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Identifying Some Factors Associated with Death Due to COVID- 19 in Babies and Children by Using Binary Logistic Regression

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ABSTRACT

Despite the direct effect of the COVID-19 virus on children is uncommon so far, the indirect effect of the global COVID-19 pandemic can be catastrophic for children, causing considerable death and suffering. Many major causes of poor health and mortality in children were increased this year as a result of the pandemic and the response. At the same time, the capacity of governments, health frameworks, and humanitarian associations to respond to child health was decreased.

In this paper, the Binary Logistic Regression Analysis technique has been employed and applied to identify the factors leading to the babies and children's deaths and building the best model for coronavirus disease data. A random sample size consists of 50 patients has been selected which 10 of them have died and the other 40 have survived. The results of the analysis showed that two variables out of eight variables were statistically significant which are Type of test and Complete Blood Count. The percentage of correct classifications was 85.7 %, which indicates the approximately high ability of the model for classification.

1. Corona Virus (Covid-19) in Children [20][18]

Few severe cases are reportable in children so far. Still, children are less prone to develop severe symptoms of COVID-19; Initial reports on COVID-19 described children as for the most part spared from severe manifestations. However, clusters of pediatric cases of severe systemic hyper inflammation and shock epidemiologically connected with COVID-19 a cardiac involvement was described in a very few of them, thus showing that the heart is a possible target of the malady at this age range as well. As the COVID-19 pandemic continues to infect immeasurable people around the world, researchers are learning more concerning however the virus affects various organs in the body. while it had been initially thought to be a respiratory illness, it' currently clear that it attacks far more than just the lungs.

The first COViD-19 impact on the heart is related to a direct myocardial injury, recently, it was hypothesized that SARS-CoV-2 might enter myocardial cells simply by binding kind a pair of angiotensin-converting-enzyme (ACE) receptors on their surface.

The second possible mechanism is hypoxia. Pneumonia caused by CoV-19 may change alveolar gas exchange, leading to hypoxia, activating anaerobic metabolism, causing metabolic acidosis, and initiating the production of oxygen free radicals, which then damage the myocardial phospholipid bilayer of the cell membrane. In summary, one of these mechanisms can cause myocardial damage because there is a substantial imbalance between oxygen request and its availability. In addition, hypoxia itself may cause calcium ions to stream into cardiomyocytes, which in turn is answerable for their apoptosis. Inflammation may play a crucial role in myocardial injury as well. a third possibility is that it can cause myocarditis, or an inflammation of the heart muscle, which might cause completely different kinds of symptoms, including chest pain, abnormal heart rhythms, and even reduced heart function.

2. Material and methods

2.1 Introduction to binary logistic regression [6][2][3][11]

Regression analysis is a statistical method for determining the relationship between variables to predict future values. In the simplest case, regression analysis needs two variables; outcome (response variables or dependent variables) and predictor (explanatory variables or independent variables).

The most popular regression method is linear regression. It is however apply if the dependent variable is continuous and Binary logistic regression analysis represents a

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special condition of linear regression analysis used when the response is binary, and the explanatory variables are quantitative or qualitative. Logistic regression uses the theory of binomial probability which represents having only two values to predict: that probability (p) is 1 instead of 0, i.e. the event belongs to one group instead of the other. It utilizes the maximum likelihood estimation method after transforming the dependent variable into a logit variable (the natural log of the odds of the dependent variable occurring or not).

2.2 Binary logistic regression Assumptions[11]

Logistic regression does not require the relationship between the independent (explanatory) variables and the dependent (response) variable to be linear, does not require normally distributed errors and homoscedasticity, and has fewer requirements in general. However, the observations must be independent, and the independent variables must be linearly related to the dependent's logit. Finally, because Maximum Likelihood coefficients are a big sample mean, the sample size must be greater than that required for logistic regression.

2.3 Logistic model [17][8][7]

The relationship between the dependent and independent variables is described in terms of logit, the natural logarithm of odd. If Y is a dichotomous outcome variable and X is a continuous predictor variable, the logistic model predicts the logit of Y from X, which is the natural log of Y's odds. The form of logistic regression model can be written as:

$$logit(Y) = ln\left(\frac{\rho}{1-\rho}\right) = \alpha + \beta x \quad .... (1)$$

ρ: Is the probability of occurring the outcome Y

$(\rho/1-\rho)$: is the odds of success; the ratio of probability of occurring the outcome Y and the probability of non-occurring the outcome Y.

α: Is a Y-intercept

β: Is a parameter of the slope,

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X can be categorical, whereas Y is always either qualitative or categorical. By taking the logarithm of Equation 1 on both sides, one can derive the following equation to estimate the probability of the desired outcome:

$$\rho(x) = P(Y|X = x) = \frac{e^{\alpha+\beta x}}{1+e^{\alpha+\beta x}} \quad .... (2)$$

Logistic model can be extended for more than one dependent (predictor) as well,

$$\text{logit}(Y) = \ln\left(\frac{\rho}{1-\rho}\right) = \alpha + \beta_1 X_1 + \cdots + \beta_p X_p \quad .... (3)$$

Therefore

$$\rho(x) = P(Y|X = x) = \frac{e^{\alpha+\beta_1 X_1+\cdots+\beta_p X_p}}{1+e^{\alpha+\beta_1 X_1+\cdots+\beta_p X_p}} \quad .... (4)$$

Equation (4) is the general form of logistic regression model for p number of predictors.

2.4 Estimation of Parameters [9][16][5]

Regression parameters β's can be estimated by either the maximum likelihood method (ML) or weighted least square method. The value of regression coefficients indicates the relationship between X's and logit of Y.

The maximum likelihood method can be used to estimate the parameters of the logistic regression model. Yi is a random variable and is independent with i=1, 2,…,n likelihood function of Yi defines as:

$$f(y_1, y_2, \dots, y_n) = \prod_{i=1}^{n} \pi(x_i)^{y_i}(1 - \pi(x_i))^{1-y_i} \quad .... (5)$$

since $\frac{\pi(x_i)}{1-\pi(x_i)} = e^{(\beta_0+\beta_1 x_i)}$ and $1 - \pi(x_i) = \frac{1}{1+e^{(\beta_0+\beta_1 x_i)}}$ then we can present equation as:

$$f(y_1, y_2, \dots, y_n, \beta_0, \beta_1) = l(\beta_0, \beta_1) = \prod_{i=1}^{n} (e^{(\beta_0+\beta_1 x_i)})^{y_i} \frac{1}{1+e^{(\beta_0+\beta_1 x_i)}}$$

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The log-likelihood function is used to simplify likelihood function. The log likelihood function is defined as follows:

$$l(\beta_0,\beta_1) = \ln(l(\beta_0,\beta_1) = \sum_{i=1}^{n} y_i(\beta_0+\beta_1 x_i) - \sum_{i=1}^{n}\ln\left(1+e^{(\beta_0+\beta_1 x_i)}\right) \text{ .... (6)}$$

The derivative of log-likelihood function with respect to B_0 is taken

$$\frac{\partial l(\beta_0,\beta_1)}{\partial\beta_0} = \sum_{i=1}^{n} y_i - \frac{e^{(\beta_0+\beta_1 x_i)}}{1+\ e^{(\beta_0+\beta_1 x_i)}}$$

Because $\pi(x_i) = \frac{e^{(B_0+B_1 x_i)}}{1+e^{(B_0+B_1 x_i)}}$ then we can present above equationas:

$$\frac{\partial l(\beta_0,\beta_1)}{\partial\beta_0} = \sum_{i=1}^{n} y_i - \pi(x_i) \ = 0$$

The derivative of log-likelihood function with respect to B_1 is

$$\frac{\partial l(\beta_0,\beta_1)}{\partial\beta_1} = \sum_{i=1}^{n} y_i x_i - x_i\frac{e^{(\beta_0+\beta_1 x_i)}}{1+\ e^{(\beta_0+\beta_1 x_i)}}$$

And can present as follows (since $\pi(x_i) = \frac{e^{(\beta_0+\beta_1 x_i)}}{1+\ e^{(\beta_0+\beta_1 x_i)}}$)

$$\frac{\partial l(\beta_0,\beta_1)}{\partial\beta_1} = \sum_{i=1}^{n}\left(y_i x_i - x_i\pi(x_i)\right) = \sum_{i=1}^{n} x_i\left(y_i - \pi(x_i)\right) = 0 \text{ .... (7)}$$

Because finding the solutions analytically is difficult, the Newton Raphson numerical iteration method should be used to obtain the values. With respect to the parameters, A(B) is defined as a matrix of the first derivative of the log-likelihood function.

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$$A(\beta) = \begin{bmatrix} \frac{\partial l(\beta)}{\partial \beta_0} \\ \frac{\partial l(\beta)}{\partial \beta_1} \end{bmatrix} = \begin{bmatrix} \sum_{i=1}^{n} y_i - \pi(x_i) \\ \sum_{i=1}^{n} y_i x_i - x_i \pi(x_i) \end{bmatrix}$$

and I(B)$^{-1}$ is:

$$I(\beta) = \begin{bmatrix} \frac{\partial^2 l(\beta)}{\partial {\beta_0}^2} & \frac{\partial^2 l(\beta)}{\partial \beta_0 \partial \beta_1} \\ \frac{\partial^2 l(\beta)}{\partial {\beta_1}^2} & \frac{\partial^2 l(\beta)}{\partial \beta_0 \partial \beta_1} \end{bmatrix}$$

$$I(\beta) = \begin{bmatrix} \sum_{i=1}^{n} \pi(x_i)(1-\pi(x_i)) & \sum_{i=1}^{n} x_i \pi(x_i)(1-\pi(x_i)) \\ \sum_{i=1}^{n} x_i \pi(x_i)(1-\pi(x_i)) & \sum_{i=1}^{n} {x_i}^2 \pi(x_i)(1-\pi(x_i)) \end{bmatrix} \quad ....(8)$$

2.5 Wald Test [16, 14]

Statistical significant of the regression coefficient can generally be tested by Wald’s test (also called the Wald Chi-Squared Test), which test the following hypothesis:

$H_0: B_i = 0$

$H_1: B_i \neq 0$

And can be obtain it as:

$$wald\ test = \frac{b_i}{SE\ (b_i)} \quad .... (9)$$

Where bi is the estimate of the coefficient of the predictor variables and SE (bi) is the standard error of bi.
The Wald test has a one-degree-of-freedom chi-square distribution. If the test's p-value is less than 0.05, the null hypothesis is rejected (significance level) which indicates that the variable is significant in the model.

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2.6 Goodness of Fit test[8]

As in linear regression, the goodness of fit in logistic regression attempts to get at how well a model fits the data. Unlike when using linear regression the r-square, measures the amount of variation in the dependent variable that is explained by the independent variables, in logistic regression, there is controversy regarding the relevance of r-square measures in assessing the predictive power of a model. It uses several pseudo-R2 statistics. In this paper, two pseudo R2 values will use: Cox and Snell R2 and Nagelkerke which computed as:

$$Cox\ and\ Snell\ R^2 = \left(\frac{-LL_0 - LL_1}{-LL_0}\right)^{\frac{n}{2}} \ \ldots.(10)$$

$$\text{Nagelkerke } R^2 = \frac{\left(\frac{-LL_0 - LL_1}{-LL_0}\right)^{\frac{n}{2}}}{1 - \ (-2LL_0)^{\frac{n}{2}}} \quad \ldots.(11)$$

Where LL_0 is the loglikelihood of the null model and LL_1 is the loglikelihood of the full model.

The Hosmer-Lemeshow goodness-of-fit statistic is another test used to assess the model fit. The test compares the predicted values against the actual values of the dependent variable. The method is similar to the chi-square goodness of fit. The Hosmer-Lemeshow test involves grouping the sample into groups based on the percentiles of estimated probability. The following formula is used to compute the Hosmer-Lemeshow test:

$$Hosmer - Lemeshow\ test = \sum_{i=1}^{k} \frac{O_i - \acute{n}_i \hat{\pi}_i{}^2}{\acute{n}_i \hat{\pi}_i (1 - \hat{\pi}_i)} \ldots.(12)$$

Where, $\acute{n}_i$ is the number of observations in the ith group, O_i is the showed outcomes in group i , The number of groups is k, and π is the estimated probability of an event outcome each group.

2.7 Omnibus Test of Model Coefficients [10][14]

Omnibus testing is an alternative to Hosmer-Lemeshow testing. It tests whether Models with predictors are significantly different from models with the only intercept. This test is interpreted as a model's ability test to predict the dependent variable when all dependent variables are used jointly. Significance corresponds to

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the conclusion that the data fits the model sufficiently, which means that at least one predictor variable is significantly related to the response variable.

2.8 Likelihood Ratio test [2][11]

The Likelihood ratio test is used for checking the significance of the difference between the likelihood ratio for the reduced model with explanatory variables and the likelihood ratio for the current model with only a constant in it. The statistic is given by:

$$G = [(-2\log L_0) - (-2\log L_1)] \quad .... (13)$$

Chi-square is used to evaluate the significance of this ratio. If the test is significant then the dropped variable will be a significant predictor in the equation whilst on the other hand If the probability is unable to reach the 0.05 significance level, we do not reject the null hypothesis then the variable is considered to be unimportant and thus will be excluded from the model.

2.9 Model selection [2][11][19]

Logistic regression, like any other model-building technique in statistics, is aimed at finding the best fitting model to assess the relationship between response variables and at least one independent variable. To obtain the best binary logistic regression model we first try to get a combination of models using best subset regression depending on Akaike Information Criterion (AIC) which can be used to select the best model. The formula for calculating AIC is:

$$\mathrm{AIC} = 2\mathrm{P} - 2\ln(\mathrm{likelyhood}) \quad .... (14)$$

Where P is the number of parameters in the model likelihood is the probability of the data given a model. AIC rewards goodness of fit and penalizes and for overfitting. A model with the lowest AIC value will be the most preferable model.

2.10 The Classification table [1][4][17]

A classification table is a good way to summarize the results of a fitted logistic regression model. This table is the result of cross classifying the outcome variable with dichotomous variables whose values are derived from the estimated logistic probabilities. The model's precision is depicted in the reclassification table. It depicts the frequencies of the predicted and observed classification of cases, as well as the

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percentage of correct predictions which depends on the logistic model. It represents the frequencies of the predicted and observed classification of cases and the percentage of correct predictions depend on the logistic regression model.

3.1 Data description

Logistic regression provides a method for modeling a binary response variable, which takes values 1 and 0. In this paper, we may wish to investigate how death (0) or survival (1) of patients can be predicted by taken explanatory variables. The used variables demonstrate in the following table.

Table2- Variable description

Number	Variable	Attribute Name
1	x_1	Age
2	x_2	Gender
3	x_3	Complete blood count
4	x_4	Chest X-Ray
5	x_5	D. Dimer
6	x_6	Type tests
7	x_7	Erythrocyte Sedimentation Rate
8	x_8	Coronary Involvement
9	Y	Patient status

The data were obtained from d. Jamal Ahmad Rashid Pediatrics Teaching Hospital in Sulaimani. The sample size of the data is 50 cases, as shown in table 2, and the data set was classified into two groups; the first group with 40 which shows 80% of observations, and the second group with 10 which represents 20% 0f observations.

Table2- Data classification

Class	**Size**	**Percentage**
Survival	40	80%
Died	10	20%

3.2 Analysis of binary logistic regression

The analysis can be showed in figure 1:

Assumptions:

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- Outcome variable follows binary distribution
- The error terms needs to be independent
- Assumes linearity of independent variables and log of odds

Creating Model:

- Outcome variable is categorical
- independent variable can be continuous or categorical

Model estimation:

- Estimate the intercept and regression coefficients

Goodness of Fit:

- Cox and Snell R^2
- Nagelkerke R^2
- Hosmer Lameshow test

Figure 1- Binary logistic regression Essential

3.2.1 Omnibus Tests of Model Coefficients

The enter method of model fitting includes entering all variables at the same time. The model chi-square and significance levels for testing the null hypothesis that all coefficients are equal to zero are shown below

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Table3- Omnibus Tests result

Model		Chi-square	df	Sig.
Enter	Step	23.289	11	0.003
	Block	23.289	11	0.003
	Model	23.289	11	0.003

The model chi-square value (chi-square values = 23.289), the null hypothesis is rejected because the sig. is less than 0.05, implying that the addition of the independent variables improved the model's predictive power. Because all values were input at the same time, the block and step values are equivalent to the model values.

3.2.2 Model selection

We apply a process that evaluates all feasible models to represent the best subsets of model selection by using automatic selection. As we mentioned before, we depend on the AIC criterion and backward stepwise (Likelihood Ratio) for this purpose.

Table 4 - Model selection

Model	AIC
x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8	41.449
x_1, x_2, x_3, x_4, x_5, x_6, x_7	39.593
x_1, x_2, x_3, x_4, x_5, x_6	37.808
x_2,x_3, x_4, x_5, x_6	36.783
x_2,x_3, x_4, x_6	35.918
x_3, x_4, x_6	35.791
x_3, x_6	35.775

As presented in table 3, the last model, which contains the two explanatory variables: x3(Complete blood count) and x6(Type of test), has the lowest AIC value among the six most effective models.

3.2.3 Model Summary

The values in the model summary show how well the model fits the data. The present model's -2 Log likelihood (goodness of fit test) values is 29.775, while the Intercept's only model was 33.914, a difference of 4.139, showing an improvement in the model after the independent variables were added. This means that by adding the variables in the model, the models' prediction power was improved.

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Table 5- Model fitting

Model	-2 log likelihood	Cox and Snell R^2	Negelkerke R^2
Intercept only	33.914		
Final model	29.775	0.293	0.476

The two other measurements (Cox and Snell R2 and Nagelkerke R2) were provided as a supplement to other more evaluative goodness of fit measures. From table 4, the response variable defines 29.3 % of the variance in explanatory variables according to Cox & Snell R2 value and 47.6% according to Nagelkerke R2 value which is the modified form of the Cox & Snell coefficient.

Also, Hosmer and Lemeshow test is commonly used to measure the goodness of fit, where the null hypothesis of the test is: model fit the data well. The test result is as follows:

Table 6 – Hosmer – lameshow test

Chi square	df	Sig.
3.360	8	0.910

Our data resulted a x^2 (8) of 3.360 with p value 0.910 (insignificant, p value > 0.05), suggesting the model was fit to the data well.

3.2.4 Estimation of Logistic Regression Parameters

Regression parameters are generally estimated by Maximum likelihood estimation technique which depends on Wald statistic.

Table 7- Results of logistic regression

Predictors	β	Std. Error	Wald	d.f	Sig.	*Odd Ratio* (e^{β})
Complete blood count	-0.008	0.003	7.822	1	0.005	0.992
Type test	1.025	1.177	6.611	1	0.010	2.787

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Constant	-0.002	1.429	0.000	1	0.999	0.998

From the above results, the fitted binary logistic regression model can write down as:

$$\text{logit(Y)} = \ln\left(\frac{\pi}{1-\pi}\right) = -0.002 + (-0.008)\ \text{Complete blood count} + 1.025\ \text{Type test}$$

The P-value (< 0.05) indicates the significance of each predictor. The predictor's Complete blood count is negatively related to the log of odds of died status. The coefficient of this predictor was -0.008, which means that. So, a unit increase in blood count leads to a decrease of (1- 0.992)* 100% = 0.8 % in the odds of death status. In other words, we can say that the odds of death for a suitable test (1.787) times higher than an unsuitable test.

3.2.5 Classification of the logistic regression model

The classification table was conducted to show the accuracy of the model, and the results as follows:

Table 8 - Classification result

Observed			Predicted		
			Died		Percentage Correct
			0	1	
Step 0	Died	0	4	6	44.4
		1	2	38	95.0
		Overall Percentage			85.7

As present in the 'classification result table', we can conclude that 38 of 40 persons from the survived group were classified correctly, and 4 of 6 persons from the dead group were classified correctly and the overall full model correct classification was 85.7% (42 out of 50 persons were classified correctly).

4. Conclusion

In this paper, we demonstrated binomial logistic regression with its application in a medical data set. The independent variables that were used in the model are age, gender, Complete blood count, Chest X-Ray, D. Dimer, Type of test, Erythrocyte sedimentation rate, and Coronary Involvement. By depending on both the AIC

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criterion and stepwise method, the best model is the model that consisting of two explanatory variables. The first variable is a Complete blood count test, the test of the count of eosinophil which is closely related to the mortality rates is a test that can aid in the early recognition of COVID-19 in patients, as well as provide prognostic information; therefore it can save the life of a Covid-19 patient.

The other variable is the type of test. It has an important impact on identify a positive or negative case of coronavirus disease and getting the right treatment which leads to a decrease death rate. In addition, the analysis showed that the binary logistic model's performance provided a high level of classification ability which is equal to 84%. Furthermore, the likelihood ratio and Wald test were used to determine the significance of the logistic coefficients. It is observed that there is a negative correlation between the Complete Blood Count test and died status but the Type of test has a positive impact on the dependent variable.

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پوخته

سەرەڕای ئەوەی ڤایرۆسی کۆرۆنا بە کەمی کاریگەری ڕاستەوخۆی هەیە، بەڵام کاریگەریە لاوەکیەکانی ئەم نەخۆشیە لەوانەیە کارەسات بیت بۆ منداڵان، کە ئەبیتە هۆکاری گەورەی موعانات ومردن. هەروەها با هۆی ئەم ناخۆشیە ولێکەوتەکانی هۆکارە سەرەکیەکانی خراپ بونی تەندروستی و مردن زیادی کردوە لە ماوەی ئەم ساڵەدا. لە هەمان کاتدا تواناى دەوڵەتان وسیستمی تەندروستی و ڕێکخراوە مرۆڤایەتیەکان تایبەت بە گرنگی دان بە تەندروستی منداڵ کەمی کردوە.

لەم توێژینەوەیەدا داچەمینەوەی لوجستی دوانی بەکارهاتووە بەئامانجی ناسین ودیاریکردنی هوکاری مردنی مندالی ساوا وە مندالی خوار تەمەنی 14 ساڵان بەپشت بەستن بە داتای ڤایروسی کۆرۆنا. ئەم زانیاریانەی وەرگیراوە پێکهاتوەلە (50) نەخوش کەبەشیوەیەکی هەرەمەکی کوکراوەتەوە کە (10) مندال مردون وە ئەوانی تر لەژیاندا ماون، لە ئەنجامی توێژینەوەکە دەرکەوت کە دوو گۆڕاو لة کۆی هەشت گۆڕاو کاریگەربوون ئەوانیش (Complete Blood Countو Type of test),ڕێژەی سەدی پۆلێنکردنەکە 84% دەرچووە کە ئەمەش پیشانی ئەدات کە مودیلەکە بەرادەیەکی زۆر گونجاوە.

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الملخص

على الرغم من أن التأثير المباشر لفيروس كوروناعلى الأطفال نادر الحدوث، إلا أن التأثير غير المباشر لهذا الوباء العالمي يمكن أن يكون كارثيًا للأطفال، مما يتسبب في قدر كبير من الوفيات والمعاناة. تم زيادة العديد من الأسباب الرئيسية لسوء الصحة والوفيات بين الأطفال هذا العام نتيجة للوباء والاستجابة. في نفس الوقت، انخفضت قدرة الحكومات والنظم الصحية والمنظمات الإنمائية والإنسانية على الاستجابة لصحة الطفل.

في هذا البحث تم استخدام تقنية تحليل الانحدار اللوجستي الثنائي لغرض التعرف وتحديد أسباب موت حديثي الولادة والأطفال تحئ سن الـ ١٤ وبناء أفضل نموذج لبيانات فيروس كورونا. تم تحديد عينة عشوائية مكونة من 50 مريضاً، 10 مريضاً ماتوا وال 40 البقية ظلوا على قيد الحياة، نتيجة التحليل أظهرت 2 من أصل 8 متغيرات كانت بارزة احصائياً المكونة من: type of test وComplete Blood Count. النسبة المئوية الصحيحة للتصنيف كانت ٨٤ ٪، التي تشير إلى القدرة العالية التقريبية للنموذج على التصنيف.