Depression and Quality of Life among Patients with Hematological Cancer in a Malaysian Hospital

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ABSTRACT

Objective: To determine the prevalence of major depressive disorder (MDD) in hematological cancer patients and to investigate MDD with quality of life. **Methods:** The research, which uses a cross sectional design, has been carried out at Ampang Hospital, Kuala Lumpur. The hospital is a tertiary referral center for cancer cases that include non-Hodgkin lymphoma, acute myelogenous leukemia, acute lymphoblastic leukemia, Hodgkin lymphoma and other hematological cancers. In total, 105 patients with hematological malignancies were included in the study. This study employed the MINI International Neuropsychiatric Interview for diagnosis of MDD, the Patient Health Questionnaire (PHQ-9) for symptom severity of depression and the European Organisation for Research and Treatment of Cancer Quality Of Life questionnaire (EORTC QLQ-C30) to assess the quality of life of the respondents. **Result:** The response rate was 83.3%. The prevalence of MDD was 24.8% (n=26) with the majority of cases classified as moderately severe depression (38.5%). About 92.3% (n=24) of depressed hematological cancer patients were diagnosed with a current episode of MDD. The depressed patients also had significantly reduced quality of life in physical, role, emotional, cognitive and social domains ($p<0.05$). They also had significantly more symptoms of fatigue, nausea and vomiting, dyspnea, insomnia, appetite loss, constipation and diarrhea in addition to having financial difficulties and poor global health statuses ($p<0.05$). **Conclusion:** The prevalence of depression among the hematological cancer patients was high and the depressed patients had reduced qualities of life. Special attention in psychotherapy would help to improve both depression level and the quality of life in these patients.

Keywords: Major depressive disorder, quality of life, hematological cancer

INTRODUCTION

Patients diagnosed with cancer not only suffer from the disease itself but they also have a higher tendency to develop psychiatric disorders. Articles have been published on psychiatric disorders of hematological cancer patients and their qualities of life in various western countries.[1-5] However, to the best of our knowledge, the research remains minimal in eastern countries, and there is no published research of such an article in Malaysia.

Hematological cancers such as leukemia, lymphoma and myeloma that exist in different forms[6] have serious emotional and physical impacts on patients.[1-2, 4-5] In 2006, a total of 21,773 patients in peninsular Malaysia were diagnosed with cancer. The hematological cancer lymphoma (3.2%) was one of the ten most frequent cancers in peninsular Malaysia. Lymphoma (4.2%) and leukemia (3.6%) were the 8th and 9th most frequent cancers among males in Malaysia. Among women, lymphoma (2.4%) was the 10th most frequent cancer.[7]

Psychiatric disorders such as depression are the most prevalent mental health problems that can be easily diagnosed in cancer patients.[1] There are nine symptoms of major depressive disorder (MDD) according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) classification. The symptoms include depressed mood, loss of interest, weight loss or weight gain, insomnia, psychomotor agitation, fatigue, worthless feelings, poor concentration and frequent thoughts of death. The person must have at least five symptoms including depressed mood or loss of interest for a two-week period of time to be diagnosed with MDD.[8]

The aim of the study was to determine the prevalence of MDD in the hematological cancer patients in Ampang Hospital and to investigate MDD with quality of life in these patients.

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METHODOLOGY

A hospital-based cross-sectional study was conducted in the hematological wards at Ampang Hospital Kuala Lumpur, Malaysia between May 2009 and December 2009. The hospital is a tertiary referral center for hematological malignancies, which include cases such as non-Hodgkin lymphoma, acute myelogenous leukemia, acute lymphoblastic leukemia, Hodgkin lymphoma and other types of hematological cancers. Sample size estimation calculated using the single proportion formula, $n = Z^2 P (1-P) / d^2$.[9] Based on the formula Z denoted for level of confidence or number of standard error away from the mean.[9] The Z value was set at 1.96 with 95% confidence interval for the result. Symbol P in the formula is the expected or anticipated proportion or prevalence.[9] Study done by Prieto, J *et al.*, found the proportion of major depressive disorder in hematological cancer patients was 9.0%[1] hence, P equals to 0.09 was determined. Symbol d in the formula is denoted for precision or measures for total percentage points of the error that will be tolerated on the either side of P. In short, symbol d is percentage points on either side of P.[9] The d value was set at 5% or d=0.05 in the study. The formula substituted with these values, $n = 1.96^2\ 0.09 (1-0.09) / 0.05^2$ and the sample size (n) = 126 hematological cancer patients was determined. The Ethical Committees of the Ministry of Health and the Faculty of Medicine and Health Sciences, University Putra Malaysia, approved the study.

All patients aged 15 years and older who were consecutively admitted to hematological wards, diagnosed with hematological cancer, able to converse in any one of these languages: English, Malay, Mandarin or Tamil, conscious and able to engage in an interview and give consent to participate were included in the study. Patient information such as disease status, medication history and socio-demographic profile were obtained from the participants and confirmed with medical records.

Many previous studies used various sets of questionnaires to screen for psychiatric disorders such as depression;[5] however, only few studies had implemented a strict systematic clinical interview based on DSM-IV criteria to make such diagnoses in hematological cancer patients.[10] In the present study, module A of the MINI International Neuropsychiatric Interview (MINI), version 6.0.0, questionnaire[11] was used to diagnose MDD. The questionnaire was developed according to DSM-IV and International Classification of Diseases (ICD-10) criteria and has 96% sensitivity and 88% specificity.[12] The module consists of five questions with multiple sub-questions to be answered either "Yes" or "No" within the time frame of the past two weeks or/and in a past episode.[11] The interviewer was trained to use the MINI by senior psychiatrists who had experience and were certified in using the MINI.

The Patient Health Questionnaire, PHQ-9 questionnaire, was used to measure the severity of depression among patients with MDD. The questionnaire is self-rated and was developed for medically ill patients based on DSM-IV criteria. It is comprised of nine questions and it is rated according to a two week time frame of symptoms on a scale from 0 to 3: 0 = not at all; 1 = several days; 2 = more than half the days; 3 = nearly every day. The final question is rated for difficulties with regards to problems, i.e., 1 = not difficult at all; 2 = somewhat difficult; 3 = very difficult; 4 = extremely difficult. The PHQ 9 scores were computed and classified according to symptoms scores as follows: (0-9) = normal to mild symptoms, (10-14) = moderate symptoms, (15-19) = moderately severe symptoms and (more than 20) = severe symptoms. The questionnaire has good internal reliability and validity.[13]

This study also used a validated[14-15] European Organisation for Research and Treatment of Cancer Quality Of Life (EORTC QLQ-C30) questionnaire to measure quality of life among the participants. The questionnaire is comprised of five functioning scales, three symptoms scales, a global health status scale and six single item scales. The functioning scale is comprised of physical functioning, role functioning, cognitive functioning, emotional functioning and social functioning. Fatigue, pain and nausea/vomiting are included in the symptom scales. Finally, the single item scale is used to measure dyspnea, insomnia, appetite loss, constipation, diarrhea and financial difficulties. The EORTC QLQ-C30 questionnaire consists of 30 questions with each set of questions belonging to each scale as mentioned above. Every question has four-point scales ranging from 1 to 4 with "not at all", "a little", "quite a bit" and "very much" as answer choices. The last two items, numbers 29 and 30, measure global health status with a seven-point numbered scale ranging from 1 to 7 ranging from "very poor" to "excellent"[14]. The raw score for each scale was calculated. Then a linear transformation of a 0-100 score was computed for each category in the scale. Thus the range of scores for each scale varies from 0 to 100. The scoring procedure was performed according to the scoring manual of EORTC QLQ-C30. A higher score is better on the functioning scale and indicates better global health status. Conversely, a higher score for the symptom scale and single item scale indicate more symptoms.[16]

All data were analyzed using Statistical Package for Social Sciences (SPSS) software version 17.0. Descriptive statistics including mean, percentages and ranges were used to describe the sample characteristics. Chi squared tests and fisher exact tests were used to find significant difference between the presence and absence of MDD and socio-demographic or clinical variables (i.e., gender, time since diagnosis, ethnicity, and religion, marital status, children status, highest level of formal education, highest certificate obtained and occupational status working sector and monthly income). T-tests were applied to gender and age of respondents to determine if there is a significant difference

between the two variables. A Mann-Whitney U test, one tailed test for non-parametric data was performed to make comparison of depressed and non-depressed hematological cancer patients with their quality of life. The significant value was set at p<0.05.

RESULTS

A total of 126 patients were approached in hematological wards during the study period. Of these patients, 6 patients refused to participate, 13 patients had non-hematological cancer diagnoses and 2 patients were unable to understand the questionnaires. Thus, the study had a response rate of 83.3%. Table 1 shows the characteristics of the respondents. Most of the respondents with hematological cancer (26.7%) fell into the 21-30 years age group followed by the 41-50 years age group (21.9%). The mean age of the participants was 40.4 years (95% CI= 37.4, 43.5). There was a significant difference (t = 1.991, df = 103, p=0.049) between the mean age of men (43.6 years, 95% CI = 39.0, 48.2) and that of women (37.5 years, 95% CI = 33.4, 41.6) who participated in this study.

Table 1.   Socio-demographic characteristics of respondents

Characteristics	Number	Percentage (%)	N
Age			
15-20	8	7.6	
21-30	28	26.7	
31-40	16	15.2	
41-50	23	21.9	
51-60	16	15.2	
61-70	11	10.5	
>70	3	2.9	105
Gender			
Female	55	52.4	
Male	50	47.6	105
Ethnicity			
Malay	63	60.0	
Chinese	26	24.8	
Indian	14	13.3	
Others	2	1.9	105
Religion			
Muslim	64	61.0	
Buddhist	20	19.0	
Hindu	12	11.4	
Christian	6	5.7	
Others	2	1.9	
No religion	1	1.0	105
Marital status			
Single	34	32.4	
Married	70	66.7	
Divorced	1	1.0	105
Children			
Yes	59	56.2	
No	46	43.8	105

Continuation
Table 1.   Socio-demographic characteristics of respondents

Characteristics	Number	Percentage (%)	N
Highest level of formal education			
Primary	15	14.3	
Secondary	57	54.3	
College/University	32	30.5	
No education	1	1.0	105
Highest certificate			
Primary School Evaluation Test (PSET)	12	11.4	
Lower Certificate of Education (LCE)	18	17.1	
Malaysian Certificate of Education (MCE)	37	35.2	
Malaysian Higher School Certificate (HSE)	3	2.9	
Certificate/Diploma	23	21.9	
Degree	10	9.5	
Master	1	1	
No education	1	1	105
Occupation status			
Working	35	33.3	
Not working	56	53.3	
House wife	8	7.6	
Pensioner	6	5.7	105
Working sector			
Government	12	12.2	
Non government	18	18.4	
Self employment	5	5.1	
Not working	63	64.3	98
Total monthly income household (RM)			
0-3000	60	85.7	
3001-6000	7	10	
6001-9000	1	1.4	
>9001	2	2.9	70

In terms of ethnicity, there was preponderance of Malays (60%) followed by Chinese (24.8%). The Indians represented a small proportion of the study population (13.3%). The majority of subjects were Muslims (61%) followed by Buddhists (19%). Hindus accounted for 11.4% and Christians for 5.7%. The majority of patients with hematological cancer were married (66.7%). In terms of education attainment, more than half of the patients (54.3%) were educated up to the secondary level. Approximately 44.8% had received tertiary education (certificate/diploma: 21.9%, degree: 21.9% and masters degree: 1%), 11.4% had primary education and 1% had not received formal schooling. A majority of the respondents were not working (53.3%). Among the working respondents, 18.4% worked in the non-government sector, followed by 12.2% in the government sector and 5.1% were self-employed. As for total monthly household income, most of the respondents had total household incomes of less than RM 3000.00 (85.7%).

Table 2 shows the clinical characteristics of the respondents. Nearly half of the respondents were diagnosed with hematological cancer less than six months prior to the study (47.6%), 26.7% were diagnosed six months to one year earlier and 25.7% were diagnosed more than one year earlier. Among the respondents, 23.8% had a diagnosis of non-Hodgkin lymphoma, 22.9% had acute myelogenous leukemia, 14.3% had acute lymphoblastic leukemia, 10.5% had Hodgkin lymphoma, and 28.5% had other hematological cancers.

Table 2.   Clinical characteristic of respondents

Characteristics	Number	Percentage (%)	N
Time since diagnosis			
Less than 6 months	50	47.6	
6 months-1 year	28	26.7	
More than 1 year	27	25.7	105
Hematological cancer diagnosis			
Acute lymphoblastic leukemia	15	14.3	
Chronic lymphocytic leukemia	1	1	
Acute myelogenous leukemia	24	22.9	
Chronic myelogenous leukemia	2	1.9	
Acute promyelocytic leukemia	3	2.9	
Hairy cell leukemia	1	1	
MDS-RAEB* towards leukemia	1	1	
MDS-CMMOL** towards chronic leukemia	1	1	
Unclassified leukemia		1	1
Hodgkin lymphoma	11	10.5	
Non-Hodgkin lymphoma	25	23.8	
Peripheral-T-Cell lymphoma	1	1	
Natural Killer-T-Cell lymphoma	3	2.9	
Central nervous system-lymphoma	2	1.9	
Intravascular lymphoma	1	1	
Follicular transform lymphoma		1	1
Unclassified lymphoma	5	4.8	
Multiple myeloma	6	5.7	
Histiocytosis	1	1	105
Stage			
Stage I	0	0 %	
Stage II	3	2.9%	
Stage III	6	5.7%	
Stage IV	26	24.8%	
Blood cell count ≥ 100			
46	43.8%		
Blood cell count > 100	3	2.9%	
Others	21	19.9%	105
Received treatment			
Yes	104	99.0%	
No	1	1.0%	105
Treatment			
Chemotherapy	97	93.3%	
Others	7	6.7%	104

* Myelodysplastic syndrome- refractory anemia with excess blasts
** Myelodysplastic syndrome-chronic myelomonocytic leukemia

The majority of the respondents (93.3%) received chemotherapy and among them 1% had received chemotherapy and radiotherapy. The remaining (6.7%) respondents received other treatments, i.e., steroid (2%), supportive treatment (1%), transplant (1%) and other medication (2.9%).

Hematological cancer was classified according to stages I, II, III, IV and blood cell counts. Approximately a quarter (24.8%) of participants had stage IV hematological cancer, 5.7% had stage III, 2.9% had stage II, and none had stage I. The majority of respondents (43.8%) had blood cell counts ≤ 100, 2.9% had a blood cell count > 100 and 19.9% had other types of blood cell counts (3% had a high blood cell count, 2% had a low blood cell count, 2% had Ig G lambda, 1% had Ig G kappa and 11.9% had unspecified or without stage).

The prevalence of MDD in the hematological cancer patients was 24.8%. From the 105 respondents, 24.8% (n=26) were diagnosed with MDD. Of 26 respondents, 92.3% (n=24) were diagnosed with a current episode of MDD and 3.8% each were determined to have a current and a recurrent episode (n=1) and a current and a past episode (n=1). Among the respondents with MDD (Table 3), the majority of them had moderately severe depression (38.5%), followed by moderate depression (30.8%), normal to mild depression (19.2%) and severe depression (11.5%).

Table 3.   Severity of symptoms of depression in respondents with major depressive disorder (n=26)

Depression (PHQ-9)	Frequency	Percentage
Normal to mild	5	19.2%
Moderate	8	30.8%
Moderately severe	10	38.5%
severe	3	11.5%

Table 4.   Quality of life mean rank scores (EORTC QLQ-C30) between depressed and non-depressed hematological cancer patients (n=105)

	Non-depressed Mean rank	Depressed Mean Rank	z	p-value
Global health status/QoL	58.68	35.73	-3.378	**0.001
Physical functioning	57.36	39.75	-2.568	**0.005
Role functioning	56.82	41.40	-2.319	*0.010
Emotional functioning	60.82	29.25	-4.607	***0.000
Cognitive functioning	56.76	41.58	-2.261	*0.012
Social functioning	59.01	34.75	-3.585	***0.000
Fatigue	48.03	68.10	-2.94	**0.002
Nausea and vomiting	48.04	68.08	-3.142	**0.001
Pain	52.37	54.90	-0.379	0.353
Dyspnea	50.51	60.58	-1.725	*0.043
Insomnia	48.09	67.9	-3.133	**0.001
Appetite loss	49.49	63.65	-2.146	*0.016
Constipation	50.07	61.09	-1.816	*0.035
Diarrhea	50.03	62.04	-2.118	*0.017
Financial difficulties	46.98	71.29	-3.669	***0.000

*p<0.05; **p<0.01; ***p<0.001.

Table 4 shows the comparison of depressed and non-depressed hematological cancer patients with their quality of life mean rank scores. The quality of life domains include functioning domains such as physical, role, emotional, cognitive and social domains. Symptom domains include fatigue, (nausea and vomiting), pain, a global health status domain and six single-item domains such as dyspnea, insomnia, appetite loss, constipation, diarrhea and financial

difficulties. A Mann-Whitney U-test, one tailed test was performed to examine the level of significance at $p<0.05$, and the result showed that the depressed hematological cancer patients had significantly reduced physical ($p=0.005$), role ($p=0.01$), emotional ($p<0.001$), cognitive ($p=0.012$) and social functioning ($p<0.001$) compared to non-depressed patients. The depressed hematological cancer patients also had significantly more symptoms of fatigue ($p=0.002$), nausea and vomiting ($p=0.001$), dyspnea ($p=0.043$), Insomnia ($p=0.001$), appetite loss ($p=0.016$), constipation ($p=0.035$), diarrhea ($p=0.017$) and financial difficulties ($p<0.001$). They also had significantly poor global health statuses ($p=0.001$).

Additionally, this study found a slightly higher prevalence of MDD in male compared to female respondents at 53.8% and 46.2% respectively. Among the depressed respondents, there was a higher preponderance of Malays (53.8%), followed by Indians (23.1%), Chinese (19.2%), other ethnic groups (3.8%). There was a high proportion of depressed respondents who were married (69.2%), achieved an educational level of MCE or less (65.4%), were working (42.3%), had a household income of RM 1000 or less (60.0%) or had children (61.5%). However, no significant difference was found between depressed hematological cancer patients and gender, time since diagnosis, ethnicity, religion, marital status, children status, highest level of formal education, highest certificate obtained, occupational status, working sector or monthly income.

DISCUSSION

This report provides information about the prevalence of MDD among hematological cancer patients in a Malaysian tertiary referral centre for hematological cancer. The present study showed that the prevalence of MDD among Malaysian hospitalized hematological cancer patients was 24.8%. The prevalence found in this study was comparable with a study among cancer patients in hospital wards by Bukberg *et al.*, which found that the overall prevalence of MDD was 24.0%[17] and severity of MDD was 24.0%.[18] Of 24.8% respondents with MDD, more than one-tenth (11.5%) had severe MDD. However, the comparison of severity of depression among cancer patients is difficult because different studies use different severity scales.

Four main causes for depression among cancer patients were identified based on various studies. First, socio-demographic factors such as age[4], gender[2, 19] and education level[19] play an important role in depression. Clinical factors such as type of cancer[19] and its treatment,[19-22] severity of cancer, [21, 23] stage[22]and duration of illness[2] were also found to be related to depression. The third most important factors are psychosocial factors like physical,[4-5, 24] role,[4, 24] emotional,[5, 24] cognitive,[5, 22, 24] social functioning,[5, 24] global quality of life[5] and coping styles.[19, 25-26] Finally, clinical symptoms such as fatigue,[4, 23] pain,[4, 23] dyspnea,[4, 23] insomnia,[4, 23] appetite loss[4] and constipation[4] also contributed to the development of depression in cancer patients. If a psychiatric disorder is left untreated it will cause shorter survival rates[1, 5] suicidality,[27] poor quality of life[20, 22-23, 28] and increased lengths of stay in hospitals.[3]

In this study, there was a preponderance of male respondents with MDD (53.8%) compared to female respondents. This finding mirrors results from a previous study by Pandey *et al.* who found that male cancer patients were more depressed compared to female cancer patients.[29] However, our finding was in contrast with other studies, which found that women scored higher in depression and anxiety measures compared to men.[2, 19] The respondents of this study represent all three predominant ethnicities of the Malaysian population, and the proportion of each ethnicity was consistent with reported proportions in the national cancer registry in 2006.[7] Among the various ethnic groups in Malaysia, the prevalence of MDD was alarmingly high in the Malays (53.8%), followed by the Indians (23.1%), the Chinese (19.2%), and other ethnic groups (3.8%).

We also found that most of the depressed patients were married (69.2%) and had an education level of MCE or less (65.4%). The higher rates of MDD in the married respondents were in contrast with the study by Staci *et al.*, who found that the married patients were less depressed compared to the unmarried group.[30] The prevalence of MDD in respondents with low educational attainment was expected and similar to that in another study that found less educated patients were more depressed compared to others.[30] There was a high preponderance of respondents who were unemployed (42.3%) and had a household income less than or equal to RM 1000 (60.0%) who were diagnosed with MDD. This is consistent with a study that found that higher distress cancer patients were coming from lower income group.[31] Patients with children were found to be more depressed in the present study. However the comparison with other studies is difficult because limited research has intensively investigated this factor.

However, MDD diagnosis did not yield any significant difference with these certain clinical and socio-demographic factors. Similarly, other studies among the cancer patients also found there is no significant correlation between depression and socio-demographic profiles.[32] The reason for non-significant result might be due to inconsistent or unequal number of patients by their gender, time since diagnosis, ethnicity, religion, marital status, highest level of formal education, highest certificate obtained, occupational status, working sector and monthly income.

Analysis also showed that compared to non-depressed hematological cancer patients, the depressed hematological cancer patients had significantly reduced physical, role, emotional, cognitive and social functioning. They also had significantly more symptoms of fatigue, nausea and vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea

and financial difficulties. The poor quality of life associated with depressed hematological cancer patients in this study is consistent with the findings of the previous study. Pamuk *et al.* found that depression among hematological cancer patients had a negative effect on the global quality of life and level of functioning. Quality of life was negatively correlated with the physical, role, emotional, cognitive, social functioning and global quality of life scores.[5]

The possible explanation for this finding could be due to side effects of the treatments received by the respondents. In a study among hematological cancer patients regarding quality of life, it was found that patients who were under active treatment had reduced physical functioning, poor appetite and fatigue compared to patients in non-active treatment.[4] On the other hand, it is also known that the worsening of quality of life of hematological cancer patients before and after treatment in the context of their physical status, energy level and systemic symptomatology was associated with fluctuations in depression level. Thus, a marked increase of depression level also contributes to poor physical health status after intensive treatment.[2]

The significance of the study is to show that hematological cancer is a life threatening illness that is not only causes significant psychological disturbances, including MDD, but also has impact on quality of life. Thus, awareness, early recognition and appropriate interventions of MDD, both pharmacological and psychosocial, in an oncology setting should become part of a holistic approach in the management of cancer patients. Thus oncologists, primary care practitioners, and mental health professionals should be informed about the psychological consequences of a hematological cancer diagnosis, and further steps must be implemented to minimize the undiagnosed MDD that is left untreated among the patients.

From the treatment perspective, intervention should be started as soon as a diagnosis is revealed to the patient because the psychological distress after receiving the diagnosis is prolonged for at least a few months and does not decrease overtime in a clinical setting. The psychiatrist or mental health professionals should carry out an individual-based support program with psychotherapy and pharmacotherapy as efficient strategies to overcome patients' psychological problems.[33] Early detection of emotional problems of hospitalized hematological cancer patients might enhance quality of life, prevent patients' difficulties in treatment and reduce the patients' sufferings.[2]

LIMITATIONS

We should note some of the limitations of this study. First, investigating depression and quality of life specifically among hematological cancer patients is a very challenging task because of the participants' difficulties in responding actively during the interview due to physical weakness and the severe nature of their illness. Thus, the results of the present study should be interpreted with caution. The response of the participants may be influenced by the physical and emotional state at the time of the interview. Furthermore, some part of this research used self-rated questionnaires that were answered by the respondents themselves or were read to them to clarify their responses. The truthfulness of the information given depended on the integrity of the respondents themselves and on the patients' memory.

CONCLUSION

The present study found that the prevalence of MDD among the hematological cancer patients in the Malaysian tertiary referral center hospital is 24.8%. Those who were depressed had reduced quality of life, especially in physical, role, emotional, cognitive and social domains and had significantly more symptoms of fatigue, nausea and vomiting, dyspnea, insomnia, appetite loss, constipation and diarrhea in addition to financial difficulties and poor global health status.

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