ORIGINAL ARTICLE

Time Series Forecasting of HFMD Cases During COVID-19 Pandemic in Tawau, Sabah, Malaysia

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ABSTRACT

Introduction: Utilization of time series forecasting models as prediction tools for HFMD have been well studied for years. However, their forecasting performance and reliability during the recent COVID-19 pandemic remained unclear. Therefore, the aim of this study is to develop a pre-pandemic fitted time series forecasting model for HFMD, to study the model's forecasting performance before and during the pandemic. **Methods:** SARIMAX model was developed using weekly HFMD surveillance data, Google Trends data, and meteorological data for Tawau, Sabah from 2013 – 2020. The model was trained using pre-pandemic dataset (2013 – 2019) and tested with dataset during the pandemic (2020). Mean average percentage error (MAPE) and root mean square error (RMSE) were used as validation metrics to compare the accuracy of the model before and during pandemic. **Results:** SARIMA (1,0,1) (0,1,1) [52] with external regressors using real time Google Trends, mean, maximum temperature and relative humidity at lag 4 weeks was the best performing model with AIC value of 1348.45. The model can forecast HFMD cases with relatively stable decay in accuracy up to 8 weeks (pre-pandemic), before declining sharply during the beginning of the pandemic at week 10 to 12. **Conclusion:** Forecasting HFMD cases during COVID-19 pandemic was challenging in terms of forecasting accuracy due to the unexpected changes in HFMD trend throughout the first year of the pandemic. Therefore, there is a need to revise previous or current models, and to take into consideration the changes in HFMD trend during the pandemic for future model development. .

Keywords: Forecasting; Public Health Surveillance; Time Series; Hand, Foot and Mouth Disease; Enterovirus

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INTRODUCTION

Hand, Foot, and Mouth Disease (HFMD) is a common childhood infectious disease "characterized by fever, vesicles in the mouth, and skin eruptions on hands and feet" (1). The disease is caused by a group of enteroviruses with Coxsackievirus A16 (CA16) and Enterovirus 71 (EV71) as the main causative agents (2). Although HFMD infection is generally self-limiting, EV71 infection can lead to severe and sometimes fatal complications (3). According to World Health Organization (WHO), HFMD outbreaks have been regularly reported in countries of the WHO Western Pacific Region such as China, Singapore, Malaysia, Vietnam, Thailand, and Japan (1). Despite being regularly reported, public health control measures for HFMD outbreaks are often still limited to non-pharmaceutical interventions. These interventions mainly include quarantine of cases and closure of premises such as schools or childcare centres, which are essentially reactive in nature (4).

Over the years, there has been an increasing attention towards the relationship between HFMD incidence and meteorological factors. This is evidently so as more and more studies have been conducted to examine the influences of meteorological factors on HFMD incidence across the Western Pacific Region (5,6). Similarly, there has also been a growing interest in the correlation between internet search query trends and HFMD cases in this region (7–10). These studies strongly suggested that meteorological as well as internet search query trends data can be used as predictors in HFMD prediction models, often with a high degree of accuracy. As a result, the utilization of time series forecasting models such as the Auto Regressive Integrated Moving Average (ARIMA) family models developed based on these predictors are increasingly common over the years as part of developing HFMD preventive strategies (7–9,11). However, majority of these models are trained using pre-pandemic dataset, which are prone to the negative effects of data drift (12). As such, forecasting performance of these models during a major global health event such as the COVID-19 pandemic is still not fully understood and should be further assessed. The early period of the COVID-19 pandemic provided us with a unique opportunity, allowing us to further assess their forecasting performance during the pandemic. Therefore, the aim of this study is to develop a pre-pandemic fitted time series forecasting model or more specifically Seasonal Autoregressive Integrated Moving Average with exogenous regressors (SARIMAX) for HFMD based on a previous study done in Sabah, Malaysia (7), to assess and compare the forecasting performance before and during the pandemic.

MATERIALS AND METHODS

Study area

Tawau is a district located in the state of Sabah, Malaysia with an estimated population density of 167 per km^2 (13). It is the third largest district in Sabah with a land area of 2240 km2 and belongs to the tropical rainforest climate zone. The total population is estimated to be around 370,000 with approximately 265,000 citizens and 108,000 non-citizens as of 2021 (13). The district is well connected to the internet with 91.6% of the households in Tawau having internet subscription at home and approximately 99.4% of the population have access to mobile phone with internet connection as of 2019 (13).

Data source

Weekly Tawau HFMD surveillance data were primarily sourced from Sabah State Health Department via online e-Notification platform provided by the Ministry of Health Malaysia. Daily Tawau meteorological data including daily rainfall (mm), daily mean relative humidity (%), daily mean temperature (°C), daily maximum temperature (°C), and daily minimum temperature (°C) were sourced from Sabah Meteorological Department. As for internet search query trends data, they were primarily sourced from Google Trends platform using the keyword "HFMD". All information was collected from 2013 to 2020.

Data analysis

Time series data for this study were transformed into weekly observations prior to data analysis. First, we described the demographic characteristics of all the HFMD cases followed by the temporal distribution and trend of all the HFMD cases in Tawau throughout the study period from 2013 to 2020. The same was done for our potential predictors such as the meteorological observations and Google Trends observations for the same period. Additionally, we also conducted cross-correlation analysis by using cross-correlation function test between HFMD cases and the potential predictors in this study. This was to identify significant predictors including their lagged functions, which were then fitted into the model as exogenous regressors.

To build the Seasonal Autoregressive Integrated Moving Average with external regressors model (SARIMAX), we split the dataset into training and test dataset, whereby dataset from 2013 to 2019 were used as training dataset representing the pre-pandemic observations, and dataset in 2020 were used as test and validation dataset, representing observations during the pandemic year. Additionally, we conducted Augmented Dickey-Fuller (ADF) and Kwiatkowski-Phillips-Schmidt-Shin (KPSS) unit root tests on the baseline HFMD time series to assess their stationarity, which is required by SARIMA and SARIMAX model, and can be achieved by differencing or log transformations (14).

For the model development, we first estimated the parameters for the baseline SARIMA model, before developing the SARIMAX model, which is an extension of the SARIMA model by including exogenous regressors into the baseline model. SARIMA model parameters can be expressed as ARIMA *(p,d,q) (P,D,Q) m* whereby *(p,d,q)* represents the non-seasonal part of the model, *(P,D,Q)* represent the seasonal part of the component, and m represent the seasonal period of the model (14). The autoregressive parameters (p,P) and moving average parameters (q,Q) were estimated by conducting the autocorrelation function (ACF) and partial autocorrelation function (PACF) test respectively, whereas the (d,D) parameters were estimated by the degree of the differencing orders to achieve stationarity. The fitness of the models with various combination of parameters were then compared based on Akaike Information Criterion (AIC), whereby lower value indicates better fit (14). Next, we conducted Ljung-Box test to ensure the residuals were independently distributed, or assumed to be "white-noise" (14). Finally, we included the significant predictors into our baseline model as external regressors to develop our SARIMAX model. The best-fit SARIMAX models were then selected again based on the lowest AIC value, and again tested with Ljung-Box test to ensure all requirements are fulfilled before testing for their forecasting performance. For forecasting performance assessment, we utilized mean absolute percentage error (MAPE) and root mean square error (RMSE) as our error metrics, whereby lower values indicate higher prediction accuracy. To further test the forecasting performance of our best-fitted SARIMAX model during the COVID-19 pandemic, we conducted a cross-validation for a forecast horizon of up to 12 weeks for year 2020, which adequately covered the period before and during the COVID-19 pandemic. All of the analyses mentioned in this study were carried out using RStudio with R version 4.1.1 and forecast-package (14).

Ethical Consideration

Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR-20-3150-57649).

RESULTS

Demographic characteristics

Throughout the eight years study period from 2013 to 2020, a total of 1832 HFMD cases were notified and registered in Tawau district. The mean age of HFMD cases was 3.63 (SD = 3.25) years. Children within the age group of one to five years old accounted for 79.1% (n=1449) of all notified and registered cases in Tawau District. Overall, male registered higher number of cases at 57.0% (n=1044), with Malaysian citizens accounted for 97.0% (n=1777) of the total cases. By ethnicity, the highest percentage of cases were found in Indigenous Sabahan, which accounted for 64.2% (n=1176), followed by Chinese (15.4%, n=282), Malay (10.3%, n=188), Indigenous Sarawakian (1.1%, n=20), and Indian (0.1%, n=2). All demographic data are shown in Table I below.

Temporal distribution, seasonal and trend decomposition analysis

The weekly HFMD incidence throughout the study period is presented in Fig. 1. Throughout the 8 years study period, 33.5% (n=613) of the cases were notified and registered from 2013 to 2017, whereas 61.8% (n=1133) of the cases were notified and registered in 2018 and 2019 (Fig. 1). However, in 2020 only a total of 86 cases of HFMD were notified and registered, of which 95.3% (n=82) of the cases were notified in the first 12 weeks of 2020. There was a noticeable decline in HFMD incidence at the beginning of week 12 in 2020 with only four HFMD cases being notified and registered after week 12. Seasonal and trend decomposition analysis as seen in Fig. 1 shows that there was an overall upward trend of cases from 2013 to 2019, peaking in mid-2019, followed by a downward trend towards 2020. A seasonal component is also observed in the analysis showing an annual bimodal peak in April and September, with April being the first and larger peak, followed by a relatively smaller second peak in September.

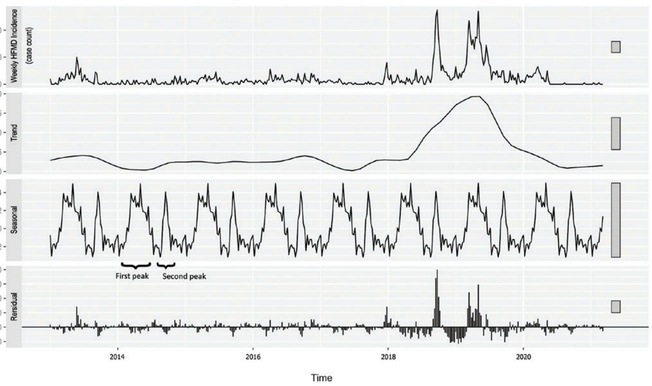

Figure 1 : Seasonal and trend decomposition of HFMD cases in Tawau, Sabah (2013 – 2020).

Table I : Demographic characteristics of HFMD cases in Tawau, Sabah (2013-2020)

Socio-demographic Characteristics		Total, n =1832	
Mean age (SD) years		3.63	(3.25)
Age Group, n (%)	**< 1 year**	139	(7.6%)
	1 – 2 years	839	(45.8%)
	3 – 5 years	610	(33.3%)
	6 – 14 years	218	(11.9%)
	≥15 years	26	(1.4%)
Gender, n (%)	**Female**	788	(43.0%)
	Male	1044	(57.0%)
Nationality, n (%)	**Malaysian**	1777	(97.0%)
	Non-Malaysian	55	(3.0%)
Ethnicity, n (%)	**Indigenous Sabahan**	1176	(64.2%)
	Malay	188	(10.3%)
	Chinese	282	(15.4%)
	Indian	2	(0.1%)
	Indigenous Sarawakian	20	(1.1%)
	Others	164	(8.9%)

Notes: SD = standard deviation

Meteorological and Google Trends data characteristics

Weekly temperature throughout the study period ranged between 21.8°C to 33.7°C. The average values of weekly mean temperature, weekly minimum and maximum temperatures were 27.0°C (range: 25.3 – 28.5°C), 23.7°C (range: 21.8 – 25.1°C) and 31.8°C (range: 29.2 – 33.7°C) respectively. The average weekly rainfall was 36.5mm (range: 0.0 – 271.8mm), whereas the average weekly mean relative humidity was 83.1% (range: 65.1 – 89.9%). The search trends for this study were generated using the term "HFMD" via Google Trends represented by relative search volume (RSV), with the highest peak of interest in epidemiological week 32 of 2018. Time series of all the data are visualized in Fig. 2.

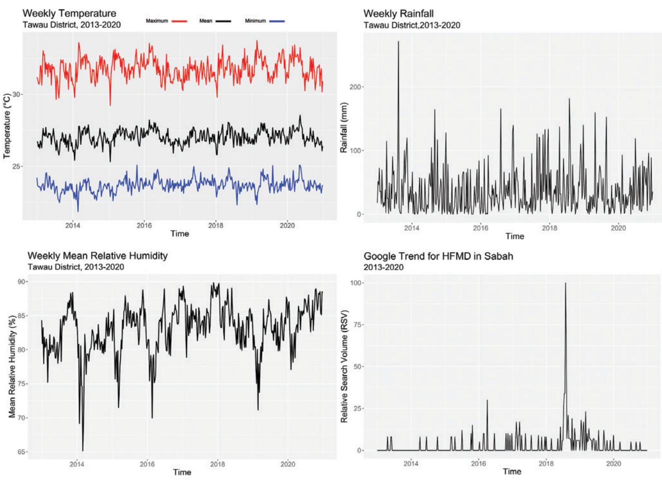

Figure 2 : Time series of Google trends data and Tawau meteorological data (2013 – 2020).

Cross-correlation analysis

Correlations between weekly HFMD incidence and the predictors (weekly meteorological data and internet search query trends) were analyzed using Spearman's rank correlation analysis. Table II shows the relationship between these variables and their lagged functions at lag 0 up to 5 weeks in Tawau, Sabah throughout the 8 years study period from 2013 to 2020. A total of 36 variables were included in this analysis, of which 20 of these variables were significantly associated with HFMD incidence.

Weekly maximum temperature at lags of 0, 2, 3, 4, and 5 weeks showed a weak positive correlation with weekly HFMD incidence, whereas weekly mean temperature at lags of 0, 3, and 4 weeks showed a weak positive correlation. Negative and positive correlations were observed for mean relative humidity and internet search query trends (Google Trend) respectively at lags of 0 – 5 weeks.

SARIMA model

After one order of differencing, baseline HFMD time series data achieved stationarity with ADF (DF = -7.33, $p < 0.01$) and KPSS (KPSS = 0.02, $p > 0.1$). SARIMA (1,0,1) (0,1,1) [52] was chosen as the best-fit model with AIC value of 1358.33 and Ljung-Box test ($p > 0.05$) suggested the model's residuals appeared to be "white-noise".

SARIMAX model

A total of 30 SARIMAX models with various combinations of exogenous regressors were computed and compared throughout this study to identify the

Table II : Coefficients of Spearman's rank correlation analysis between HFMD incidence and predictors

Lagged functions	Maximum temperature	Minimum temperature	Mean temperature	Relative humidity	Rainfall	Google trend
Lag 0	0.12*	0.03	0.11*	-0.2**	-0.04	0.36**
Lag 1	0.06	0.02	0.07	-0.18**	-0.03	0.35**
Lag 2	0.11*	0.01	0.1	-0.19**	-0.01	0.35**
Lag 3	0.13**	0.01	0.1*	-0.2**	-0.02	0.32**
Lag 4	0.13**	0.03	0.12*	-0.23**	0.22	0.31**
Lag 5	0.12*	0	0.1	-0.24**	-0.02	0.32**

Notes: *Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level best-fit and best performing model. SARIMA (1,0,1)(0,1,1) [52] with exogenous regressors using real time Google trend, mean temperature at lag 4 weeks, relative humidity at lag 4 weeks, and maximum temperature at lag 4 week was identified as the best performing model with AIC value of 1348.45 and Ljung-Box test ($p > 0.05$).

Forecast horizon accuracy with cross-validation

To test the forecasting performance of our best-fitted SARIMAX model during the COVID-19 pandemic, we conducted cross-validation for a forecast horizon of up to 12 weeks for year 2020, which adequately covered the period before pandemic (before epidemiological week 10) and during the COVID-19 pandemic, including the beginning of movement control order (MCO) (epidemiological week 10 – 12). As mentioned previously, there were only four HFMD cases being reported after epidemiological week 12 in 2020, with most of the weeks having not reported any cases. Therefore, we only used forecast horizon of up to 12 weeks for this study. Table III shows the forecasting accuracy of the model by forecast horizon of up to 12 weeks. The forecasting accuracy of our model steadily decayed over the first 8 weeks (MAPE increased steadily from 2.9% to 19.7%, RMSE increased steadily from 0.2 to 1.6). This observation is expected because the forecasting accuracy of time series model tend to decay over time. However, beginning at week 10 and onwards, we noticed the forecasting performance destabilized with both MAPE and RMSE increased sharply by almost 5 times as shown in Table III. The rapid deterioration in forecasting performance beginning at week 10 – 11 coincided with the beginning of COVID-19 global pandemic and the implementation of movement control order nationwide in Malaysia as shown in Fig. 3.

Table III : Accuracy of model predictions by week of forecast

Forecast horizon (week)	MAPE (%)	RMSE
1	2.97817	0.238253
2	7.90169	0.744807
3	8.81451	0.909093
4	12.31294	1.678614
5	10.61876	1.509341
6	9.63798	1.384460
7	18.27404	1.663071
8	19.73759	1.643472
9	66.68035	3.330536
10	101.51810	4.107814
11	97.21823	4.244133
12	101.50920	4.262652

Notes: MAPE = mean absolute percentage error; RMSE = root mean square error

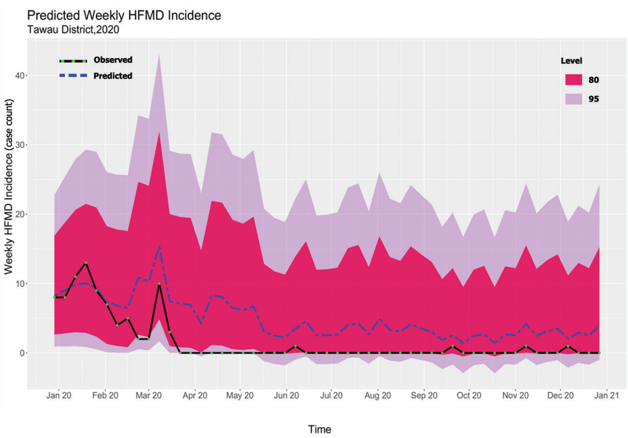

Figure 3 : Forecasted Weekly HFMD Incidence vs Observed Weekly HFMD Incidence in Tawau, Sabah (2020)

DISCUSSION

This study found that, the demographic characteristics of our HFMD cases in terms of age group and gender were very similar to other studies in which those infected were predominantly children in the age group of one to five years old and males (7,15,16). Those in the age group of one to five years old were mostly in their pre-school going age, on top of having poorer self-hygiene due to young age, thus increasing their risk of exposure and infection (17). Although HFMD cases were predominantly reported among male children in various studies as previously mentioned, oftentimes there were no direct explanations for such observation. Our study also found that, cases in Tawau were mostly reported among Malaysian citizens. One possible explanation for this observation could be due to the underreporting of cases among non-Malaysian citizens in this region. However the percentage of reported HFMD cases among non-Malaysian citizens in Tawau was slightly higher at 3.0%, compared to studies done in Peninsular Malaysia, whereby only 0.8% of the reported cases in Selangor involved non-Malaysian citizens (18). In term of seasonality, HFMD cases in Tawau exhibit an annual bimodal peak in the month of April and September, similar to previous study done in Sabah (7), potentially due to the beginning of school semesters in those months. Studies in other countries also showed similar bimodal peak, albeit in different months, possibly due to different school semester period or different climatic pattern (19).

In this study, we analyzed the correlation between HFMD cases with 5 meteorological parameters at various lags totaling up to 30 different variables. We found that 14 of these meteorological variables were significantly correlated with HFMD cases, whereby maximum and mean temperature at various lags were positively correlated, while relative humidity at various lags were negatively correlated. Minimum temperature and rainfall were both not significantly correlated, as opposed to similar study done in Sabah (7) whereby the results differed slightly. In that study, the mean rainfall at lag 0 to 1 week were negatively and significantly correlated. The differing results could potentially be due to the usage of data from different meteorological stations from different districts in Sabah.

As for the internet search query trends data, we found a significant positive correlation at lag 0 to 5 week, with the highest correlation coefficient at lag 0 or real time. This finding is slightly different compared to the same study done in Sabah (7), whereby the authors found that the highest correlation coefficient for Google Trends was at lag 1 week. The differing result was potentially due to the study being conducted prior to 2019, whereby internet accessibility during that period was much lower compared to our current study (13). The availability of internet access in real-time potentially encouraged and enabled parents of HFMD infected children to conduct quick online search for relevant information pertaining to HFMD either before, during or shortly after consultations with healthcare providers, hence explaining higher correlation at lag 0 or real time (20).

Although HFMD cases were generally reported all year round from 2013-2019 in Tawau, one notable finding in this study was that there was a sharp decline in number of cases being reported at the beginning of week 13 in 2020 towards the end of the year. Throughout that period, only four cases were being reported, as opposed to 82 cases being reported prior to week 13 in the same year. Upon further inspection on this sharp decline, we found that the beginning of week 13 in 2020 coincided with the fourth day following the implementation of national movement control order (MCO) on 18th of March 2020 (21). The sharp decline of cases being reported in the beginning of the movement control order could possibly be due to the movement restriction of the local population during that period, resulting in lower case detection and underreporting of cases in healthcare facilities. However, the unusually low HFMD incidence throughout the remaining of the year could also be due to closure of pre-schools and nurseries during that period in addition to restrictions of outdoor activities. The closure of preschools and movement restrictions might have potentially reduced the risk of HFMD transmissions among the high-risk groups, especially the pre-school children, which were commonly associated with HFMD infection (17). These observations however, are not exclusive to HFMD, as similar trends were also observed in other infectious diseases like pertussis, varicella, and mumps (22) due to the implementation of non-pharmaceutical interventions such as social distancing during the pandemic.

Forecasting HFMD cases during the pandemic period was challenging and evidently so, as our model's forecasting performance deteriorated sharply during the beginning of the pandemic. This was mainly due to the utilization of pre-pandemic dataset to train the model, coupled with the sudden unexpected changes in the HFDM trend following the COVID-19 pandemic. Such observation is not uncommon due to the effect of data drift following the pandemic, which is known to negatively impact model performances (12). Despite the low forecasting accuracy during the pandemic, our model was able to capture the overall downward trend of HFMD cases during the first year of the pandemic as shown in Fig. 3, signifying its potential application in disease trend monitoring.

CONCLUSION

The observed level shift in HFDM time series during the first year of the pandemic pose a huge challenge not only for time series models developed prior the pandemic, but also for current and future time series models development. This is due to the nature and limitation of time series forecasting models whereby they have the tendency to reproduce abnormal patterns from previous time series with outliers, such as the one observed during the pandemic. Therefore, there is a need to revise previous or current models, and to take into consideration the changes in HFMD trend during the first year of the pandemic for future model development. As this phenomenon is not exclusive to HFMD alone, there is also a need to investigate time series forecasting models for other diseases developed prior to the pandemic.

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