Identifying Factors affecting the Severity of Asthma

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ABSTRACT
The factors that significantly affect the severity and the relationship between those identified factors and severity level were examined in the study. The forward stepwise binary logistic regression analysis was done to identify factors affecting the severity of asthma. Results showed that the factors, living in urbanized areas, having stress, cigarette smoking, exposing to smoke from mosquito coils and other chemical gasses had a strong effect for asthma to be severe. Out of them exposing to smoke of mosquito coils was the most significant factor for asthma to be severe and the odds of being severe rather than being not severe increased by a factor of 24.43 by exposing to smoke of mosquito coils rather than not exposing to smoke from mosquito coils.

Key words: Asthma, severity, stepwise logistic regression analysis, odds ratio
1. INTRODUCTION
Asthma is defined by the Global Initiative for Asthma as "a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The word asthma comes from the Greek word for "panting." People with asthma pant and wheeze because they cannot get enough air into their lungs. Asthma was first recognized in ancient Egypt. During the 1930s–50s, asthma was considered as a psychological illness. A paper published on the subject in 1873 tried to explain the pathophysiology of the disease. Especially in Sri Lanka hospital admissions and deaths due to asthma have increased significantly over the last two decades. Asthma has become very common with immense social impact.

Asthma is a common chronic inflammatory disorder of the airways that leads to wheezing, coughing, chest tightness and shortness of breath particularly at night. Asthma is an episodic disease, with acute exacerbations interspersed with symptom-free periods. However, there can be a phase in which the patient experiences some degree of air way obstruction daily. So Asthma severity can be classified as the disease occurs daily which is the severe asthma and the disease does not occur daily which is not severe. Asthma is a frustrating disease for both patients and health care providers. Patients with asthma often feel that their disease is not treated effectively. Surveys reveal that most asthmatic patients limit their activities because of respiratory symptoms and as a consequence, report dissatisfaction with their lifestyles. Health care providers recognize that routine asthma care requires millions of office visits annually and that acute asthma problems prompt many additional emergency department visits.

300 million people worldwide are affected by asthma and estimated 300 million people worldwide suffer from asthma, with 250,000 annual deaths attributed to the disease. It is estimated that the number of people with asthma will grow by more than 100 million by 2025. The number of people with asthma continues to grow. One in 12 people (about 25 million, or 8% of the population) had asthma in 2009, compared with 1 in 14 (about 20 million, or 7%) in 2001 Asthma accounts for about 10.1 million missed work days for adults annually and it has become a major cause of work and school absence and loss of productivity. Therefore it has many costs to society as well as to the individual affected.

Sometimes the attacks of asthma may lead to acute ventilator failure and even death. Genetic and environmental factors may contribute to its initiation and continuation. Bryant-Stephens T. (1) states that children live in urban environments experiencing high asthma morbidity and mortality. Tatum AJ et.al. (2) states that outdoor air pollution and tobacco smoke affect health in persons with asthma. Though these factors are possible exacerbation factors of asthma they are not clearly identified as exact exacerbation factors. The researchers are still studying whether they actually affect significantly for the severity. Therefore this research was carried out to identify factors which significantly affect for the severity of asthma then describe the relationship of those factors with the severity of the disease. The study is significant in statistically. Logistic regression analysis is mainly used to obtain the results for the objectives of the study. The study is significant in medicine as well as it is significant in statistically. The study is significant in medicine since there is currently no cure for asthma and no single exact cause has been identified. Therefore, understanding the changes that occur in asthma, factors affect for the severity of the disease and how it can behave over time is vital.

Logistic regression analysis is a statistical technique that is used extensively in numerous disciplines, including the medical and social science fields. For example, the Trauma and Injury Severity Score (TRISS), which is widely used to predict mortality in injured patients, was originally developed by Boyd et al using logistic regression. Understanding the changes that occur in asthma, factors affect for the severity of the disease and how it can behave over time is vital. This knowledge empowers patients to take an active role in their own health care in avoiding triggering factors and maintaining a good clinical management.
Severity of asthma
Asthma is an episodic disease, with acute exacerbations interspersed with symptom-free periods. However, there can be a phase in which the patient experiences some degree of airway obstruction daily. So Asthma severity can be classified as the disease occurs daily which is the severe asthma and the disease does not occur daily which is not severe. Asthma is a frustrating disease for both patients and health care providers. Patients with asthma often feel that their disease is not treated effectively. Surveys reveal that most asthma patients limit their activities because of respiratory symptoms and as a consequence, report dissatisfaction with their lifestyles. Health care providers recognize that routine asthma care requires millions of office visits annually and that acute asthma problems prompt many additional emergency department visits. Sometimes the attacks of asthma may lead to acute ventilator failure and even death. Asthma causes deaths, especially in high risk inner city populations. Persistent asthma can cause deterioration in lung function over time, e.g. conversion from reversible airflow obstruction to irreversible airflow obstruction as seen in chronic obstructive pulmonary disease.

Factors affecting the severity of asthma
From an etiologic standpoint, asthma is a heterogeneous disease and genetic and environmental factors may contribute to its initiation and continuation. The possible factors that may affect the severity are cigarette smoke, household dust, using mosquito coils, chemical gasses, animal dander, perfumes, emotional stress, aspirin etc. Though these factors are possible exacerbation factors of asthma they are not clearly identified as exact exacerbation factors, but the researchers are still studying whether they actually affect significantly for the severity. The recent studies are being done to identify whether there is a possibility that genetic factors may influence not only the presence of asthma, but the severity of the asthma condition, as well and also the duration of the disease, age, gender and geographical variation that is whether living in an urbanized area with air pollution or a rural area can affect the severity of asthma.

2. METHODOLOGY
The target population was registered asthmatic patients in the main chest clinic in Kegalle district. Using simple randomized sampling technique a sample of 225 asthmatic patients was selected. By distributing questionnaires to the sample of asthmatic patients the data were obtained. On statistical analysis, data were analyzed using statistical package for social sciences (SPSS) software. The statistical significance and difference were considered at p<0.05.

2.1 Sample Design
The sampling method was based on the simple randomized sampling procedure. For the objective, to predict the morbidity rate which is the proportion of severe asthmatic patients, a sample was taken to represent the population. Among children, asthma occurs at all ages but it does not continue of many children. Therefore the populations of adult asthmatic patients who are above 12 years are taken for the study. The population had 2599 registered asthmatic patients up to the time the study was carried out. Considering the proportion of severe patients as the parameter p, the sample size was calculated. First a pilot survey was carried out to get an estimate for p. It was conducted among 20 randomly selected asthmatic patients and p was obtained as 20%.

By using the formula, \[ n = \frac{(pq/v)}{1 + ((pq/v) - 1)/N) \]
where \( v = (d/z_a)^2 \) d is chosen as 5 and at 5% significance level \( z_a \) is 1.96 n was calculated as 225.
To identify the factors which significantly affect the severity of asthma, a number of suspicious facts were used as input variables for the analysis. Those input variables were age, gender, living area, whether having cats and/dogs at home, exposure to household dust, smoking, exposure to chemical gases, exposure to smoke from mosquito coils, usage of perfumes, usage of aspirin, having stress, duration of the disease and the family history. The severity assessed using the two severity levels, mild (the disease does not occur daily) and severe (the disease occurs daily).

A forward stepwise logistic regression was performed to evaluate the factors which significantly affect the severity and model the relationship between significant factors with the severity of the disease. Odds ratios were obtained to get a measure of association between the categories of identified significant factors across the severity levels.

2.2 Overview of Logistic Regression

Logistic regression allows one to predict a discrete outcome, such as group membership, from a set of variables that may be continuous, discrete, dichotomous, or a mix of any of these. Generally, the dependent or response variable is dichotomous, such as presence/absence or success/failure. Discriminant analysis is also used to predict group membership with only two groups. However, discriminant analysis can only be used with continuous independent variables. Thus, in instances where the independent variables are a categorical, or a mix of continuous and categorical, logistic regression is preferred.

2.3 The Logistic Regression Model:

The dependent variable in logistic regression is usually dichotomous, that is, the dependent variable can take the value 1 with a probability of success $\theta$, or the value 0 with probability of failure $1-\theta$. This type of variable is called a Bernoulli (or binary) variable. Although not as common and not discussed in this treatment, applications of logistic regression have also been extended to cases where the dependent variable is of more than two cases, known as multinomial or polytomous [Tabachnick and Fidell (1996) use the term polychotomous].

As mentioned previously, the independent or predictor variables in logistic regression can take any form. That is, logistic regression makes no assumption about the distribution of the independent variables. They do not have to be normally distributed, linearly related or of equal variance within each group. The relationship between the predictor and response variables is not a linear function instead, the logistic regression function is used, which is the logit transformation of $\theta$:

$$\theta = \frac{e^{(\alpha + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_n x_n)}}{1 + e^{(\alpha + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_n x_n)}}$$

where $\alpha$ = the constant of the equation and, $\beta$ = the coefficient of the predictor variables.

An alternative form of the logistic regression equation is:

$$\text{logit} [\theta(x)] = \log \left( \frac{\theta(x)}{1-\theta(x)} \right) = \alpha + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_n x_n$$

The goal of logistic regression is to correctly predict the category of outcome for individual cases using the most parsimonious model. To accomplish this goal, a model is created that includes all predictor variables that are useful in predicting the response variable. Several different options are available during model creation. Variables can be entered into the model in the order specified by the researcher or logistic regression can test the fit of the model after each coefficient is added or deleted, called stepwise regression.

There are two main uses of logistic regression. The first is the prediction of group membership. Since logistic regression calculates the probability or success over the probability of failure, the results of the
analysis are in the form of an odds ratio. Logistic regression also provides knowledge of the relationships and strengths among the variables.

The logistic equation: Logistic regression predicts the log odds of the dependent event. The “event” is a particular value of Y, the dependent variable. By default the event is Y = 1 for binary dependents coded 0, 1, and the reference category is 0. The natural log of the odds of an event equals the natural log of the probability of the event occurring divided by the probability of the event not occurring.

\[ \ln(\text{odds (event)}) = \ln(\text{prob (event) / prob (nonevent)}) \]

\[ \text{Exp (b)} = \text{the odds ratio for an independent variable = the natural log base raised e to the power of b.} \]

The odds ratio is the factor by which the independent increases or (if negative) decreases the log odds of the dependent.

**2.4 Stepwise logistic regression**

The forward or backward stepwise logistic regression methods, available in binary and regression in SPSS, determine automatically which variables to add or drop the model. As data-driven methods, stepwise procedures run the risk of modeling noise in the data and are considered useful only for exploratory purposes.

**2.5 Binary logistic regression:**

Since the probability of an event must lie between 0 and 1, it is impractical to model probabilities with linear regression techniques, because the linear regression model allows the dependent variable to take values greater than 1 or less than 0. The logistic regression model is a type of generalized linear model that extends the linear regression model by linking the range of real numbers to the 0-1 range.

Start by considering the existence of an unobserved continuous variable, Z, which can be thought of as the "propensity towards" the event of interest. In the case of the loan officer, Z represents a customer's propensity to default on a loan, with larger values of Z corresponding to greater probabilities of defaulting.

In SPSS offers these variants in the Method area of the main binary logistic regression dialog: forward conditional, forward LR, Forward Wald, backward conditional, backward LR, or backward Wald. The conditional options uses a computationally faster version of the likelihood ratio test, LR options utilize the likelihood ratio test (chi-square difference), and the Wald options use the Wald test. The LR option is most often preferred. The likelihood ratio test computes -2LL with the target variable removed. The conditional option is preferred when LR estimation proves too computationally time consuming. The conditional statistic is considered not as accurate as the likelihood ratio test but more so than the third possible criterion, the Wald tests. The stepwise procedures are selected in the method dropdown list of binary logistic regression dialog.

**Wald Test:**

A Wald test is used to test the statistical significance of each coefficient (β) in the model. A Wald test calculates a Z statistic, which is:

\[ z = \frac{\hat{\beta}}{SE} \]

This Z value is then squared, yielding a Wald statistic with a chi-square distribution. However, several authors have identified problems with the use of the Wald statistic. Menard (1995) warns that for large coefficients, standard error is inflated, lowering the Wald statistic (chi-square) value. Agresti (1996) states that the likelihood-ratio test is more reliable for small sample sizes than the Wald test.
Hosmer-Lemshow Goodness of Fit Test:
The Hosmer-Lemshow statistic evaluates the goodness-of-fit by creating 10 ordered groups of subjects and then compares the number actually in the each group (observed) to the number predicted by the logistic regression model (predicted). Thus, the test statistic is a chi-square statistic with a desirable outcome of non-significance, indicating that the model prediction does not significantly differ from the observed.

3. RESULTS AND DISCUSSION
To identify the factors which significantly affect the severity of Asthma, a number of suspicious factors were used as input variables for the analysis. Those input variables were age, gender, living area, whether having cats and/dogs at home, expose to house hold dust, smoking, expose to chemical gasses, expose to smoke from mosquito coils, usage of perfumes, usage of aspirin, having stress, duration of the disease and the family history. The severity assessed using the two severity levels, mild (the disease does not occur daily) and severe (the disease occurs daily).
The results of the binary logistic regression analysis suggested that five factors significantly affect the severity of asthma at 5% level of significance.
Those factors were
1. Exposing to smoke of mosquito coils
Out of those five factors, exposing to smoke of mosquito coils was the most significant factor for asthma to be severe. The odds of being severe rather than being not severe increased by a factor of 24.43 by exposing to smoke of mosquito coils rather than not exposing to smoke from mosquito coils. If an asthmatic patient avoid usage of mosquito coils it can be greatly helpful to control the disease.
2. Having stress
Having stress is also has a considerable impact for asthma to be severe. If an asthmatic patient can avoid going through stressful events as much as possible the severity can be controlled.
3. Living area
Another significant factor is living in urbanized areas rather than living in rural areas. The air pollution with urbanization affect for the severe asthma. So it is important to control the air pollution in urbanized areas.
4. Smoking
The harmful smokes from cigarette smoking lead for severe asthma. If an asthmatic patient can avoid smoking it helps to control the severity.
5. Exposing to chemical gasses.
One can expose to other harmful chemical gasses such as sulphur dioxide nitrogen dioxide, carbon monoxide, ozone specially when doing occupations in some manufacturing factories. These chemical gasses also affect for asthma to be severe. It is recommended to avoid exposing to these chemical gasses as much as possible to control the severity.
The model for Severity of Asthma was obtained as
\[
\log_e \left( \frac{P \text{ (severe)}}{P \text{ (not severe)}} \right) = -7.241 + 2.497 \times \text{Living Area} [\text{Urbanized}] \\
+ 3.196 \times \text{Expose to smoke of mosquito coils} [=\text{yes}] \\
+ 2.112 \times \text{Expose to Chemical Gasses} [=\text{yes}] \\
+ 2.990 \times \text{Having Stress} [=\text{yes}] \\
+ 1.441 \times \text{Cigarette Smoking} [=\text{yes}].
\]
Overall, 93.8% of the cases are predicted correctly. Hosmer-Lemshow goodness of fit test and pseudo R-squared statistic indicated that the model adequately fits the data.
Exposing to smoke of mosquito coils was the most significant factor for asthma to be severe and the odds of being severe rather than being not severe increased by a factor of 24.43 by exposing to smoke of mosquito coils rather than not exposing to smoke from mosquito coils. For having stress, the odds of being severe rather than being not severe increased by a factor of 19.88 by having stress rather than not having stress. The odds of being severe rather than being not severe increased by a factor of 12.144 by living in an urbanized area rather than living in a rural area. For the factor, exposing to chemical gasses, the odds of being severe rather than being not severe increased by a factor of 8.261 by exposing to chemical gasses rather than not exposing to chemical gasses and smokes. And the odds of being severe rather than being not severe increased by a factor of 4.233 by smoking rather than not smoking.

Cox and Snell's R2 is based on the log likelihood for the model compared to the log likelihood for a baseline model. However, with categorical outcomes, it has a theoretical maximum value of less than 1, even for a "perfect" model.

McFadden's R2 is another version, based on the log-likelihood kernels for the intercept-only model and the full estimated model.

It was 0.541 for Cox & Snell’s R square and 0.785 for McFadden’s R square at the last iteration for this model. So it indicates that more of the variation is explained by the model (Table 1).

The test statistic is a chi-square statistic with a desirable outcome of non-significance at the last step in the Hosmer and Lemeshow Test, indicates that the model prediction does not significantly differ from the observed. (Table 2). From the Contingency Table for Hosmer and Lemeshow Test, it shows that expected values are not significantly different from observed values (Table 3).

147(95.5%) of the patients who are not severe are classified correctly. 51(89.5%) of the severe patients are classified correctly. Overall, 93.8% of the cases are classified correctly. Hence the model is suitable to describe the relationship between severity of asthma and the factors affect the severity (Table 4).

It should be noted that the interaction terms are included only when it is unable to satisfactorily explain the variation of dependent variable with only main effects in the model. Therefore the interaction terms were not included in this model since the model satisfactorily explains the variation of severity with only main effects which are the factors affect the severity.

Due to practical limitations; the study was carried out only in Kegalle district. But the results can be generalized to the whole country since Kegalle consists of the geographical variations such as urbanized areas, rural areas and areas with hills and those geographical variations were considered in this study.

4. CONCLUSIONS

The results of the binary logistic regression analysis suggested that out of those many possible factors, five factors significantly affect the severity of asthma at 5% level of significance. Out of them exposing to smoke of mosquito coils was the most significant factor for asthma to be severe. If we can educate the patients to avoid those identified factors which significantly affect the severity as much as possible it may be helpful for the asthmatic patients to control their severity. It will be a benefit for the individual as well as for the society.

REFERENCES


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### Table 2. Hosmer and Lemeshow Test

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a. The cut value is .500