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Study the Risk Factors Associated with ICU Admission for Children that are infected with Influenza

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Abstract: Many patients get infected with flu, but some of them develop severe disease that mandates ICU admission. The aim of this study is to improve careful measures in dealing with the disease for children and reduce the possibility of children entering the ICU if they get infected with flu. We checked some parameters and its association with admitting the children infected with flu to the ICU. We used a logistic regression model to represent the data and to determine significant and insignificant factors. As this study focused on children aged 0-16 years old, the study shows that the gender and premature birth are significant factors that play an important role in children entering the ICU. We discovered that children who were had early birth, were more likely to enter the ICU. We also found out that female children were more likely to need intensive care unit more than male children.

Keywords: ICU, SAS, Risk Factor.

1. INTRODUCTION

Influenza is an infectious disease that affects the respiratory system caused by influenza viruses that infect the throat and nose and sometimes infect the lungs. The flu causes mild to severe illness and may even cause death *[1]*. Adults and children can get infected by the flu; if we focus on children, most children will get infected by the flu for a week or less. But for some children, the risk of disease could be increased. It may need to enter the intensive care unit) ICU), in some cases, influenza may also cause lung injury or death for children *[2]*.
To understand why some children need to be entered the (ICU) we use statistical analysis to determine the main factors that affect entering (ICU) for those children that have the flu. Binary logistic regression has made in this study. A binary logistic regression represents the relationship between a binary response variable and a set of predictors called factors. It has only two possible values, yes or no, and the binary regression model is used to understand

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how the factors considered are related to the probability of an event occurring *[3]*. The factors that are considered to study the association between the flu and entering ICU for children are age, gender, BMI, premature, and primary immunodeficiency.

studied the high youth mortality rate that was observed during the flu pandemic that occurred in Spain in 1918. Those who were 28 years old, were more likely to die during the epidemic and argue that as a result of direct exposure to influenza, they found out an increase in deaths. Also, they indicated that knowing the age pattern of exposure to the resulting deaths Flu can improve the performance of the crisis during influenza epidemics in the future *[4]*.

It was found that exposure to influenza infection by age has important implications for learning about disease dynamics and controlling it and being able to choose optimal vaccination strategies *[5]*. The efficiency of Triple IIV against hospital admission due to acute respiratory infection (ARI) infection was examined for ≥50-year-olds in Thailand. It was slightly effective, but IIV coverage was low *[6]*.

Male and female behavioral and societal differences contribute to different outcomes of exposure to influenza virus infection, Physiological differences between males and females, including immune responses to infection and vaccination, are taken into account differences in hormone concentrations to see how dangerous the disease is affected *[7]*. Antibodies show elevated female responses compared to males regardless of age. Studies show a strong correlation between androgenic participation genes in the fat metabolism process, which indicates the potential role of these findings in the reason for differences in immune responses between males and females *[8]*.

The likelihood of developing newborns with influenza is high due to the negative levels of the transmitted antibody. Modern treatments have proven that they can reduce the severity of the disease in adults, as such therapies are not used in newborns. Care and measures must be provided to restrain the infection and prevent its spread in the event of newborns influenza infection *[9]*.

2. MATERIALS AND METHODS

I. Data collection

Patient data were collected through a survey that was presented at King Abdullah University Hospital in Jordan on 209 cases of children with influenza from new-borns to the age of 16 years. The survey included the question about the patient's age, gender, height, and weight for the patient to calculate the body mass index for each patient and knowing whether he is facing immune deficiency or not and whether the patient had an early birth or not.

II. Variables

Status of entering ICU (yes, no) considered as outcome variables (response variable), the predictor variables are divided into two types. The first one is categorical type of data, which include gender (male, female) and premature (yes, no) and primary immunodeficiency (yes, no). the second type is continuous data such as, and body mass index.

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III. Statistical analysis

a. Collected data will be analyzed statistically using the logistic regression model considering category data analysis. Statistical Analysis System (SAS) software tool will be considered.

b. The model formulation:

$\text{Log}(\pi ij/(1-\pi ij) = \beta.+ \beta 1*X1 + ... \beta m *Xm$

c. Data analysis and discussion

The response (ICU) has two-levels (yes, no), the probability is (ICU) = yes. The frequency of each one is shown in table 1, and class model information shown in table 2. Age and body mass index (BMI) are continuous data, and age has values from (0-16) and (BMI) has the values dependent on each person's Hight and Wight.

Table 1: frequency of each level for (ICU)

Response Profile		
Ordered Value	**ICU**	**Total Frequency**
1	**NO**	**180**
2	**YES**	**28**

Table 2: Class Level Information

Class Level Information			
Class	**Value**	**Design Variables**	
gender	**female**	1	0
	meal	0	1
premature	**NO**	1	0
	Yes	0	1
primary immunodeficiency	**NO**	1	0
	yes	0	1

Firstly, the test was made on Global Null Hypothesis: BETA=0, to test that at least one of the predictors' regression coefficient is not equal to zero in the model [9]. the results were shown in table 3, it was concluded that at least one predictors' regression coefficient is not equal to zero because p-value in three tests is less than 0.05.

Testing Global Null Hypothesis: BETA=0			
Test	**Chi-Square**	**DF**	**Pr > ChiSq**
Likelihood Ratio	13.6066	5	0.0183

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Score	11.5100	5	0.0422
Wald	12.0674	5	0.0339

Table 3: Testing Global Null Hypothesis: BETA=0

The analysis of effects of each factor appears that we have two significant factors that effected on entering (ICU), the factors are gender and premature, This can be explained by low values of p-values for gender and premature factors, the other factors have no effect on entering (ICU) for children if they have influenza because have more than 0.05 values for p-value, The result shown in table 4.

Table 4: Analysis of Effects

Type 3 Analysis of Effects			
Effect	**DF**	**Wald Chi-Square**	**Pr > ChiSq**
gender	1	4.2635	0.0389
premature	1	5.2171	0.0224
primary immunodeficiency	1	0.8252	0.3637
age	1	0.0386	0.8442
BMI	1	1.6364	0.2008

The third important component of model evaluation is R-square, R-square is a statistical measure of how close the data are to the fitted regression line (How To Interpret R-squared and Goodness-of-Fit in Regression Analysis - Data Science Central, n.d.), R-square in our model is just 0.06, so that indicates how the model fits the data and because the p-value is low, it was concluded that the model is not appropriate to represent the data, this may be due to the need for more data than taken. Table 5 shows this result.

Table 5: R-square value

R-Square	0.0633	**Max-rescaled R-Square**	0.1159

The next step before analysing the remaining measurements we must remove the insignificant factors from the model, the results after removing the insignificant factors listed in table 6.

Analysis of Maximum Likelihood Estimates						
Parameter		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
Intercept		1	-1.8357	0.3409	28.9931	<.0001
gender	**female**	1	0.8866	0.4183	4.4935	0.0340
gender	**meal**	0	0	.	.	.
premature	**NO**	1	-0.9988	0.4361	5.2453	0.0220

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premature	**Yes**	0	0	.	.	.

Table 6: Analysis of effects after removing insignificant factors

The most important concepts to understand the relationship between factors and response is the odds ratio, in logistic regression, the odds ratio represents the constant effect of a predictor X, on the likelihood that one outcome will occur [10] , [11]. The results of odds ratio for the model are shown in table 7 and interpreting it.

Table 7: odds ratio estimates

Odds Ratio Estimates			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
gender female vs meal	2.427	1.069	5.509
premature NO vs Yes	0.368	0.157	0.866

The odds ratio for gender tells that if the patient is female, there are 2.42 times more likely to be entered (ICU) than if the patient is male. Confidence interval indicates that on 95% of the patient the odds ratio will be between (1.069 - 5.509), that's mean the odds of entering (ICU) for the female is getting between (1.069 – 5.509) times higher than odds for the male to entering (ICU) to 95% of cases.

But regarding the odds ratio for premature, it tells that the patient who gave birth prematurely there are 2.7 times more likely to be entered the (ICU) than if the patient was not born with premature birth. And the same for confidence interval here, the odds of entering (ICU) for who gave birth prematurely is getting between (1.069 – 5.509) times higher than odds for the patient was not born with premature birth to entering (ICU) to 95% of cases. The odds ratio represented as a graph in figure 1.

One of the important measurements that can be used to check the model fit at each observation is Pearson residuals; Pearson residuals are defined to be the standardized difference between the observed frequency and the predicted frequency. From the scattered plot shows in graph 2, it can be found out that the data appeared randomized. And there are some data that have a standardized residual above 2, which means there is a highly standardized difference between the observed frequency and the predicted frequency. (Too many observations compared to independence).

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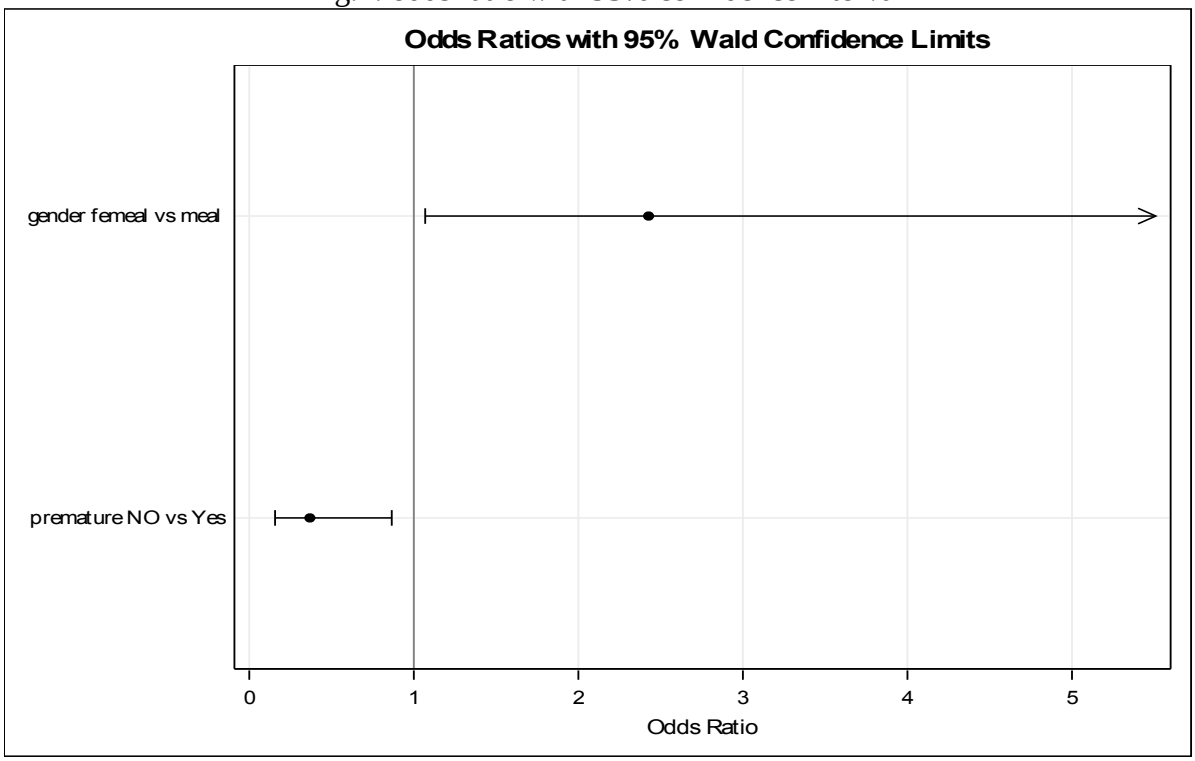
Fig.1: odds ratio with 95% confidence interval



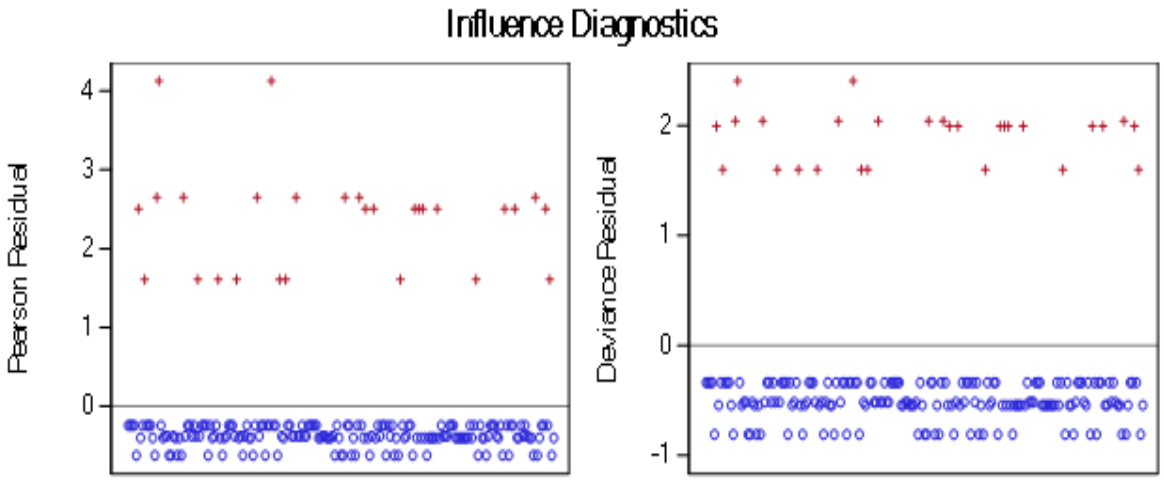


Fig.2: influence diagnostic

3. CONCLUSIONS

The binary logistics model was developed and solved to study the effects of different factors on the (ICU) response using the SAS software. Based on the results achieved, the following points can be concluded:

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- The factors affecting entry into the intensive care unit are gender and premature birth because they have p-value less than 0.05.
- Body mass index, age and primary immunodeficient factors have no effect on the response because they have p-value more than 0.05.
- The odds ratio for gender factor tells us that if the patient is female there are 2.42 times more likely to be entered the (ICU) than if the patient is meal.
- The odds ratio for premature factor tells us that the patient who gave birth prematurely there are 2.7 times more likely to be entered the (ICU) than if the patient was not born with premature birth.

This analysis helps us to understand the effect of both the person's gender and early childbirth on the severity of influenza affected by the occurrence of other complications, and how the necessary precautions can be taken in these cases until any serious complications leading to death are prevented.

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