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Acknowledgement
EDITORIAL

Positive Emotions in Treatment of Depressive Patients

Azhar MZ

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I was asked the above question recently and asked to comment the Malaysian perspective on this question. These are some of my thoughts. Depression is a very common psychiatric disorder. The rate increases with increasing age. Children are less diagnosed than adults though the rates are increasing especially in adolescents. It is said that in the community the rates are 2% for school age children and 5% for adults. However depression is not a single disease, there are cases of Major Depressive Disorder (MDD), Dysthymic Disorder, and Bipolar Disorder and when taken together the rates are higher.

The diagnostic criteria in the fourth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) for Major Depressive Disorder, Dysthymic Disorder, and Bipolar I Disorder are the same for children and adolescents as they are for adults with some minor modifications. The modifications are that in children the mood may not be depressed but irritable and that weight loss or gain is not as important as failure to make expected weight gains in children compared to adults. To make a diagnosis of a Depressive Disorder the most defining symptom is depressed mood. DSM–IV describes it as depressed mood most of the day, nearly every day indicated by subjective report or observation by others. The other defining symptom is anhedonia (loss of pleasure) which DSM-IV describes as markedly diminished interest or pleasure in all, or almost all, activities for most of the day, nearly every day.

In my clinical practice and as I teach students, I emphasize these two points or symptoms in order to diagnose MDD. The way the symptoms presents as a continuous low mood and anhedonia not affected by environmental factors indicates biological abnormalities rather than purely psychological effects. The depressed mood that is involuntary to environmental change has been investigated in several studies. Functional neuroimaging studies have most commonly associated depressed mood and sadness with abnormal neuronal activity in the medial prefrontal cortex, including the anterior cingulated and orbitofrontal cortex [1, 2]. These areas receive innervations from serotonergic, noradrenergic and dopaminergic pathways. As such low levels of NE, 5-HT, and DA may be associated with low mood. Reduced dopaminergic activity has been linked to decrease incentive motivation [3], anhedonia [4], and loss of interest [5]. Increased functional dopaminergic activity has been linked to positive affect [6].

In view of the above, it is clinically important to view negative emotions, viz low mood, anhedonia and blunting of affect as a diagnostic tool to make the correct diagnosis of biological depression and to take into account the amount of positive emotion present during the first visit to establish the severity of MDD. The lower the presence of positive emotion, the more severe the MDD. Scales for measuring negative and positive emotions must be used so that an objective measurement is made and patients can see the lowering of negative emotions and increase of positive emotions as they progress in their treatment.

In conclusion, MDD or Dysthymic Disorder or Bipolar I Depressive Disorder are biological disorders and changes in positive and negative emotions in these patients are due to biological abnormalities. As such, in the treatment of these patients, the initial assessments and measurements of negative and positive emotions will help to determine treatment efficacy and progress and assist in establishing better compliance and even better prognosis for patients who are able to experience and monitor the change from high negative emotions to low negative emotions and low positive emotions to high positive emotions.

REFERENCES


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Outcome of Total Thyroidectomy and Subtotal Thyroidectomy in Non Toxic Multinodular Goiter: Hospital Universiti Sains Malaysia Experience

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ABSTRACT

Introduction: Thyroid enlargement is one of the common surgical presentations in the Department of Surgery, Hospital Universiti Sains Malaysia (HUSM). Among them, benign non-toxic multinodular goiter constitutes one third (30%) of patients who underwent thyroidectomy. Common complications of thyroidectomy include recurrent laryngeal nerve (RLN) injury, hypocalcaemia, and recurrence of the thyroid lesion. Objective & Methods: This is a retrospective study of patients diagnosed with multinodular goiter treated in HUSM between January 1996 and December 2005. A total of 111 patients were studied and 52 of them underwent subtotal thyroidectomy while 59 underwent total thyroidectomy. The outcome in terms of RLN injury, hypocalcaemia and mass recurrence were analyzed. Results: Post operative complications were studied in both groups. Permanent recurrent laryngeal nerve injury occurs in 2.4% (1 case) in subtotal thyroidectomy group compared to total thyroidectomy group (3.6%, 2 cases). Five cases from total thyroidectomy group suffered from permanent hypocalcaemia but none in the other group. 70.7% (29 cases) from subtotal thyroidectomy group have functional remnant of thyroid tissue. Recurrence rate post subtotal thyroidectomy after 5 years is only 4.9% (2 cases). Conclusion: The post operative outcome in patients who underwent subtotal thyroidectomy in HUSM from January 1996 to December 2005 was better than total thyroidectomy with significant functional thyroid remnant.

Keywords: Thyroidectomy, subtotal, complication, benign

INTRODUCTION

Goiter is one of the common surgical presentations in the general surgical unit. In an 8-year review (1996-2003) in HUSM, a total of 492 thyroidectomies were performed. The diagnosis of multinodular goiter (MNG) was established in 149 patients (30%).

MNG affects 5% of the general population of non endemic areas and 15% in endemic area.1 2 Although the pathogenesis of MNG is still controversial, the possible aetiologies are association with increased sensitivity of the thyroid follicular cells to thyroid stimulating hormone (TSH), growth stimulating antibodies and thyroid stimulating peptides. The other causative factors associated with goiter are goitrogens, iodine deficiency and excess, genetic factor, angiogenesis, dyshormogenesis and radiation exposure in head and neck in childhood.3 4

The treatment options for non toxic multinodular goitre include thyroidectomy, radio-iodine therapy, and L-thyroxine therapy.5 The type of thyroidectomies for MNG include hemithyroidectomy, bilateral subtotal, near total and total thyroidectomy is still controversial.6-9

The advantages of performing total thyroidectomy in MNG are minimizing the risk of goiter recurrence thus avoiding completion thyroidectomies which possess more complications and simultaneously treating an occult primary in the thyroid that is missed during pre-operative work-up. The incidence of incidental finding of thyroid carcinoma could be as high as 6.2%.10 11 Although total thyroidectomy carries few drawbacks such as long term thyroxine replacement therapy with its side effects, the advantages outweigh the risk of complications and in expert hand, total thyroidectomy for MNG becomes a preferable option in many centres.10 13 14

On the contrary, subtotal thyroidectomy retains thyroid function and some authors revealed 70-80% of remnants are functioning.15-17 Though these remnants can result in recurrence of up to 10-30% in non toxic MNG,8-18 the recurrence rate following STT demonstrate dependency on extent of resection, and risk factors such as very young age

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and presence of gross multinodules.\textsuperscript{16,19} One of techniques to reduce the recurrence and to preserve the function in remnant thyroid is to retain the remnant thyroid volume (critical volume) of 4-5 ml on each side.\textsuperscript{20,21}

**METHODOLOGY**

All patients diagnosed as MNG and who underwent subtotal and total thyroidectomy were included in the study. The study duration was 10 years, from January 1996 to December 2005. Only patients with non-toxic goiter were included. Serum calcium and thyroid function tests results must be available in every patient as inclusion criteria. The exclusion criteria are:

- 1. Thyroid malignancy or other form of thyroiditis.
- 1. Follow-up period of less than one and half years
- 2. Patients who had not undergone indirect laryngoscopy or 70° laryngoscopic findings documented before and after operation by Otorhinolaryngologist.

Serum calcium level and RLN function were checked for 24 hours after the operation. After that, serum calcium was rechecked at interval of one month, 3 months, 6 months & 18 months. Low calcium level (< 1.9 mmol/l), hoarseness of voice less than 6 months were considered as temporary and more than 6 months were regarded as permanent lesion.

Low thyroxine level (Total T4 < 60 mmol/l, Free T4 < 7.7 pmol/l and TSH > 5 mIU/l) more than 6 months are regarded as hypothyroidism or non functioning thyroid remnant. Any visible thyroid mass after 6 months to 1 year are regarded as recurrence.

Some patients (13) had no documented result of T4 and TSH post operatively to determine functional thyroid remnant. We contacted these patients and sent questionnaires to enquire if they were on medication (thyroxine, calcium) or have symptoms and signs of hypothyroidism and if recurrent thyroid swelling were present. The patients who took no medication and had no symptoms and signs of hypothyroidism and no recurrent thyroid swelling were considered as having functional remnant.

The complications and other observed outcomes were recorded based on the type of operation category, subtotal thyroidectomy (STT) and total thyroidectomy group (TT).

**RESULTS**

During the 10-year period, a total of 111 patients with MNG were operated, 52 underwent STT and 59 underwent TT. Among these patients, 96 fulfilled the criteria. Fifteen patients (11 patients from STT group and 4 patients from TT group) were excluded from the study. After 6 months to 1 year, 25 patients defaulted from the clinic follow up. We followed up the patients by questionnaire or contacted them by phone. Eleven patients from STT group were not contactable and excluded from the study.

### Table 1.

**Demographic distribution (sex & age) of patients in STT and TT groups**

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Number of Patients</th>
<th>Male (sex)</th>
<th>Female (sex)</th>
<th>Age group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtotal Thyroidectomy</td>
<td>41</td>
<td>3 (7.3%)</td>
<td>38 (92.7%)</td>
<td>11-20 yo= 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>21-30 yo=10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>31-40 yo=12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>41-50 yo=13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>51-60 yo=  6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mean = 36.2</td>
</tr>
<tr>
<td>Total Thyroidectomy</td>
<td>55</td>
<td>4 (7.3%)</td>
<td>51 (92.7%)</td>
<td>11-20 yo= 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>21-30 yo=5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>31-40 yo=11</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>41-50 yo=24</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>51-60 yo=5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>61-70 yo=6</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>Mean = 42.7</td>
</tr>
</tbody>
</table>
Female patients predominate the study sample in both groups, of more than 90% (Table 1). Mean age of patients were 36.2 years and 42.7 years in subtotal and total group respectively. Mean follow up of study was longer in subtotal group.

Transient RLN injury occurred in 2 STT patients (4.9%) and 4 TT patients (7.27%). Permanent RLN injury occurred in 1 STT patient (2.4%) and 2 TT patients (3.6%).

Transient hypocalcaemia developed in 7 STT patients (17%) and 9 TT patients (16.4%). None of the STT patient (0%) and 5 TT patients (9.1%) developed permanent hypocalcaemia (Table 2). Functioning thyroid remnants in STT were observed in 29 patients (71%).

<table>
<thead>
<tr>
<th>Type of Operation</th>
<th>Number of Patients</th>
<th>RLN Injury</th>
<th>Hypocalcaemia</th>
<th>Functional Remnant</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Transient</td>
<td>Permanent</td>
<td>Transient</td>
<td>Permanent</td>
</tr>
<tr>
<td>Subtotal Thyroidectomy</td>
<td>41</td>
<td>2 (4.9%)</td>
<td>1 (2.4%)</td>
<td>7 (17%)</td>
<td>0 (29%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Thyroidectomy</td>
<td>55</td>
<td>4 (7.3%)</td>
<td>2 (3.6%)</td>
<td>9 (16.4%)</td>
<td>5 (100%)</td>
</tr>
</tbody>
</table>

Table 2. Frequency of RLN injury, hypocalcaemia, functional remnant & recurrence in subtotal and total thyroidectomy

Two STT patients (4.9%) developed recurrence in subtotal group and none in TT group. Incidental malignancy was detected in 3 (2.7%) patients: 2 papillary carcinoma and 1 micropapillary carcinoma. There were no patients with carcinoma in STT group.

**DISCUSSION**

Total thyroidectomy (TT) is adopted as the standard treatment for non-toxic MNG cases in our centre since 2002. In this study, the mean follow up of the patients was 62 months in STT group and 24.2 months in TT group because the majority of the STT patients were operated earlier in the period of study (1996-2005).

In the past 20 years, total thyroidectomy is gradually replacing the subtotal thyroidectomy because of some advantages such as avoidance of recurrence, no need for completion surgery and simultaneously treating incidental thyroid carcinoma. However the patients have to bear the disadvantages of life long thyroxine therapy and its side effects. Despite the emerging evidences, the ideal surgical treatment for non toxic multinodular goitre remain controversial. The exact nature and aetiology of the disease is still unknown.

In this cohort retrospective study we compared the outcome of both procedures applied to non toxic MNG. As this study extended to 10 years, some limitation need to be considered, for example multiple surgeons involved (as compared to a single surgeon/operator study) and the follow up.

**RLN injury & hypocalcaemia**

The prevalence of transient RLN injury in our study was lower in STT group. However this difference is not statistically significant (p=0.49). In comparison with other studies, transient RLN injury varies from 3-3.8% for STT group and 3-6.9% for TT group. Thus, our local data is comparable with those studies.

Permanent RLN injury occurred in 2.4% in STT group and 3.6% in TT group in our study. However its difference was not statistically significant (p=0.6). In comparison with other studies, permanent RLN injury varies from 0.8-1% for subtotal group and 1.4-2.3% for total group. The overall incidence of transient RLN injury in other series were 2.5-4% and 0.5-2% for permanent RLN injury following all types of thyroidectomy (subtotal, total and completion thyroidectomy).

In our study, the incidence of transient hypocalcaemia was not statistically significant (p=0.92) for both studied groups (17% in STT group and 16.4% in TT group). Permanent hypocalcaemia only occurred in TT group comprised of 9.1% and none in STT group. This difference is borderline significant in statistically (p=0.057).

Overall reported incidence of temporary hypocalcaemia in other series were 1.6% to as high as 53.6%, and 0-8%
for permanent hypocalcaemia following thyroidectomy.\textsuperscript{[31]} However, these results were not comparable to our finding because those operations included non toxic multinodular goiter and other pathologies.

**Functional Remnant**

Following subtotal thyroidectomy, functioning thyroid remnant was observed in 29 patients (71%). This is the desired outcome of STT for non toxic MNG and in our study was highly significant (p<0.001). Data from other centers showed 70-80\% of thyroid remnants are functioning following STT.\textsuperscript{[15-17]}

However, out of these 29 post STT with functioning remnant, only 16 patients had T4 and TSH values more than 6 months. Thirteen patients had no biochemical documentations and defaulted clinic follow up. They were contacted by phone and questionnaires. All 13 patients admitted that they were not on thyroxine following the operation. They had no symptoms and signs of hypothyroidism, no recurrent thyroid swelling up to at least 2 years post operation. These patients were also considered as functioning remnant.

One of the drawbacks of STT is recurrence, thus the extent of resection and volume of remnant following thyroidectomy is important. The standard volume (critical volume) in order just to maintain function should be 4-5 ml on each gland.\textsuperscript{20,21} In our study, the long term thyroxine therapy and its side effects was achieved in more than 70\% of patients who underwent subtotal thyroidectomy.

**Recurrence**

Among the 41 patients of STT group, 2 patients (4.9\%) developed recurrence during the 10 years period and 62 months of means follow up. Other studies reported that the recurrent rate following STT varies from 10-30\% in long term period follow up of more than 15-20 years.\textsuperscript{[6,18]} Although our study showed lower rate, the follow-up period was very much less as compared to their studies.

Recurrence is significant when revision surgery is considered. This is because fibrosis and disruption of normal anatomical landmarks will impose additional risk to the RLN to be injured. Besides that, the risk of hypocalcaemia are also increased in reoperative surgery.\textsuperscript{[13,32]} However not all patient need a reoperation or a completion surgery. The rate can be as low as 4\% from 21\% of recurrent cases following non total thyroidectomy and it can be without additional morbidity.\textsuperscript{[13]} Furthermore, this complication can be avoided in cases of early stage of recurrence non toxic MNG by radioiodine (I131) treatment and thyroxine therapy.\textsuperscript{[5,33-34]}

**Incidental finding of Thyroid Carcinoma**

Out of total 111 thyroidectomies, 3 patients (2.7\%) had incidental carcinoma in their histopathological specimens (2 papillary and 1 micropapillary). In other studies, incidental finding of occult carcinoma in the thyroid gland specimens varies from 4.6-10\%.\textsuperscript{[10,35,36]} These undetected carcinoma at pre operative stage is an advantage if total thyroidectomy is performed. However, incidental finding of occult malignancy is higher rate in endemic area of MNG.

**CONCLUSION**

RLN injuries from subtotal and total thyroidectomy were not statistically significant (p=0.48 and p=0.61). There was borderline significance in the difference of permanent hypocalcaemia (p=0.05) which was better in STT group. A highly significant functioning remnant thyroid gland was achieved in STT group but at the risk of recurrence of less than 5\%. The incidental finding of thyroid carcinoma was 2.7\%.

From this study, STT can be considered in non toxic MNG in view of less post operative morbidities, acceptable recurrence rate and avoidance of lifelong thyroxine therapy in more than 70\% of patients. However, risk stratification should be applied in the selection of patient in order to reduce the possibility of needing a revision or completion surgery.

**REFERENCES**


Outcome of Total Thyroidectomy and Subtotal Thyroidectomy in Non Toxic Multinodular Goiter: Hospital Universiti Sains Malaysia Experience


Dietary Habits and Dental Caries Occurrence Among Young Children: Does The Relationship Still Exist?

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ABSTRACT

Introduction: The role of diet in the aetiology of dental caries occurrence has been questioned recently. Aim: This cross-sectional study was conducted to determine the relationship between dietary habits and dental caries among 105 children aged 2 to 5 years old in Kuala Lumpur. Methodology: Subjects were selected using convenient sampling method. Their body weight and height were measured and their dental check-up was performed by qualified dental nurses. A Structured questionnaire and 3-day food diaries were distributed to their parents/caretakers to obtain socio-demographic data, oral health practice and dietary habits of the subjects. The dft (decayed, filled teeth) score was used to describe dental caries incidence. Results: Caries was found in 36.6% subjects with mean dft score of 1.95±3.59 (range: 0-16). Energy (r=-0.334, p=0.008), carbohydrate (r=-0.353, p=0.005), fat (r=-0.325, p=0.01), protein (r=-0.264, p=0.038), and calcium (r=-0.470, p<0.001) intake were significantly correlated with dft score. The negative association between frequency of milk consumption and dental caries incidence was lost after other confounding factors were considered. Dental caries incidence was associated with age of subjects started brushing their teeth (Adjusted OR=5.46, 95% CI=1.74 – 17.17). There was no relationship between frequency of daily meals (p=0.800) and sugary food/drinks consumption (p=0.489) with dental caries occurrence. Conclusion: Dental caries is prevalent among young children and related with dietary factors and oral health practices. Therefore, healthy dietary habits and oral health practice should be integrated in the oral health promotion targeted to parents/caregivers and young children in order to improve their dental health status.

Keywords: Dental caries, dietary habits, sugary foods, sugary drinks, young children

INTRODUCTION

Dental caries also known as tooth decay is a common disease among children all over the world particularly in developing countries[1]. It occurs with the presence of dental plaque as the result of enamel demineralization process which is stimulated by organic acids produced by oral bacteria such as Streptococcus Mutans and lactobacilli[2, 3]. These bacteria metabolised carbohydrate from the diet as substrate to produce organic acids that will lower the dental pH plaque and form biofilm structure which attached itself to the teeth structure[4, 5].

Various factors contribute to the occurrence of dental caries; they include condition of saliva (buffer capacity, composition, flow rate)[3, 5], fluoride exposure[6], oral health practice[6], biological/maternal factor[7], diet[4, 5] (amount, composition, frequency)[8], fermentable carbohydrates[3, 5] and also socio-demographic (education level, income)[7]. In the 1900’s, diet was one of the main factor blamed for dental caries. After World War 2, caries data among caries-free children had increased as a result of wartime diets[9]. Diet is one of caries aetiological factor through various sugary foods and drinks[9-11]. The theory of diet and caries occurrence was proven by the legendary Vipeholm study (1945-1954) where sugar consumption was found significantly related to dental caries occurrence[12]. In young children, their dietary habits were linked to caries development through several ways such as frequent consumption of sugary foods and drinks, prolonged bottle feeding and pacifier usage[13, 14]. However, for the last 40 years, the relationship between diet and risk of dental caries has been debateable as the decline of caries prevalence was observed among children in industrialized countries[15]. In some parts of the world, water fluoridation programmes and usage of fluoride-tooth paste were reported as the preventive factors which contributed to the declining trend in dental caries[8, 16, 17]. However, certain groups of the population are still suffering from dental caries and the prevalence is increasing in some of the

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developing countries that experienced changes in dietary practice\textsuperscript{11,16,18}.

In Malaysia, data on incidence of dental caries and its link to dietary habits among children less than 5 years of age is limited as compared to older age groups. The National Oral Health School Survey in 1995 reported that 87.1\% of 5-year old children had dental caries\textsuperscript{19}. The latest Oral Health National Survey conducted in 2005 showed that 76.2\% of the children of the same age had dental caries\textsuperscript{20}. Nevertheless, contributing factors particularly dietary habits as explanation of the high prevalence of dental caries among young children in Malaysia has not been reported. Hence, the aim of this study was to determine the relationship between dietary habits and dental caries among children aged 2 to 5 years old in Kuala Lumpur. It was hypothesized that dietary habits were related to dental caries among children aged 2 to 5 years.

**MATERIAL AND METHODS**

**Data collection**

This cross-sectional study was carried out amongst 105 Malay children aged 2-5 years from five kindergartens around Kuala Lumpur. The kindergartens and the subjects of the study were selected by convenience sampling. Based on the sample size calculation\textsuperscript{21} and with the assumption of 10\% rejection rate, 106 subjects were required. Prevalence of dental caries in a previous study among 565 children aged 12-38 months in Jakarta Indonesia was used in the formula\textsuperscript{11}. Prior to data collection pre-visits were arranged to the selected kindergartens to meet up with the teachers and the teachers’ assistants. An invitation letter to participate in the study was sent out to parents/caregivers of all children aged 2-5 years. The inclusion criteria included: All children aged 2-5 years with parental/guardian consent. Children with any chronic diseases; physical or mental disabilities or being non-Malaysian were excluded.

Ethical approval was obtained from the Medical Research Ethics Committee of Universiti Kebangsaan Malaysia Medical Centre while approval to conduct this study was granted by the respective kindergartens and the Kuala Lumpur City Council. The information sheet about the study was distributed to parents/guardians and their consents were obtained.

**Anthropometric Measurements**

Height and weight of participants were measured in minimal indoor clothing and without shoes. Body weight was measured to the nearest 0.1 kg using a digital weighing scale (Tanita 318, Japan). Height without shoes was measured to the nearest 0.1cm using a SECA portable body meter (SECA 206, Germany). The anthropometric status of the subjects was classified based on the World Health Organization Growth Reference\textsuperscript{22}.

**Questionnaire and Food Diary**

Questionnaires on socio-demographic data and oral health practice together with the 3-day food diaries were distributed to the parents/guardians. Teachers in the selected kindergartens assisted in distributing the questionnaires to the parents/guardians and re-collecting them. The structured questionnaire was designed based on previous studies\textsuperscript{23,24}. Then, the questionnaire was translated into Malay Language and pilot-tested for face and content validity among 15 Malay parents with children of similar age around Selangor. The value of cronbach obtained was 0.77. Amendments to the questionnaire were then made accordingly.

The questionnaire was divided into four sections: Socio-demographic profile, health status, dietary habits and oral health practices of the children. Parents/guardians were required to record their children’s food intake in the food diary on two weekdays and one weekend. In order to guide parents/guardians in filling up the food diary, detailed and easy-to-understand instructions were attached with the food diary. In addition, a complete example of one day food diary was also attached with the instructions. Food intake by subjects on two weekdays at the kindergarten were recorded in a form by the teachers and supervised by the researcher. Data from food diaries and food records were used to analyse the energy and nutrient intake, average daily frequency of meals, consumption of sugary food and drinks. The 3-day food diary method was also applied in previous studies\textsuperscript{13,24,25} to determine the frequency consumption of sugary foods and drinks. Nutritionist Pro TM 2003 software was used to perform the dietary analysis.

The frequency of food/drink consumption was calculated as one ‘episode’ when the food/drink was taken at one same time or consumed within a 30-minute interval after the previous food/drink intake. Calculation of the food and sugary drinks frequency per day was also based on the same method\textsuperscript{25}.

**Dental Check-ups**

The dental check-up of the subjects was performed by qualified dental nurses from the Department of Dental Public Health, Faculty of Dentistry, Universiti Kebangsaan Malaysia. The check-up involved a dental probe and mouth mirror under consistent illumination. The position of nurse and the children during the examination was in line with the
recommendation by WHO (1997)\textsuperscript{[26]}. The dft (decayed, filled teeth) index was used to describe the incidence of dental caries.

The dft (decayed, filled teeth) and DMFT (decayed, missing and filled teeth) index are the indicators of dental caries for primary and permanent dentition respectively\textsuperscript{[27,28]}. The dft index was applied for preschool children as they do not experience tooth loss caused by dental caries. The calculation of the dft and DMFT index involved the counting of teeth that has been affected with decay (decayed), loose tooth (missing) or teeth filling (filled). Zero dft/DFMT index shows that a person is caries-free whereas higher dft/DFMT signifies the incidence of caries\textsuperscript{[28,29]}. Subjects were regarded as having dental caries if there is a decay or dental filling even on only one tooth\textsuperscript{[29,30]}. The dental check-ups were followed by an oral health education session which also included demonstration on brushing of teeth by the dental nurses.

**Statistical Analysis**

Data were analyzed using the Statistical Package for Social Sciences software (SPSS) version 17.0. Data were presented as means, standard deviations and ranges. The normality of the data was assessed using Kolmogorov-Smirnov test. The Mann-Whitney test was performed to compare continuous and categorical variables while Chi square test was applied to test the different of two categorical variables. The association between continuous data was analysed by using the Spearman’s Correlation test. The occurrence of dental caries was dichotomised by presence or absent of caries (Yes/No) and the quantitative data of dft index. Further analysis was carried out using binary logistic regression to calculate adjusted odd ratio (AOR) with the inclusion of confounding factors such as gender, parents’ educational status and parents’ income. P values of less than 0.05 were considered statistically significant.

**RESULTS**

Approximately 280 invitation letters and information sheets were distributed to the parents/guardians in the selected kindergartens. A total of 146 children were eligible to participate in this study but the final number of subjects included

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total n (%)</th>
<th>Had Caries n (%)</th>
<th>p value\textsuperscript{a}</th>
<th>dft index (mean±S.D)</th>
<th>p value\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>59 (56.2)</td>
<td>22 (59.5)</td>
<td>0.64</td>
<td>1.82±3.11</td>
<td>0.79</td>
</tr>
<tr>
<td>Girls</td>
<td>46 (43.8)</td>
<td>15 (40.5)</td>
<td></td>
<td>2.11±4.17</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>105 (100.0)</td>
<td>37 (36.6)</td>
<td></td>
<td>1.95±3.59</td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-3 years old</td>
<td>36 (35.7)</td>
<td>4 (10.8)</td>
<td>\textless0.001</td>
<td>0.61±2.70</td>
<td>\textless0.001</td>
</tr>
<tr>
<td>4-5 years old</td>
<td>69 (64.3)</td>
<td>33 (89.2)</td>
<td></td>
<td>2.69±3.82</td>
<td></td>
</tr>
<tr>
<td><strong>Mother’s education level</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attend schools/Others</td>
<td>40 (39.6)</td>
<td>19 (51.4)</td>
<td>0.07</td>
<td>2.37±3.30</td>
<td>0.07</td>
</tr>
<tr>
<td>Diploma/Degree/Master/PhD</td>
<td>61(60.4)</td>
<td>18 (48.6)</td>
<td></td>
<td>1.67±3.78</td>
<td></td>
</tr>
<tr>
<td><strong>Father’s education level</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attend schools/Others</td>
<td>40 (41.2)</td>
<td>15 (42.9)</td>
<td>0.81</td>
<td>2.15±3.30</td>
<td>0.56</td>
</tr>
<tr>
<td>Diploma/ Degree/Master/PhD</td>
<td>57 (58.8)</td>
<td>20 (57.1)</td>
<td></td>
<td>1.75±3.80</td>
<td></td>
</tr>
<tr>
<td><strong>Mother’s income (RM 1= USD 0.33)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>\textless RM 2000</td>
<td>44 (43.6)</td>
<td>19 (51.4)</td>
<td>0.30</td>
<td>1.86±3.13</td>
<td>0.30</td>
</tr>
<tr>
<td>RM 2000-3000</td>
<td>31 (30.7)</td>
<td>8 (21.6)</td>
<td></td>
<td>1.13±2.43</td>
<td></td>
</tr>
<tr>
<td>\textgreater RM 3000</td>
<td>26 (25.7)</td>
<td>10 (27.0)</td>
<td></td>
<td>3.08±5.06</td>
<td></td>
</tr>
<tr>
<td><strong>Father’s income (RM 1= USD 0.33)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>\textless RM 2000</td>
<td>34 (34.3)</td>
<td>11 (30.6)</td>
<td>0.83</td>
<td>1.09±1.85</td>
<td>0.64</td>
</tr>
<tr>
<td>RM 2000-3000</td>
<td>36 (36.4)</td>
<td>14 (38.9)</td>
<td></td>
<td>1.94±3.46</td>
<td></td>
</tr>
<tr>
<td>\textgreater RM 3000</td>
<td>29 (29.3)</td>
<td>11 (30.6)</td>
<td></td>
<td>2.79±4.86</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}Chi Square test between socio-demographic characteristics and dental caries occurrence
\textsuperscript{b}Spearman’s correlation test for the association between socio-demographic characteristics and dental caries occurrence
\textsuperscript{†}Total number of subject in some sections are inconsistence due to incomplete information from some of parents/guardians.
in the study was 105, giving a response rate of 72%. The remaining subjects did not return completed questionnaires and food diaries. Nonetheless, some parents did not answer some of the questions. The data were analyzed based on those who responded.

The socio-demographic characteristics and Body Mass Index (BMI) of subjects are shown in Table 1. Out of 105 subjects, 56.2% were boys and 43.8% of girls. The mean age of the subjects was 3.90 ± 1.05 years. A total of 35.7% of the subjects aged 2-3 years and 64.3% aged 4-5 years old. Most of the parents/caregivers had completed their education level at Diploma/Degree/Master/PhD. There were 43.6% of mothers and 34.3% of fathers who had monthly income of less than RM 2000.

Table 2. Associations of dental caries occurrence with nutritional status of subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>N (%)</th>
<th>Had Caries n (%)</th>
<th>p value</th>
<th>dft index (mean±S.D)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI status c†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thinness</td>
<td>8 (8.9)</td>
<td>3 (8.8)</td>
<td>0.91</td>
<td>1.95±3.92</td>
<td>0.91</td>
</tr>
<tr>
<td>Normal</td>
<td>45 (50.0)</td>
<td>16 (47.1)</td>
<td></td>
<td>2.04±3.52</td>
<td></td>
</tr>
<tr>
<td>At risk of overweight, Overweight, Obese</td>
<td>37 (41.1)</td>
<td>15 (44.1)</td>
<td></td>
<td>2.87±4.32</td>
<td></td>
</tr>
<tr>
<td>Height-for-Age d†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>57 (63.3)</td>
<td>18 (54.5)</td>
<td>0.19</td>
<td>1.91±3.90</td>
<td>0.22</td>
</tr>
<tr>
<td>Stunting</td>
<td>33 (36.7)</td>
<td>15 (45.5)</td>
<td></td>
<td>2.45±3.55</td>
<td></td>
</tr>
<tr>
<td>Weight-for-Age e†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>75 (83.3)</td>
<td>28 (84.8)</td>
<td>0.77</td>
<td>1.96±3.60</td>
<td>0.85</td>
</tr>
<tr>
<td>Underweight</td>
<td>15 (16.7)</td>
<td>5 (15.2)</td>
<td></td>
<td>2.87±4.57</td>
<td></td>
</tr>
</tbody>
</table>

a Chi Square test between nutritional status and dental caries occurrence
b Spearman’s correlation test for the association between nutritional status and dental caries occurrence
c Z scores: Obese (+3 SD); Overweight (+2 SD) – (+3 SD); Risk of overweight (+1 SD – (+2 SD); Normal (-1 SD – (+1 SD); Thinness (-2SD) – (-1 SD); Severe thinness (<-3 SD), these categories were re-grouped for purpose of statistical analysis
d Z scores: Stunting (<-2 SD) height-for-age
e Z scores: Underweight (<-2 SD) weight-for-age
† 15 subjects (14.3%) were not measured anthropometrically; 6 subjects did not attend the kindergarten during the measurement days and 9 subjects had left the kindergarten.

Table 3. The correlation between the mean nutrients intake with dft score

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean±S.D</th>
<th>r value</th>
<th>p* value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy Intake (EI) (kcal)</td>
<td>1163±427</td>
<td>-0.334</td>
<td>0.008</td>
</tr>
<tr>
<td>% of RNI</td>
<td>128</td>
<td>-0.473</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>145±57</td>
<td>-0.353</td>
<td>0.005</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>47±19</td>
<td>-0.325</td>
<td>0.010</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>41±13</td>
<td>-0.264</td>
<td>0.038</td>
</tr>
<tr>
<td>% of RNI</td>
<td>184</td>
<td>-0.355</td>
<td>0.005</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>657±400</td>
<td>-0.470</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% RNI</td>
<td>132</td>
<td>-0.494</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Spearman’s correlation test for the association between variables
The percentage of subjects with dental caries was not statistically significant between genders. However, a significantly greater percentage of subjects in older age group had dental caries (89.2%) compared to the younger age group (10.8%). A slightly higher percentage of caries incidence were observed in the subjects whose parents had lower education level (51.4%) compared with their counterparts whose mothers had higher level of education (48.6%). However, this difference was not statistically significant.

Results from the anthropometric assessments show that half of the subjects (50%) had normal BMI-for-age while 41.1% was at risk of overweight, overweight and obese (Table 2). Only 8.9% was classified as moderately thin. More than one-third (36.7%) of the subjects were stunted and 16.7% of subjects were underweight. Lower dft scores were observed among thin subjects compared to their counterparts who were normal, at risk of overweight, overweight or obese. However, this difference was not statistical significant.

The nutrient analysis shows that subjects of this study had adequate nutrients intake as recommended by Recommended Nutrients Intake of Malaysia (RNI)\textsuperscript{[31]} for energy and selected nutrients (Table 3). There were significant associations in the mean intake of all nutrients with dft score. Energy and calcium intake were strongly associated with dft score.

Dietary Habits and Dental Caries Occurrence

Table 4 shows the prevalence of dental caries occurrence according to dietary habits of the subjects. The majority of subjects (78.2%) had daily meals more than four times a day and about less than a quarter (21.8%) of them had less than four times a day (Table 4). Almost 19% of subjects were given pacifier and 60.4% of subjects were put to bed with bottle of juice/milk at most bed times. Only 6.2% were given pre-chewed food by their parents/caregivers and 85.7% had stopped being breastfed. A total of 18.9% of subjects received sweets as rewards from their parents/guardians.
There were no associations between these dietary practices with dental caries. However, the frequency of formula milk consumption was positively associated with dental caries occurrence (p=0.032). Caries free subjects were more likely to report often consumed milk (91.9%) compared with their counterparts with caries (76.7%). The odds of having caries experience was lower (OR=0.25, 95% CI=0.07-0.95) among subjects who consumed milk more frequently. Almost 10% of subjects consumed sugary food/drinks more than 4 times a day. The average of daily frequency of sugary food/drink consumption was not significant between subjects with and without caries (p=0.489) (Figure 1).

**Table 5.** The prevalence of dental caries among the subjects according to their oral health practices

<table>
<thead>
<tr>
<th>Oral health practices</th>
<th>Had caries n (%)</th>
<th>No Caries n (%)</th>
<th>Total n (%)†</th>
<th>p^a</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brush own teeth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>29 (78.4)</td>
<td>47 (78.3)</td>
<td>76 (78.4)</td>
<td>0.996</td>
<td>1.00</td>
</tr>
<tr>
<td>No</td>
<td>8 (21.6)</td>
<td>13 (21.7)</td>
<td>21 (21.6)</td>
<td>.</td>
<td>0.57-2.70</td>
</tr>
<tr>
<td>Age of started tooth brushing (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1 - 2</td>
<td>18 (56.3)</td>
<td>49 (84.5)</td>
<td>67 (74.4)</td>
<td>0.030</td>
<td>4.24</td>
</tr>
<tr>
<td>After 2</td>
<td>14 (43.8)</td>
<td>9 (15.5)</td>
<td>23 (25.6)</td>
<td>.</td>
<td>1.56 - 11.47</td>
</tr>
<tr>
<td>Frequency of tooth brushing per day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Once</td>
<td>12 (32.4)</td>
<td>17 (27.4)</td>
<td>29 (29.3)</td>
<td>0.596</td>
<td>0.79</td>
</tr>
<tr>
<td>Twice or more</td>
<td>25 (67.6)</td>
<td>45 (72.6)</td>
<td>70 (70.7)</td>
<td>.</td>
<td>0.32 - 1.91</td>
</tr>
<tr>
<td>Duration of brushing of teeth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One minute or less</td>
<td>24 (64.9)</td>
<td>40 (64.5)</td>
<td>64 (64.6)</td>
<td>0.972</td>
<td>0.99</td>
</tr>
<tr>
<td>More than 1 minute</td>
<td>13 (35.1)</td>
<td>22 (35.5)</td>
<td>35 (35.4)</td>
<td>.</td>
<td>0.42-2.31</td>
</tr>
<tr>
<td>Use toothpaste during brushing teeth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>36 (97.3)</td>
<td>60 (95.2)</td>
<td>96 (96.0)</td>
<td>0.612</td>
<td>0.56</td>
</tr>
<tr>
<td>No</td>
<td>1 (2.7)</td>
<td>3 (4.8)</td>
<td>4 (4.0)</td>
<td>.</td>
<td>(0.06-5.54)</td>
</tr>
</tbody>
</table>

^a Chi Square test oral health practices and dental caries prevalence

^Total number of subject in some sections are inconsistence due to incomplete information from some of parents/guardians

**Oral Health Practices and Dental Caries Occurrence**

Data on oral health practices by subjects are shown in Table 5. The majority of the subjects (78.4%) brushed their teeth on their own. About three-quarters of the subjects (74.4%) had started brushing their teeth at less than 2 year of...
age and a quarter (25.6%) did so after 2 years. More than half (70.7%) brushed their teeth twice or more a day while 29.3% only once a day. Subjects who were caries-free were more likely to brush their teeth at an early age i.e. less than 1 year – 2 (84.5%) compared with those with caries (56.3%) (p=0.030). More than half (64.6%) of the subjects spent one minute or less brushing their teeth. Almost all of the subjects (96.0%) used tooth paste to brush their teeth. There was significant association between the age of subjects when they started brushing their teeth, with dental caries risk even after gender, parents'/guardians' educational level and income were taken into consideration (Table 6). Those who brushed their teeth later had 5.46 times more risk to have dental caries (OR=5.46, 95% CI=1.74 – 17.17) than those who did so earlier. After adjustment of confounding factors, binary logistic regression analysis shows that the risk of dental caries occurrence was not significant with frequency of milk consumption (Table 6).

### Table 6. Binary Logistic Regression Model for amount of dietary habits and oral health practice

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of milk formula consumption in bottle/cup</td>
<td>0.25 (0.07-0.95)</td>
<td>0.65 (0.23 – 1.84)</td>
</tr>
<tr>
<td>Age of tooth brushing started (years)</td>
<td>4.24 (1.56 - 11.47)</td>
<td>5.46 (1.74 – 17.17)</td>
</tr>
</tbody>
</table>

*Adjusted OR for gender, parents educational status and parents/guardians income.

## DISCUSSION

The present study has yielded important information on the dietary habits and other factors that are related to dental caries occurrence among children aged 2 to 5 five years. This study shows that more than a third of the subjects had dental caries experience with mean df index of 1.95±3.59. The percentage of subjects with dental caries in the present study was lower compared to previous studies. A recent study conducted by Zahara et al. [39] among children aged 5 to 6 years in Kuala Lumpur showed 62% of subjects had caries with df score of 3.72. In Thailand, 95.4% of 2-12 years old children had dental caries with dmft (decay, missing, filling primary teeth) score of 7.4±4.6 [6]. This difference may be due to subjects recruited in the current study were younger. Similar trend was observed in the study of which the older age group were more likely to experience dental caries compared to the younger age group. Previous studies in Hong Kong [40] and Nigeria [41] also found similar results. Colonization of oral bacteria i.e. Streptococcus Mutans is high as the age increases which contributes to higher risk of dental caries [42]. Children with high colonization of Streptococcus Mutans are more prone to experience dental caries than children with lower level of Streptococcus Mutans [35].

To the best of our knowledge, the latest study on dental caries among children less 5 years in Malaysia was conducted by Chin et al. [40] among children aged 36 -71 months in Kelantan, Malaysia. They reported that a higher percentage of subjects with dental caries (88.7 %) with df index of 7.3 ± 5.01. The majority of their subjects (53.6%) brushed their teeth once a day and 85.7% consumed sugary food/drink of more than 4 times per day. In contrast, this findings show that the majority of the subjects (70.7%) brushed their teeth more than twice a day and only 9.8% had sugar exposures of more than 4 times a day. Moreover, subjects recruited in their study were those who attended dental clinics and most likely had dental problems. These differences may explain a higher percentage of subjects with dental caries in the aforementioned study.

There was no significant difference between dental caries occurrence between genders. This finding is consistent with the finding of previous studies among children aged 3.9±0.7 years in Hong Kong [39] and children aged 3-5 years in Saudi Arabia [42]. Studies in the USA [37] and Australia [43] reported that dental caries prevalence was lower in children of more educated parents. We found a similar trend here but it did not reach a statistical significance (p=0.07) which may be due to the small sample size. Moreover, there wasn’t any significant association between household income and dental caries occurrence. In contrast, Sugito et al. [1] reported that that children aged 12-38 months from families with higher socioeconomic levels in Indonesia generally had lower dental caries incidence than those from the lower socioeconomic levels. In the present study, we did not take into account the number of children/dependents in a family. This factor may affect the ability of families to provide a healthy diet and oral health care for their children.

In the present study, we observed that there is no statistical significant association between df index and anthropometric status of the children. Findings from previous studies show the relationship between BMI and risk of dental caries were inconsistent [38-42]. Studies among children with primary dentition in the USA [46, 41] and China [42] show, no association between childhood obesity and caries experiences. However, studies in Brazil [40] and in Thailand [43] reported that malnourished preschoolers were more vulnerable to dental caries compared with their counterparts.
It was hypothesized that malnutrition compromised tooth integrity, thus increase risk for dental caries [48]. Studies in Finland [49] and Germany [50] suggested that obesity was a predicting indicator for caries experience. A longitudinal study with a bigger sample size is needed to investigate the association between nutritional status with primary and permanent dentition.

The results of the present study show significant negative correlations between energy, carbohydrate, fat, protein and calcium intake with the incidence of dental caries. These negative associations may be because most of the children in the present study consumed milk as their main food item in their diet. Based on the food diaries collected, most of the children drank milk twice or more per day. Full cream milk is rich in energy, carbohydrate, protein, fat and calcium [48]. Although milk contains carbohydrate i.e. lactose, it has protective factors against dental caries [13, 49]. Calcium is described as an important component in the process of repairing teeth and dental remineralisation process along with phosphate and fluorine [50]. Protein intake was also found to be negatively correlated with caries occurrence. Dietary protein has been associated with dental caries prevention by the mechanism of salivary polymorphic protein towards the binding capacity of bacteria induced-caries like Streptococcus Mutans [51].

The negative correlations between nutrients intake and caries are consistent with the finding in this study that children who often consumed milk had lower incidence of caries compared to those who seldom did so. Milk has low cariogenic potential and contains cariostatic factors against dental caries [52]. Cariogenic potential can be defined as the foods’ ability to drop plaque pH significantly, demineralise the enamel or can lead to more caries occurrence [49]. Many studies showed that milk has potential caries protective factor as it contains calcium, phosphorus and casein which are believed to inhibit the occurrence of caries [19, 49]. The mechanism of milk as caries protective factor can be explained by high buffering capacity characteristic which balances the demineralization and remineralisation process of saliva [5, 13]. Nonetheless, the cariogenicity potential should be considered along with the frequency and manner of consumption so that the ‘effective cariogenicity’ can be determined. In this study we did not ask the parents/guardians to record the duration of milk drinking neither to specify whether milk was taken in bottle or cup in the food diary. Drinking milk in cup is highly recommended for children starting from their first birthday as this can reduce the prolonged contact of children teeth with milk at the bottle pacifier [53]. The variability of milk consumption manner and other factors may interfere with the result of positive association between milk and dental caries occurrence [49]. This was proven when frequency of milk consumption did not show significant association with caries when other confounding factors were taken into consideration in the multivariate analysis.

The present study did not find any significant relationship between the frequency of daily meal and sugary food/drinks consumption with dental caries occurrence. This result is in line with the earlier study by Zahara et al. [32] which found no statistical significant relationship between frequencies of sugary food and drink consumption with dft score. The insignificant relationship between daily meal and sugary food/drinks consumption with dental caries occurrence can also be explained by the cross-sectional design of the study. Cross-sectional study may not reflect the true dietary habits of the children before dental caries occurred as dietary habits of several months earlier are responsible for the current caries development. The parents may also have changed the food served to their children due to the presence of dental caries on the children’s teeth. Like other studies that require subjects or their parents to write down the diet intake, the result of food intake may suffer from biases as the parents may tend to report socially acceptable foods [54] and underreport cariogenic foods.

We found that the younger the age of the children when they started to brush their teeth, less likely were to experience dental caries. This finding is in agreement with previous studies conducted among children in different populations in Saudi Arabia [32] and Hong Kong [52]. This may be related with the effect of cariogenic bacteria removal during tooth brushing [41]. In addition, the American Academy of Pediatric Dentistry [55] recommends that oral hygiene measures in children should be no later than the time of eruption of the first primary tooth i.e. one year old. Parents should be educated on dental health as this will help them to inculcate good oral health practice among their children. They should be advised on the usage of fluoride tooth paste, dietary control (reduce consumption and frequency of cariogenic sugars in food and drinks), plaque control (by highly effective tooth brushing twice a day) and having oral examination more frequently than once a year [56].

The main limitation of this study is the study design employed which should be addressed. The nature of cross-sectional design is that it does not take into account the previous dietary habits and dental hygiene practices which may have been changed when the study was conducted. Oral health education is usually integrated as one of the activities in most kindergartens in Malaysia for example, dental checkups and demonstration of tooth brushing by dental nurses and tooth brushing routine at a designated area in kindergartens. It is more beneficial for future studies to apply longitudinal and cohort study designs so that the dietary and oral health practice habits of the subjects can be identified when dental caries incidence occur. Another limitation of this study is the small sample size recruited which only involved Malay children from five kindergartens in Kuala Lumpur, therefore, it limits the generability of our findings to the general population. Finally, there were parents/guardians who did not answer some of the questions in the questionnaire. Due to limited time for data collection, we did not contact them. It is possible that those who
completed the questionnaire had better dietary and oral health practices than those who did not. It would be beneficial to replicate this study with a larger sample size to determine risk factors of dental caries occurrence among young children. Parents/guardians should be contacted if their questionnaires are not completed.

CONCLUSIONS
This study has shown that more than a third of the young children aged 2 to 5 had dental caries. On the whole, the findings presented in this study suggest that several dietary habits and oral health practices are associated with dental caries occurrence. Thus, it is important for the parents or caretakers to enhance their oral health knowledge and inculcate good practices on dietary habits and oral health practices for their children in order to prevent dental caries at young age.

ACKNOWLEDGEMENTS
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REFERENCES


Vitamin D Intake and Sun Exposure Among Malaysian Athletes in National Sports Institute, Bukit Jalil

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ABSTRACT
Introduction: Vitamin D plays an important role in maintaining the physical health as well as the performance of athletes. This cross-sectional analytical study was conducted to determine vitamin D intake, sun exposure and skin types of both indoor and outdoor Malaysian athletes in the National Sports Institute, Bukit Jalil. Method: A total of 28 indoor (badminton, shooting, wushu and fencing) and 36 outdoor (athletics, football and hockey) athletes were recruited for this study. The dietary vitamin D intake was estimated using Vitamin D-specific Food Frequency Questionnaire (FFQ). The Sun Exposure Index (SEI) was calculated from Seven-day Sun Exposure Record while the skin types of athletes were determined using Fitzpatrick Skin Typing Questionnaire. Results: The mean age of the athletes was 21.02±4.11 years and their mean Body Mass Index (BMI) was 22.20±2.22 kg/m². The mean body fat percentage of outdoor athletes was significantly lower than indoor athletes (p<0.001). Forty two athletes (65.6%) met the recommended nutrient intake (RNI) value for vitamin D and the outdoor athletes had significantly greater amount of vitamin D intake compared to RNI (p<0.05) and the indoor athletes (p<0.05). The indoor athletes spent significantly less time outdoor per day (p<0.05) and had lower SEI per day (p<0.05) than outdoor athletes. Most of the indoor athletes (53.6%) had type II of Fitzpatrick skin type while the outdoor athletes (47.2%) had type III of Fitzpatrick skin type. Conclusion: The outdoor athletes had higher intake of vitamin D and more sun exposure than indoor athletes. There is a need to ensure the adequacy intake of vitamin D among indoor athletes.

Keywords: Vitamin D intake, sun exposure, Fitzpatrick skin type, athletes

INTRODUCTION
Vitamin D, which is also known as sunshine vitamin, is the most accessible vitamin in our daily life especially in tropical countries like Malaysia. Vitamin D can be synthesized endogenously when the skin is exposed to ultraviolet B (UVB) radiation (wavelength range of 290-315nm). However, the problem of low vitamin D status was found in the countries with abundant sunshine, where high amounts of sun exposure do not ensure the adequacy of vitamin D. There are various factors that may limit or inhibit the amount of sun exposure and the synthesized of vitamin D. Aging, skin pigmentation, sunscreen use, clothing, cloud cover, atmospheric pollution, time of day, indoor activity, geographic location are examples of factors that can impair vitamin D synthesis. Vitamin D can be obtained from diet oily fish (such as salmon, mackerel and sardine), fish oil (such as cod liver oil), egg yolks and food fortified with vitamin D (such as fortified milk, margarine and cereal products) are good sources of dietary vitamin D.

Vitamin D is important for the development and maintenance of bone as well as for the maintenance of normal calcium and phosphorus homeostasis. Recent studies have revealed the roles of vitamin D in cancer prevention, reducing the risk for diabetes mellitus and promoting body’s autoimmunity, cardiovascular diseases and osteoporosis prevention as well as improving athletes’ performance.

In athletes, vitamin D plays major role in maintaining their physical health and performance. Active individuals required sufficient vitamin D for the bone health and bone injury prevention. The risk of stress fracture which is common among athletes is significantly increased when serum 25(OH)D, an indicator of vitamin D status, is defined as insufficient. Moreover, the study by Halliday et al. (2011) in college athletes also demonstrated the positive association between vitamin D status and the frequency of documented illness. Although there is no evidence to show the direct relationship between vitamin D status and athlete’s performance, vitamin D inadequacy in athletes can hamper their performance, indirectly since their health could become poor due to insufficient vitamin D.

Vitamin D is the micronutrient which is normally ignored in sport nutrition even though it can hamper or promote

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the performance of athletes.\textsuperscript{11} The aim of this study was to determine the intake vitamin D and sun exposure among athletes in Malaysia is currently no data is available in this country.

**METHODOLOGY**

**Subjects**

All Malaysian male and female athletes from National Sports Institute aged between 18 years and above were invited to participate in the study which was approved by the Medical Research Ethics Committee of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. The inclusion criteria for subjects’ recruitment were male and female, aged 18 and above. Moreover, the subjects had to be Malaysians since this study aim is to determine the vitamin D intake and sun exposure among Malaysian athletes. The information sheets and consent forms were given out before data collection so that the participants could have a brief understanding of the study. The subjects were classified as either indoor- or outdoor-based athletes depending on their sport. In this study, the indoor athletes were defined as those who trained and competed indoor while the outdoor athletes are those who trained and/or competed outdoor.

**Study design & sampling method**

This was a cross-sectional analytical study, which was conducted at a single point in time. Convenience sampling method was used to recruit subjects due to availability and accessibility of subjects during the time of data collection. Although the recruited sample might not be representative, this was the sampling method which could reach the targeted number of subjects in the limited duration and the most feasible method for this study.

**Sample size**

Since the comparison of vitamin D and sun exposure between indoor and outdoor athletes is involved, comparing two population means was used in determining the sample size for each group as shown below\textsuperscript{12}:

$$n_i = 2 \left( \frac{Z_{1 - \alpha/2} + Z_{1 - \beta}}{\sigma} \right)^2$$

Where $\alpha = 0.05$, $\beta = 0.8$ and $ES = \frac{|\mu_1 - \mu_2|}{\sigma}$

However, since data for $\sigma$ is not available, we used $S_p = \sqrt{\frac{(n_1 - 1) \sigma^2_1 + (n_2 - 1) \sigma^2_2}{n_1 + n_2 - 2}}$ to calculate the value for $\sigma$. Study by Halliday et al.\textsuperscript{2011} that showed significant difference between vitamin D status of indoor ($n=12, 39.9 \pm 8.9$ ng/ml) and outdoor ($n=29, 53.1 \pm 17.4$ ng/ml) athletes was used for the calculation.

$$S_p = \sqrt{\frac{(12 - 1) (8.9)^2 + (29 - 1) (17.4)^2}{12 + 29 - 2}} = 15.48$$

So,

$$ES = \frac{139.9 - 53.1}{15.48} = 0.85$$

With the above value of ES, the number of subjects in each group was computed as below:

$$n_i = 2 \left( \frac{Z_{1 - \alpha/2} + Z_{1 - \beta}}{ES} \right)^2 = 2 \left( \frac{1.96 + 0.84}{0.85} \right)^2 = 21.7$$

According to the formula, the calculated sample size for each group was 22 persons. Thus, the total sample size required for this study was 44 persons. However, to overcome the problem of incomplete questionnaires, more subjects have to be recruited to allow for attrition. Assuming that 20% of the subjects failed to complete the questionnaires, a total number of 56 subjects were needed (28 subjects per group) for this study.

**Instruments**

A brief socio-demographic background of the subjects was recorded including body weight and height as well as body fat percentage using a self-administered bilingual (Bahasa Malaysia and English) questionnaire.

The dietary vitamin D was estimated by using Vitamin D-specific Food Frequency Questionnaire (FFQ) from Wu et al.\textsuperscript{2009} which consists of a list of 35 specific food items known as source of dietary vitamin D. The list of food items had been modified according to the food available in the country. Subjects were required to recall the frequency
of food and supplements that were consumed for the past one month. The average of the vitamin D daily intake was calculated by expressing the response to the food item as a portion of daily use, which was then multiplied by the amounts of the specified portion sizes and by the vitamin D content of the food. The values of vitamin D content in food were obtained from the food labels and food databases of USDA and New Zealand.

The Sun Exposure Index (SEI) was calculated from Seven-day Sun Exposure Record. Subjects were requested to record total minutes spent outdoor for each period from 7am-7pm as well as the clothing, sunscreen use and outdoor activity for those minutes. Body surface area (BSA) exposed was estimated referring to the guidelines of clothing key. Minutes and SEI are used to estimate the sun exposure where SEI is the product of time spent outdoor and BSA exposed. The average SEI, where the total SEI is divided by total minutes, was calculated for each subject using this record.

Fitzpatrick Skin Typing Questionnaire was used to determine the skin type of subjects. The Fitzpatrick skin phototypes were developed by Thomas B. Fitzpatrick in 1975 based on an individual’s skin colour and responses to sun exposure in terms of degree of burning and tanning. There are three components in this questionnaire including genetic disposition, reaction to sun exposure and tanning habits. A scale of zero to four is used to measure the response to each question. The total score, summation of score for all questions, is used to classify the skin type corresponding to Fitzpatrick skin type.

Data analysis

The collected data was analyzed using the SPSS version 17.0. The descriptive data such as mean age, height and weight, types of sport, skin types, minutes spent outdoor, SEI per day and daily vitamin D intake were used to describe the characteristics of the subjects. On the other hand, single sample t-test was used to test the significant difference between vitamin D intake and RNI for vitamin D (5µg) among athletes. Independent or unpaired samples t-test was used to test the significant differences in vitamin D intake and sun exposure between indoor and outdoor athletes.

RESULTS

Socio-demographic background

Initially in total, 80 athletes volunteered to participate in the study, however, 16 of them were excluded in the analysis due to incomplete data and for not fulfilling the indoor or outdoor athletes classification of subject recruitment. Hence, the study sample size was 64 athletes, which consisting of 28 indoor and 36 outdoor athletes. The socio-demographic characteristics of the subjects are shown in Table 1.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Indoor (n=28)</th>
<th>Outdoor (n=36)</th>
<th>Total (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16 (57.1%)</td>
<td>32 (88.9%)</td>
<td>48 (75.0%)</td>
</tr>
<tr>
<td>Female</td>
<td>12 (42.9%)</td>
<td>4 (11.1%)</td>
<td>16 (25.0%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>10 (35.7%)</td>
<td>33 (91.7%)</td>
<td>43 (67.2%)</td>
</tr>
<tr>
<td>Chinese</td>
<td>17 (60.7%)</td>
<td>0 (0.0%)</td>
<td>17 (26.6%)</td>
</tr>
<tr>
<td>Indian</td>
<td>-</td>
<td>3 (8.3%)</td>
<td>3 (4.7%)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (3.6%)</td>
<td>-</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elite</td>
<td>11 (39.3%)</td>
<td>4 (11.1%)</td>
<td>15 (23.4%)</td>
</tr>
<tr>
<td>Back-up</td>
<td>17 (60.7%)</td>
<td>32 (88.9%)</td>
<td>49 (76.6%)</td>
</tr>
<tr>
<td>Accommodation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hostel</td>
<td>25 (89.3%)</td>
<td>28 (77.8%)</td>
<td>53 (82.8%)</td>
</tr>
<tr>
<td>Home</td>
<td>-</td>
<td>7 (19.4%)</td>
<td>7 (10.9%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (10.7%)</td>
<td>1 (2.8%)</td>
<td>4 (6.3%)</td>
</tr>
<tr>
<td>Type of sports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Badminton</td>
<td>6 (21.4%)</td>
<td>-</td>
<td>6 (9.4%)</td>
</tr>
<tr>
<td>Shooting</td>
<td>9 (32.1%)</td>
<td>-</td>
<td>9 (14.1%)</td>
</tr>
<tr>
<td>Wushu</td>
<td>9 (32.1%)</td>
<td>-</td>
<td>9 (14.1%)</td>
</tr>
<tr>
<td>Fencing</td>
<td>4 (14.3%)</td>
<td>-</td>
<td>4 (6.3%)</td>
</tr>
<tr>
<td>Athletics</td>
<td>-</td>
<td>13 (36.1%)</td>
<td>13 (20.3%)</td>
</tr>
<tr>
<td>Football</td>
<td>-</td>
<td>19 (52.8%)</td>
<td>19 (29.7%)</td>
</tr>
<tr>
<td>Hockey</td>
<td>-</td>
<td>4 (11.1%)</td>
<td>4 (6.3%)</td>
</tr>
<tr>
<td>Age (mean ± SD)*</td>
<td>23.11 ± 4.89</td>
<td>19.39 ± 2.41</td>
<td>21.02 ± 4.11</td>
</tr>
</tbody>
</table>

*Significant differences between indoor & outdoor groups at level p<0.001
As shown in Table 2, the mean height of subjects was 169.44 ± 8.46 cm with the mean height of outdoor athletes significantly higher than indoor athletes (p<0.05). The average weight of subjects was 63.99 ± 9.77 kg. The average weight of outdoor athletes was greater than indoor athletes as well. However, similar BMI was found between indoor and outdoor athletes groups with the mean BMI of subjects at 22.20 ± 2.22 kg/m². For body fat percentage, the average reading for all subjects was 18.47 ± 5.89. The indoor athletes was having significantly greater percentage of body fat than the outdoor athletes (p<0.001).

According to the BMI classifications by WHO (2004) the majority of the subjects were normal in their BMI classification (92.2%). One subject from the indoor group was classified as underweight (1.6%) and four subjects were categorized as overweight (6.3%), which comprised two athletes from each group.

Since athletes are physically active, it might be more suitable and meaningful to describe the body composition of athletes instead of BMI. The body fat percentage of the subjects was classified according to ratings of body-fat percentage levels for males and females aged 18-30. Most of the subjects were in the range of good (31.3%) and acceptable (53.1%). Five of them were rated with athletic category, which usually applies particularly to athletes who compete in events where excess body fat may be a disadvantage. On the other hand, five subjects were rated as overweight and obese. It was found that more indoor athletes were found to have greater body fat percentage. However, only a small number of athletes had excess body fat.

**Vitamin D intake**

The daily intake of vitamin D intake was calculated using data obtained from Vitamin D-specific FFQ and shown in Table 3. The mean daily vitamin D intake and intake from supplements of outdoor athletes was significantly higher than indoor athletes (p<0.05). The significant difference in total vitamin D intake between these two groups could be explained by the significant difference in supplements consumption.

| Table 2. Anthropometric measurements and body fat percentage of subjects |
|-----------------------------|-----------------------------|-----------------------------|
| Measurements                | Indoor (n=28) |  | Outdoor (n=36) |  | Total (n=64) |  |
|                            | mean ± SD | mean ± SD | mean ± SD |  |
| Height, cm*                | 166.34 ± 7.77 | 171.85 ± 8.28 | 169.44 ± 8.46 |
| Weight, kg                 | 61.42 ± 9.31 | 65.99 ± 9.78 | 63.99 ± 9.77 |
| BMI, kg/m²                 | 22.14 ± 2.60 | 22.24 ± 1.91 | 22.20 ± 2.22 |
| Body fat percentage**      | 22.15 ± 6.11 | 15.60 ± 3.77 | 18.47 ± 5.89 |

Significant differences between indoor & outdoor groups (*p<0.05, **p<0.001)

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| Table 3. Vitamin D intake of subjects |
|------------------------------------|-----------------------------|-----------------------------|
| Daily intake (µg)                  | Indoor (n=28) |  | Outdoor (n=36) |  | Total (n=64) |  |
|                                    | mean ± SD | mean ± SD | mean ± SD |  |
| Food                               | 5.40 ± 4.44 | 6.66 ± 5.70 | 6.11 ± 5.18 |
| Supplements*                       | 1.70 ± 4.09 | 6.82 ± 8.43 | 4.58 ± 7.29 |
| Total*                             | 7.10 ± 6.86 | 13.47 ± 10.50 | 10.68 ± 9.57 |

*significant differences between indoor & outdoor groups at level p<0.05

The recommended vitamin D intake as stated in RNI is 5 µg per day for all age groups except the elderly. There was a relatively high number of subjects (34.4%) who did not meet the recommended intake. Almost half of the indoor athletes (46.4%) and a quarter of the outdoor athletes (25.0%) failed to consume a sufficient amount of vitamin D. Significant difference between RNI and vitamin D intake of all subjects was found in one sample t-test (p<0.001). Moreover, the intake of outdoor athletes also showed a significantly higher intake compared with RNI (p<0.05). According to the list of food items in vitamin D-specific FFQ, fresh milk was the major source of vitamin D among subjects. Furthermore, UHT milk, sandwich bread, salmon and eggs also contributed to the vitamin D intake of the subjects.
Sun exposure

Sun exposure measurements of subjects included average minutes spent outdoor per day, percent body surface area (BSA) exposed per day, Sun Exposure Index (SEI) and SEI with sunscreen are shown in Table 4. These measurements are important in determining how much time and body surface area of a subject are exposed to sunlight, enabling the dermal synthesis to occur. The average minutes, percent BSA exposed were determined every day that a subject went outside and the average did not take into account days in which the subjects did not go outside.

Table 4. Sun exposure measurements of subjects

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Indoor (n=28)</th>
<th>Outdoor (n=36)</th>
<th>Total (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean ± SD</td>
<td>mean ± SD</td>
<td>mean ± SD</td>
</tr>
<tr>
<td>Minutes per day**</td>
<td>22.61 ± 13.49</td>
<td>195.51 ± 64.03</td>
<td>119.87 ± 99.14</td>
</tr>
<tr>
<td>BSA per day</td>
<td>28.25 ± 9.42</td>
<td>32.17 ± 6.90</td>
<td>30.45 ± 8.26</td>
</tr>
<tr>
<td>SEI per day**</td>
<td>639.78 ± 430.35</td>
<td>6119.63 ± 1830.75</td>
<td>3722.20 ± 3073.86</td>
</tr>
<tr>
<td>SEI with sunscreen per day**</td>
<td>586.01 ± 397.01</td>
<td>5809.63 ± 1474.30</td>
<td>3524.29 ± 2845.46</td>
</tr>
</tbody>
</table>

**significant differences between indoor & outdoor groups at level p<0.001

The percent of BSA exposed was affected by the clothing and sunscreen use of subjects. The average percent BSA exposed of subjects was 30.45 ± 8.26 %, corresponded to the face, neck, arms and hands (t-shirt), legs (shorts near the knees) and feet (sandals) being exposed to the sun. The mean value of percent BSA exposed among indoor athletes was lower than outdoor athletes which could be due to the clothing of indoor athletes that covered more body surface area to minimize the sun exposure when they went outside.

There was no significant difference between average SEI and SEI with sunscreen among the subjects. This may be due to the small number of sunscreen users (n=10) in this sample. The mean of SEI with sunscreen in outdoor athletes was significantly higher than indoor athletes as well. This showed that, despite the usage of sunscreen, outdoor athletes tend to received more sun exposure than indoor athletes.

Types of activities and percent of time spent performing the outdoor activities were obtained from the sun exposure records besides sun exposure measurements and sunscreen use. Walking was the most frequent activity where indoor athletes spent the modest percent of their time (67.8%) when they were outside, followed by riding motorbike (13.5%), outdoor training (9.7%), hiking (4.7%), playing badminton (1.6%), washing car (1.2%), jogging (0.8%) and sitting (0.8%). For outdoor athletes, the majority of their time was spent on outdoor training (80.0%). They spent 10.7% of the time on walking, 5.0% on having a match and 1.8% on jogging.

Skin type

The skin type of a subject was relatively important in determining how much of Ultraviolet-B could reach into the skin for dermal synthesis process. Three subjects (4.7%) had skin type II, the skin type that burns easily and tans minimally with difficulty after a long exposure to the sun. The skin types of type III and IV had modest number among all subjects, twenty six persons (40.6%) for each type. Those with skin type III burn moderately as well as tan moderately and uniformly after being exposed to the sun for a long period of time. While the subjects with skin type IV were more likely to be burned minimally and tanned moderately and easily. The rest of the subjects (14.1%) had the skin type V, which rarely burns and tans easily. Table 5 also showed that overall outdoor athletes had darker skin than indoor athletes.

Table 5. Fitzpatrick skin type classification of subjects

<table>
<thead>
<tr>
<th>Classification</th>
<th>Indoor (n=28)</th>
<th>Outdoor (n=36)</th>
<th>Total (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type II</td>
<td>2 (7.1%)</td>
<td>1 (2.8%)</td>
<td>3 (4.7%)</td>
</tr>
<tr>
<td>Type III</td>
<td>15 (53.6%)</td>
<td>11 (30.6%)</td>
<td>26 (40.6%)</td>
</tr>
<tr>
<td>Type IV</td>
<td>9 (32.1%)</td>
<td>17 (47.2%)</td>
<td>26 (40.6%)</td>
</tr>
<tr>
<td>Type V</td>
<td>2 (7.1%)</td>
<td>7 (19.4%)</td>
<td>9 (14.1%)</td>
</tr>
</tbody>
</table>
Ethnicities (genetic disposition) do influence the skin types of subjects, in which indirectly related to the cutaneous synthesis of vitamin D with the same Sun Exposure Index (SEI) across ethnicities. Table 6 shows the classification of skin type according to ethnicity of subjects.

Table 6. Classification of skin type according to ethnicity of subjects

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Fitzpatrick skin type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type II (n=3)</td>
</tr>
<tr>
<td>Malay</td>
<td>2 (66.7%)</td>
</tr>
<tr>
<td>Chinese</td>
<td>1 (33.3%)</td>
</tr>
<tr>
<td>Indian</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Others</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

DISCUSSION

The surprising finding of this study was that vitamin D intake was significantly different between indoor and outdoor groups. It was believed that the type of sports do not differ them in terms of vitamin D intake from food and supplements. The differences occurred may be due to cultures and ethnicities of subjects which shaped them with different food habits or supplement use. Moreover, taste preference, familiarity and religion do affect the food choices of subjects. Food accessibility and availability are also factors that determine the diet patterns of subjects.

Furthermore, attention should be paid on vitamin D intake of athletes since about one third (n=22, 34.4%) of the subjects in this study sample did not meet the requirement of Malaysian RNI. There was more concern on indoor athletes who did not achieve RNI rather than outdoor athletes because outdoor athletes would be exposed longer under the sun which might help in reducing the risk for poor vitamin D status.

The average body fat percentage in both indoor as well as outdoor athletes was in the range of good and acceptable, according to the rating scale of body fat percentage levels in this study, which promoting optimal vitamin D production with ideal body fat percentage level. Only few athletes were found to be overweight and obese and attention should be paid to them. Body fat percentage of athletes should be monitored regularly in order to maintain in healthy range, which could optimize the capability of the skin in producing vitamin D.

In this study sample, types of sports do play an important role in determining the chances to be exposed to the sun. The training patterns, extensive training hours and locations for indoor athletes diminished their opportunities to carry out their activities under the sun. Higher sun exposure in outdoor athletes was mostly due to their training patterns and locations. The study by Halliday et al. (2011) also found that the vitamin D status of the athletes who were involved in their study is correlated with the estimated weekly outdoor practice time, but not the leisure time.

Persons with low sun exposure are those spending 20 minutes per day averagely in direct sun with about 18% BSA exposed while those spending an average of 90 minutes per day in direct sun with about 35% BSA exposed are known as having high sun exposure. Indoor athletes in this study could be categorized as slightly low sun exposure whereas the outdoor athletes had relatively high sun exposure. It was found that indoor athletes were more likely to have the habits of sunscreen use too. Therefore, indoor athletes who spent lesser time outside, with lower percent BSA exposed and SEI, would have higher probability of low vitamin D status.

The skin type of subjects, which were determined by their ethnicities and skin pigmentation, is one of the components in determining the quantity of cutaneous synthesized vitamin D. Outdoor athletes were more likely to have darker skin due to their ethnicities (Malay and Indian) as well as greater melanin production as a result of response to greater sun exposure. On the other hand, indoor athletes might tend to have fairer skin for the same reasons as well.

Hall (2009) estimated that persons with low skin reflectance or darker skin would need 6-9 times the amount of time under the sun compared to those with high skin reflectance. In other words, subjects with darker skin or greater number of melanin, the natural sunscreen in the skin, are required a longer duration of sun exposure compared to fairer-skinned subjects in order to obtain the same amount of dermally synthesized vitamin D. It be said that darker-skinned subjects would have higher risk of having low vitamin D status for this reason.

However, persons with darker skin are less sensitive and less likely to experience sunburn. Thus, persons who have greater skin type (darker skin) could spend longer time under the sun. Besides skin colour, sun sensitivity or photosensitivity of skin is another characteristic described in Fitzpatrick skin type classification. Using the same classification, the study by Chan, Jaceldo-Siegl and Fraser (2010) found that those with greater ability to tan, minimal or insensitive skin, spend more time outside explaining the higher levels of serum 25(OH)D with increasing skin type. Therefore, skin type not only determines the amount of vitamin D production, but also the duration of sun
Vitamin D intake is the alternative source of vitamin D besides sun exposure. Hence, intake of vitamin D could be adjusted in order to meet optimal vitamin D status depending on the sun exposure habits of athletes. Hall et al. (2010) suggested that persons with high skin reflectance (fairer skin) and high sun exposure are at low risk of vitamin D inadequacy and a supplemental intake of 25 µg (100 IU) to 63.75 µg (2550 IU) per day is needed for those persons depending on the season to maintain optimal vitamin D status. For those who have low skin reflectance (darker skin) and low sun exposure they need to be supplemented with 52.5 µg (2100 IU) to 77.5 µg (3100 IU) per day all year-round to achieve and maintain optimal serum 25(OH)D. Thus, indoor athletes should be supplemented with vitamin D or increase their vitamin D consumption from food to maintain their vitamin D status.

In conclusion, these findings showed that indoor athletes were more vulnerable to vitamin D insufficiency since they spent relatively less time under the sun and tended to use sunscreen protective than outdoor athletes. Furthermore, their vitamin D intake from food and supplement were also lower than outdoor athletes. This again increased the risk of vitamin D inadequacy among indoor athletes. The results also showed that almost half of the indoor athletes did not meet the RNI for vitamin D as well. Due to limited resources, the major outcome, vitamin D status, was not measured via serum 25(OH)D in this study. Hence, the current status of subjects and the relationship or impact of the determined factors in this study could not be determined.

ACKNOWLEDGEMENTS
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REFERENCES


ABSTRACT
The objective of the study was to determine the proportion of sound HIV knowledge and common misconceptions about HIV among university students. A set of pre tested and validated questionnaire assessing sound HIV knowledge and common misconceptions about HIV was used in this cross sectional study. HIV knowledge was defined as sound when one was able to identify correctly two ways of preventing the sexual transmission of HIV and reject three major misconceptions about HIV.
Out of 300 respondents, 298 completed the questionnaire giving a response rate of 99.3%. A total of 40.9% of university students have sound HIV knowledge. The majority of those who lacked sound HIV knowledge were young (60.2%) and female (60.4%). A significant proportion still believed that HIV can be transmitted via social contact (13.8%), by sneezing or coughing (11.4%) and mosquito bites (10.1%). About 6.7% were believed wrongly that HIV can be treated by vaccine and healthy-looking people cannot have HIV.

Keywords: Sound HIV knowledge, misconceptions, university students

INTRODUCTION
Human immunodeficiency virus (HIV) infection in Malaysia has become a significant health problem after it was first identified in 1986. Young people aged between 13 to 29 years old account for 34.7% of the reported infections[1]. The prevalence of HIV among people aged between 15 to 24 years old is estimated at about 0.45% in Malaysia[2]. Malaysian HIV data from 1986 to 2010 based on sectors or occupations has shown that 0.34% of students made up the total number of people living with HIV (PLWH) with half of them having progressed into AIDS[3]. Although it was low, percentage college or university students may not be excluded from being a risk of contracting HIV. The reasons being campus living environment provides opportunity for students’ independence and self determination, and peer influence may trap them into risky situations such as early drugs and sexual experimentation.

Students in colleges and universities who are at their prime and are aged between 18 to 25 years old are vulnerable to HIV infection due to many factors. One of the risk factors is that they lack knowledge of HIV[4]. Knowledge about HIV/AIDS is defined as sound when one is able to identify correctly, two ways of preventing the sexual transmission of HIV and reject three major misconceptions about HIV[5]. A study in a Malaysian public university has reported that the level of HIV knowledge among the students was not satisfactory. More than 60% had major misconceptions about HIV transmission despite correctly identifying that the use of a condom may lower the risk of HIV spread through sexual transmission[6].

A nationwide survey on young people aged between 15 and 24 years old in Malaysia reported that almost 20% of the respondents did not know that condom use during sexual intercourse can prevent HIV transmission[7]. Misconceptions were still a major problem as up to 50% of them either believed that HIV infected people could be recognized or had no idea about it at all. More than half of the respondents believed that mosquitoes could transmit HIV and about 30% answered that HIV could be transmitted through sharing plates with HIV infected people. The ministry of Health (MOH) Malaysia has reported that only 22.6% of 6000 young people who were national service conscripts had sound knowledge about HIV/AIDS[8]. It was still far from the 95% target for sound HIV knowledge among young people as set out in United Nations General Assembly Special Session (UNGASS) Declaration of Commitment for 2010[9]. The findings reflect that accurate information about HIV/AIDS is not reaching the youth and there is an urgent need to address this problem.

Many previous studies in Malaysia used different set of assessment of HIV knowledge on mainly general youth population or school children. This study aims to examine sound HIV knowledge among university students using
the questionnaire that is recommended by the Joint United Nations Programme on HIV/AIDS (UNAIDS) which reflects the sufficient level of basic knowledge on HIV that youth must acquire in order to reduce their susceptibility to HIV infection. As such, it would help to determine the necessity to integrate HIV/AIDS prevention program into the curriculum of the university.

**METHODOLOGY**

A cross-sectional study was carried out to determine the proportion of university students with sound HIV knowledge and who would be able to dispel common misconceptions about HIV. The study was conducted at a selected faculty of a Malaysian public university. The list of all names of first and second year students in six undergraduate programs in the faculty served as the sampling frame. The respondents were selected from the sampling frame using a simple random sampling method. The inclusion criterion comprised all first and second year students studying at faculty because of their availability to be in campus on a full-time basis during the study period. Therefore, all of them could be available during the sampling procedure. The exclusion criteria for the study were respondents who did not give their consent. In addition, international students were also excluded from the study due to differences between them and local students with regards to demographic, social, and cultural backgrounds. The ethical committee of the university granted permission to conduct the study.

Data were collected using a set of validated and pretested English version questionnaire. It was self-administered and consisted of two sections. Section A collected information on the demographic profile of the respondents which included age, gender, ethnicity, and bachelor program enrolled. Section B consisted of seven questions on HIV knowledge. There were five core indicator questions for assessing sound HIV knowledge and two additional questions on common misconceptions about HIV. The five core indicator questions were adopted and modified from Guidelines on Construction of Core Indicators: 2010 reporting by UNAIDS [10].

- Can people protect themselves from HIV by having one uninfected faithful sex partner?
- Can people protect themselves from HIV, the virus that causes AIDS by using a condom correctly every time they have sex?
- Do you think that a healthy-looking person can be infected with HIV, the virus that causes AIDS?
- Can a person get the HIV virus from mosquito bites?
- Can a person get HIV by sharing a meal with someone who is infected?

The two additional questions were as follow:

- Can coughing or sneezing spread HIV, the virus that causes AIDS?
- Can a vaccine treat HIV infection?

All questions were answered by Yes or No. A correct answer scored one mark while no mark was given for an incorrect answer. The respondents were identified to have sound HIV knowledge if they correctly answered all five core indicator questions.

Data were collected and entered manually into statistical computer software of SPSS version 18 [11]. Percentage was used to describe the proportion of respondents with or without sound HIV knowledge. Chi-square test was used to determine the association between respondents' socio-demographic variables and sound HIV knowledge. All significant levels were set at a standard p value of less than 0.05 (p < 0.05).

**RESULTS**

Out of 300 respondents, 298 completed the questionnaire giving a response rate of 99.3%. Table 1 shows the demographic profile of the respondents. The mean age of the respondents was 20.5 years old (SD=3.29, 95% CI = 20.1-20.8). The age ranged from 18 to 40 years old. The majority in the age group of 18 to 20 years old (84.2%). Females made up the majority of the respondents (78.9%). Almost three quarters of the respondents (72.9%) were of Malay ethnicity. Medical students represented one third (31.2%) of the respondents while students from Dietetics program formed the smallest group (6.0%) in the study.

Table 2 shows the distribution of respondents' sound HIV knowledge by their age group, gender, ethnicity, and programs enrolled at the university. The percentage of respondents with sound HIV knowledge was 40.9% while those who did not have sound HIV knowledge was 59.1%. Up to 60% of those in the younger age group did not have sound HIV knowledge as compared to those whose age were 21 and above (53.2%). However, there was no significant difference shown in sound HIV knowledge by their age group (χ²=0.795, p = 0.373). There were more male respondents (46.0%) who had sound HIV knowledge as compared to their female counterparts (39.6%). However, the difference was not statistically significant (χ²=0.857, p = 0.355). Although, the Malays formed the majority of those...
without sound HIV knowledge (61.8%) as compared to the non Malays (51.9%), there is no significant difference shown between the two groups ($\chi^2 = 2.391, p = 0.122$). With regards to the program enrolled, those who were in other health sciences programs (41.8%) has more sound HIV knowledge than those who enrolled into medical and nursing programs (39.7%). However, it was not significantly different ($\chi^2 = 0.130, p = 0.719$).

**Table 1.** Demographic profile of the respondents (n=298)

<table>
<thead>
<tr>
<th>Profile of respondents</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-20</td>
<td>251</td>
<td>84.2</td>
</tr>
<tr>
<td>21 and above</td>
<td>47</td>
<td>15.8</td>
</tr>
<tr>
<td>Total</td>
<td>298</td>
<td>100.0</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>63</td>
<td>21.1</td>
</tr>
<tr>
<td>Female</td>
<td>235</td>
<td>78.9</td>
</tr>
<tr>
<td>Total</td>
<td>298</td>
<td>100.0</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>217</td>
<td>72.8</td>
</tr>
<tr>
<td>Chinese</td>
<td>60</td>
<td>20.1</td>
</tr>
<tr>
<td>Indian</td>
<td>12</td>
<td>4.1</td>
</tr>
<tr>
<td>Others</td>
<td>9</td>
<td>3.0</td>
</tr>
<tr>
<td>Total</td>
<td>298</td>
<td>100.0</td>
</tr>
<tr>
<td>Program enrolled</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biomedical Science</td>
<td>55</td>
<td>18.5</td>
</tr>
<tr>
<td>Dietetics</td>
<td>18</td>
<td>6.0</td>
</tr>
<tr>
<td>Environmental Health</td>
<td>34</td>
<td>11.4</td>
</tr>
<tr>
<td>Medicine</td>
<td>93</td>
<td>31.2</td>
</tr>
<tr>
<td>Nursing</td>
<td>23</td>
<td>7.7</td>
</tr>
<tr>
<td>Nutritional Health</td>
<td>75</td>
<td>25.2</td>
</tr>
<tr>
<td>Total</td>
<td>298</td>
<td>100.0</td>
</tr>
</tbody>
</table>

**Table 2.** Sound HIV knowledge by age group, gender, ethnicity and program enrolled of the respondents (n=298)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency, n and percentage, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sound HIV knowledge</td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
</tr>
<tr>
<td>18-20</td>
<td>100(39.8)</td>
</tr>
<tr>
<td>21 and above</td>
<td>22(46.8)</td>
</tr>
<tr>
<td>Total</td>
<td>122(40.9)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>29(46.0)</td>
</tr>
<tr>
<td>Female</td>
<td>93(39.6)</td>
</tr>
<tr>
<td>Total</td>
<td>122(40.9)</td>
</tr>
<tr>
<td>Malays</td>
<td>83(38.2)</td>
</tr>
<tr>
<td>Non Malays</td>
<td>39(48.1)</td>
</tr>
<tr>
<td>Total</td>
<td>122(40.9)</td>
</tr>
<tr>
<td>Program enrolled</td>
<td></td>
</tr>
<tr>
<td>Medicine-Nursing</td>
<td>46(39.7)</td>
</tr>
<tr>
<td>Others</td>
<td>76(41.8)</td>
</tr>
<tr>
<td>Total</td>
<td>122(40.9)</td>
</tr>
</tbody>
</table>
Table 3 shows the distribution of responses to common misconceptions about HIV among the respondents. The majority of the respondents gave correct responses (86.2% to 93.3%) to all five common misconceptions about HIV. However, up to 10% of the respondents believed that mosquito bites can transmit HIV. Almost 14% of them agreed that HIV can be spread by sharing a meal with someone who is infected while 11% believed that sneezing or coughing can transmit HIV. A small percentage (6.7%) of the respondents believed that a healthy looking person cannot have HIV and HIV can be treated with a vaccine.

**DISCUSSION**

The study was able to determine the percentage of respondents who had sound HIV knowledge using a structured questionnaire with five core indicator questions on the knowledge scale. The results of the study showed that only 40.9% of the respondents had sound knowledge of HIV. The percentage was higher than that reported from a worldwide survey from 1999 to 2003. It was reported that only 29% of young people aged 15 to 24 years old had sound knowledge using the same measured outcome[12]. However, with advances in HIV prevention effort, a recent report from UNAIDS has demonstrated that the proportion has increased to 40%[13] which supports the result of the present study.

The present study showed higher percentage of respondents (40.9%) with sound knowledge of HIV as compared to that reported from the Ministry Health of Malaysia[8](22.6%). The lower reported figure was obtained from a group of young people who came from diverse socioeconomic and educational backgrounds. In the present study, university students were a more selected group of youth with much better educational attainment and higher socioeconomic status than the general youth population which explains the difference. Another local study had used similar questions to assess sound knowledge of HIV on 2259 adolescents aged 14 to 17 years old[14]. The cross sectional study revealed that only 3.81% of the total respondents had sound knowledge of HIV. The figure (3.8%) was very much lower than that of the present study (40.9%). The marked difference also concurs with the finding of the previous study that age had a significant association with the presence of sound knowledge of HIV among the respondents. Although the difference was not significant in the present study, it was shown (46.8%) that those in the older age group have more sound...
majority of the population are safe from HIV/AIDS and therefore they do not need to take safety precaution on behaviour change. In addition, stigmatizing at risk or affected groups would create a false sense of security that AIDS. It can contribute to discriminative attitudes from the respondents towards HIV/AIDS and thus has an impact percentage of university students with the above three common misconceptions about HIV compared to the previous university students in health sciences program which indicated better educational attainment than the respondents. The respondents from the previous study were younger as compared to the result of the previous study (53.0%). The findings from both studies differed because of the socioeconomic and educational background of respondents. The respondents from the previous study were younger than those in the present study. The mean age of the respondents in the previous study was 19.4 with half of them being in the age range of 15 to 19 years. Three quarters of them only had formal education up to secondary level and a significant proportion came from low to middle socioeconomic status. In the present study, respondents were university students in health sciences program which indicated better educational attainment than the respondents from the previous study.

Another previous local study on university students has shown that more respondents believed that a healthy looking person cannot have HIV (35.9%), mosquito bites can transmit HIV (38.7%) and the possibility of HIV being transmitted by sharing plates with HIV infected person (19.6%)\(^6\). However, the present study showed a lower percentage of university students with the above three common misconceptions about HIV compared to the previous study. Although the numbers were low, these misconceptions could trigger off prejudices against those who have HIV/AIDS. It can contribute to discriminative attitudes from the respondents towards HIV/AIDS and thus has an impact on behaviour change. In addition, stigmatizing at risk or affected groups would create a false sense of security that majority of the population are safe from HIV/AIDS and therefore they do not need to take safety precaution\(^6\).

Acquiring sound HIV knowledge and dispelling common misconceptions about HIV in general does not necessarily translate individual’s low risk behaviour pertaining to HIV infection. Rozina, et al., (2009) reported that even with correct knowledge on HIV sexual transmission and condom use, it was not translated into practice as two thirds of university students engaged in unprotected sexual encounters\(^6\). Some other reasons may contribute to this finding but one of the reasons could be the students believed wrong that HIV would not happen to them. Co existence of high risk behaviours, particularly unsafe sexual behaviour, together with inadequate knowledge and major misconceptions regarding HIV/AIDS contribute to increased vulnerability of university students to HIV infection\(^6\).

The results of the present study should be viewed in the light of the study’s strengths and limitations. One of the strengths of the study was the use of five core indicator questions in measuring sound HIV knowledge among the respondents. The questions are accepted internationally and are particularly useful in countries whose populations have poor knowledge of HIV/AIDS. It allows for a serial incremental improvement on HIV knowledge to be measured easily. While in countries where HIV knowledge is high, the core indicator questions are used to ensure that the pre existing knowledge is constantly maintained.

However, a few limitations of the study require the findings to be interpreted with caution. The cross sectional study design did not help in determining the causal relationship between demographic factors and sound HIV knowledge among the respondents. In addition, the design also did not permit the use of more complex statistical analysis in order to examine the relationship of the variables. Although the sample size was adequate to differentiate between those who were with or without sound knowledge, a larger sample size would be recommended to determine the associated factors of sound HIV knowledge among the respondents. The findings of the study were only generalizable to a specific group of university students.
CONCLUSION
The majority of the university students still lack sound knowledge of HIV and a significant proportion of them have common misconceptions about HIV particularly with regards to HIV spread via social contact and other modes of transmission. Although many efforts for HIV prevention have been implemented, they are still insufficient and it was reflected in the findings of the study. University students were not well informed about HIV and even if they did, the information that reached them was not accurate. Therefore, it is high time to integrate HIV education program into the university curriculum so as to improve their knowledge about HIV and subsequently reduce their susceptibility to HIV infection.

ACKNOWLEDGEMENT
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REFERENCES
Comparison Between Healthy Cities and Adipura in Indonesia

1,2 S Palutturi*, 1 S Rutherford, 1 P Davey & 1 C Chu

1 Centre for Environment and Population Health, Griffith University, Australia
2 School of Public Health Hasanuddin University, Indonesia

ABSTRACT
Urban health problems are very complex and affected by many factors, ranging from social and economic to environment and living conditions. In the middle of the 1980s, WHO introduced the Healthy Cities concept in Europe as a pilot project in response to a variety of urban problems including health issues. Then, in 1996 in Indonesia, the Ministry of Health and Home Affairs, began to develop Healthy Cities, including establishing a set of indicators to monitor improvements in urban health. However in 1986, ten years before the concept of Healthy Cities was formally recognised by WHO, the Indonesian State Ministry of Environment had developed Adipura – a clean cities program. The aims of both these programs are similar but they have a different history and were established by different departments. They also bring with them different policies, indicators and implementation methods. Both the Healthy Cities and Adipura programs operate without sufficient coordination to assess their effectiveness. Thus, they seem to be overlapping and competing, potentially leading to inefficient resource use. Based on an extensive literature review and document analysis, this paper compares and reviews the policies and existing indicators used by Healthy Cities and Adipura. This analysis has identified that the programs have similar goals in addressing urban problems, but have different agendas and performance indicators and different stakeholders involved in managing them. Therefore, strengthening the partnership between the key players involved in both approaches is an important strategy for improving the health and environmental conditions in Indonesian cities.

Keywords: Healthy Cities, indicators, Adipura, Indonesia

INTRODUCTION
Urban health problems are very complex and are affected by many factors, ranging from social and economic to environmental and living conditions [1, 2]. Problems ranging from air pollution, traffic congestion, inadequate health services, inadequate water supply, slum areas up to social and economic problems such as street children and buskers, homelessness, HIV/AIDS, narcotics use and urban poverty occur in both developed countries and developing countries including Indonesia [3]. Urban problems are becoming more complex because urban areas are growing. People moving to urban areas have inherent problems, and urbanisation due to migration from the countryside to the cities has brought additional problems associated with blending of cultures, social structures, values, beliefs, habits and behaviour. Consequently, urban problems are becoming more and more difficult to address [4, 5].

In the middle of the 1980s, in response to a variety of urban problems including health problems, the World Health Organisation (WHO) introduced Healthy Cities in Europe as a pilot project [5]. Since then the Healthy Cities movement has grown and is now a worldwide movement, including in Indonesia [6]. In 1996, the Indonesian government, through the Ministry of Home Affairs (MOHA) and the Ministry of Health (MOH) began to develop Healthy Cities including establishing a set of indicators to monitor improvements in urban health. Although this WHO concept of Healthy Cities has been established in Indonesia since 1996, the implementation of Healthy Cities became most significant after issuing the joint regulation between the Ministry of Home Affairs and the Ministry of Health in 2005. However, around ten years before the formal concept of Healthy Cities was defined, the Indonesian State Ministry of Environment had introduced the Adipura program – a clean cities program [7-12]. Healthy Cities and Adipura have similarities in objectives, in particular the aspect of clean cities, but they have a different history and were established by different departments. According to the joint regulation between the Ministry of Home Affairs and the Ministry of Health No: 34/2005 and No: 1138/Menkes/ PB/ VIII/2005, the aims of Healthy Cities in Indonesia are to achieve clean, comfortable, safe and healthy districts/cities to be occupied as a working place for their citizens. They should do this by implementation of various health programs in conjunction with other sectors, in order to improve facilities and productivity and community income [13]. The aims of the Adipura program as mentioned in the regulation of The State Ministry of Environment No. 01/2009 are to encourage districts/cities

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governments and communities in realizing clean and green cities through application of good governance principles in the field of environmental management \[12, 14, 15\]. In the aspect of achieving a cleaner environment, their aims have similarities but numerous questions remain unanswered - why do they not work together? What kinds of policies, indicators, and implementation methods make it difficult for them to work together? Have the early histories of Healthy Cities and Adipura caused them to work independently without enough coordination or effort to assess their program implementation and effectiveness?

This paper aims to compare and review the policies and existing indicators used by the Healthy Cities and Adipura programs in Indonesia. Through this appraisal, recommendations will be made to increase the effectiveness and efficiency of resources used for the programs.

**METHODS**

For this study, six dimensions are used for the comparative review of Healthy Cities and Adipura in Indonesia. They are: history of Healthy Cities and Adipura; focus, principles, and legislation; organizational structure; assessment approach and methods; award system; and budgeting. Information needed on these dimensions was obtained from published research papers and government documents. For the Healthy Cities context, the main document used was the national guideline of Healthy Districts/Cities implementation which is the joint regulation between the Ministry of Home Affairs and the Ministry of Health No. 34/2005 and No. 1138/Menkes/PB/VIII/2005 \[13\] while in the Adipura context, the primary document reviewed was the regulation of the State Ministry of Environment No. 01/2009 on Adipura program \[14\]. Both these main documents are written in the Indonesian language (bahasa Indonesia). Search strategies included key word searches in Bahasa Indonesia such as “kota sehat”, “kabupaten sehat”, and “Adipura” and in English - such as “Healthy Cities” or “Healthy City” from Google and Google Scholar.

**HISTORY OF HEALTHY CITIES AND ADIPURA**

The Healthy Cities policy was developed by the Ministry of Home Affairs and the Ministry of Health following the WHO World Health Day theme “Healthy Cities for better life” in 1996. This was the starting point for Indonesia in implementing Healthy Districts/Cities \[16\]. In October 1998, in Jakarta, the Ministry of Home Affairs launched a Healthy Cities Pilot Project in 6 cities: Cianjur district, Bakti Kpapan city, Bandar Lampung, Pekalongan, Malang, and East Jakarta. Subsequently the central government agreed to develop activities of Healthy Districts /Cities especially in the field of tourism in 8 cities: Anyer Area in Serang District, Batu Raden Area in Banyumas District, Kotagede in Yogyakarta City, Brastagi Tourism Area in Karo District, Senggigi Beach Area in West Lombok District, Bunaken Beach and Coast in Manado City, Tana Toraja District and Nongsa & Marina Area in Batam \[17\]. Currently, Indonesia has developed 216 Healthy Districts/Cities among 497 districts/cities in Indonesia \[11\].

In 1986, ten years before the WHO notion of Healthy Cities was conceptualised, the Indonesian State Ministry of Environment developed the Adipura Program or clean cities program which focuses on improving the quality of the environment in cities \[7, 9, 10\]. According to the Java Calender, Adi means having an edge in everything and a lot of new things \[18\] while Pura (from Sanskrit) that has the meaning of city, fortified city, towered city. According to the Indonesian Ministry of Education, officially Adipura means the most clean and beautiful cities. In bahasa Indonesia it is called kota yg terbersih dan terindah \[19\]. It differs from the Healthy Cities concept, in which the WHO is the international umbrella, as Adipura does not have any official relationship to WHO or other international agencies. Twelve years after its initial implementation, the Adipura program stopped due to the Indonesian internal political crisis (the reformation era). It was re-launched by the State Ministry of Environment in Bali in June 2002 and is still continuing. Since 2002 a further 59 cities have developed an Adipura program, and now there are a total of 375 cities in Indonesia that have developed the Adipura program.

Some cities have implemented both programs. Adoption of these programs indicates a commitment to achieving beyond the minimum health and environmental legislative standards.

**FOCUS, PRINCIPLES AND LEGISLATION**

The Healthy Cities and Adipura have different program aims, policy documents and regulations. The key words for Healthy Cities are “clean, comfortable, safe and healthy districts/cities” while those for Adipura are “clean and green districts/cities”. The definitions indicate clearly that there is overlap between Adipura’s aims and those of Healthy Cities’. To achieve the Healthy Cities’ aims eight policies have been established by the Indonesian government:

1. A Healthy District/City is implemented at district/city level gradually, and is begun by prioritizing community programs at sub-district and village level, considering the social, economic and cultural aspects in the areas.
2. A Healthy District/City is implemented with the community as main actors through forming or utilizing City Forums or other names agreed by community and local government and getting resources from related sectors.
3. Each district/city establishes potential areas as “an entry point”. Hence, the program starts with simple activities, agreed by the community, and then develops the program in one area or a larger area.

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4. A Healthy District/City implementation emphasises more process than output, runs continually, is begun from
prioritised activities in one setting and achieves outcomes in a time-frame based on community ability and all
stakeholders’ support.
5. Agreement on selected Healthy District/City settings and activities as well as types and magnitude of its indicators
is established by Healthy District/City Forums together with local government.
6. Local government facilitates selection of community activities including providing the community resources
needed.
7. Programs which are not prioritised by community are carried out regularly by each sector and gradually socialised
to the community and related sectors through meetings of Healthy District/City Forums.
8. A Healthy District/City implementation is fully funded and implemented by the concerned region and community
using the concept of community empowerment, from, by and for community.

On the other hand, the Adipura program has four principles which are the basis of policy development, namely:
1. Environmental conservation needs strong political will from decision makers
2. Society needs to demand their right to obtain a good and healthy environment
3. Effective democratic mechanisms that are sensitive to the demands of society are needed, and
4. Governments, both at central and regional levels, need to have the ability to implement good governance in the
field of environmental management or good environmental governance [20].

The general difference in these sets of principles is that Healthy Cities is very focussed on community needs and
specific process issues, while the Adipura principles and process are more broad and less prescriptive.

Although Healthy Cities initiatives were started in 1996 [23], officially the Healthy Cities policy was only well
documented in the guideline for the implementation of Healthy Districts/Cities (joint regulation between the Ministry
Indonesia in 2005. The guideline consists of seven chapters, 19 articles/ clauses and two appendices. It contains general
provisions; Healthy District/City application (community empowerment, Healthy District/City Forums, and the role
of an advisory team); Healthy District/City classification and criteria; assessment; awards; development system; and
budgeting. The main guideline only provides general dimensions of Healthy Districts/Cities while the Appendix
provides a detailed explanation about Healthy Districts/Cities including a general description; aims and targets;
policies and strategies; Healthy District/City application; settings; classification and criteria; indicators; and more
details on the evaluation and development system (supervising, advising, coordinating and developing capacities) and
funding. In addition, the Appendix also provides an evaluation form for healthy districts/cities consisting of evaluation
variables; criteria; and scores [23].

In relation to formal legislation, at the national level there is no specific act regarding Healthy Districts/Cities.
However, one Indonesian city, Palopo in South Sulawesi province, has a special Healthy City act (Peraturan Daerah),
No. 10/2008 [23], developed by the Palopo local government. On the other hand, the latest Adipura document was
stipulated by the State Ministry of Environment No. 01/2009. It is a revision of the regulation of the State Ministry
of Environment No. 99/2006 and regulation of The Ministry of Environment No. 14/2006. This guideline covers
general provisions (terms and definitions); Adipura application (including Adipura program officer, evaluation system,
assessor team, cities classification); development system; sanctions (ethical code for assessor team); funding; and final
provisions. As with Healthy Cities, there is no specific national act governing and managing Adipura. However, in
many cities in Indonesia there is a local act regarding city cleanliness, hygiene and waste management such as the
of these regulations support activities relating to Healthy Cities.

**ORGANIZATIONAL STRUCTURE**

The organisational structure of Healthy Cities differs from Adipura. This organisational structure explains the role
of each organisational level. Healthy Cities have organisational support at all levels of government in Indonesia:
national, provincial and districts/cities level. For example, at the national level, Healthy Cities is the responsibility of
two ministries: the Ministry of Home Affairs and the Ministry of Health. Healthy Cities in the Ministry of Home
Affairs is the responsibility of the Directorate General for Regional Development while at the Ministry of Health,
it is the responsibility of the General Disease for Control and Environmental Health. These two departments have
different functions. The Ministry of Health implements and facilitates the Healthy Cities for activities related to health,
while the Ministry of Home Affairs supports, encourages, and commands other departments to contribute to Healthy
Cities achievement. The Ministry of Home Affairs undertakes general guidance such as providing a Healthy Cities
guide, conducting supervision, improving capacity through training, and giving direction, while the Ministry of Health provides technical guidance on how to implement Healthy Cities including advocating local government.

**Provincial and district/city level**

At the provincial level, Healthy Cities is managed by the Regional Development Planning Board and the Provincial Health Office. The roles of central and provincial governments are quite similar. The provincial government only provides guidance to districts/cities government implementing Healthy Districts/Cities. Thereafter, the real implementation of Healthy Cities is at the local level (districts/cities level). As Healthy Cities implementation is at local government level, the local government plays an important role in achieving it. In the Healthy Cities context, the Head of Regional Development Planning Board at district/city level acts as Head of an Advisory Team (*Tim Pembina*). The Advisory Team coordinates, integrates, synergizes, and synchronizes Healthy Cities programs among governmental bodies and offices in the regional development.

In contrast to Healthy Cities, Adipura does not have any formal organisational structure at the provincial and district/city level. The organisational structure of Adipura is at the national level. However, to help with program implementation, the State Ministry of Environment has divided Indonesia into several regions according to the Environmental Management Centre: the regional office for Sumatera region is in Pekanbaru, Riau; the regional office for Balf and South East Nusa is in Denpasar, Bali; the regional office for Java region is in Condong Catur, East Depok and Sleman, Jogjakarta; the regional office for Sulawesi, Maluku and Papua (SUMAPAPUA) is in Makassar; and the regional office for Kalimantan is in Balikpapan. In general, the roles of the regional offices are to coordinate the implementation of policy and provide technical guidance, to supervise and to monitor the environment in accordance with laws and regulations applicable in each of the regional areas.

**EVALUATION: APPROACH AND METHODS**

Evaluation is an important part of health management. It is a multistep process that aims to assess to what extent the aims and objectives of program implementation have been achieved. Evaluation can include assessing the level of implementation achieved, the degree of success and identification of a variety of challenges influencing program achievements [25-27]

The assessment of Healthy Cities and Adipura differs in the assessment period, choice of indicators, categories, and assessor team. Healthy Cities evaluation is generally carried out in June, July or August every two years. There is no specific period of assessment like a month, a semester, or a year. This differs from the *Adipura* assessment system which is conducted from July in the current year up to June the following year so that the assessment period runs for around one year.

Three kinds of indicators are evaluated in Healthy Cities, namely main indicators, general indicators and specific indicators. The main indicators include literacy rate, and domestic income per capita and Infant Mortality Rate (IMR) per 1000 live births. The general indicators are focussed on process and include the availability of local government support, functioning of the district/city forums; village communication forums, and village working groups. Then, the specific indicators are based on the selected settings. In the Healthy Cities implementation, there are 9 settings established by central government, namely healthy settlement areas and public facilities; traffic facilities areas and transportation services; healthy mining areas; healthy forestry areas; healthy industry and office areas; healthy tourism areas; food and nutrition security; self-reliant healthy community life; and healthy social life. These nine settings can be selected and adopted by local government according to local problems and resources as well as community needs. Each setting has specific and complex indicators. Duplication of the indicators can occur between the Healthy Cities and *Adipura* in certain circumstances.

For example “City A” developed a Healthy Cities program and the “healthy settlement areas and public facilities” setting was selected. Hence it established indicators for clean water, clean river water, individual and public water supply, water disposal, waste management, housing and settlement, gardening and city forest, schools and market management. A number of these indicators are quite similar to the *Adipura* indicators.

For assessment purposes, *Adipura* divides cities into four types according to the population size or other characteristics of the city: metropolitan, large cities, medium cities and small cities [28]. Both physical aspects and non-physical aspects are assessed as part of the assessment program. The physical assessment consists of two types: obligatory assessment and non-obligatory assessment. The obligatory assessment includes settlement areas, urban facilities such as markets, schools, offices, hospitals and parks as well as sanitation facilities (waste management), while the non-obligatory assessment includes transportation facilities and tourist beaches. Further, non-physical assessment consists of three aspects: institution, management and responsiveness. Institution aspects assessed include the availability of law, policy, budget and facilities. Management aspects include planning, implementation and monitoring, and responsiveness aspects including community participation. Therefore, in terms of achieving a healthier environment
“healthy settlement areas and public facilities” is one of the Healthy Cities settings which have similarities with the *Adipura* program. The difference is that ‘the healthy settlement areas and public facilities’ program is handled by the Department of Public Works and the Regional Environmental Impact Control Board while *Adipura* is managed by the State Department of Environment. Both departments work with little coordination although the goal of Healthy Cities and Adipura is almost the same in the context of this particular setting.

There is a difference in the evaluation step relating to who assesses the districts/cities. The Healthy Cities evaluation is conducted at two levels: provincial and national. For the provincial level, the provincial government selects and determines which districts/cities will be evaluated as healthy districts/cities. This assessment is conducted by a provincial advisory team on behalf of the Governor. This team consists of the provincial government and related institutions’ representatives such as the Provincial Regional Development Planning Board, Health Office and university representatives. The results of the Healthy Districts/Cities assessment by the provincial team are submitted by the Governor to the Ministry of Health with a copy to the Ministry of Home Affairs, to be further evaluated at the national level. The national assessor team consists of representatives from the Ministry of Health and the Ministry of Home Affairs and related ministries.

Unlike Healthy Cities, the *Adipura* program has a single evaluation. *Adipura* directly evaluates all districts/cities whether metropolitan; large cities; medium cities; or small cities. The State Ministry of Environment representatives appointed by the State Ministry of Environment and provincial representatives appointed by the governor evaluate those districts/cities. Provincial assessor team members consist of provincial environmental institutions, universities, mass media, NGOs, agencies or board representatives stipulated by the Governor’s Decree. The *Adipura* guideline explains in more details the assessor team while the Healthy Cities assessor team is only explained in general (see Table 2 - a summary table on assessment system between Healthy Cities and *Adipura*).

<table>
<thead>
<tr>
<th>Policy Document and Regulation</th>
<th>Healthy Cities</th>
<th>Adipura</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title</strong></td>
<td>Guidelines for the implementation of healthy districts/cities (joint regulation between the Ministry of Home Affairs (MOHA) and the Ministry of Health (MOH) No. 34/2005 and No. 1138/Menkes/PB/VIII/2005)</td>
<td>State Ministry of Environment No. 01/2009 on <em>Adipura</em> Program</td>
</tr>
<tr>
<td><strong>Year</strong></td>
<td>2005</td>
<td>2009</td>
</tr>
<tr>
<td><strong>Corporate Author(s)</strong></td>
<td>MOH and MOHA</td>
<td>State Ministry of Environment (SMOE)</td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td>Bahasa Indonesia</td>
<td>Bahasa Indonesia</td>
</tr>
<tr>
<td><strong>Publisher</strong></td>
<td>MOH and MOHA</td>
<td>SMOE.</td>
</tr>
<tr>
<td><strong>Publisher place</strong></td>
<td>Jakarta</td>
<td>Jakarta</td>
</tr>
<tr>
<td><strong>Physical description</strong></td>
<td>69 pages (2 pages for title and table of content; 8 main pages; 38 pages for Appendix I and 21 pages for Appendix II), A4</td>
<td>62 pages, 5 appendixes, A4</td>
</tr>
<tr>
<td><strong>Status of document Act</strong></td>
<td>Guideline</td>
<td>Guideline</td>
</tr>
<tr>
<td><strong>• There is no national healthy district/city Act</strong></td>
<td>• There is no national <em>Adipura</em> Act</td>
<td></td>
</tr>
<tr>
<td><strong>• Palopo City has a local Act (<em>Perda</em>) of Healthy Cities</strong></td>
<td>• Many cities have a local Act regarding cleanliness and waste management</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Assessment system comparison between Healthy Cities and Adipura in Indonesia

<table>
<thead>
<tr>
<th>Assessment System</th>
<th>Healthy Cities</th>
<th>Adipura</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment period</td>
<td>There is no specific period of time like a month, a semester, or a year</td>
<td>From July in the running year up to June next year (1 year)</td>
</tr>
<tr>
<td>Evaluated indicators</td>
<td>Three indicators: main indicators; general indicators and specific indicators</td>
<td>Physical assessment and non-physical assessment</td>
</tr>
<tr>
<td>Categories</td>
<td>There is no specific city classification</td>
<td>Metropolitan, large cities, medium cities, and small cities</td>
</tr>
<tr>
<td>By whom</td>
<td>Provincial level • Selection is conducted by provincial advisory team on behalf of Governor • Provincial advisory team consists of the provincial government and related institutions representatives</td>
<td>National level • State Ministry of Environment representatives appointed by the State Ministry of Environment and • Provincial representatives appointed by the governor, consisting of representatives from provincial environmental institutions, universities, mass media, NGOs, agencies or boards stipulated by governor</td>
</tr>
</tbody>
</table>

AWARD SYSTEM OF HEALTHY CITIES AND ADIPURA

An important part of both approaches is an award system. Such a system builds recognition for the programs and promotes good practice and sharing between participating communities. Awards given for Healthy Cities and Adipura are also prestigious for both community and city government. They are proof that the government and people are concerned about their health and the environment. For Healthy Cities, an award system is identified in detail in the joint regulation between the Ministry of Home Affairs and the Ministry of Health. It includes an award name, categories; year the awards are given; by whom; occasion and type of award. The name of a Healthy Cities award is Swasti Saba. A Swasti Saba is an award given by the central government to the community through Regent(s)/City Mayor(s) who are successful in implementing Healthy Cities. In Sanskrit, Swasti means healthy and prosperous and “Shaba” means city. Thus, “Swasti Saba” means healthy and prosperous city [29].

Figure 1. Healthy Cities and Adipura logos used in Indonesia

There are three levels of Swasti Saba: Swasti Saba Padapa (basic achievement); Swasti Saba Wiwerda (middle achievement), and Swasti Saba Wistara (high/good achievement). All cities/districts that meet indicators/requirements...
Comparison Between Healthy Cities and Adipura in Indonesia

The Healthy Cities budgeting is based on the purposes, sources and types of activities. Money is allocated for three kinds of purposes: operational funding, general assistance and technical assistance. The operational funding is charged to the Revenue and Expenditure Budget of Districts/Cities (APBD) in accordance with the selected settings: Healthy settlement areas and public facilities; traffic facilities areas and transportation services; healthy mining areas; healthy forestry areas; healthy industry and office areas; healthy tourism areas; food security and nutrition; healthy self-reliant community life; and healthy social life. Activities relating to general guidance are charged to the State Revenue and Expenditure Budget of the Department of Home Affairs, the Provincial and Districts/Cities Revenue and Expenditure Budget, while technical assistance is charged to the State Revenue and Expenditure Budget of Department of Health, the Provincial and Districts/Cities Revenue and Expenditure Budget.

For the Adipura program, the documentation does not make clear the purposes of the budget. Budgeting for Adipura is also from the State Revenue and Expenditure; the Provincial Revenue and Expenditure the Districts/Cities Revenue and Expenditure Budget or other sources in accordance with stipulated decrees. Therefore, both healthy districts/cities and Adipura budgeting are from the central government allocated in the State Revenue and Expenditure Budget (APBN) either by the Ministry of Health, the Ministry of Home Affairs, the State Ministry of Environment or other related ministries; the Provincial Revenue and Expenditure Budget (APBD); the Districts/Cities Revenue and Expenditure Budget (APBD) or other sources stipulated by decrees or regulation.

Table 3. Comparison between Healthy Cities and Adipura budgeting in Indonesia

<table>
<thead>
<tr>
<th>Purposes</th>
<th>Healthy Cities</th>
<th>Adipura</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• General assistance</td>
<td>There is no specific explanation</td>
</tr>
<tr>
<td></td>
<td>• Technical assistance</td>
<td></td>
</tr>
<tr>
<td>Source</td>
<td>• The State Revenue and Expenditure Budget (APBN) of Department of Home Affairs, the Provincial and District/City Revenue and Expenditure Budget (APBD) for general guidance</td>
<td>• The Revenue and Expenditure Budget of Districts/Cities (APBD) for operational funding</td>
</tr>
<tr>
<td></td>
<td>• APBN of the Department of Health, the Provincial and District/City Revenue and Expenditure Budget for technical assistance</td>
<td>• Other sources</td>
</tr>
<tr>
<td></td>
<td>• APBN; the Provincial District/City APBD</td>
<td></td>
</tr>
<tr>
<td>Types of activities</td>
<td>Depends on the selected settings</td>
<td>There is no specific explanation</td>
</tr>
</tbody>
</table>

RECOMMENDATIONS AND CONCLUSION

Healthy Cities and Adipura are two parallel national policies in Indonesia that have similarities in policy aims and objectives but that are implemented under the governance of different ministries. Both are implemented at the local level across Indonesia. Healthy Cities has a stronger emphasis on process rather than specific health outcomes, and
as part of this emphasis, community engagement and leadership are important aspects of the implementation of Healthy Cities in Indonesia. In contrast, Adipura emphasises environmental outcomes more than process and is more government led.

As Healthy Cities covers a range of broad issues, their indicators are tiered: main indicators, general indicators, and specific indicators by settings. However, they really do not emphasise some of the essential problems of the urban environment such as hygiene and sanitation. By contrast, Adipura indicators are quite simple and more specific, but they do not really cover social problems and other determinants of health. Both programs have similarities, in particular in the setting of Healthy City, namely Healthy Settlement Areas and Public Facilities. The existence of the joint regulation between the Ministry of Home Affairs and the Ministry of Health and organisational structure at all levels of government system are strong points for Healthy Cities while the assessment system used for the Adipura is a good system as it involves assessment of the dimensions over a period of time. However, Adipura is better known than Healthy Cities, especially at local government level. Major challenges for urban areas are shortage of resources and lack of community participation. Therefore, in order to create a healthier environment and to improve the effective and efficient use of resources, building partnerships and working together among the Ministry of Health, the Ministry of Home Affairs and the State Ministry of Environment should be strengthened. The Ministry of Home Affairs would be the best department to facilitate this partnership. Strengthening partnerships, should optimise the health and environment benefits to the communities of the cities where the programs are implemented.

ACKNOWLEDGEMENT

A part of this paper work was presented at the 4th Global Conference Alliance for Healthy Cities in Seoul South Korea on 26-29 October, 2010. Therefore, I would especially like to thank the conference committee who provided the opportunity to present this paper as well as travelling grant. My thanks also go to the Ministry of Education, Indonesia who gave me the chance to undertake a PhD Program at The Centre for Environment and Population Health, Griffith University, Australia.

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Comparison Between Healthy Cities and Adipura in Indonesia


Pain Interference Level and its Effects on Patients’ Quality of Life and Depression: A Study on Breast Cancer Survivors in Hospital Kuala Lumpur, Malaysia

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4Dept of Psychiatry, Cyberjaya University College of Medical Sciences, Cyberjaya, Selangor, Malaysia

ABSTRACT

Introduction: Cancer pain is a complex experience and is one of the most common and distressing symptom of breast cancer which affects patients’ functioning in daily activities, their quality of life (QOL), and mood. Yet, there is a great lack of data on breast cancer and pain in Malaysia. Methods: A cross-sectional study using the Breast Cancer Patient Version of Quality of Life (QOL) Instrument (translated into Malay) and Depression Anxiety and Stress Scale (DASS) were conducted on 87 female breast cancer patients to investigate the impact of pain interference level on their quality of life and depressive level. Results: The patients were divided into 4 groups based on their rating of how pain and aches have been a problem to them (i.e not a problem [n=18 (20.7%)], mild [n=29 (33.3%)], moderate [n=18 (20.7%)]) and severe [n=22(25.3%)]. Pain and aches were reported to be the most severe interference problems in QOL physical domain by patients (mean=5.8, SD=2.8), followed by fatigue (mean=6.0, SD=3.1) and sleep changes (mean=6.2, SD=3.5). Patients who reported that pain and aches had severely affected them showed significantly lower score on many aspects of quality of life (Fs > 5, p < 0.005; p < 0.0001) and patients reported pain was not a problem at all demonstrated highest score on all aspects of QOL. Patients with most severe pain interference level showed highest depressive score [F (3, 84) =3, p < 0.05]. Conclusion: The study underscores the impact of pain interference on patients’ quality of life and depressive level. The pain assessment deserves significant attention and therefore a comprehensive biopsychosocial assessment of pain to rule out any related underlying issues is warranted in the management of breast cancer to ensure appropriate intervention given to the patients.

Keywords: Pain, breast cancer, quality of life, Malaysia, depression

INTRODUCTION

Breast cancer is the commonest cancer in women and is the leading cause of cancer deaths among women worldwide.1-2 In 2003, 3,738 new cases of breast cancer were reported, giving an age-standardized incidence rate (ASR) of 46.2 per 100,000 women [3]; which suggests that 1 in 20 women in Malaysia will develop breast cancer in her lifetime.4 Despite improvements in oncology treatments and survival rates [5], breast cancer is still experienced as life threatening and its treatments are associated with numerous highly aversive symptoms and adverse side effects. At least half of all breast cancer patients will experience emotional distress as part of their psychosocial problems related to the illness.6 Among the psychological reactions documented are denial, anger, intense fear towards the disease and treatment process and preoccupation with thoughts of illness and death.7 There is a variation of the prevalence of depressive disorders, ranging from 1.5 to 46%; and this is attributed to the differences in time evaluation, measurements and population studied [8-9].

While psychological distress issues in breast cancer have been extensively documented in the body of literature, pain which is one of the common side effects of breast cancer and its treatment, has received less attention despite its significant effects on patients. As with distress, patients typically experience pain at some point of their treatment regardless of the stages of illness and treatment [10]. Pain in breast cancer has been associated with chemotherapy, radiotherapy, [11] surgery and hormonal therapy [12]. Known risk factors for pain in breast cancer may include age (<40 years), psychosocial factors, preoperative breast pain and acute postoperative pain intensity. [13] Almost half of the breast cancer patients reported experiencing pain [14] with scar pain and arm pain being the most common types reported by them. In another study, pain was stated to have occurred in 51% of breast cancer survivors 15 months after surgery. [15]

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A few studies have shown significant relationships between pain and psychological distress amongst breast cancer patients. For example, a study has indicated that patients who reported having more arm problems after surgery, including weakness, stiffness, pain, numbness, swelling causing restricted range of movement are more likely to experience higher psychological distress.\(^{[14]}\) Another study showed that when compared those who reported pain and those who did not, breast cancer patients who complained of pain had significantly higher level depression, anger, total mood disturbance and lower psychological well-being on their quality of life measures.\(^{[15]}\) Similarly, significant positive associations were also found between pain interference level with function and patients’ psychological and social well-being as well as their mental health.\(^{[16]}\) Additionally, it was documented that pain increases in breast cancer patients before death.\(^{[19]}\) A critical review on cancer pain and psychological distress has provided evidence that the relationship between psychosocial factors and chronic cancer pain is considered strong for psychological distress, that is, increased distress is associated with more intense pain.\(^{[20]}\)

Despite its high prevalence and significant effects on patients well-being that have been documented world-wide, there have been no published studies on cancer pain in Malaysia. The present study aims to investigate the impact of pain interference level on the many aspects of quality of life and depression level in breast cancer patients in a General Hospital in Malaysia. Generally, there are 2 dimensions of pain that have been widely researched, that is, ‘sensory’ and ‘reactive’. The sensory dimension refers to the severity of pain whilst the reactive dimension refers to the degree to which pain interferes with the patient’s function and quality of life\(^{[21]}\); and providing both dimensions will yield a useful representation of pain. However, it has been shown that pain severity, however measured, is probably not linearly related to interference with function\(^{[21, 22]}\); implying that it is equally important to address pain interference level with patients overall functioning in order to have a meaningful understanding of the impact of pain on patients’ quality of life. This study therefore focuses on the reactive dimension of pain, that is, assessing the degree to which pain has been interfering with breast cancer patients’ overall quality of life and its relations with their depressive level.

**METHODS**

Participants and Setting

A comparative cross-sectional study design was conducted amongst female breast cancer patients who were undergoing treatment in a general hospital in Malaysia, Hospital Kuala Lumpur. Subjects were recruited using purposive sampling from the breast cancer clinic, day care centre, radiology departments and wards of the Oncology and Radiotherapy Department, Hospital Kuala Lumpur. Data collection was carried out after the permission to conduct the study was obtained from the Hospital Director and the Head of Department of Oncology and Radiotherapy.

A study information sheet and an informed consent form were distributed and a set of self-administered questionnaires were given upon consent given by the patient to be involved in the study. In the case where the respondents were illiterate, the researchers (who had been trained by the first author to conduct an interview) would read the items to them and their responses were recorded in the questionnaire. The exclusion criteria were; non Malaysian patients, male breast cancer patients, patients who were also diagnosed with other types of cancer, patients who were not currently receiving treatment and patients who suffered from any mental illnesses. Confidentiality was assured by respondents’ anonymity. The protocol for this study had been approved by the Universiti Putra Malaysia Ethics Committee, which conformed to the provisions of the 1995 Declaration of Helsinki.

Instruments

The sample was administered using a questionnaire, that has been divided into 3 main sections. The first section was about patients’ demographic and illness background data. The second section was the Breast Cancer Patient Version of QOL Instrument adopted from City of Hope\(^{[23]}\). While the third section was 21-Depression, Anxiety and Stress Scales (DASS).\(^{[24]}\) ‘Back-translation’ method was employed to translate these questionnaires into Malay language to accommodate patients’ language preference in responding to the questionnaire. The second section of the questionnaire consisted of five aspects which were physical well-being (8 items), psychological well-being and patient’s experience of illness and treatment (22 items), social well-being (9 items) and spiritual well-being (7 items). The scale used for each questions was ordinal scale which ranged from 0 to 10. The scoring was generally based on a scale from 0 which indicated worst outcome to 10, to indicate best outcome except for several items which have reverse anchors, indicating the requirements to be reversely coded to have a meaningful score.

The Principle Component Analysis using varimax rotation method was carried out on psychological and patient’s experience of illness domain specifically to obtain a meaningful structure of this domain. Table 1 reveals an extraction of four distinct factors with two non-fitting items being removed. These factors, which had eigenvalues greater than one, accounted for 67.3 percent of the item variance. The four-factor solutions are labelled as ‘illness-related matters’, ‘perception of satisfaction in life’, ‘self esteem and emotional distress’ and ‘cancer treatment matters’. Cronbach’s coefficients were calculated to examine the reliability of each of the sub-domain and the alphas obtained reflect a

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**Table 1**

<table>
<thead>
<tr>
<th>Domain</th>
<th>Questions</th>
<th>Alphas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness-related matters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perception of satisfaction in life</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self Esteem and Emotional distress</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer Treatment matters</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Malaysian Journal of Medicine and Health Sciences Vol. 9 (1) January 2013
reasonably high inter-item consistency for each domain (Table 1). These subdomains will be used to further describe the results in this article. Cronbach alpha coefficients for other domains also yielded an acceptable inter-item consistency, that is physical (alpha=0.75), social (alpha=0.70) and spiritual (0.65). The total score for each domain was calculated by summing up the scores for all of the items in the respective domains.

The third section was DASS-21 which measured the negative emotional states of depression (7 items), anxiety (7 items) and stress (7 items). Subjects were asked to use 4-point severity or frequency scales to rate the extent to which they had experienced each state over the past one week. The score of each question were obtained by multiplying the scale by two. Therefore, the scores for depression, anxiety and stress were calculated by summing the scores for the relevant items. Cronbach’s alpha coefficients result suggested that the scales for depression, anxiety and stress in Malay language possessed excellent internal consistency that is, alpha = 0.96, alpha = 0.93, alpha = 0.93 respectively. However, only depression domain is reported in the present study.

Table 1. Factor Structure of Psychological Well-being and Patient’s Experience of Illness and Treatment domain

<table>
<thead>
<tr>
<th>Factors</th>
<th>Factor 1 (Illness-related matters)</th>
<th>Factor 2 (Perception of satisfaction in life)</th>
<th>Factor 3 (Self esteem and emotional distress)</th>
<th>Factor 4 (Cancer treatment matters)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastasis of cancer</td>
<td>.90</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence of cancer</td>
<td>.88</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Having a second cancer</td>
<td>.83</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Future diagnostic tests</td>
<td>.68</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial diagnosis</td>
<td>.51</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Satisfaction about life</td>
<td>.81</td>
<td>.71</td>
<td>.68</td>
<td>.68</td>
</tr>
<tr>
<td>Self usefulness</td>
<td>.74</td>
<td>.68</td>
<td>.60</td>
<td>.45</td>
</tr>
<tr>
<td>In control of things in life</td>
<td>.67</td>
<td>.61</td>
<td>.60</td>
<td>.45</td>
</tr>
<tr>
<td>Happiness</td>
<td>.65</td>
<td>.45</td>
<td>.40</td>
<td></td>
</tr>
<tr>
<td>Quality of life</td>
<td>.47</td>
<td>.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty in coping today due to treatment</td>
<td>.71</td>
<td>.68</td>
<td>.60</td>
<td></td>
</tr>
<tr>
<td>Difficulty in coping today due to disease</td>
<td>.68</td>
<td>.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in self concept</td>
<td>.61</td>
<td>.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in appearance</td>
<td>.60</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>.45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>.40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer radiation</td>
<td>.68</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completion of treatment</td>
<td>.65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer surgery</td>
<td>.48</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer chemotherapy</td>
<td>.45</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cronbach’s alpha coefficients for factor 1, 2, 3, and 4 were 0.92, 0.81, 0.84, and 6.05 respectively.

Analyses

Data was tabulated in SPSS program version 18. The socio-demographic profile of samples from different groups were analysed using chi square test. The differences of quality of life between groups were analysed using ANOVA One-way with the application of Scheffe post-hoc for further group comparisons.
Results

Eighty-seven respondents were included in this study and the overall response rate was 90.6%. The patients were divided into 4 groups based on their rating of how pain and aches had been a problem to them [18 (20.7%) indicated pain not giving them problem at all, 29 (33.3%) as mild problem; 18 (20.7%) as moderate; and 22 (25.3%) as severe]. The categorisation of pain interference level in the present study was a reverse score based on the study done by Serlin et al.[21], that is, 10= no interference; 7-9 = mild interference; 5-6 = moderate; and 0-3 = severe.

As can be seen in Table 2, in terms of patients’ demographic characteristics, there were no significant differences found between groups with respect to their age group, ethnicity, marital status, current stage of cancer and the presence of surgical treatment. Nonetheless, significant differences were found between pain interference level groups in relation to their occupational status and level of education. Specifically, most of the patients who reported having no pain interference and severe pain interference were unemployed. Items in physical domain were analysed and it was found that pain and aches were reported to be the most severe problems by patients (mean=5.8, SD=2.8), followed by fatigue (mean=6.0, SD=3.1) and sleep changes (mean=6.2, SD=3.5).

Table 2. Socio-demographic characteristics of patients according to pain interference levels

<table>
<thead>
<tr>
<th>Demographic variables</th>
<th>Pain Interference Levels</th>
<th></th>
<th></th>
<th></th>
<th>χ²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not at all</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-49</td>
<td>5 (27.8)</td>
<td>13 (44.8)</td>
<td>11 (61.1)</td>
<td>12 (54.5)</td>
<td>4.67 ns</td>
</tr>
<tr>
<td>50-79</td>
<td>13 (72.2)</td>
<td>16 (55.2)</td>
<td>7 (38.9)</td>
<td>10 (45.5)</td>
<td></td>
</tr>
<tr>
<td>Ethnic group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>8 (44.4)</td>
<td>17 (58.6)</td>
<td>13 (72.2)</td>
<td>14 (63.6)</td>
<td>7.34 ns</td>
</tr>
<tr>
<td>Chinese</td>
<td>6 (33.3)</td>
<td>10 (34.5)</td>
<td>3 (16.7)</td>
<td>3 (13.6)</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>4 (22.2)</td>
<td>2 (6.9)</td>
<td>2 (11.1)</td>
<td>5 (22.7)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>14 (77.8)</td>
<td>22 (75.9)</td>
<td>15 (88.2)</td>
<td>20 (90.9)</td>
<td>2.63 ns</td>
</tr>
<tr>
<td>Not married</td>
<td>4 (22.2)</td>
<td>7 (24.1)</td>
<td>2 (11.8)</td>
<td>2 (9.1)</td>
<td></td>
</tr>
<tr>
<td>Occupational status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>1 (5.6)</td>
<td>11 (37.9)</td>
<td>9 (50.0)</td>
<td>8 (36.4)</td>
<td>8.83*</td>
</tr>
<tr>
<td>Unemployed</td>
<td>17 (94.4)</td>
<td>18 (62.1)</td>
<td>9 (50.0)</td>
<td>14 (63.6)</td>
<td></td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>12 (66.7)</td>
<td>13 (44.8)</td>
<td>3 (16.7)</td>
<td>7 (31.8)</td>
<td>13.45*</td>
</tr>
<tr>
<td>Secondary</td>
<td>4 (22.2)</td>
<td>13 (44.8)</td>
<td>8 (44.4)</td>
<td>10 (45.5)</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>2 (11.1)</td>
<td>3 (10.3)</td>
<td>7 (38.9)</td>
<td>5 (22.7)</td>
<td></td>
</tr>
<tr>
<td>Current stage of cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>2 (11.1)</td>
<td>7 (24.1)</td>
<td>3 (16.7)</td>
<td>3 (13.6)</td>
<td>4.24 ns</td>
</tr>
<tr>
<td>Stage 2</td>
<td>9 (50.0)</td>
<td>8 (27.6)</td>
<td>6 (33.3)</td>
<td>7 (31.8)</td>
<td></td>
</tr>
<tr>
<td>Stage 3</td>
<td>5 (27.8)</td>
<td>8 (27.6)</td>
<td>5 (27.8)</td>
<td>8 (36.4)</td>
<td></td>
</tr>
<tr>
<td>Stage 4</td>
<td>2 (11.1)</td>
<td>6 (20.7)</td>
<td>4 (22.2)</td>
<td>4 (18.2)</td>
<td></td>
</tr>
<tr>
<td>Surgical treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16 (88.9)</td>
<td>22 (75.9)</td>
<td>15 (83.3)</td>
<td>19 (86.4)</td>
<td>1.65 ns</td>
</tr>
<tr>
<td>No</td>
<td>2 (11.1)</td>
<td>7 (24.1)</td>
<td>3 (16.7)</td>
<td>3 (13.6)</td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>18 (20.7)</td>
<td>29 (33.3)</td>
<td>18 (20.7)</td>
<td>22 (25.3)</td>
<td></td>
</tr>
</tbody>
</table>

ns: P >0.05, * P<0.05
Table 3. Comparisons of QOL domain mean scores according to pain interference levels

<table>
<thead>
<tr>
<th>QOL domains and pain interference levels</th>
<th>Mean (SD)</th>
<th>95% CI for mean</th>
<th>F- statistic (df)</th>
<th>p- value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all (G1)</td>
<td>53.1 (3)</td>
<td>-11.2</td>
<td>47.5</td>
<td>-58.6</td>
</tr>
<tr>
<td>Mild (G2)</td>
<td>54.2 (3)</td>
<td>-7.73</td>
<td>51.3</td>
<td>-57.3</td>
</tr>
<tr>
<td>Moderate (G3)</td>
<td>40.1 (3)</td>
<td>-11.1</td>
<td>34.4</td>
<td>-45.5</td>
</tr>
<tr>
<td>Severe (G4)</td>
<td>35.6 (3)</td>
<td>-15.1</td>
<td>28.9</td>
<td>-42.2</td>
</tr>
<tr>
<td><strong>Illness-related matters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all (G1)</td>
<td>21.9 (3)</td>
<td>-17.4</td>
<td>13.8</td>
<td>-30.6</td>
</tr>
<tr>
<td>Mild (G2)</td>
<td>20.1 (3)</td>
<td>-15.6</td>
<td>14.12</td>
<td>25.9</td>
</tr>
<tr>
<td>Moderate (G3)</td>
<td>20.2 (3)</td>
<td>-16.3</td>
<td>12.1</td>
<td>28.3</td>
</tr>
<tr>
<td>Severe (G4)</td>
<td>6.8 (3)</td>
<td>-11.3</td>
<td>8.9</td>
<td>11.12</td>
</tr>
<tr>
<td><strong>Perception of satisfaction in life</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all (G1)</td>
<td>35.8 (3)</td>
<td>-9.1</td>
<td>31.3</td>
<td>-40.4</td>
</tr>
<tr>
<td>Mild (G2)</td>
<td>36.3 (3)</td>
<td>-9.1</td>
<td>32.8</td>
<td>-59.9</td>
</tr>
<tr>
<td>Moderate (G3)</td>
<td>33.3 (3)</td>
<td>-10.9</td>
<td>27.8</td>
<td>-38.7</td>
</tr>
<tr>
<td>Severe (G4)</td>
<td>28.2 (3)</td>
<td>-11.1</td>
<td>23.3</td>
<td>-33.2</td>
</tr>
<tr>
<td><strong>Self esteem and emotional distress</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all (G1)</td>
<td>48.1 (3)</td>
<td>-13.2</td>
<td>41.5</td>
<td>-54.6</td>
</tr>
<tr>
<td>Mild (G2)</td>
<td>42.9 (3)</td>
<td>-11.3</td>
<td>38.5</td>
<td>-47.3</td>
</tr>
<tr>
<td>Moderate (G3)</td>
<td>35.1 (3)</td>
<td>-13.7</td>
<td>28.2</td>
<td>-41.8</td>
</tr>
<tr>
<td>Severe (G4)</td>
<td>23.6 (3)</td>
<td>-14.2</td>
<td>17.3</td>
<td>-29.9</td>
</tr>
<tr>
<td><strong>Cancer treatment matters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all (G1)</td>
<td>32.3 (3)</td>
<td>-6.8</td>
<td>28.9</td>
<td>-35.7</td>
</tr>
<tr>
<td>Mild (G2)</td>
<td>26.4 (3)</td>
<td>-9.8</td>
<td>22.7</td>
<td>-30.2</td>
</tr>
<tr>
<td>Moderate (G3)</td>
<td>25.6 (3)</td>
<td>-8.1</td>
<td>21.6</td>
<td>-29.6</td>
</tr>
<tr>
<td>Severe (G4)</td>
<td>19.1 (3)</td>
<td>-11.7</td>
<td>13.8</td>
<td>-24.2</td>
</tr>
<tr>
<td><strong>Social</strong></td>
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</tr>
<tr>
<td>Not at all (G1)</td>
<td>62.8 (3)</td>
<td>-18.3</td>
<td>53.2</td>
<td>-71.4</td>
</tr>
<tr>
<td>Mild (G2)</td>
<td>61.7 (3)</td>
<td>-14.3</td>
<td>56.3</td>
<td>-67.2</td>
</tr>
<tr>
<td>Moderate (G3)</td>
<td>50.6 (3)</td>
<td>-17.9</td>
<td>41.7</td>
<td>-59.5</td>
</tr>
<tr>
<td>Severe (G4)</td>
<td>44.2 (3)</td>
<td>-12.6</td>
<td>38.6</td>
<td>-49.7</td>
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<tr>
<td><strong>Spiritual</strong></td>
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</tr>
<tr>
<td>Not at all (G1)</td>
<td>45.6 (3)</td>
<td>-16.5</td>
<td>37.4</td>
<td>-53.9</td>
</tr>
<tr>
<td>Mild (G2)</td>
<td>50.1 (3)</td>
<td>-10.4</td>
<td>46.1</td>
<td>-54</td>
</tr>
<tr>
<td>Moderate (G3)</td>
<td>51.7 (3)</td>
<td>-11.1</td>
<td>46.23</td>
<td>-57.2</td>
</tr>
<tr>
<td>Severe (G4)</td>
<td>49.1 (3)</td>
<td>-10.2</td>
<td>44.52</td>
<td>-53.5</td>
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<td><strong>Depressive level</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Not at all (G1)</td>
<td>6.6 (12.8)</td>
<td>.25 - 12.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (G2)</td>
<td>12.8 (14.9)</td>
<td>7.13 – 18.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (G3)</td>
<td>16.8 (16.8)</td>
<td>8.39 – 25.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe (G4)</td>
<td>19.7 (12.8)</td>
<td>14.03 – 25.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*aOne-way ANOVA test was applied
Post-hoc Scheffe's procedure was administered with the application of Bonferonni type Correction for multiple comparison (p ≤ 0.01).

bG1 vs G3, p < 0.001; G1 vs G4, G2 vs G3, G2 vs G4, p < 0.0001

cG1 vs G4, G2 vs G4, G3 vs G4, p < 0.05

dG1 vs G3, G3 vs G4, p < 0.05; G1 vs G4, G2 vs G4, p < 0.0001

eG1 vs G4, p < 0.05; G2 vs G4, p < 0.0001
fG1 vs G4, p < 0.05; G2 vs G4, p < 0.0001

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Table 3 illustrates significant differences found between levels of pain interference groups reported by patients in most of the quality of life domains. For physical domain, patients who reported pain as severely interfering with their life scored the lowest in the QOL score [not at all=53.1, severe=35.6; F(3, 84)=15.1, p<0.05]. Post-hoc Scheffe’s analysis revealed that patients who stated that pain and aches was not a problem to them scored significantly lower than those who reported that pain and aches was affecting them moderately and severely. Likewise, in terms of matters regarding illness and treatment, patients who rated that pain and aches were severely affecting them scored significantly lower in their QOL than those who reported it as not a problem, mild or moderate. This pattern was also true in matters involving patients’ perception of satisfaction in life. That is, patients who were affected severely by pain and aches scored significantly lower score in QOL as compared to their counterparts who rated pain as not a problem or affected by pain in mild or moderate level.

Table 3 also shows that Quality of Life scores on issues regarding self esteem and emotional distress were found to be significantly different amongst pain interference groups. Specifically, Post Scheffe’s analysis indicated that those who felt that pain has been severely interfering them had significantly lower QOL scores on self esteem and emotional distress in comparison to those who were not affected at all, mildly and moderately affected by the pain and aches. Similarly, patients who were severely affected by pain reported significantly lower quality of life scores on matters regarding cancer treatment as well as in the social domain. Nonetheless, there was no significant difference between groups in spiritual domain of quality of life. With regards to patients’ depressive level, those who felt that pain was not a problem at all reported significantly lower scores on depression as compared to those who reported their pain as interfering with their life in mild, moderate or severe manner.

Pearson correlation coefficients analyses were carried out to examine the relationship between individual items in the physical domain and other domains in the quality of life. Table 4 illustrates that amongst the physical items, pain and aches as well as fatigue were found to be correlated positively with every other domain in quality of life (r = 0.28 – 0.58, p<0.01, p<0.05).

Table 4. Relationships between physical domain items and other domains of QOL

<table>
<thead>
<tr>
<th>Items</th>
<th>Illness-related matters</th>
<th>Perception of satisfaction in life</th>
<th>Self esteem and emotional distress</th>
<th>Cancer treatment matters</th>
<th>Social</th>
<th>Spiritual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>.35**</td>
<td>.28**</td>
<td>.56**</td>
<td>.33**</td>
<td>.44**</td>
<td>-0.09</td>
</tr>
<tr>
<td>Appetite changes</td>
<td>.23*</td>
<td>0.19</td>
<td>.43**</td>
<td>0.19</td>
<td>.33**</td>
<td>-0.09</td>
</tr>
<tr>
<td>Pain and aches</td>
<td>.32**</td>
<td>.28**</td>
<td>.58**</td>
<td>.43**</td>
<td>.44**</td>
<td>-0.07</td>
</tr>
<tr>
<td>Sleep changes</td>
<td>0.21</td>
<td>0.2</td>
<td>.57**</td>
<td>.29**</td>
<td>.49**</td>
<td>-0.19</td>
</tr>
<tr>
<td>Weight gain</td>
<td>0.17</td>
<td>0.12</td>
<td>.53**</td>
<td>.24*</td>
<td>.28**</td>
<td>-0.12</td>
</tr>
<tr>
<td>Vaginal dryness/ menopausal symptoms</td>
<td>.33**</td>
<td>.23*</td>
<td>.41**</td>
<td>.23*</td>
<td>.24*</td>
<td>-0.04</td>
</tr>
<tr>
<td>Menstrual changes/fertility</td>
<td>0.04</td>
<td>0.07</td>
<td>.29**</td>
<td>0.04</td>
<td>0.19</td>
<td>-0.06</td>
</tr>
</tbody>
</table>

** p<0.01; *p < 0.05 (2-tailed)

A series of multiple linear regressions using stepwise method were conducted to further ascertain the proportion of each individual item in physical domain that significantly contributed to the patients’ severity of quality of life level in other domains. As can be seen in Table 5, with respect to illness-related matters, fatigue and pain aches were accounted for 18% of the variance in level of quality of life. Pain and aches were found as the only physical domain that was accounted for 18% of the variance in the perception of satisfaction in life. For self esteem and emotional distress, 47% of the variability was significantly explained by three physical items namely, pain aches, fatigue and menstrual changes (b=2.1, CI, 2.56 – 17.45; p < 0.0001); (b=1.4, CI, .45-2.42; p<0.005); (b=.91, CI, .21-1.61; p<0.01) respectively. This suggests that of all these physical items, pain and aches made the largest unique contribution to the proportion explained. Similarly, pain and aches were the only physical item associated with cancer treatment matters, accounted for 20% of the score variance. With regard to social domain, sleep changes accounted for 27% of the score variance.
variance. For the overall quality of life score, two physical items were found to be significantly associated with its score, namely pain and aches as well as fatigue, both accounting for 37% of its variance. As shown in Table 5, pain and aches contributed largely to the variance ($b=6.89$, CI, 3.36-10.41; $p<0.0001$) as compared to fatigue ($b=4.68$, CI, 1.16-8.21; $p<0.01$). With regards to depressive domain, pain and aches together with menopausal symptoms were found to explain the 20% of the score variance in the level of depression.

### Table 5. Physical domain items associated significantly with other domains of QOL

<table>
<thead>
<tr>
<th>Domains</th>
<th>Significant physical domain item(s)</th>
<th>$R^2$</th>
<th>$b$</th>
<th>(95% CI)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness-related matters</td>
<td>Fatigue</td>
<td>0.18</td>
<td>1.5</td>
<td>(0.38, 2.5)</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>Pain and aches</td>
<td>0.14</td>
<td>(1.7, 2.6)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Perception of satisfaction in life</td>
<td>Pain and aches</td>
<td>0.16</td>
<td>0.94</td>
<td>(0.26, 1.62)</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>Pain and aches</td>
<td>0.47</td>
<td>2.1</td>
<td>(0.56, 17.45)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Self esteem and emotional distress</td>
<td>Fatigue</td>
<td>0.16</td>
<td>1.4</td>
<td>(0.45, 2.42)</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Menstrual changes</td>
<td>0.91</td>
<td>(1.21, 1.61)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Cancer treatment matters</td>
<td>Pain and aches</td>
<td>0.2</td>
<td>0.42</td>
<td>(0.80, 2.10)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Social</td>
<td>Sleep changes</td>
<td>0.27</td>
<td>1.66</td>
<td>(0.56, 2.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Overall quality of life</td>
<td>Pain and aches</td>
<td>0.57</td>
<td>6.89</td>
<td>(3.36, 10.41)</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
<td>0.57</td>
<td>6.89</td>
<td>(3.36, 10.41)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Depressive level</td>
<td>Menopausal symptoms</td>
<td>0.2</td>
<td>0.53</td>
<td>(0.80, 2.4)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Pain and aches</td>
<td>0.42</td>
<td>(.71, 1.94)</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

* Adjusted regression coefficient

$R^2$ coefficient of determination

Stepwise multiple linear regression method applied for every model; model assumptions are fulfilled.

There were no interactions amongst independent variables. No multicollinearity detected.

### DISCUSSION

The present study reported the impact of pain interference level on the quality of life and depression of the breast cancer patients in a hospital in Malaysia. As mentioned earlier, previous studies have focused on the relationship between psychological factors and quality of life, without taking into consideration some physical symptoms such as pain. To our knowledge, this is the first study in Malaysia that examined the effects of pain interference level on patient’s quality of life and depression in breast cancer patients. Pain has been reported to be a mild to severe problem for approximately 79% of the respondents in this study. Other outcomes consistently showed that the reported level of interference pain in patients’ life corresponds to the level of psychological disturbance experienced by them. This is independent of the patients’ age group, ethnicity, marital status, current stage of cancer and the presence of surgical treatment. Similarly, the pain and aches were found to affect other domains of quality of life, namely, illness-related matters, perception of satisfaction in life, self esteem and emotional distress, cancer treatment matters and the overall quality of life as reported by patients.

The most common issues reported by patients in the physical domain of quality of life are pain, fatigue and sleep changes. This finding lends support to a study undertaken by Rukiye et al which asserted that patients suffered from pain, anorexia and fatigue, which did not only shorten their lives, but also decreased their quality of life [25]. Approximately 79.3% of the patients in this study reported having pain interfering ranging from mild to moderate with their life regardless the stage they ware at. Whilst the literature has documented that the prevalences of persistent pain after breast cancer surgery is between 20% to 65% [13, 26], the pain interference level in this study was reported to be slightly higher than in previous findings. There maybe a few explanation for this: firstly, reported pain severity and its relationship with pain interference has been found to be non-linear [21]; secondly, not all the pain reported by patients will become chronic in nature, that is, for some patients, the pain is likely to subside within three months. It is noteworthy that the present study did not examine the pain severity and duration of pain (chronicity of pain as studied
by previous research) experienced by the patients. Furthermore, the present study suggests that the patients reported pain interference level regardless of the cancer stage and the presence of surgery in their treatment.

The present study indicated that patients who were affected severely by pain and aches scored significantly lower score in most of the QOL domains as compared to their counterparts who rated pain as not a problem or affected by pain in mild or moderate level. Likewise, patients who indicated having mild to moderate pain reported higher level of depressive symptoms compared to those who did not. These findings are in line with the ones found in the previous studies, which asserted that women who developed chronic pain after breast cancer surgery demonstrate diminished health-related quality of life, including impaired physical functioning and increased psychological distress[14, 27, 28]. As mentioned earlier, there are only a few studies that examine the relationship between pain and quality of life in breast cancer patients. Nonetheless the current findings lend support to the results found in earlier studies on these matters. Ferrell et al revealed that the amount of pain reported by patients has linear relationship with the social well-being domain[32]. In other words, this implies that those patients with higher level of pain were having poorer social well-being. Another study which studied the relationship between pain and life stress in women with recurrent breast cancer found that there is an association between pain and overall life stress[32].

In line with the current findings, it was also found that 47% of the patients studied reported experiencing cancer-related pain and these patients indicated high scores in mood disturbance and lower level of quality of life as well as functional status compared to those without pain[37]. This is also consistent with the findings obtained from a study that examine pain and psychological status in Hong Kong. Physical symptoms such as pain and fatigue were found to be related with patients’ level of anxiety and depression. Patients under treatment were found to have inadequate social support, experienced higher levels of symptoms and were more likely to have a poorer quality of life[31]. Likewise, breast cancer patients reported symptoms of distress corresponding to the amount of pain that they experienced following surgical treatment at three months and the pain persisted at eighteen months follow up[39]. Other studies also concur with the present study’s result, that is, pain had a significant component affecting different aspects of patients’ quality of life. Pain severity was found to have a positive correlation with patients’ emotional, psychosocial and mental health. Similarly, higher pain frequency was associated with lower level of psychosocial scores; whilst the high level of pain interference was associated with lower functional ability and poorer psychological health status[40]. In another study, it was established that patients with pain were more likely to report low levels of social activity and became less resilient in their social networking as compared to those without pain. Similarly, patients with low levels of social activity and social support were more likely to report pain and impaired functional level compared to those with high levels of social activity[32]. A somewhat inconsistent finding was found in a study on breast cancer patients who were scheduled for autotransplantation; it was indicated that there was no relationship between types of coping strategies and overall pain intensity. This study also showed that level of catastrophizing, which is usually present in people with anxiety and depression was not related to pain intensity, sensory and affective pain[39]. On the other hand, a study on breast cancer patients who had undergone surgery reported that the level of catastrophizing had a linear relationship with pain intensity[34]. The discrepancy in findings could be attributed to the experience of treatment; those who were scheduled for transplant had no real experience of treatment effects whilst those who had undergone surgery and experienced the surgery effects were more able to relate their level of catastrophe with matters regarding pain.

The strength of this study is that it has brought into attention the importance of addressing pain issues in the assessment and management of breast cancer patients. More importantly, pain was found to be one of the physical symptoms that affects patients’ quality of life and level of depression. Thus, the clinicians must not only inquire about pain intensity of interference level, but should also assess and monitor factors associated with pain. In addition, this study focused on how much the pain has affected people’s life as compared to previous studies that focused much on the pain severity and duration. Whilst this can be a limitation, it can also be a strength as it has been emphasized that the amount of pain severity is not necessarily followed by the level of interference experienced by patients[31]. That way, it can be asserted that examining the level of interference will be more meaningful in the context of studying patients’ level of quality of life.

The main limitation of this study is that its generalizability to other patients. This study was carried out in a hospital setting and it is probably generalizable to only hospital-based patients. Furthermore, the sample is relatively small and it is a cross-sectional study that only assesses pain after primary treatment was given. Hence it did not provide information on if and how the reported pain interference level will subside or substantiate with time since breast cancer treatment. The study also had no information about pertinent issues related to the pain such as pain intensity, duration, pain sites and types that can be pertinent to issues regarding to quality of life and depression. Thus it is highly recommended for future studies to address those pain issues in order to obtain more meaningful study results.

**CONCLUSION**

The present study found that approximately 79% of breast cancer patients reported pain interference level ranging from mild to severe in Hospital Kuala Lumpur. The reported level of pain interference in patients’ life corresponded to...
the level of psychological disturbance experienced by them. This is independent of the patients’ age group, ethnicity, marital status, current stage of cancer and the presence of surgical treatment. Pain and aches were found to affect patients’ other domains of quality of life, namely, illness-related matters, perception of satisfaction in life, self esteem and emotional distress, cancer treatment matters and the overall quality of life as well as level of depression.

ACKNOWLEDGEMENT

The authors would like to thank all the doctors and staff nurses of the Oncology and Radiotherapy Department of Hospital Kuala Lumpur for their great cooperation throughout the completion of this project. Our warmest gratitude also goes to all breast cancer survivors for their perseverance and kind cooperation throughout the data collection phase.

REFERENCES


Demographic Differences of Preference, Intake Frequency and Craving Hedonic Ratings of Sweet Foods Among Malaysian Subjects in Kuala Lumpur

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ABSTRACT
As the sugar intake of Malaysians is one of the highest in the Asia Pacific region, we wanted to investigate how this high prevalence of ‘sweet tooth’ is influenced by biological determinants like age, gender, ethnicity and Body Mass Index (BMI). Therefore, this study was to determine the demographic and BMI differences of preference, intake frequency and craving of a list of sweet beverages and food among Malaysian subjects. Convenience sampling was performed around Kuala Lumpur, with informed consents, involving 367 multi-ethnic subjects (163 males, 204 females; 83 Malays, 201 Chinese, 83 Indians; 209 lean, 158 overweight). Demographics and anthropometric measurements were taken and questionnaire on the preference/frequency/craving of a list of 22 sweet food and beverages with a 7 point hedonic scale (from 1= very unpleasant/never/never crave to 7 = very pleasant/at least once a day/always crave) was performed. Females significantly preferred more, took less frequently but had equal craving of sweet foods compared to males. Lean subjects and those <25 years showed significantly higher preference, intake frequency and craving of sweet foods. The ethnic differences in rating the preference, intake frequency and cravings seemed to be food-specific and culturally-related, where overall, ethnic Chinese had significantly higher intake frequency but lesser craving of sweet foods compared to Malays and Indians. Understanding the demographic and anthropometric factors that may affect the preference, intake frequency and craving of certain sweet foods can help to plan for strategies to prevent the detrimental health burden of high sugar intake among Malaysians.

Keywords: Food preference, diet records, addictive behavior, Body Mass Index, Malaysia

INTRODUCTION
People who have a persistent desire to eat sweet products are said to have a ‘sweet tooth’[1]. The 2007 Food Supply Quantity for sugar and sweeteners revealed that Malaysians have one of the ‘sweetest teeth’ in the Asia Pacific region, with 40.7 kg/capita/year – way higher than China (8.7) and India (19.8), and ranked second among Southeast Asian countries after Brunei (47.4)[2]. In the same survey, sugar and sweeteners account 13.5% (395 kcal/day) of the total energy intake of Malaysians[2]. According to the Malaysian Adults Nutrition Survey (MANS) 2003, highly-sweetened food like local desserts known as kuih, and drinks like tea, coffee, chocolate-flavoured drink (all likely to be sweetened with condensed milk) and cordial are among the top ten daily consumed food and beverages in Malaysia among all ethnicities[3]. The mean sugar intake was about 4 teaspoons/day or around 21g, which was under-represented by only sugar added to beverages like tea, coffee and chocolate-based drinks[3]. If the sugars from the commonly consumed very sweet snacks and desserts (like the Malaysian kuih) and beverages (like soft drinks, cordials) were to be taken into consideration in the study, the dietary energy proportion would be substantially more.

There are few methods that are designed to measure ‘sweet tooth’. As reviewed by Reed & McDaniel (2006)[4], hedonic assessment such as intake frequency, preference and craving and assessment of sensitivity as in perceived intensity and quality/pleasantness are examples of methods used to measure ‘sweet tooth’. Intake frequency measurement is defined as how often the sweet foods and beverages are consumed, while sweet preference is the desire and acceptance of sweet products that are chosen due to pleasure and satisfaction[4]. The term “sweet craving” is defined as a consuming desire or yearning of sweet foods and beverages[4]. The preference, intake frequency and craving for sweet products vary not only between individuals, but also between different groups of age, gender, ethnicity, and Body Mass Index (BMI) status. For instance, African Americans prefer higher concentrations and Pima Indians prefer lower concentrations of sugar compared with those of European ancestry[5]. However, ethnic differences may generalize only to specific food types. For instance, Taiwanese students rate sucrose solutions as more pleasant,
but sweetened cookies as less pleasant, than do students of European descent\[6\]. Studies of sex differences suggest that male and female infants do not differ in sweet preference\[7\], but that older boys and men prefer higher concentrations of sweet compared with women\[8\]. Food cravings are also extremely common, particularly among women and are frequently reported for specific type of foods, including chocolate and foods high in both sugar and fat\[9\].

High sugar intake poses a serious public health threat to Malaysians, which is thought to contribute to the current high prevalence of diabetes at 14.9% for adults ≥30 years and overweight/obesity at 43.1%\[10\]. To date, there is limited research on understanding how the reported high prevalence of ‘sweet tooth’ among Malaysians is influenced by biological determinants like age, gender, ethnicity and BMI status. Therefore, the main objective of this study was to perform a questionnaire survey of hedonic assessment on the preference, intake frequency and craving of a list of 22 commonly consumed Malaysian sweet food and beverages. Demographic data and anthropometric measurements such as Body Mass Index (BMI), Waist-to-Hip Ratio (WHR) and Total Body Fat (TBF) were taken to associate how different age, gender, ethnicity and body compositions may affect the hedonic ratings of the sweet food list.

**MATERIALS AND METHODS**

**Subjects**

Convenience sampling was performed in this study from October 2009 to February 2010 to recruit student, staff and faculty populations of Kolej Tunku Abdul Rahman and Universiti Tunku Abdul Rahman campuses, two major private institutions of higher learning in Setapak, Kuala Lumpur, and from the local Setapak community. The ideal sample size for this study with a 5% margin error, 95% confidence level and 50% response distribution in the Setapak population of around 66,000 people\[11\] is 382 subjects. In this study, we recruited 367 healthy and unrelated subjects, consisting of three major Malaysian ethnicities - Malays, Chinese and Indians with the median age of 21.0 ± SD 14.5 years (range 17 - 77). The institutional board approved this study, all individuals participating in this study signed informed consent forms and all samples were taken in accordance with the Declaration of Helsinki (as revised in Seoul 2008).

**Demographic data and anthropometric measurements**

Demographic data such as age, gender and ethnicity were collected. The height of the subjects was measured to the nearest 0.1 cm using a meterstick affixed to a flat wall. Besides, waist and hip circumferences were determined to the nearest 0.1 cm with the subjects in standing position using a measuring tape. Waist-to-Hip Ratio (WHR) was calculated by dividing the waist circumference by hip circumference. A bio-impedence body fat weighing scale (Salter Body Analyser and Scale, UK) was used to determine the weight (in nearest 0.25 kg), Body Mass Index (BMI - Weight (kg) / [Height (m) x Height (m)] ; calculated to the nearest 0.1 kg/m\(^2\)) and Total Body Fat (TBF; to the nearest 0.1%). Subjects with the BMI cut-off point of ≥ 23 kg/m\(^2\) were considered overweight\[12\].

**Hedonic assessment of sweet food preference, intake frequency and craving**

A self-administered questionnaire on the preference, intake frequency and craving of a list of 22 types of commonly available Malaysian sweet food and beverages (according to the Malaysian Dietary Guidelines)\[13\] was presented. These included *ais kacang* (a syrup-sweetened shaved ice dessert with condiments such as *attap chee* (palm seed), red beans, sweet corn and grass jelly), *cendol*, (a palm sugar-sweetened shaved ice dessert with condiments such as coconut milk, a worm-like jelly made from rice flour with green food coloring), *cincau* drink (a grass jelly or *Mesona chinensis* drink sweetened with syrup), cola/carbonated drink, cordial/rose syrup/Ribena\® , fruit juice, Milo\® / Horlicks\® /Vico\® (malt-based chocolate drinks), packet drinks (like Yeo’s\®/Drinhu\®), sweet dessert soup (like red or mung bean dessert), *quis batik* (pancake, normally with coarse sugar and peanut fillings), apple pie, brownies, cake, candy/sweets, chocolate, doughnuts, egg/fruit tart, ice-cream, jelly/jam/kaya (a coconut egg jam) on bread, *pisang goreng* (fried banana fritters), pudding and sweet *kuih* (bite-sized snack or dessert foods usually made from rice or glutinous rice flour like *bingka ubi kayu*, *kuih talam*, *kuih seri muka*, etc.). In order to aid a better recall of the preference, intake frequency and craving of the foods, subjects were also presented with images of the foods, with appropriate serving sizes to reflect high sugar content. Subjects were required to rate the sweet foods and beverages based on how much they like the item (preference), how frequently they consume the item (intake frequency), and how often they experience a craving for the item over the past month (craving) using a 7-point hedonic scale\[14\]. The response alternatives for preference were 1 = very unpleasant, 2 = fairly unpleasant, 3 = slightly unpleasant, 4 = neither pleasant nor unpleasant, 5 = slightly pleasant, 6 = fairly pleasant and 7 = very pleasant; frequency were 1 = never, 2 = once a month or less often, 3 = 1-2 times a month, 4 = once a week, 5 = a couple of times a week, 6 = almost everyday and 7 = at least once a day and for craving, 1 = never, 2 = very rarely, 3 = rarely, 4 = sometimes, 5 = often, 6 = very often and 7 = always/almost every day.

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*BTL Sia, SY Low, WC Foong, MP Pramasivah, CZ Khor & YH Say*
Statistical Analysis

The data obtained was statistically analyzed by the Statistical Package for Social Sciences, SPSS® for Windows® Version 16.0 software (SPSS, Chicago, IL). Descriptive statistics was used to compute frequencies and percentages for demographic data. The results for preference, intake frequency and craving are given as means ± standard error (SE). The differences between two or more groups were assessed by Mann-Whitney U test or Kruskal-Wallis test for continuous variables. The p value of < 0.05 was considered as statistically significant.

RESULTS

Demographic and anthropometric characteristics of subjects

Table 1 represents the demographic information and anthropometric measurements of the subjects involved in this study. A total amount of 367 subjects were recruited and among these subjects, 44.4% of them were males while 55.6% were females. Subjects were categorized into two different age groups in this study - < 25 years were considered as the ‘younger’ group, while subjects ≥ 25 years old were considered as the ‘older’ group. The majority of the subjects in this study were aged < 25 with females more than males. This phenomenon is due to the study being conducted primarily in university campuses comprising of young students. In this study, the largest ethnic group was Chinese (n = 201, 54.8%) of which the majority of them were females. An equivalent number of Malay and Indian subjects participated in this study. The majority of the subjects were lean (56.9%), with lean and overweight subjects well-balanced for males. WHR, BMI and TBF were all significantly different among gender, with males having higher WHR and BMI (mean was in the overweight category).

Table 1. Demographic and anthropometric characteristics of the subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Male (n = 163)</th>
<th>Female (n = 204)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>36 (22.1)</td>
<td>47 (23.0)</td>
</tr>
<tr>
<td>Chinese</td>
<td>91 (55.8)</td>
<td>110 (54.0)</td>
</tr>
<tr>
<td>Indian</td>
<td>36 (22.1)</td>
<td>47 (23.0)</td>
</tr>
<tr>
<td>Age groups (year)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>125 (76.7)</td>
<td>131 (64.2)</td>
</tr>
<tr>
<td>≥25</td>
<td>38 (23.3)</td>
<td>73 (35.8)</td>
</tr>
<tr>
<td>BMI status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lean</td>
<td>80 (49.1)</td>
<td>129 (63.2)</td>
</tr>
<tr>
<td>Overweight</td>
<td>83 (50.9)</td>
<td>75 (36.8)</td>
</tr>
<tr>
<td>Anthropometric measurements (Mean ± SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHR</td>
<td>0.86 ± 0.07</td>
<td>0.80 ± 0.07</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.62 ± 15.82</td>
<td>22.74 ± 5.46</td>
</tr>
<tr>
<td>p</td>
<td>0.016</td>
<td></td>
</tr>
<tr>
<td>TBF (%)</td>
<td>22.16 ± 10.83</td>
<td>25.75 ± 12.01</td>
</tr>
<tr>
<td>p</td>
<td>0.003</td>
<td></td>
</tr>
</tbody>
</table>

WHR – waist-to-hip ratio, BMI – body mass index, TBF – total body fat; Numbers in brackets are percentage of total variable of the same column; p values by Mann-Whitney U test, significant at <0.05

Preference, intake frequency and craving hedonic ratings

Gender

For sweet beverages, females significantly preferred fruit juice and sweet dessert soup more; drank or ate less frequently ais kacang, cola/carbonated, chocolate malt and packet drinks but had equal craving of sweet foods compared to
males (Figure 1A). As for sweet food, females significantly preferred brownies, cake, chocolate and pudding; ate less frequently apple pie, ice cream, jam on bread and pisang goreng, but had equal craving for sweet food compared to males (except for cake) (Figure 1B).

**Figure 1.** Means of hedonic ratings of preference (p), intake frequency (f) and craving (c) of (A) sweet beverages and (B) sweet foods among genders. Significant difference of means between genders was compared by Mann-Whitney U test, with levels of significance, *p* <0.05 and **p** <0.01 as indicated. Error bars are standard errors.
Age group

The age group of <25 significantly preferred cola/carbonated, malt and packet drinks more; drank cincau, cola/carbonated, fruit juice, malt and packet drinks and sweet dessert soup more frequently; and craved cola/carbonated, fruit juice, malt and packet drinks and sweet dessert soup more than the ≥25 age group (Figure 2A). Furthermore, they also significantly preferred, ate and craved more brownies, cake, candy, chocolate, doughnuts, tart and ice cream more than the ≥25 age group (Figure 2B).

Figure 2. Means of hedonic ratings of preference (p), intake frequency (f) and craving (c) of (A) sweet beverages and (B) sweet foods among age groups. Significant difference of means between age groups was compared by Mann-Whitney U test, with levels of significance, *p<0.05 and **p<0.01 as indicated. Error bars are standard errors.
Ethnicity

Ethnic Malays had significantly higher preference, intake frequency and craving of cordial drinks and pisang goreng compared to other ethnicities (Figure 3). Ethnic Chinese had significantly higher intake frequency of cola/carbonated and chocolate malt drinks, candy, chocolate and ice-cream, and significantly higher preference and craving for sweet dessert soup and tarts. Of note, ethnic Indians tend to have a significantly higher preference of sweet kuih compared to Malays or Chinese (Figure 3B).

Figure 3. Means of hedonic ratings of preference (p), intake frequency (i) and craving (c) of (A) sweet beverages and (B) sweet foods among Malaysian ethnicities. Significant difference of means between ethnicities was compared by Kruskal-Wallis test, with levels of significance, *p<0.05 and **p<0.01 as indicated. Error bars are standard errors.
BMI status

Lean subjects significantly ate or drank and craved cincau, chocolate malt, packet drinks and sweet dessert soup more compared to the overweight group (Figure 4A). As well, they significantly preferred, ate and craved cake, candy, chocolate and pudding more compared to the overweight group (Figure 4B).

Figure 4. Means of hedonic ratings of preference (p), intake frequency (f) and craving (c) of (A) sweet beverages and (B) sweet foods among BMI status (lean and overweight). Significant difference of means between BMI groups was compared by Mann-Whitney U test, with levels of significance, *p<0.05 and **p<0.01 as indicated. Error bars are standard errors.
DISCUSSION

Consumption of sweet foods is influenced by a variety of biological, psychological, sociological, and environmental factors and on an individual level, taste preference for sweetness has been shown to have an influence on sugar consumption\textsuperscript{[19]}. Sweet food intake is hard to measure accurately because of memory issues and disinclination of subjects to correctly report the food they eat. Individuals might under- or over-report intakes\textsuperscript{[18]}. For instance, a person who is attempting to lose weight may tend to report smaller portions than were actually eaten. In this study, we investigated the determining patterns of the reported high prevalence of ‘sweet tooth’ among Malaysians of different ethnicities, by using a 7-point hedonic scale to estimate the preference, intake frequency and craving of a list of 22 commonly consumed Malaysian sweet food and beverages. Demographic (gender, age groups and ethnicity) and anthropometric (BMI status) differences were also compared.

The current study shows that Malaysian women significantly preferred more, ate or drank less frequently but had equal craving of sweet foods compared to men. Pertaining to preference, in contrast with our study, previous studies on sex differences revealed that although male and female infants do not differ in sweet preference\textsuperscript{[17]}, older boys and men prefer higher concentration of sweets as compared to women\textsuperscript{[9]}. The higher mean of intake frequency of sweet foods in men compared to women supports the finding of earlier research at Italy which found that male ate food rich in saturated fats such as fried food, meat and sugar drinks more frequently than female did\textsuperscript{[17]}. This is because female seemed to be more concerned about their weight and diet by eating healthy food, such as vegetables, more frequently than men did\textsuperscript{[17]}. Meanwhile, studies on sweet craving suggest that women, more often than men, experience food cravings in general\textsuperscript{[18]}. It has been reported that oestrogen may play a role in changes of sweet craving during the menstrual cycle\textsuperscript{[19]}. However, our study found no evidence of gender difference in sweet food craving.

As for age, the group <25 years showed significantly higher preference, intake frequency and craving of sweet foods than ≥25 years, as expected. Preference for sweetness is affected by ageing as demonstrated by some studies\textsuperscript{[20]}. Young people also had higher frequency of sweet intake than do elderly people in Japan\textsuperscript{[21]}. Also, the investigation conducted by Drewnowski et al. (1997)\textsuperscript{[16]} agreed with this finding. This phenomenon can be explained by changes in caloric requirements for growth, or the onset of puberty\textsuperscript{[16]}. Meanwhile, sweet craving changes over the life span, and older women report less craving for sweet foods compared with younger women\textsuperscript{[9]}. The ethnic differences in rating the preference, intake frequency and cravings seemed to be food-specific and culturally-related, as expected. For Malays, they seemed to have higher affinity towards cordial drinks and pisang goreng, Chinese - sweet dessert soup and tarts and Indians – sweet kuih. A pilot study among Malaysian children\textsuperscript{[22]} found that although the difference in sweet preference between boys and girls was not statistically significant, the ethnic variation was. They suggested that diet and sugar eating habits, in particular sweet preference levels, are gradually nurtured over time by culturally accepted dietary norms\textsuperscript{[22]}. This ethnic variability in the hedonic ratings of preference, intake frequency and craving is also supported by previous studies in other populations. For example, in Australia, Malaysian students (mainly ethnic Malays) had significantly higher sweetness perception but lower sweetness preference for high-sucrose orange juice samples, compared to their Caucasian counterparts\textsuperscript{[23]}.

It is commonly assumed that people with a sweet tooth will over-consume sweet foods, consequently causing a proportional rise in obesity (reviewed in \textsuperscript{[24]}). Our study showed that the lean subjects showed significantly higher preference, intake frequency and craving of sweet foods than the overweight subjects. This result is supported by some studies which demonstrate that lean people prefer sweet food or drinks and consume more calories, as sugar, compared with obese people\textsuperscript{[25]}. The reason for lean subjects to have a stronger craving for sweet foods could be explained by their high temptation in controlling the intake of high sugar-content-foods, while overweight subjects who might be less concerned about the consequences of sweet food intake, appear to have less craving for sweet items\textsuperscript{[26]}.

There were several limitations in this study. Firstly, the age of the subjects was more skewed towards young university and college students, although elderly subjects were included in this study. We are also aware of the small sample size, therefore limiting the power for statistical analysis and could not be generalized to reflect the entire Malaysian population. A larger sample size may prevent sampling bias. There may be also under-reporting of the sweet food preference, intake frequency and craving due to responder fatigue, memory recall and interviewer and subject bias. Sweet food preference, intake frequency and craving could also be associated with sweet genetic markers, like the sweet taste receptor genes TAS1R2 and TAS1R3, and leptin and leptin receptor genes, LEP and LEPR (reviewed in \textsuperscript{[27]}). Studies in mice have indicated that the exchange of Ile to Thr at amino acid codon 60 of T1R3 (encoded by Tas1R3 gene; homologue for human TAS1R3) is attributed to lower sweetness preference\textsuperscript{[28]}. While studied in humans have indicated that single nucleotide polymorphisms rs307355 and rs35744813 of the TAS1R3 gene\textsuperscript{[29]} and LEP A19G and LEPR K109R\textsuperscript{[30]} are associated with sucrose sensitivity and sweet preference.

CONCLUSIONS

All in all, Malaysian females in this study significantly preferred more, ate or drank less frequently but had equal craving of sweet foods compared to males, whereas lean subjects and those <25 years showed significantly higher preference,
intake frequency and craving of sweet foods. Among ethnic groups, Chinese had significantly higher intake frequency but lesser craving of sweet foods compared to Malays and Indians. The Malaysian Dietary Guidelines generally recommend eating food and drinking beverages that are low in sugar (NCC, 2010). In addition to that, understanding the demographic and anthropometric factors that may affect the preference, intake frequency and craving of certain sweet foods can help to plan for more strategies in preventing the detrimental health effects of high sugar intake among Malaysians.

ACKNOWLEDGEMENTS
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REFERENCES


GyrA Gene Mutations of M. tuberculosis and Previous Use of Ciprofloxacin and Ofloxacin in Quinolone Resistance

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ABSTRACT

Objectives: This study assessed quinolone resistance in MDR and non-MDR cases. It also analyzed the duration of ciprofloxacin (Cfx) and ofloxacin (Ofx) use in resistance and sensitive isolates. The position and type of gyrA gene mutations in quinolone resistant isolates were also evaluated.

Methods: This was a combined analytic observation with cross-sectional timed and biomolecular qualitative study using a total of 35 M. tuberculosis clinical isolates between 2007 and 2009. The susceptibilities of isolates to Cfx and Ofx were determined by using MIC method on LJ medium. Amplification of gyrA gene was done using PCR with touch-down program to all resistant-isolates. PCR product was then further used as a template for DNA sequencing.

Results: Quinolone resistance among the MDR isolates was significantly higher than non-MDR (p=0.008). Compared to sensitive isolates, the duration of previously used Cfx was 10.46 weeks longer in resistant isolates (p=0.021). There was no significant difference in the duration of Ofx between resistant and sensitive isolates with 22.75 weeks and 17.02 weeks of mean rank respectively (p=0.218). Quinolone resistance exhibited point mutations at Asp89Val (16.7%), Asp94Gly (50%), Asp94Ala (16.7%), Asp94Asn (16.7%), Ser95Thr (83.3%), Ser95Asn (16.7%).

Conclusion: Quinolone resistance among MDR isolates is high in rate. All of quinolone-resistant isolates shows missense mutations on gyrA gene with high-level resistance. Cfx has been used more frequently and longer than Ofx in MDR and non-MDR cases.

Keywords: Quinolones, M. tuberculosis, gyrA

INTRODUCTION

Indonesia is the fourth country with the highest number of patients with tuberculosis (TB) patients. Anti-tuberculosis drug resistance has emerged in tuberculosis control. Multidrug-resistant TB (MDR-TB) which has not yet been overcome is now followed by extensively drug-resistant TB (XDR-TB). WHO formulated XDR-TB as a resistance to rifampicin (R) and isoniazid (H) as well as resistance to any one of fluoroquinolones (FQ) and to at least one of three injectable second-line drugs: capreomycin, kanamycin and amikacin. The resistance prevalence of ciprofloxacin (Cfx) and ofloxacin (Ofx), the two largest FQ used in TB, in Indonesia has not yet been clearly known because it does not have a routine examination. WHO recommended second-line and injection drug susceptibility test of MDR isolates to determine the proportion of XDR-TB among MDR-TB.

FQ is one of second-line drug used to treat MDR, besides, it is considered as a broad spectrum antibiotic which is commonly used in infectious diseases. The widespread use of this drug in the tuberculosis treatment without properly diagnostic criteria increases the risk of resistance because of inadequate therapy.

Generally, the causes of antibiotic resistance are due to microbial aspects of gene mutation and clinical aspects of drug use. It is known that gyrA gene mutation of M. tuberculosis in quinolone-resistance-determining region (QRDR) is responsible for FQ resistance. Missense mutations possibly change the structure and function of GyrA protein in DNA gyrase in which FQ binds. These lead FQ to fail in DNA gyrase negative supercoil activity. Consequently, M. tuberculosis DNA is not damaged and remains alive. From the clinical aspect, the irrational use of Cfx and Ofx in both indications and duration, exposes microbes to sub-lethal drug concentration leading to resistant strains which are potentially dominant in population. The epidemiology studies found that MDR cases have a higher risk in anti-tuberculosis drug resistance affecting FQ therapy outcomes. The detection of gyrA gene mutation rapidly predict the sensitvity of FQ especially in MDR case.

This study aimed to analyze gyrA gene mutations in Cfx and Ofx resistance. It included the number of mutation,

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the position of codon and the type of mutation. The previous use of FQ and FQ resistance in MDR and non-MDR cases were also evaluated.

**METHODS**

*M. tuberculosis* isolates. The total of 35 clinical isolates from culture collection of the year 2007-2009 were derived from patients having medical record of Cfx and Ofx use in tuberculosis treatment. All were recultured on Lowenstein-Jensen (LJ) medium for *M. tuberculosis* identification and drug susceptibility test.

**Catalase and Nitrate Test.** These tests chemically identified *M. tuberculosis* which was negative in 68 °C catalase test and positive in nitrate reduction test. On the catalase test, one loopfull of bacteria was transferred to a tube containing PBS pH 7.0. Each tube was then incubated at 68 °C for 20 minutes. After the mixture of H2O2 and fresh Tween-80 10% were added, the forming of bubble was identified. It was considered negative when the bubble did not form within 20 minutes. In the nitrate test, one loopfull colonie was added to a solution of 0.85% NaCl and nitrate reagent and then incubated in a water bath at 37 °C for 2 hours. The existence of pink color with minimum standard of +3 was identified as positive after the addition of HCl 50%, sulfanilamide 0.2% and N-Naphthylen 0.1%.

**Drug Susceptibility Test (DST).** The DST to rifampicin (R), isoniazid (H), kanamycin (Km) referred to WHO standards. FQ susceptibilities were determined by proportion method on LJ medium. After an inoculums source was made through standard suspension and dilution, it was then inoculated on LJ medium containing Cfx (Bayer) and Ofx (Bayer) with each concentration of 0.5 µg/mL, 1 µg/mL, 2 µg/mL and 4 µg/mL and LJ medium without drug as a control. The culture media were incubated at 37 °C and the colony growth reading were recorded for two days, on day 28th and 42nd. The MIC was determined by colony forming unit (cfu) counting. The strain of H37Rv was tested as a control isolate which was sensitive to all tested drugs.

**DNA Isolation of *M. tuberculosis*.** One colony cultured on LJ medium was transferred into an aliquot containing 100 µL lysis solution (Sigma Molecular Biology). It was then heated on boiling water for 15 minutes. After that, the aliquot was centrifuged at 10.000 rpm for 10 minutes. The supernatant was transferred to a new aliquot. DNA concentration was then measured with a spectrophotometer at 260m and 280nm.

**GyrA Gene Amplification.** Amplifying 320 bps region of gyrA, the Polymerase Chain Reaction (PCR) method with touch-down program used primers gyrA-f 5'-CAGCTACATCGACTATGCGA-3' and gyrA-r 5'GGCTTCGGTGTACCTCAT -3' from the AlphaDNA. A total of 25 µL PCR mixture contained 10x PCR Buffer, 6 µM MgCl 2, primers (each) 4µM, 50 µM dNTPs, H2O PCR, 1 IU Taq polymerase, and 50 µM DNA. The mixture was then put in the thermal Cycler (Hybaid Om-E) with following PCR program of denaturation, annealing and extension: 95 ° C for 3 minutes

- 2 cycles: 95 ° C for 1 minute, 58 ° C for 1 minute, 72 ° C for 1 minute
- 2 cycles: 95 ° C for 1 minute, 57 ° C for 1 minute, 72 ° C for 1 minute
- 2 cycles: 95 ° C for 1 minute, 56 ° C for 1 minute, 72 ° C for 1 minute
- 2 cycles: 95 ° C for 1 minute, 55 ° C for 1 minute, 72 ° C for 1 minute

Phase extension: 72 ° C for 5 minutes

- 6µL of PCR amplification product was mixed with 1 mL loading dye (Promega) then they were poured into ehibium bromide colored 3% agarose gel (Invitrogen). The DNA Ladder used a bench top PCR (Promega). Electrophoresis was performed for 30 minutes in 1x TAE buffer at 100V at room temperature. Gel was visualized in a Dark Reader Transiluminator (Vilbert Loumart).

**DNA Sequencing.** PCR product was sent to Macrogen Inc.. Korea for purification and single sequencing of gyrA gene using the same forward and reverse primer in the PCR. The result was then analyzed with the Genious program. Alignment was then performed with the BLAST (Basic Local Alignment Search Tools) program from the NCBI (National Center for Biotechnology Information). The difference of nuncleotide sequence was analyzed to identify the position and the type of gyrA gene mutation.

**Statistical Analysis.** This study used univariate and bivariate analysis. The difference of quinolone resistance between MDR and Non-MDR isolates was analyzed by the Fisher Exact Test. The Mann-Whitney Test was used to identify significant differences of duration of quinolones use between resistant and sensitive isolates. Data analysis was performed by SPSS for windows version 13.0 on 95% of CI with significant difference of p value ≤ 0.05.
RESULTS

Clinical Characteristics of M. tuberculosis Isolates.

Clinical characteristics of M. tuberculosis isolates which include the type of TB patients and the previous use of Cfx and Ofx in the non-MDR, MDR and fluoroquinolone-resistance group can be seen in Table 1.

Cfx and Ofx were mostly used on chronic cases (41.2%) in MDR group. Meanwhile, in non-MDR group they were mostly used on drop out cases (33.3%). Surprisingly, these drugs were also widely used on new cases in both of the group. Cfx only was the most frequent drug used in all cases (57.2%), followed by Cfx and Ofx combination (37.1%) and Ofx only was the least common drug used (5.7%). Most of MDR isolates (58.8%) had Cfx and Ofx combination prior use while the majority of FQ resistant isolate used Cfx only in tuberculosis treatment.

![Table 1. Clinical Characteristics of M. tuberculosis Isolates](image1)

<table>
<thead>
<tr>
<th>Patients Type*</th>
<th>Overall (n=35)</th>
<th>Non MDR (n=18)</th>
<th>MDR (n=17)</th>
<th>Resistant to FQ (MIC &gt; 2µg/ml) (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New</td>
<td>5 (14.3%)</td>
<td>3 (16.7%)</td>
<td>2 (11.8%)</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td>Relapse</td>
<td>9 (25.7%)</td>
<td>4 (22.2%)</td>
<td>5 (29.4%)</td>
<td>0</td>
</tr>
<tr>
<td>Failed</td>
<td>1 (2.9%)</td>
<td>0</td>
<td>1 (5.9%)</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>Drop Out</td>
<td>8 (22.9%)</td>
<td>6 (33.3%)</td>
<td>2 (11.8%)</td>
<td>0</td>
</tr>
<tr>
<td>Chronic and other</td>
<td>12 (34.3%)</td>
<td>5 (27.8%)</td>
<td>7 (41.2%)</td>
<td>3 (50%)</td>
</tr>
</tbody>
</table>

Use of Fluoroquinolones

- CiprOfx Only: 20 (57.2%) 14 (77.8%) 6 (35.3%) 2 (33.3%)
- Ofx Only: 2 (5.3%) 1 (5.6%) 1 (5.3%) 1 (16.7%)
- CiprOfx and Ofx: 13 (37.1%) 3 (16.6%) 10 (58.3%) 2 (33.3%)

Table 2. MIC of Ciprofloxacin and Ofloxacin

<table>
<thead>
<tr>
<th>Drug</th>
<th>No. (%) of Sensitive Isolates with MIC (µg/ml)</th>
<th>Cut-off</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>4 (11.4%)</td>
<td>10 (28.6%)</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>5 (14.3%)</td>
<td>14 (40%)</td>
</tr>
</tbody>
</table>

DST of Ciprofloxacin and Ofloxacin

The inhibition of M. tuberculosis by Cfx and Ofx at different concentration is shown in Table 2. Using >2 cut-off resistant, a total of 29 (82.9%) isolates were sensitive to the concentration of 4 µg/ml. Ofx had higher antimicrobial activity than Cfx at concentration ≤ 2 4 µg/ml. The standard strain of H37Rv was sensitive to all concentrations.

The Duration of Cfx and Ofx Previous Use in FQ Resistance

Of 35 isolates, there were 6 (17.1%) of FQ resistance, and MDR group had 0.647 higher risk of FQ resistant than Non-MDR group (p=0.008) as shown on Table 3. Table 4 shows that the duration (mean rank of week) of Cfx exposure was...
associated with Cfx resistance ($p<0.05$), but there was no correlation between Ofx duration and Ofx resistance ($p>0.05$). Compared to Ofx, Cfx was used longer with maximum duration of 44 weeks and 144 weeks respectively and the most frequent duration for Cfx was 4 weeks.

**Table 3.** Quinolone Resistance on MDR and non-MDR Isolates

<table>
<thead>
<tr>
<th>Variable</th>
<th>Resistant</th>
<th>Sensitive</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>MDR</td>
<td>6</td>
<td>35.3%</td>
<td>11</td>
<td>64.7%</td>
</tr>
<tr>
<td>Non-MDR</td>
<td>0</td>
<td>0%</td>
<td>18</td>
<td>100%</td>
</tr>
<tr>
<td>Overall</td>
<td>6</td>
<td>17.1%</td>
<td>29</td>
<td>82.9%</td>
</tr>
</tbody>
</table>

*Significance difference ($p<0.05$) in Fisher’s Exact test

MDR, multi-drug resistance

**Table 4.** Exposure Duration on Ciprofloxacin and Ofloxacin Resistance

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean Rank</th>
<th>SR</th>
<th>p values</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resistant</td>
<td>26.67</td>
<td>160</td>
<td>0.021*</td>
<td>6</td>
</tr>
<tr>
<td>Sensitive</td>
<td>16.21</td>
<td>470</td>
<td></td>
<td>29</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resistant</td>
<td>22.75</td>
<td>136.50</td>
<td>0.218</td>
<td>6</td>
</tr>
<tr>
<td>Sensitive</td>
<td>17.02</td>
<td>493.5</td>
<td></td>
<td>29</td>
</tr>
</tbody>
</table>

* Significance difference ($p<0.05$) in Mann-Whitney test

**Figure 1.** *GyrA* gene PCR product of *M. tuberculosis*

Lane 1 : Marker
Lane 2 : Positive Control
Lane 3 : Negative Control
Lane 4-8 : PCR Product of 320 bp
Amplification of *M. tuberculosis* gyrA gene by PCR.

PCR amplification was performed on six resistant isolates and one sensitive isolate of wildtype H37Rv. PCR product showed one single band of gyrA gene at 320 bp as shown in Figure 1. This product included QRDR on gyrA. PCR results were then used as templates for DNA sequencing.

Sequencing results.

The position and the type of mutations are shown on Table 5. Along QRDR hotspot regions, all resistant isolates had mutations at codon 94 and codon 95. Substitute point mutations in all position generally changed amino acid and caused missense mutations. Of 6 resistant isolates, the mutation patterns were Asp89Val (16.7%), Asp94Gly (50%), Asp94Ala (16.7%), Asp94Asn (16.7%), Ser95Thr (83.3%), Ser95Asn (16.7%).

**Table 5. GyrA Gene QRDR Mutation Patterns of M. tuberculosis Isolates Resistant to Ciprofloxacin and Ofloxacin**

<table>
<thead>
<tr>
<th>Codon</th>
<th>Nucleotide Mutation</th>
<th>Type</th>
<th>Amino Acid Change</th>
<th>Mutation Frequency (isolate)%</th>
</tr>
</thead>
<tbody>
<tr>
<td>76</td>
<td>TCG → TTG</td>
<td>Substitution</td>
<td>Ser → Leu</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>77</td>
<td>GTT → GTC</td>
<td>Substitution</td>
<td>Val → Val</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>78</td>
<td>GCC → GCG</td>
<td>Substitution</td>
<td>Ala → Ala</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>89</td>
<td>GAC → GTG</td>
<td>Substitution</td>
<td>Asp → Val</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>94</td>
<td>GAC → GGC</td>
<td>Substitution</td>
<td>Asp → Gly</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td>94</td>
<td>GAC → GCC</td>
<td>Substitution</td>
<td>Asp → Ala</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>94</td>
<td>GAC → AAC</td>
<td>Substitution</td>
<td>Asp → Asn</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>94</td>
<td>GAC → GGA</td>
<td>Substitution</td>
<td>Asp → Gly</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>95</td>
<td>AGC → ACC</td>
<td>Substitution</td>
<td>Ser → Thr</td>
<td>5 (83.3%)</td>
</tr>
<tr>
<td>95</td>
<td>AGC → AAC</td>
<td>Substitution</td>
<td>Ser → Asn</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>96</td>
<td>CTG → CCG</td>
<td>Substitution</td>
<td>Leu → Pro</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>97</td>
<td>GTG → GGG</td>
<td>Substitution</td>
<td>Val → Gly</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>99</td>
<td>ATG → AAG</td>
<td>Substitution</td>
<td>Met → Lys</td>
<td>1 (16.7%)</td>
</tr>
</tbody>
</table>

DISCUSSION

This study shows a high rate of FQ resistance and the MDR. FQ resistance rate among all isolates were 17.3%, two times lower than MDR isolates (35.3%). Compared to previous studies, these were higher than the rate in Taiwan but lower than the rate in the Philippines. The prevalence of FQ resistance in Taiwan was 3.3% in general and 19% in MDR isolates. Another study in Taiwan found 6.2% of FQ resistance incidence and 22.2% among MDR isolates. In the Philippines, FQ resistance was 35.3% in general and 51.4% in MDR isolates. However, fortunately, we found that there was no XDR-TB because all isolates were sensitive to kanamycin, a second-line antituberculosis injection drug, which WHO showed 2% of resistance. This study suggests that kanamycin is empirically effective for treating MDR.

Having exposed to Cfx and Ofx, both of non-MDR and MDR groups had similar risk to be resistant. Therefore, it is very important to perform FQ sensitivity test in order to determine the appropriate regimen because Cfx and Ofx has been widely used among non-MDR cases. This means that Cfx which is not recommended for neither sensitive nor resistant tuberculosis is still commonly used in Indonesia. This is because of efficient cost and high availability of Cfx.

The duration of Cfx exposure associated with its resistance as well as previous studies which found that Cfx administration in tuberculosis treatment is rapidly followed by resistance. M. tuberculosis isolate which is not
exposed to Cfx have a little opportunity to be resistant with 1 CFU per 2 x 10^6 CFU of resistance incidence on day 0 and 1 CFU per 7.9 x 10^5 CFU of resistance incidence on day 13. Exposing \textit{M. tuberculosis} with 1 CFU per 7.9 x 10^5 CFU of Cfx increases rapid resistance from 0.00003% of the total population on the beginning to 0.27% on day 3 and 54.5% on day 7.\[13\]

FQ resistance is more common in the MDR for the differences of DnaE2 levels between resistant and sensitive \textit{M. tuberculosis}.\[14\] DnaE2 has an important role in DNA repair which promotes mutation. DNA repair mechanism is the only way for bacteria to survive. \textit{M. tuberculosis} within the host’s body gets genotoxic stressors which come from the body’s immune response as well as antituberculosis drug exposure causing DNA damage resulting in cell damage and death. Translesion synthesis, one of DNA repair mechanism in \textit{M. tuberculosis}, is a process allowing replication of DNA template damage. This process is performed by the “tend to go wrong” DNA polymerase C enzyme encoded by DnaE2 gene. There is an accumulation of mutations in rpoB and katG genes in MDR \textit{M. tuberculosis}.

We found that all resistant isolate had gyrA gene mutation. The frequency of gyrA and gyrB gene mutation among resistant strains varied from 10.3% in India, 50% in Taiwan, 55.2 -58.8% in Hong Kong, 60% in Thailand, 89.5% in Italy and Abkazia to 100% in Japan.\[15\] The mutation of codon 94 in this study is similar to previous studies that found hotspot areas of codon 88, 89, 90, 91, and 94.\[6, 7, 16, 17\] The detection of codon 90, 91 and 94 is an effective way predicting FQ resistance in \textit{M. tuberculosis}. Compared to other mutations, mutation of Asp94 (Gly / Ala) showed high levels of resistance which generally has double missense mutations.\[7\]

The Asp94Gly mutations (50%) and Ser95Thr mutations (83.3%) potentially change the subunit protein structure of DNA gyrase GyrA 3 α helix-shaped. Aspartic acid (Asp) is acidic polar amino acid, whereas glysin (Gly) is a neutral non polar amino acids. The alteration from Asp to Gly possibly changes structure or function of protein. These may cause FQ resistance through either change binding site of FQ on DNA gyrase-DNA complex or decrease supercoiling activity of DNA gyrase.

There was 83.3% of Ser95Thr mutation which is the most frequent polymorphisms found in some studies. This does not have a direct role in the development of resistance. Polymorphisms of codon 95 found in 15% of strains is a kind of genetic evolution which is not associated with resistance increase.\[13\]

In regions with high incidence of antituberculosis drug resistance, detection of target gene mutation for resistance identification will improve the diagnosis of MDR and XDR tuberculosis. Identification of gene mutation which is responsible for rifampichyn and FQ resistance using gene \textit{rpoB}, \textit{gyrA} and \textit{gyrB} is a rapid test to give the most appropriate therapy especially in multi-resistant case.

**CONCLUSION**

Based on the previous use, Cfx was the most frequently used drug among FQ. Cfx and Ofx were used in all type of TB patients from new case to chronic case. For this widely use, as well as WHO guidelines, Cfx is not recommended in neither sensitive nor resistant TB. All resistant isolates had \textit{gyrA} gene mutation at codon 94 which potentially changes structure or function of DNA gyrase as FQ target. Detection of \textit{gyrA} gene mutation codon 94 targeted should be performed for rapid diagnostic test of FQ resistance.

**ACKNOWLEDGEMENTS**

We would like to thank Beasiswa Pascasarjana (BPPS) DIKTI 2008 for the scholarship that made this research possible and Prof. Wasmen Manalu for reviewing this article.

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GyrA Gene Mutations of M. tuberculosis and Previous Use of Ciprofloxacin and Ofloxacin in Quinolone Resistance


Comparison of Anterior Tooth Size Discrepancies Among Different Malocclusion Groups

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ABSTRACT

Background: Discrepancies between tooth sizes can cause orthodontic problems such as crowding and improper occlusion. By identifying these problems, better orthodontic treatment outcome can be achieved. The aim of this study is to identify anterior tooth size discrepancies among 4 different types of malocclusion i.e. Class I; Class II division 1 (II/1); Class II division 2 (II/2); and Class III. Methods: A retrospective study was carried out using 200 orthodontic study models where 50 study models were taken for each of the 4 malocclusion groups. The samples were selected using random sampling technique based on the orthodontic waiting list in the Orthodontic Department, Dental Faculty, UKM. All anterior teeth were measured by the same examiner at the largest mesio-distal dimension, using a digital caliper recorded up to 0.01 mm. Comparison between the 4 groups of malocclusion were made intra-arch using individual tooth size measurement and inter-arch using Anterior Bolton Index (ABI).

Results: For the intra-arch assessment, Class II/1 had significantly the largest upper and lower anterior tooth size except for its upper canine and lower central incisor. Class III group had insignificantly the smallest mandibular anterior teeth compared to other malocclusion groups. For inter-arch assessment, Anterior Bolton Index (ABI) of all samples was 79.2 ± 3.94%. The highest ABI was noted in Class II/2 of 80.3 ± 4.71%. However, no significant differences were found among the 4 malocclusion groups (p>0.05). Conclusion: Most of the anterior teeth in Class II division 1 were the largest of all. No significant difference in the inter-arch tooth size discrepancies were detected among all malocclusion groups.

Keywords: Tooth size discrepancy, malocclusion, Bolton discrepancy

INTRODUCTION

Discrepancies of the tooth sizes can be a local aetiological factor for malocclusion. Any deviation in the tooth size within the arch can cause malalignment such as crowding or spacing\[1, 2\]. Moreover, inter-arch tooth size discrepancy can cause poor interdigitation of the presenting occlusion\[3\]. Sometimes, these discrepancies are not noticeable till the end of the orthodontic treatment\[4-5\]. Because of these discrepancies, at the end of an orthodontic treatment, good occlusion and interdigitation may not be achievable. When the anterior maxillary anterior teeth are too large in relation to the mandibular teeth, abnormal overbite or overjet can be the clinical manifestations\[3\]. On the other hand, if the mandibular anterior teeth are too large in relation to the maxillary teeth, end to end relationship of teeth, spacing in the maxillary anterior segment and improper occlusion of posterior teeth can be seen\[6\]. By identifying which type of malocclusion has the most tooth-size discrepancies, treatment can be modified and appropriate measures can be implemented to gain a good post-treatment interdigitation. Measures such as the removal or addition of tooth structure could be included in the initial treatment plan.

Inter-arch tooth size discrepancies are assessed by an index called Bolton Index\[13\]. Bolton introduced two indices, the Anterior Bolton Index (ABI) that involves the measurements of the six front teeth and the Overall Bolton Index (OBI) which incorporates the total mesio-distal size of 12 teeth from incisors to the first permanent molar. In order to compare tooth size discrepancies between different types of malocclusion which uses the incisor’s relationship as its reference, thus the Anterior Bolton Index (ABI) is more suitable than the overall Bolton index. By comparing the ABI norms value, the applicability of the ABI to all the different types of malocclusion in Malaysia can be determined.

Many studies have been done to compare the inter-maxillary tooth size relationship among different malocclusions, and had controversial results. Some studies have noted that there were no significant differences among the malocclusion groups\[4, 7, 8\]. However, there are a number of studies with contradictory results. These studies found that Class III individuals had greater tooth size discrepancies when compared to Class I and Class II malocclusions\[3, 9, 10, 11, 12\].

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Therefore, the aim of this research is to compare the mesio-distal tooth width (intra-arch) and anterior tooth size discrepancies (inter-arch) among different types of malocclusion i.e. Class I, Class II division I, Class II division 2 and Class III in orthodontic patients attending UKM’s dental clinic.

**METHODOLOGY**

**Samples’ selection**

This was a retrospective study of orthodontic study models taken from Orthodontic department, Universiti Kebangsaan Malaysia from the year 2005-2008. Orthodontic study models were selected using stratified random sampling technique based on the orthodontic waiting list. A total of 200 study models with equal number of sample in each type of malocclusion were retrieved. The inclusion criteria for selecting the samples are shown in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Inclusion criteria</th>
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<tr>
<td>Inclusion Criteria</td>
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<tr>
<td>• Good quality of pretreatment models</td>
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<tr>
<td>• Presence of all 6 anterior teeth from incisors to canine for each quadrant</td>
</tr>
<tr>
<td>• Absence of dental prosthesis</td>
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<tr>
<td>• Absence of partially erupted teeth</td>
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<tr>
<td>• No tooth deformity (eg, conical shaped lateral incisor)</td>
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<td>• No record of restoration or stripping of incisor and canine teeth.</td>
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</tbody>
</table>

**Tooth width measurement**

All the six front teeth were measured at the largest mesio-distal dimension, perpendicular to its long axis using a digital caliper accurate to 0.01 mm (ABSOLUTE Digimatic, Mitutoyo USA). The readings were recorded at the 0.01 mm level and were calculated manually. All the measurements were triplicated and done by single examiner to avoid bias. The measurements of all 200 study models were done within the 3-month period of data collection with an average of 4 study models per day. The anterior tooth size discrepancies were calculated based on the formula described by Bolton as shown below:

\[
\frac{\text{sum mandibular “3-3”}}{\text{sum maxillary “3-3”}} \times 100 = \text{Anterior Bolton Index %}
\]

All statistical analyses were performed using the SPSS software package (Statistical Package for Social Sciences, version 19.0). All data collected were analyzed descriptively using percentages and frequencies. Comparison tests were performed using independent T-test since the data were normally distributed as shown by Kolmogorov-Smirnov analysis (p>0.05).

**RESULTS**

**Analysis of error**

Intra-examiner reliability test was performed by randomly re-measuring 10% of the samples (n=20) after a one-week interval. The re-measurements involved the individual reading of the mesio-distal width dimension of the six front teeth. Reliability testing was performed using Pearson correlation coefficient test. Result showed that both readings were strongly related with Pearson’s r values of 0.9.

**Intra-arch assessment**

There were a total of 200 orthodontic study models that were used in this study which comprises of 50 study models for each malocclusion groups i.e. Class I, Class II division 1, Class II division 2 and Class III.
Comparison of Anterior Tooth Size Discrepancies Among Different Malocclusion Groups

Table 2 shows overall number of teeth, mean ± standard deviation of each tooth. In the upper arch, central incisor was 8.63± 0.56mm, lateral incisor was 7.09± 0.74mm and canine was 7.84 ± 0.64mm. While in the lower arch, average size of central incisor was 5.48 ± 0.43mm, 6.12 ± 0.53mm for lateral incisor and 6.92 ± 0.52mm for canine.

Table 2. Total number of samples (N), mean ± standard deviation of each upper and lower anterior teeth.

<table>
<thead>
<tr>
<th></th>
<th>Upper</th>
<th></th>
<th></th>
<th>Lower</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Central Incisor</td>
<td>Lateral Incisor</td>
<td>Canine</td>
<td>Central Incisor</td>
<td>Lateral Incisor</td>
<td>Canine</td>
</tr>
<tr>
<td>N</td>
<td>400</td>
<td>400</td>
<td>400</td>
<td>400</td>
<td>400</td>
<td>400</td>
</tr>
<tr>
<td>Mean</td>
<td>8.63± 0.56</td>
<td>7.09± 0.74</td>
<td>7.84± 0.64</td>
<td>5.48± 0.43</td>
<td>6.12± 0.53</td>
<td>6.92± 0.52</td>
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</table>

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Figure 3 shows comparison of each tooth to the 4 different types of malocclusions groups i.e. Class I, Class II division 1 (CI II/1), Class II division 2 (CI II/2) and Class III. Upper central incisor of Class II/1 was the largest among other types of malocclusion of 8.74 ±0.05mm with significant differences (p<0.05) were detected when compared to Class II/2 and Class III. Among all upper lateral incisors, Class II/1 was the largest of 7.33±0.51mm with significant differences were detected when compared to other 3 malocclusion groups. Upper canine had almost similar size in all 4 malocclusion groups ranging from 7.75mm to 7.94mm with no significant differences detected in between the groups (p>0.05). No significant differences were detected in size of the lower central (p>0.05). As for the lower lateral incisor, Class II/1 showed the largest of all with measurement of 6.23± 0.56mm and significant differences (p<0.05) were noted when compared to Class I and Class III. Similarly, Class II/1’s lower canine was the largest of all but only significant difference was found when compared to Class III (p<0.05). Overall, it was shown that the Class II/1’s teeth had the largest tooth size in each of the tooth type except for the lower central incisor as shown in Figure 3.

Table 3. Mean and standard deviation of Anterior Bolton Index (ABI) in 4 different types of malocclusion groups

<table>
<thead>
<tr>
<th>Types of malocclusion</th>
<th>Anterior Bolton Index (%)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Class I</td>
<td>78.83</td>
</tr>
<tr>
<td>Class II/1</td>
<td>78.75</td>
</tr>
<tr>
<td>Class II/2</td>
<td>80.53</td>
</tr>
<tr>
<td>Class III</td>
<td>79.09</td>
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</tbody>
</table>

Inter-arch assessment using Anterior Bolton Index (ABI)

The ABI for overall samples was 79.3 ±3.94%. Mean percentage and standard deviation of each malocclusion groups presented in Anterior Bolton Index (ABI) are shown in Table 3. ABI in Class II/2 was the highest of 80.3 ± 4.71%. Class III malocclusion had ABI 1.24 lesser than the Class II division 2 malocclusion. Both Class I and Class II/1 has almost similar ABI of 79%. No significant differences were detected in between each of 4 malocclusion groups (p>0.05).
**DISCUSSION**

Assessment of tooth size discrepancies can be an important factor to determine orthodontic treatment outcome. In our study, we wanted to determine whether there is a difference in anterior tooth size among different malocclusion groups in orthodontic patients attending UKM’s dental clinic. No discrimination of gender and side i.e. left/right were made as previous studies showed no statistical difference in tooth size when comparing between gender or between sides [14, 15, 16].

**Intra-arch assessment**

In a study by Fattahi *et al.* (2006), they found that Class III individuals had smaller maxillary teeth compared to Class I and Class II subjects [17]. The result does correlate with our study where we found that Class III’s maxillary anterior teeth were in fact the smallest for upper central incisors and the second smallest for upper lateral incisors and upper canines. We also found that Class III subjects had the smallest mandibular anterior teeth compared to other malocclusion groups which were not in agreement to the study by Lavelle (1972) and Sperry *et al.* (1977) that reported the mesio-distal width of lower teeth in Class III malocclusion subjects is larger when compared with Classes I and II (divisions 1 and 2) [10, 17]. We also found that Class II/1 had the largest mesio-distal width of anterior tooth size for both maxillary and mandibular teeth except for the lower central incisor.

**Inter-arch assessment**

Intermaxillary tooth size discrepancies can be assessed using ABI. For a correct anterior occlusion, Bolton has recommended the ABI of 77.2 ± 1.65%. In our study, the ABI for the whole samples was 79.3 ±3.94% in which is slightly higher than in the Bolton’s sample. There are studies which found that their ABI were different from the Bolton’s norms [18, 19, 20]. Paredes *et al.* (2006) suggested a different norm for their Spanish population as their result showed significant differences between the Spanish’s and Bolton’s values [18]. Result from this study is in agreement with a study done in Iran by Fattahi *et al.* (2006) which had similar number of samples (n=200) [15]. Their ABI was 79.01%. Another study done in Pakistan by Batool *et al.* (2008) also found that their ABI was 79.3% [20]. Recently, a Malaysian study reported that their Malaysian ABI’s value was similar to the Bolton’s value. This contradiction in our finding may be due to the smaller number of samples compared to those recruited by the previous study [15]. However, when looking at the individual ethnic ABI values as presented in the Malaysian study, our ABI was closely related to the Malay ABI of 78.93 ± 2.68 as compared to the Malaysian Chinese and Indian values. [21] This similar findings could be reflected by the fact that the majority of people who attended our clinic in UKM were Malay.

The difference of ABI in the 4 types of malocclusion are shown in these few studies. Class III has been shown to have greater anterior tooth discrepancies than the other 3 malocclusion groups [3, 9, 10]. In Brazil, Araujo and Souki (2003) also found that the mean anterior tooth size discrepancy for Class III subjects was significantly greater than that for Class I and Class II malocclusion [11]. However in our study, by using Anterior Bolton Index (ABI), we found that Class II division 2 had the highest ABI with a percentage of 80.33 ±4.06. However, no statistically significant differences were found when compared to the other 3 malocclusions (p>0.05). Our findings different from the Brazilian’s study maybe because of the differences in the classification used. They classified their subjects based on skeletal pattern. This study used incisor’s classification instead of the skeletal pattern’s classification thus making the number of samples for Class II doubled.

Similarly, Crosby and Alexander (1989) compared the tooth size ratios among different malocclusion groups, as in our study [4]. They found that there were no significant differences among Class I, Class II division 1, Class II division 2, and Class III groups. In Japanese orthodontic population as studied by Endo 2008, no significant inter-arch tooth size discrepancies were noted between the malocclusion groups [12]. Akyalc *et al.* (2006) identified only the skeletal Class I and measured the tooth size discrepancies in all malocclusion groups. The result showed no significant difference in Class I, II or III malocclusions [22]. Results from these two studies also support this finding [11, 23].

**CONCLUSION**

This study found that Class II division 1 malocclusion had the largest anterior mesio-distal tooth size for both maxillary and mandibular teeth except for the lower central incisor. Class III individuals had the smallest mandibular anterior teeth compared to other malocclusion groups. The Anterior Bolton Index (ABI) for Class II division 2 was the highest among all malocclusion groups. However, there were no significant differences of Anterior Bolton Index among the 4 different types of malocclusion group.
ACKNOWLEDGEMENT

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REFERENCES


Intracranial Germinoma – A Case Report

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ABSTRACT

Intracranial germinomas belong to the class of germ cell tumors which are relatively rare intracranial tumors. Early recognition of this neoplasm is vital as germinomas are highly radiosensitive and effective/early radiation therapy can result in relatively favourable overall prognosis. In this article we describe a 19 years old man who presented with pituitary tumor in the suprasellar region for which transsphenoidal decompression and biopsy was done. The histopathological examination confirmed it to be germinoma and he underwent craniospinal radiotherapy.

Keywords: Germinoma, germ cell tumor, radiotherapy

INTRODUCTION

Intracranial germ cell tumors are broadly classified into germinomas and nongerminatous tumors. Germinomas are being the commoner type with peak incidence in children and adolescents. Intracranial germinomas occur mainly in the pineal and suprasellar regions.[1] Less common sites include thalamus, basal ganglia, ventricular system, cerebellum, frontal lobes and septum pellucidum. The clinical presentation depends upon the tumor location and size and it mainly includes endocrine abnormalities, visual field defects and signs of increased intracranial pressure.[2] The diagnosis of an intracranial germ cell tumor usually requires imaging and histological confirmation. Surgery is indicated to obtain a tissue specimen for diagnosis. Intracranial germinoma has relatively good prognosis when treated with radiation therapy.[1, 2, 3].

CASE REPORT

A 19 years old man presented with progressive visual loss, recurrent episodes of head ache associated with vomiting over a period of several months. He also complained of generalized lethargy and loss of weight. He had no history of fever, seizures or trauma. On examination his vital signs were stable. He had bitemporal hemianopia with no other neurological deficits. His endocrine work up demonstrated panhypopituitarism and was subsequently placed on hydrocortisone, testosterone, thyroxine and desmopressin. MRI scan of brain revealed an enhancing lesion in the suprasellar region compressing the optic chiasma. An endoscopic transsphenoidal biopsy was done. Intraoperatively, erosion in the sella turcica floor was noted. Histopathology was consistent with germinoma. Serum tumor markers, alpha fetoprotein, beta human chorionic gonadotropin, cancer antigen, prostatic specific antigen and carcinoembryonic antigen all were normal. His ultrasound scan of the abdomen revealed no organomegaly. He was then referred to an oncologist and he underwent 28 cycles of craniospinal radiotherapy. During follow up his vision remained the same with no further deterioration of symptoms. He was lost to follow up after radiotherapy.

DISCUSSION

Primary intracranial germ cell tumors are rare central nervous system neoplasms. Germinomas are the most common accounting for 50-70 % of all germ cell tumors.[1] Most germ cell tumors occur before the second decade. Males are two times more likely than females to develop this tumor.[2] Approximately 95% of the primary germ cell neoplasm’s are found in the midline, in the pineal and suprachiasmatic region. The pineal region is the most common site for an intracranial germinoma compared to suprasellar region by a ratio of 2:1.[2, 3] Germ cell tumors will also occur in other sites including thalamus, basal ganglia region and fourth ventricle.

Clinical presentation of germ cell tumors depended on the location of the tumor in the central nervous system, the size of the lesion and age of the patient.[4, 5] Our case report highlights the unusual presentation in our patient, a 19 years old man with progressive visual deficits and symptoms of increased intracranial pressure confirmed to be having primary suprasellar germinoma. Suprasellar germinomas are observed more often in females and are the site

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of approximately 30% of intracranial germ cell tumors.

Germ cell tumors in the pineal region most commonly present with signs of increased intracranial pressure due to hydrocephalus, visual disturbances, pyramidal tract signs and ataxia. Symptoms such as nausea, vomiting and visual complaints can lead to an early diagnosis. The most common presenting symptoms for patients with suprasellar germ cell tumors are hypothalamic pituitary abnormalities such as diabetes insipidus, growth hormone deficiency and precocious puberty. Patients with isolated endocrine abnormalities are often diagnosed later. Patients with suprasellar germinoma rarely present with signs of increased intracranial pressure. Suprasellar germinomas are considered to have a poorer prognosis compared to those lesions arising in the pineal region. Germinomas can disseminate the neuroaxis at any time in course of the illness. The differential diagnosis of an intracranial germinoma includes craniopharyngioma, pituitary macro adenoma, metastatic cancer, malignant glioma, nongerminatous germ cell tumor and Langerhans cell histiocytosis.

MRI with gadolinium is the diagnostic test of choice. It shows tumor size, vascularity, homogeneity and the relationship of the tumor to the surrounding structures. Germ cell tumors are relatively isointense to normal white matter on T2-weighted images and enhance with gadolinium. Calcification is likely to be seen in suprasellar and pineal region germinomas. CSF dissemination of primary intracranial germinoma throughout the ventricular system and subarachnoid space is common. Therefore before any surgical intervention, MRI of the entire spine is essential for the detection of metastasis.

The presence or absence of specific tumor markers produced and secreted by tumor cells has been an extremely important adjuvant in the diagnosis of germ cell tumor. Serum and cerebrospinal fluid tumor markers i.e. alpha fetoprotein and beta human chorionic gonadotropin may be helpful. A pure germinoma is usually not associated with elevation of these markers. The presence of elevated beta human chorionic gonadotropin (HCG) in patients with germinoma may correlate with a less favourable prognosis.

In the majority of clinical situations biopsy of the intracranial tumor is required for a specific diagnosis. Endoscopic biopsy of the marker negative germ cell tumors is a safe and reliable method of establishing a diagnosis of germinoma. Intracranial germ cell tumors encompass a variety of histological subtypes including germinomas and nongerminomatous tumors. Nongerminomatous tumors include highly malignant tumors such as embryonal carcinoma, choriocarcinoma, teratomas, which have extremely poor prognosis. The clinical manifestations, radiological characteristics and immunohistochemical evaluation of these tumors are similar to germinoma. Therefore accurate initial histological diagnosis and staging are very crucial to plan appropriate therapy since their treatment responses and prognosis differ considerably. Germinomas are extremely radiosensitive, allowing the successful treatment without surgical debulking. Thus surgery is required in the majority of patients for diagnosis alone. The role of extensive surgery is debatable. Radiation therapy has been the main modality of treatment for primary intra cranial germinoma. Whole brain irradiation may result in neurocognitive and endocrine sequelae. The rationale for the use of chemotherapy has been either to improve survival in these patients with disseminated disease or reduce sequelae, by limiting the amount of radiation in patients with localized disease. Chemotherapy has been of greatest value in nongerminatous malignant germ cell tumor.

CONCLUSION

Germinomas are rare intracranial neoplasms which pose a challenge to clinician because of its variable clinical presentation with peak incidence in children and young adults. The diagnosis of these neoplasm requires imaging and histological confirmation. We describe this case in order to highlight the fact that early diagnosis of this rare locally destructive neoplasm is vital as these tumors are readily curable with radiation therapy alone or in combination with chemotherapy.

REFERENCES


Death from Malaria Infection in a Military Personnel After a Peace Keeping Mission

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ABSTRACT
Military personnel who are deployed for peace-keeping missions are exposed to many hazards, including infectious diseases. One of the most common and fatal infectious disease is Malaria. Although well controlled in Malaysia, this deadly disease is still widely endemic in many other countries especially Africa. We would like to report the case of a military personnel who was infected with Malaria during a peace-keeping mission in Sudan and subsequently died after returning home. We hope that by reporting this case in depth, strategic actions can be taken to avoid similar unfortunate events in future.

Keywords: Malaria, screening, detection, Peace-Keeping mission, military personnel, Malaysia

INTRODUCTION
Malaria is a very common communicable infectious disease worldwide. In fact, approximately half of the world’s population is at risk of Malaria infection and most cases occur in the Sub-African Continent where an estimated 247 million cases have been reported with nearly one million deaths.[1]

Many developed and developing countries of the world from North America, Europe, Middle East, Asia, South Pacific Region and South East Asia including Malaysia (under the mandate of United Nations) send their military troops for peace-keeping missions in Sub-African Continent countries. Military missions to these countries in conflict expose military personnel to a variety of hazards which may result in significant morbidity and mortality. There have been several reports of military personnel from the Unites States as well as Europe who were infected with Malaria in the Sub-African Continent, resulting in significant morbidity and mortality. Ciminera & Brundage reported a total of 423 cases of Malaria, which involved their military personnel from 2003 to 2005 during United States missions to countries which included the Sub-African Continent. Plasmodium vivax and Plasmodium falciparum infection contributed 80% of the reported cases.[2]

Malaysia has deployed military forces for peace keeping missions under the United Missions since 1960’s. These missions have been to countries such as Bosnia-Herzegovina, Cambodia, Southern Philippines, Timor Leste, Southern Lebanon, Afghanistan and Sub-African Continent’s countries like the Republic of Congo, Somalia, Ethiopia, Western Sahara and Southern Sudan. The Malaysian Armed Forces implements a stringent medical check-up in accordance to the United Nations Health Standard requirements, including post mission malaria screening upon returning from malaria endemic areas. Prophylaxis for malaria is a must for military personnel returning home from malaria endemic areas. In spite of this, there have been cases of Malaria infection among military personnel of the Malaysian Armed Forces during and post-missions, some resulting in deaths.

In this paper, we would like to report the case of a military personnel who died from complications of mixed Malaria infection after returning home from a mission in Southern Sudan, Africa. The aims are: (1) to highlight Malaria infection as a significant cause of morbidity and mortality during military missions, and (2) make several recommendations to improve post mission detection and management of Malaria infection among military personnel.

A CASE REPORT
This case involved a military personnel from Malaysia who was deployed for a United Nation Peace Keeping mission in Sudan. He completed a pre-deployment United Nation Health Standard clearance in Malaysia and was prescribed Malaria prophylaxis (Tablet Mefloquine 250mg weekly). He had no history of travel to other highly endemic Malaria areas. His tour of duty was uneventful until his arrival in Southern Sudan a year later, where he developed acute

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appendicitis and was admitted to a military field hospital. He underwent an appendicectomy, and was admitted for wound recovery in the same room with another patient, an African military personnel who was being treated for Malaria. After discharge from the hospital (four days post-operation), he remained in transit in Southern Sudan to complete his out-processing documentation, and departed for home two weeks' later. He arrived in Malaysia the next day, and completed his post-mission medical screening examination at a military hospital. A Rapid Diagnostic Test (RDT) investigation for Malaria was conducted. As the RDT was found to be non-reactive, the personnel was not subjected to any post-mission quarantine.

A week later, the military personnel was brought by his wife to a military hospital in an acute confused state. He had developed high intermittent fever associated with chills and rigor, which began the day after arriving back to Malaysia. He was admitted to the hospital, and a Blood Film Malaria Parasite (BFMP) was done on admission. It was found to be positive for *Plasmodium falciparum*. Further investigations revealed Malaria complications of acute renal failure, liver derangement, thrombocytopenia and cerebral malaria. He was immediately started on Intravenous Quinine and Tablet Primaquine, which are standard regimes of anti-malaria drugs. All the above complications were also treated accordingly, but his condition worsened and the patient was transferred to a government hospital for respiratory support in the Intensive Care Unit. A repeated BFMP showed the presence of *Plasmodium malariae* infection as well. Intravenous Artersunate and Tablet Doxycycline were added to his regime of treatment. Despite that, the patient’s condition deteriorated and he succumbed to the infection. The cause of death was multi-organ failure secondary to severe mixed Malaria infection.

**DISCUSSION**

The military personnel died of severe mixed *Plasmodium falciparum* and *Plasmodium malariae* infection, which led to multi-organ failure. Aggressive treatment with standard regimes of anti-malaria drugs failed to combat the infection. The clinical findings were consistent with complications secondary to *Plasmodium falciparum* infection. These complications such as altered consciousness, acute respiratory arrest syndrome, renal and liver failure, and circulatory collapse were poor prognostic markers. The BFMP also showed 110,000 mature trophozoites and schizonts (parasitaemia > 10,000). These indicators are poor prognostic markers for survival.\(^{[1]}\)

**Source of the Malaria infection**

There are many possibilities of how this personnel was infected with mixed Malaria parasites. From the epidemiological tracing conducted, he was infected when hospitalised following his appendicectomy. Post-appendicectomy he was warded together with a confirmed malaria patient, who was probably the source of infection.

**Non-compliance or Resistance to Malaria Prophylaxis – Tablet Mefloquine**

Military personnel posted to Malaria endemic areas are required to take Tablet Mefloquine weekly during their missions and to continue doing so 4-weeks post-missions. However; it is difficult to determine whether this military personnel was compliant to the required Malaria prophylaxis regime. Although Tablet Mefloquine was prescribed, there was no record of him taking the medication. As he was already in a state of altered consciousness when he was admitted in the military hospital in Malaysia, serum for Mefloquine level was not measured. Therefore there was no evidence of the military personnel ever taking Mefloquine.

Resistance to Mefloquine may also be a factor in this case. In a drug sensitivity study using in-vivo testing, it was found that 13.4% of the subjects showed resistance to Mefloquine.\(^{[1]}\) In this case, the personnel could have also been infected during his stay in Sudan in the previous year because longer incubation periods may be likely in individuals who are semi-immune, or in those taking ineffective anti-malaria prophylaxis.

**BFMP as the screening method of choice for post-mission detection of Malaria infection**

The BFMP method for direct laboratory diagnosis of Malaria remains the gold standard in diagnosing Malaria.\(^{[4]}\) There are two kind of blood films; thick and thin. The thick film is used for quick identification and quantification of parasites, and the thin film is used for differentiation of parasite species. In this case, the post-mission screening for Malaria infection was done using RDT (which was found to be non-reactive), where as the BFMP was done 8 days after the military personnel had developed signs and symptoms of Malaria infection. Cornelio documented that indirect diagnostic tests for Malaria (such as RDT) may not be diagnostic of acute Malaria infection because it does not differentiate the different Malaria species, and RDT only detects antibodies due to past malaria infections.\(^{[4]}\) Monsef Rabhi recently published a study which compared the effectiveness of a RDT (known as Now(R), Malaria) to BFMP in diagnosing Malaria among 105 blood samples of serviceman deployed in an endemic area in the Republic of Congo.\(^{[8]}\) The findings showed that the RDT had a sensitivity of 77% and a specificity of 73%. However while the positive predictive value (PPV) was high at 96%, the negative predictive value (NPV) was very low at only 27%.
Therefore the author concluded that due to its low NPV, the use of RDT alone is insufficient for the clinical diagnosis of malaria infections in populations with very high prevalence of Falciparum Malaria. This is because a negative result with the RDT is insufficient to rule out the possibility of Malaria infection. Therefore in highly endemic areas, it is essential to use the BFMP as the diagnostic tool for Malaria infection.

**CONCLUSION AND RECOMMENDATIONS**

Based on this case, we would like to propose an approach of 6–components in preventing infectious diseases during military deployment. This 6–component approach should include comprehensive pre-deployment preparation, health education and promotion, personal protective measures, vaccines, chemoprophylaxis, and medical surveillance. It is essential that thorough medical check-ups be conducted, with preferably the BFMP as the compulsory screening investigation for all military personnel returning to Malaysia from Malaria endemic areas. All Armed Forces Laboratory Technicians should be competent in performing BFMP procedures. Any fever arising post-missions should be investigated in-depth for Malaria infection and other infectious diseases as well. This should be explained during post-debriefing missions to the military personnel involved. Military personnel returning from overseas mission should be advised to report immediately to the nearest Armed Forces Medical Centre or government medical facility if they develop any fever. Quarantine procedures should be enforced strictly to all personnel returning from endemic areas.

Compliance to Malaria prophylaxis among all military personnel should also be enforced. The given malaria chemo-prophylaxis must be strictly adhered to based on the current protocols and regulations. The intake of the drugs should be clearly recorded for each military personnel. Briefing and debriefing for pre-and-post military missions should clearly state the hazards and risks of infectious diseases, including Malaria. This is to ensure that all military personnel understand and comply with the chemoprophylaxis given. When deployed to malaria endemic areas, military personnel should also be provided with personal protective measures such as mosquito nettings and repellents, and be taught on how to use these measures correctly.

Malaria infection among military personnel is preventable, provided that the recommended primary prevention approaches are enforced. These improvements need to be made in the management approach of military personnel sent overseas for peace-keeping missions. The important lesson learnt is that we can avoid mortality due to Malaria if all military personnel tasked overseas are conscious and adhere strictly to the recommended policies and procedures.

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**REFERENCES**


A Case of Clinical Vampirism in Asia

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ABSTRACT
Clinical vampirism in psychiatric practice is very rare and usually associated with schizophrenia, antisocial personality disorder or paraphilia. An Asian case of clinical vampirism is described. It is about a 24-year-old Malay female, paramedic student, who craved for blood since childhood. She injured her sister and herself so that she could access and drink blood. There was no associated psychosis or medical problems. The craving for blood may represent her underlying craving for parental love and attention.

Keywords: Schizophrenia, vampire, psychosis, Malaysia, blood

INTRODUCTION
Vampires are mythological beings who survive by feeding on the blood of living creatures. The vampire myth is widespread in various cultures including those in Asian countries. Some authors have reviewed the possible link between the vampire myth and medical conditions such as porphyria [1]. Clinical vampirism in psychiatric practice is extremely rare, and usually associated with schizophrenia, antisocial personality disorder or paraphilia [2]. An Asian case of female clinical vampirism is described in this article.

THE CASE
A 24-year old female Malaysian started craving and ingesting human blood at the age of five years old. She would injure her sister by pushing or scratching her while playing, making it look accidental, and then licked the blood from the wounds (2-3 times per week). At the age of eight, she stopped taking blood from her sister as she refused to play with her anymore. Following this, she would lick blood from any of her own wounds that were sustained accidently (2-3 times per month). She enjoyed the taste of blood, likening it to ‘candy.’

Her craving for blood became more intense when she first had her menses. After a period of unsuccessful attempting to inhibit her craving, she once bit her sister’s finger in the middle of the night for blood. Later as she was afraid that she would hurt others, she decided to bite her own tongue or lip for blood (1-2 times per week). This continued until the age of 18 when she saw a documentary on discovery channel on vampirism; a boy who ingested his blood using a syringe. Since then, she also syringed blood directly from her brachial and popliteal veins, and drank the blood from the syringe (about 15 cc fortnightly). She enjoyed the smooth texture, metallic and bitter sweet taste of her blood and would have anxiety symptoms (sweating, palpitation, tremor, restlessness, body weakness) if she was deprived of blood. The symptoms would only disappear when she ingested more blood or distracted herself with activities. When she was attending a paramedic course at the age of 23, she would prick herself 3-4 times a week for blood with a lancet (besides the 15 cc of syringed blood every two weeks). One day, while she was attending a class on using glucometer, she had an intense craving for blood. At that time, in an attempt to stop her habit, she was already deprived of blood for about three weeks – the longest period of ‘abstinence’. During the intense craving, she had repeated thoughts such as, “I want blood now!” and “I must get to the toilet with a lancet to get blood!” She felt very sick, and was subsequently brought to medical attention in the college. She confided her unusual craving to her supervisor and was subsequently referred for psychiatric assessment.

Besides her sister earlier, she had never harmed anyone or any animals for blood. There was no criminal record. She seemed to crave more for her own blood rather than others people’s blood. The cravings were usually triggered by the smell of blood and less whenever she was busy or tired. There were no depressive symptoms, substance abuse, hallucinations, delusional believes and erotic feeling associated with blood, or any symptoms suggestive of obsessive-compulsive spectrum disorders. She had photosensitivity causing skin rash and watery eyes since the age of sixteen. There was also prominent hair loss, and she had haematuria before twice.

There was no family history of mental illness, but there seemed to be a lot of anger towards her father, an army officer. She described her father with these words: “irresponsible,” “controlling,” “abusive,” “gambler,” and “womanizer.” At
the age of 4-5 (coinciding with the onset of blood ingestion), her father was frequently abusive towards her mother – he once kicked her mother during pregnancy resulting in miscarriage. Her onset of blood craving around this time could be due to her unconscious craving for a better relationship among family members – ‘blood’ here represents ‘family relationship.’ Her mother was a school teacher; she was never close to her parents and three other siblings. She yearned for a happy family and often thought, “Why my family is not like a family?! Everyone is in their own world and nobody communicates.” She always felt good whenever she was needed (e.g. doing voluntary work and paramedic service). Birth and developmental history were uneventful. She claimed that she had bi-sexual orientation, but was not sexually active, and there was no history of sexual abuse.

She was underweight (BMI = 17) and appeared pale on physical examination. There was hepatosplenomegaly (2 cm), but ultrasonography of abdomen was normal. Mental state examination showed that she was guarded and irritable whenever she was asked about her parents. Full blood count, renal profile, liver function, thyroid function, antinuclear antibody, erythrocyte sedimentation rate, urine porpyrins, porphobilinogen, uroporphobilinogen, delta-aminolaevulinic acid (δ-ALA), Hepatitis B & V, and HIV tests were all normal. She was referred to the haematology team for an opinion but was discharged with no abnormality.

A Diagnostic & Statistical Manual of Mental Disorders (DSM-IV) diagnosis of Impulse Control Disorders Not Elsewhere Classified was made. Attempt to explore more on her relationship with her parents was met with resistance. No medication was started. After three clinic appointments, and with the help of supportive counseling and some distraction techniques, she was able to gradually stop ingesting blood. Without blood ingestion, there were no anxiety symptoms; but occasional longing for blood was still present. This was usually triggered by the smell of chocolate, instead of blood as in previous episodes – could be symbolic representation of craving for intimate relationship. Upon reflection, she admitted that her craving for blood usually coincided with moments when she felt lonely. She completed her paramedic training, but was not allowed to work at the medical centre that was associated with the college. She managed to move on with life and found a job which is not related to healthcare. She also engaged in some voluntary service and was happy as she felt appreciated, a feeling that she admitted yearning from her parents.

DISCUSSION
Clinical vampirism associated with schizophrenia has been reported in America [1] Sweden, France, and United Kingdom [2]. This is the first reported case of clinical vampirism in an Asian country.

Prins has classified clinical vampirism into four groups [3]; 1. Complete vampirism which involves blood ingestion, necrophilia (sexual arousal stimulated by a dead body) and necrosadism (mutilation of corpse for sexual arousal), 2. Vampirism without ingestion of blood, but with sexual satisfaction from touching or having sexual intercourse with a cadaver, 3. Vampiristic activity without death being involved, and 4. Auto-vampirism which is further subdivided into a) self-induced bleeding with blood ingestion, b) voluntary bleeding with reingestion of blood, and c) auto-haemotetishism.

The case in this report is considered predominantly under the fourth type i.e. auto-vampirism, and it is not associated with schizophrenia, antisocial personality or paraphilia. It is postulated that her craving for her own blood is actually craving for a better relationship with her family members - “blood” in an Asian culture often represents “family relationship.” This is supported by the following evidence in history: 1. The lack of supportive family relationship since childhood (especially from the absent father), 2. The onset of blood craving (age 4-5) that coincided with her father’s frequent abusive behavior towards the mother (e.g. kicking her mother during pregnancy), 3. The worsening of blood craving (from biting her tongue/lip to syringing of blood) during adolescent years – often a period of emotional turbulence whereby extra family care is often needed. It was also during this period that she was away from home and staying in a boarding school, 4. The craving for blood that was triggered by the smell of chocolate which is often a symbolic representation of intimate relationship, 5. The preference for activities that made her feel needed or appreciated, e.g. voluntary and paramedic service – a feeling that she missed from her family. Her vampirism is indeed a ‘relationship vampirism,’ an ‘Asian vampirism.’

CONCLUSION
Clinical vampirism in psychiatric practice is also found in Asia and may not necessary be associated with schizophrenia, antisocial personality disorder or paraphilia. Consistent with the Asian culture of emphasis on family cohesiveness, this could be a case of clinical vampirism with underlying craving for parental love and family attention.

REFERENCES


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