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Prediction of Cumulative Death Cases in Indonesia Due to COVID-19 Using Mathematical Models

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ABSTRACT

Different growth models such as Baranyi-Roberts, Von Bertalanffy, modified Gompertz, Morgan-Mercer-Flodin (MMF), modified Richards, modified Logistics and Huang utilized in fitting and analyzing the COVID-19 outbreak pattern showing the cumulative number of SARS-CoV-2 deaths in Indonesia as of 15 July 2020. Out of all the models tested MMF was found to be the best one considering its highest adjusted R^2 and the lowest RMSE values. Parameter such Accuracy and Bias Factors were found to have values close to unity (1.0). Values generated from the MMF model includes the maximum growth of death rate (log) of 0.051 (95% CI from 0.34 to 0.49), the curve constant (δ) that affects the inflexion point of 0.4212 (95% CI from 1.029 to 1.171), lower asymptote value (β) of -1.72 (95% CI from -2.53 to -1.22) and the maximal total number of death (y_{max}) of 889,201 (95% CI from 260,016 to 7,464,488). The MMF forecasted that the total death toll in Indonesia would be 5.315 (95 per cent CI from 5.079 to 5.562) and 6.857 (95 per cent CI from 6.450 to 7.289) on the 15th August and 15th September 2020 respectively. The prediction accuracy of the model used in this research article is a powerful tool for epidemiologists to monitor and evaluate the level the severity of COVID-19 in Indonesia in the coming months. Besides that, just like any other model, due to the intermittent nature of the COVID-19 dilemma both in the local and global context, these values must be considered with caution.

INTRODUCTION

A novel viral infection had been discovered in Wuhan, China at the end of 2019. Many scientists considered novel beta coronavirus to be the cause of this infectious disease, which attributed to the extreme acute respiratory syndrome. It affects the lungs and has symptoms such as cough, fever, fatigue, and hard breathing. The virus identified and named as 2019-nCoV, SARS-CoV-2, and COVID-19.[1, 2]. Sadly, the spread of the 2019-nCoV in Hubei Province was too fast and developed an outbreak in late January 2020[3]. The Chinese Government then forced quarantine restrictions to stop the outbreak. It also announced a ban on foreign travels. It wasn't effective though, and the disease has spread across the globe. Meanwhile, this disease affects a large number of nations, such as the USA, Italy, Spain and Germany, and governments seek to combat coronavirus by imposing social distancing. Indonesia is considered to be the fourth most populous nation in the world and is therefore expected to suffer immensely as a result of COVID 19 pandemic compared to the less populous[4]. Early cases of COVID-19 in Indonesia were reported on 2 March 2020 with two cases reported. The first death of COVID 19 in Indonesia was reported on the 11th of March 2020[5]. Mathematical modeling is very important for forecasting and understanding pandemic trends such as that of COVID 19[6]. Typically, the growth curve of viruses and microorganisms on the substrate, such as nutrients or other organisms, even humans, followed a sigmoidal path, beginning with the lag segment just after t = 0, accompanied by a logarithmic phase, and afterwards, the organism entered the stationary phase and finally moved to the death phase or decreased developmen[7,8]. Various sigmoidal functions are utilized to describe organism growth curve, notably the Von Bertalanffy, the Baranyi-Roberts, a modified Richards, a modified Gompertz and modified Logistics [9] including Morgan-Mercer-Flodin (MMF) [10]. Valuable parameters of the growth curve include the maximum specific growth rate (μm), the lag period and the asymptotic values.

Analysis techniques of the COVID-19 outbreak comprising theoretical, quantitative and simulation of the total death toll using statistical models. Models such as the modified Gompertz, von Bertalanffy and logistics have been used for the COVID-19 pandemic mode [11] with good predictive capabilities. The objective of this work is to test various models available such as Logistic [9,12], Gompertz [9,13], Richards [9,14], Morgan-Mercer-Flodin (MMF) [10], Baranyi-Roberts [15], Von Bertalanffy [16,17], Buchanan three-phase [18] and most recent Huang model [19] in fitting and evaluating the COVID-19 epidemic trend in the form of a total death case of SARS-CoV-2 in Indonesia as of 15th of July 2020.

MATERIALS AND METHODS

Data from Worldommeter [20] for the Indonesian's cumulative or the total number of death cases as of 15th of July 2020 were obtained and were first converted to logarithmic values and the time after first death was utilized for time zero.

Statistical analysis

Statistically significant differences between models were determined using multiple methods, including the adjusted coefficient of determination (R^2), the accuracy factor (AF), the bias factor (BF), the root-mean-square error (RMSE) and the revised AICc (Akaike Information Criterion) as before[21].

Eqn. (1) below was used to calculate the RMSE,
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 used to calculate the quality of nonlinear models according to the formula where RMS is Residual Mean Square and S_y^2 is the total variance of the y-variable ad calculated as follows;

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

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

The Akaike information criterion (AIC) [22] 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 smallest AICc value is highly likely correct [23]. Accuracy Factor (AF) and Bias Factor (BF) as suggested by Ross was calculated as follows;

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

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

Fitting of the data

GraphPad Prism (v 8.0 trial version) was utilized for the fitting of the curves using various growth models (**Table 1**).

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 death cases lower asymptote;
y_{max}= maximum no of death cases upper asymptote;
μ_m = maximum specific growth rate of death;
v= affects near which asymptote maximum no of death cases occurs.
λ=lag time
e = exponent (2.718281828)
t = time after first death 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 death 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 the 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.**

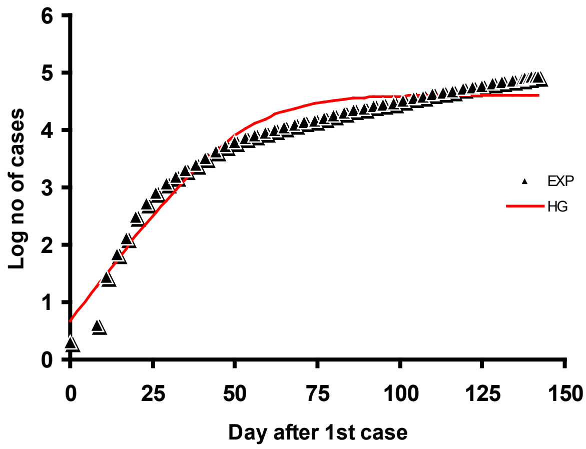

Fig. 1. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the Huang model.

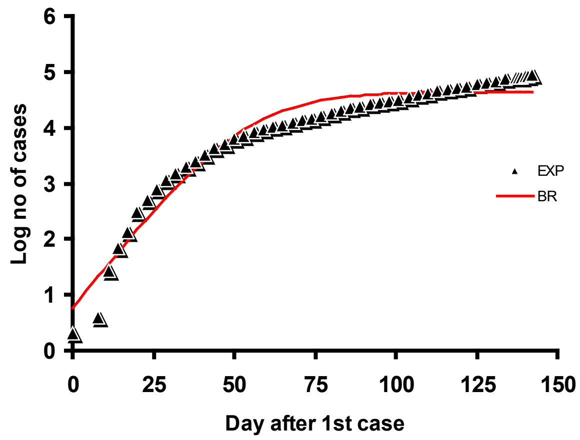

Fig. 2. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the Baranyi-Roberts model.

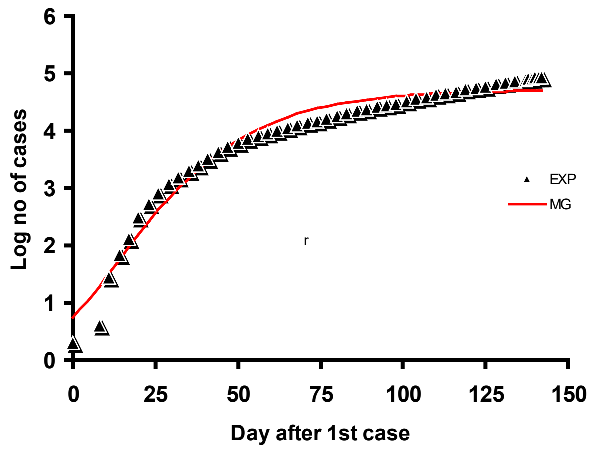

Fig. 3. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the modified Gompertz model.

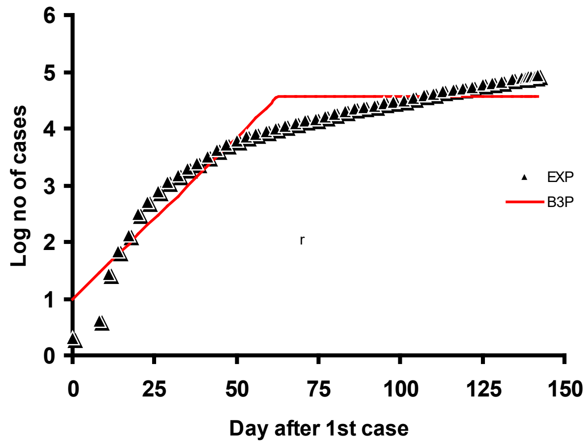

Fig. 4. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the Buchanan-3-phase model.

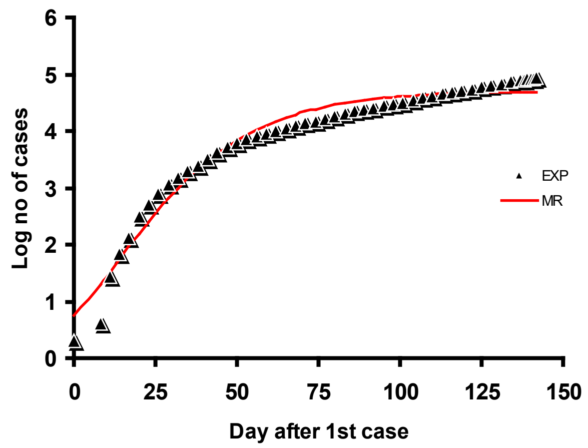

Fig. 5. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the modified Richard model.

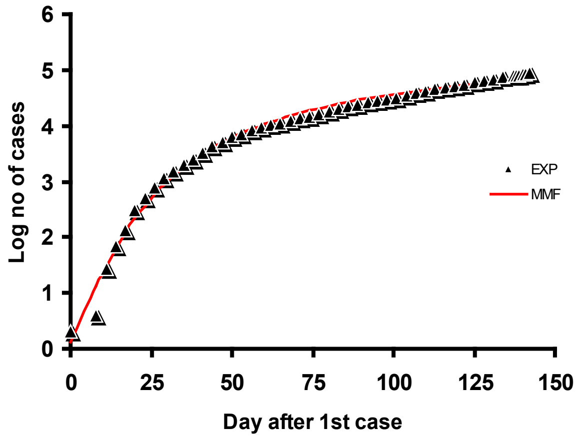

Fig. 6. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the MMF model.

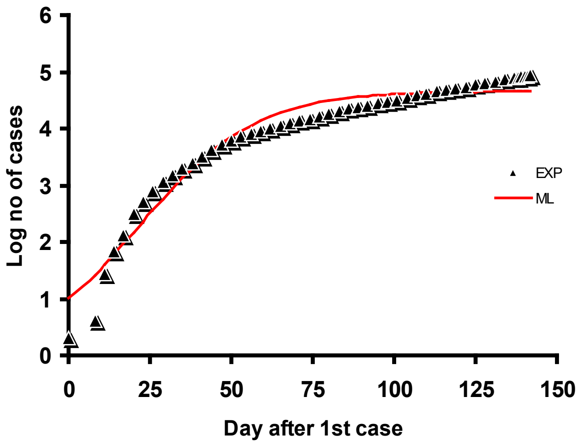

Fig. 7. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the modified logistics model.

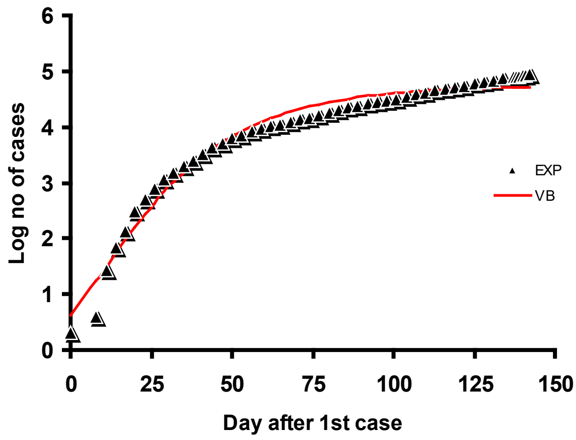

Fig. 8. Total no of SARS-CoV-2 cases in Indonesia as of 15th of July 2020 as modelled using the von Bertalanffy model.

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

Model	*p*	RMSE	R^2	adR^2	AF	BF	AICc
Huang	4	0.261	0.878	0.868	1.045	1.03	-118.99
Baranyi-Roberts	4	0.266	0.874	0.863	1.038	1.02	-117.32
modified Gompertz	3	0.257	0.878	0.870	1.056	1.02	-123.94
Buchanan-3-phase	3	0.282	0.988	0.987	1.056	1.00	-114.69
modified Richards	4	0.260	0.878	0.867	1.036	1.02	-119.46
MMF	4	0.220	0.921	0.914	1.021	1.02	-136.41
modified Logistics	3	0.286	0.843	0.833	1.037	1.02	-113.45
von Bertalanffy	3	0.245	0.891	0.884	1.036	1.02	-128.72

Note: p is no of parameter

Table 3. Coefficients as modelled using the MMF model.

Parameters	Value	95% Confidence interval		
μ_M	0.051	0.042	to	0.060
δ	0.4212	0.34	to	0.49
y_{max}	889,201	260,016	to	7,464,488
β	-1.72	-2.53	to	-1.22

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	889,201	260,016to	7,464,488
Maximum number of total cases by 15th of August 2020	5,315	5,562to	5,079
Maximum number of total cases by 15th of September 2020	6,857	7,289to	6,450

The parameters obtained from the MMF model include maximum growth of death rate (log) of 0.051 (95% CI from 0.34 to 0.49), curve constant (δ) that affects the inflection point of 0.4212 (95% CI from 1.029 to 1.171), lower asymptote value (β) of -1.72 (95% CI from -2.53 to -1.22) and the maximal total number of death (y_{max}) of 889,201 (95% CI from 260,016 to 7,464,488). The MMF anticipated that the total number of death cases for Indonesia on the coming 15th of August and 15th of September 2020 will be 5,315 (95% CI of 5,079 to 5,562) and 6,857 (95% CI of 6,450 to 7,289), respectively. This projection has to be taken with caution since the model failed 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 much larger.

The MMF model was initially developed to describe a wide variety of nutrient-response relationships in higher organisms [10]. To date, the model has found utility in several modelling exercises involving animals such as rabbit, sheep, horse, microorganisms [25–29], a yield of oil palm [30], ethanol [31] and even in finance [32]. Whether the predicted data is correct or not will depend on a case by case basis and include the effectiveness of lockdown, mutation of the virus that increases the infectivity rate of the virus to name a few. Certainly, the models will be revisited every few months to remodel the data so a better prediction can be obtained.

CONCLUSION

In conclusion, the MMF model was the best in modelling *x* number in wastewater based on statistical tests such as corrected AICc (Akaike Information Criterion), bias factor (BF), adjusted coefficient of determination (R^2) and root-mean-square error (RMSE). Parameters obtained from the fitting exercise were maximum growth rate (μ_m), the curve constants () and maximal total number of death cases (Y_{max}). The parameters obtained from the MMF model include maximum growth of death rate (log) of 0.051 (95% CI from 0.34 to 0.49), curve constant (δ) that affects the inflection point of 0.4212 (95% CI from 1.029 to 1.171), lower asymptote value (β) of -1.72 (95% CI from -2.53 to -1.22) and maximal total number of death (y_{max}) of 889,201 (95% CI from 260,016 to 7,464,488). The MMF predicted that the total number of death cases for Indonesia on the coming 15th of August and 15th of September 2020 will be 5,315 (95% CI of 5,079 to 5,562) and 6,857 (95% CI of 6,450 to 7,289), respectively. The model allows for prediction of total number of death cases and this prediction will vary according to various number of factors. Despite this, the predictive ability of the model utilized in this study is a powerful tool for epidemiologist to monitor and assess the severity of COVID-19 in Indonesia in months to come.

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