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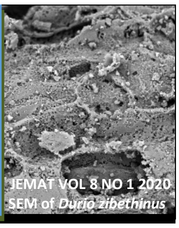

Predictive Mathematical Modelling of the Total Number of COVID-19 Cases for Indonesia

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ABSTRACT

In the current article, we showcase various growth models like Von Bertalanffy, Baranyi-Roberts, Morgan-Mercer-Flodin (MMF), modified Richards, modified Gompertz, modified Logistics and Huang in the fitting and analysis of the COVID-19 epidemic trend as of 15 July 2020 in Indonesia in the form of the total number of SARS-CoV-2 infections. The MMF model was proved as the suitable model with the highest adjusted R^2 value and lowest RMSE value. The Accuracy and Bias Factors values were near to unity (1.0). The parameters obtained from the MMF model consist of maximum growth rate (μ_m) (log) of 0.025 (95% CI from 0.020 to 0.028), curve constant (δ) that affects the inflection point of 0.770 (95% CI from 0.691 to 0.849), lower asymptote value (β) of 0.297 (95% CI from 0.229 to 0.365) and maximal total number of cases (y_{max}) of 4,634,469 (95% CI from 1,967,886 to 15,417,005). The MMF forecast that the total number of cases in Indonesia on the coming 15th of August and 15th of September 2020 will be 113,179 (95% CI of 103,477 to 123,790) and 154,235 (95% CI of 136,542 to 174,220), respectively. The predictive capability of the model applied in this paper is likely a reliable tool for epidemiologist to monitor and evaluate the severity of COVID-19 death cases in Indonesia in few months to come. Undoubtedly, the models will be reexamined after every few months in the event unwarranted phenomena lead to an exponential increase or wave of new infection.

INTRODUCTION

The SARS-CoV-2 virus is the agent responsible for the world pandemic COVID-19 that is still devastating to human being with the present death tolls above half a million individuals with more than 10 million persons left ill. The respiratory ailment, Covid-19, is a current universal health issue that spread into many countries so far. A great task of global researchers is to find cure and vaccines against Covid-19 [1]. Global societies and markets have remained a near-complete stoppage for the first time in a near history due to this virus. The virus belongs to the family of coronavirus (CoV), that is responsible for the zoonotic infections over the past decades on many occasions [2]. In the fall of 2019, SARS-CoV-2 first emerged near Wuhan City, in the People's Republic of China [2–5].

To date there is no therapeutic treatments available for corona virus, and therefore the pandemic overcome healthcare facilities of even well-equipped countries. The only prevention measure rely only on interaction tracing, isolation of infected persons and distancing [6]. Due to extensive effects of deleterious pandemic on the well-being and economy of the world, it is cognizance to study the trend of transmission of COVID 19 and this can be realistic using mathematical tools. Mathematical modelling is quite significant in prediction and comprehension a pandemic such as COVID 19 [7].

Indonesia is regarded as the fourth most populated nations of the globe, and therefore predicted to suffer immensely due to covid-19 pandemic as compared less populated nations [8]. The early cases of covid-19 in Indonesia was reported on March 2, 2020 with two confirmed cases. It increases to 1285 cases across 30 provinces. Jakarta, West Java, Banten, East Java and Central Java were the provinces with the highest pandemic [9]. At the end of March 2020, the number of cases increases to 1528 and 136 number of deaths were recorded. The country's case fatality rate (CFR) was quite higher than reported cases of China where the pandemic started (8.9% against 4%) [10]. In April 2, 2020, Indonesia recorded 1790 confirmed cases, 113 fresh cases, 170 deaths and 112 recoveries [8]

The growth curve of viruses and microorganisms on substrates such as nutrients or other organisms including humans usually followed a sigmoidal pattern, starting with the lag section just after t = 0, followed by the logarithmic section and then the organism enters the stationary phase and finally moves to the phase of death or decline. There are various sigmoidal functions to describe the growth curve of organisms, such as Von Bertalanffy, Baranyi-Roberts, modified Richards, modified Gompertz and modified Logistics [11], including Morgan-Mercer-Flodin (MMF) [12]. The valuable parameters of the growth curve include the maximum specified growth rate (μm), the lag period and asymptotic values.

COVID-19 pandemic analysis can be carried out using mathematical models including theoretical, quantitative and simulation. Models such as the modified Gompertz, von Bertalanffy and logistics have been utilized to model COVID-19 pandemic [13] with good predictive ability. The objective of this work is to evaluate several available models such as Logistic [11,14], Gompertz [11,15], Richards [11,16], Morgan-Mercer-Flodin (MMF) [17], Baranyi-Roberts [18], Von Bertalanffy [19,20], Buchanan three-phase [21] and more recently the Huang model [22] in fitting and analyzing the COVID-19 epidemic trend in Indonesia as of 15 July 2020 in the form of the total SARS-CoV-2 infection case.

MATERIALS AND METHODS

Data were acquired from Worldommeter [23] for the total number of infected cases from Indonesia as of 15 July 2020. Data were first converted to logarithmic values, and time zero was used as time after first infected case.

Statistical analysis

The statistically significant difference between the models was calculated using different methods including the adjusted determination coefficient (R^2), accuracy factor (AF), bias factor (BF), root-mean - square error (RMSE), and corrected AICc (Akaike Information Criterion) as reported by [24]. The RMSE was computed using Eq. (1), where Pd_i are the values predicted by the model and Ob_i are the experimental data, n is the number of experimental data, and p is the number of parameters of the assessed model.

$$RMSE = \sqrt{\frac{\sum_{i=1}^{n}(Pd_i - Ob_i)^2}{n-p}} \qquad \text{(Eqn. 1)}$$

The adjusted R^2 is applied to calculate the inferiority of nonlinear models on the basis of the formula where RMS is Residual Mean Square and S_y^2 is the total variance of the calculated y-variable and calculated as follows;

$$Adjusted\left(R^2\right) = 1 - \frac{RMS}{s_Y^2} \qquad \text{(Eqn. 2)}$$

$$Adjusted\left(R^2\right) = 1 - \frac{\left(1-R^2\right)(n-1)}{(n-p-1)} \qquad \text{(Eqn. 3)}$$

The Akaike information criterion (AIC) [25] was calculated as follows;

$$AICc = 2p + n\ln\left(\frac{RSS}{n}\right) + 2(p+1) + \frac{2(p+1)(p+2)}{n-p-2} \qquad \text{(Eqn. 4)}$$

Where n is the number of data points and p is the number of parameters of the model. The model with the lowest AICc value is greatly likely to be correct [26].

Accuracy Factor (AF) and Bias Factor (BF) as described by Ross [27] were calculated as follows;

$$\text{Bias factor} = 10^{\left(\sum_{i=1}^{n}\log\frac{(Pd_i/Ob_i)}{n}\right)} \qquad \text{(Eqn. 5)}$$

$$\text{Accuracy factor} = 10^{\left(\sum_{i=1}^{n}\log\frac{\left|(Pd_i/Ob_i)\right|}{n}\right)} \qquad \text{(Eqn. 6)}$$

Fitting of the data

The data was fitted using as far bacterial growth curve using different growth models (Table 1) using the GraphPad Prism (v 8.0 trial version).

Table 1. Models used in this study.

Model	p	Equation
Modified Logistic	3	$y=\frac{A}{\left\{1+\exp\left[\frac{4\mu_m}{A}(\lambda-t)+2\right]\right\}}$
Modified Gompertz	3	$y=A\exp\left\{-\exp\left[\frac{\mu_m e}{A}(\lambda-t)+1\right]\right\}$
Modified Richards	4	$y=A\left\{1+v\exp(1+v)\exp\left[\frac{\mu_m}{A}(1+v)\left(1+\frac{1}{v}\right)(\lambda-t)\right]\right\}^{\left(\frac{-1}{v}\right)}$
Morgan-Mercer-Flodin (MMF)	4	$y = y_{max} - \frac{(y_{max}-\beta)}{1+(\mu_m t)^{\delta}}$
Baranyi-Roberts	4	$y=A+\mu_m x+\frac{1}{\mu_m}\ln\left(e^{-\mu_m x}+e^{-h_0}-e^{-\mu_m x-h_0}\right)$ $-\ln\left(1+\frac{e^{\mu_m x+\frac{1}{\mu_m}\ln\left(e^{-\mu_m x}+e^{-h_0}-e^{-\mu_m x-h_0}\right)}-1}{e^{(y_{\max}-A)}}\right)$
Von Bertalanffy	3	$y=K\left[1-\left[1-\left(\frac{A}{K}\right)^3\right]\exp^{-\left(\mu_m x/3K^{\frac{1}{3}}\right)}\right]^3$
Huang	4	$y=A+y_{\max}-\ln\left(e^A+\left(e^{Y_{\max}}-e^A\right)e^{-\mu_m B(x)}\right)$ $B(x)=x+\frac{1}{\alpha}\ln\frac{1+e^{-\alpha(x-\lambda)}}{1+e^{\alpha\lambda}}$
Buchanan Three-phase linear model	3	Y = A, IF X < LAG Y=A + K(X−λ), IF λ ≤ X ≥ X_{MAX} Y = Y_{MAX}, IF X ≥ X_{MAX}

Note:
A= maximum no of cases lower asymptote;
y_{max}= maximum no of cases upper asymptote;
μ_m= maximum specific growth rate;
v= affects near which asymptote maximum no of cases occurs.
λ=lag time
e = exponent (2.718281828)
t = time after first case is reported
α,β,δ and k = curve fitting parameters
h_0 = a dimensionless parameter quantifying the initial physiological state of the reduction process. The lag time (h^{-1}) or (d^{-1}) can be calculated as h_0=μ_m
When data at time zero is 0 (Day after 1st case log 1=0 for COVID-19) the MMF is reduced to a 3-parameter model

RESULTS AND DISCUSSION

All the curves tested indicated visually satisfactory fitting with the exclusion of the Buchanan-3-phase model which indicated non-satisfactory curve (**Figs 1** to **8**). The most suitable performance was the MMF model having the lowest value for RMSE, AICc and the uppermost value for adjusted R^2. The AF and BF values were equally excellent for the model with their values nearer to unity (1.0). The lowest performance was the modified logistics model (**Table 2**). The coefficients for the MMF model are presented in **Table 3**. The Predictions of COVID-19 pandemic for Indonesia based on the MMF model are presented in **Table 4.**

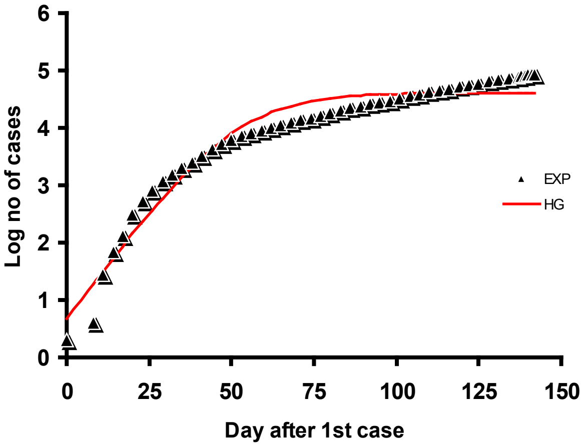

Fig. 1. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the Huang model.

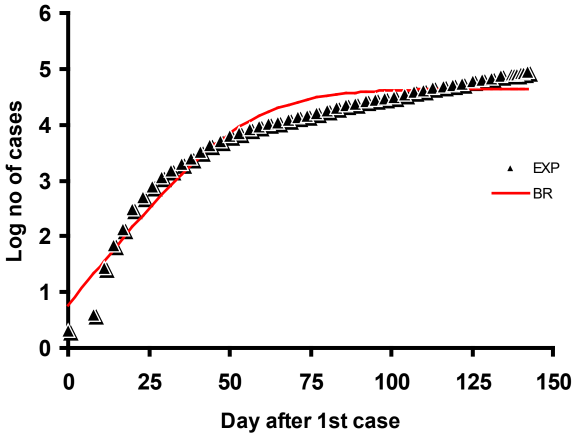

Fig. 2. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the Baranyi-Roberts model.

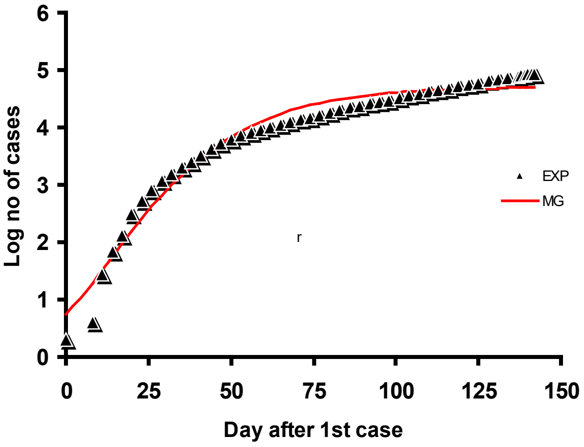

Fig. 3. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the modified Gompertz model.

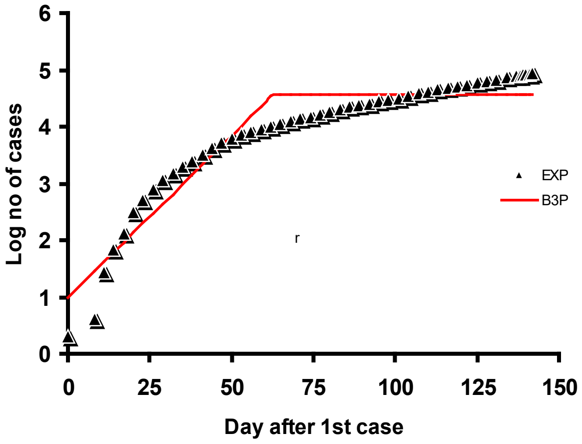

Fig. 4. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the Buchanan-3-phase model.

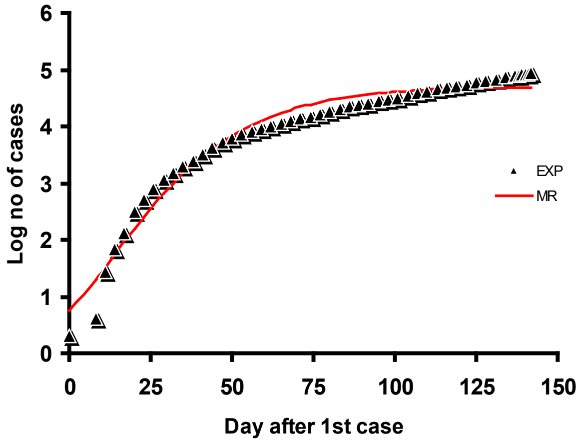

Fig. 5. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the modified Richard model.

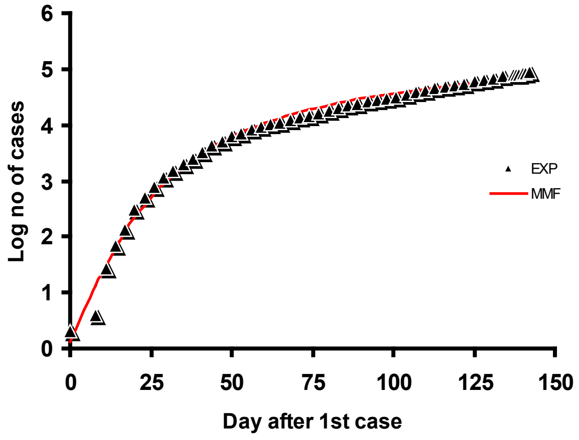

Fig. 6. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the MMF model.

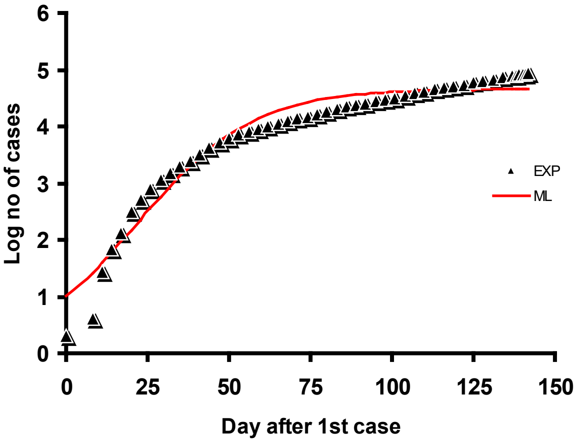

Fig. 7. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the modified logistics model.

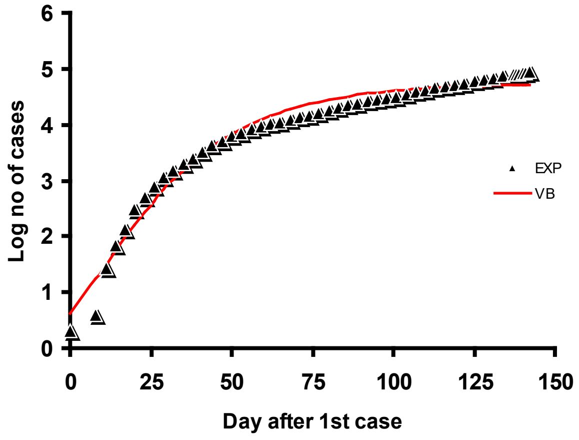

Fig. 8. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the von Bertalanffy model.

Table 2. Statistical tests for the various models utilized in modelling the total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020.

Model	*p*	RMSE	R^2	adR^2	AF	BF	AICc
Huang	4	0.247	0.950	0.945	1.033	1.00	-124.56
Baranyi-Roberts	4	0.245	0.950	0.945	1.031	1.00	-125.26
modified Gompertz	3	0.205	0.964	0.962	1.045	1.00	-146.87
Buchanan-3-phase	3	0.330	0.906	0.900	1.045	1.00	-98.98
modified Richards	4	0.207	0.964	0.961	1.024	1.00	-142.40
MMF	4	0.111	0.990	0.990	1.011	1.00	-204.67
modified Logistics	3	0.252	0.944	0.940	1.029	1.00	-126.21
von Bertalanffy	3	0.185	0.972	0.970	1.022	1.00	-157.04

Note: p is no of parameter

Table 3. Coefficients as modelled using the MMF model.

Parameters	Value	95% Confidence interval
μ_m	0.025	0.020 to 0.028
δ	0.770	0.691 to 0.849
y_{max}	4,634,469	1,967,886 to 15,417,005
β	0.297	0.229 to 0.365

Table 4. Predictions of COVID-19 pandemic for Indonesia based on the MMF model.

Prediction	Mean	95% Confidence interval
Maximum number of total cases by the end of COVID-19	4,634,469	1,967,886 to 15,417,005
Maximum number of total cases by 15th of August 2020	113,179	103,477 to 123,790
Maximum number of total cases by 15th of September 2020	154,235	136,542 to 174,220

The parameters obtained from the MMF model include maximum growth rate (μ_m) (log) of 0.025 (95% CI from 0.020 to 0.028), curve constant (δ) that affects the inflection point of 0.770 (95% CI from 0.691 to 0.849), lower asymptote value (β) of 0.297 (95% CI from 0.229 to 0.365) and maximal total number of cases (y_{max}) of 4,634,469 (95% CI from 1,967,886 to 15,417,005). The MMF model predicted that COVID-19 will end about 1,513.53 days (95% CI of 833.58 to 2,193.48) days from 15th of July 2020 based on the lower bound of the 95% CI from the calculated maximum number of total cases (y_{max}) while the mean and upper 95% CI bound values failed to be predicted by the software for their number of days. The MMF predicted that the total number of cases for Indonesia on the coming 15th of August and 15th of September 2020 will be 113,179 (95% CI of 103,477 to 123,790) and 154,235 (95% CI of 136,542 to 174,220), respectively. This prediction has to be taken with caution since the model refusede to predict the number of days for the mean and upper 95% CI values and the number of days for COVID-19 to end may be greatly larger.

The MMF model has never been used to model growth of infectious cases unlike modified Gompertz and logistics. It was developed initially to describe a broad range of nutrient-response relationships in higher organisms [17]. The growth of animals such as rabbits, sheep, horses, microorganisms [28–32], yield of oil palm [33], ethanol [34] and also in finance [35] all have benefitted from this model. The resulting modelling prediction in this work is dependent upon effective lockdown no virus mutations which increases the virus' infection rate. Undoubtedly, the models will be reexamined after every few months in the event these phenomena lead to an exponential increase or wave of new infection to remodel the data so as a better prediction can be achieved.

CONCLUSION

Conclusively, the findings of this study indicated that, the MMF model was proved to the best model in modelling the total number of COVID-19 cases for Indonesia based on statistical tests like corrected AICc (Akaike Information Criterion), bias factor (BF), adjusted coefficient of determination (R^2) and root-mean-square error (RMSE). The parameters acquired from the MMF model include maximum growth rate (μ_m) (log) of 0.025 (95% CI from 0.020 to 0.028), curve constant (δ) that affects the inflection point of 0.770 (95% CI from 0.691 to 0.849), lower asymptote value (β) of 0.297 (95% CI from 0.229 to 0.365) and maximal total number of cases (y_{max}) of 4,634,469 (95% CI from 1,967,886 to 15,417,005). The MMF predicted that the total number of cases for Indonesia on the coming 15th of August and 15th of September 2020 will be 113,179 (95% CI of 103,477 to 123,790) and 154,235 (95% CI of 136,542 to 174,220), respectively. The model permits for prediction of total number of cases and this prediction will differ based on several number of factors. Despite this, the predictive capability of the model applied in this study is an influential tool for epidemiologist to monitor and evaluate the harshness of COVID-19 in Indonesia in months to come.

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