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Clinical Study of Risk Factors of Schizophrenia

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Absteact: This Research is design to statistically analyze the genetic, social and environmental factors affecting on schizophrenic patients. It is a case control study. Hospitals of Rawalpindi and Islamabad were approached to collect the data for cases and approached universities and local public for control. Through logistic regression Technique, factors were analyzed. Results showed that hereditary, seasonal birth, low birth weight, paternal age, childhood abuses, substances uses, suicidal attempts, viral infection, famine, maternal blood pressure, sleeping disturbances, lack of oxygen, neurological problems, epilepsy, depression are significant factors of schizophrenia. Apply logistic regression on all the significant variables together showed the significant result. Stepwise binary logistic regression is also applied on the variables and depression is found most significant factor for schizophrenia.

Key words: Schizophrenia · Chi square · Cox and Snell R^2 · Negelkerke R^2 · Logistic regression

INTRODUCTION

Schizophrenia is a mental and a psychological disorder. It is estimated that about 1 per cent. Pakistani population is suffering from schizophrenic disorder. In Pakistani culture, native faith healers are found in every where especially on shrines. Pakistan is a developing country and people are not well educated having little awareness regarding schizophrenia disorder. Word schizophrenia was being introduced by Swiss Psychiatrist. The two Greek words 'schizo' (split) and 'phren' (mind) are the origin of this term (mind) are the origin of this term [1]. Social and psychological pressures can play significant role to trigger the psychological illnesses. According to the nature of disease psychiatrists and psychologists made treatment plan to treat the illness. Now-a-days care shifted to the community awareness and people suffering from schizophrenia have better chances of the treatment than earlier [2]. The use of Electro Convulsion Therapy (ECT) in schizophrenia increased with the use of medicines [3]. Schizophrenic patients have disturbed functioning of cognition and emotions such as inferential thinking, communication, language problems, fluency of speech and communication. According to [5] these problems are also extended to attitude, hallucination and delusions which are main and major symptoms of these patients. Six per cent of the population of schizophrenic patients is at the risk of committing suicide because of severe depression and severe depression evolves when patients lose hope for survival [6]. There is a positive relationship of child sexual abuse and onset of hallucination, delusion and thought is a positive relationship of child sexual abuse and onset of hallucination, delusion and thought disorders [7]. Life stresses, pre or post pregnancy depression can develop schizophrenic person in later age [12]. Child abuse was a important predictor of aural and tactile hallucinations, even in the absence of adult abuse [8]. The family history of schizophrenia is a well-built single judge for an entity having the risk of

Schizophrenia. Schizo-affective disorders and bipolar affective disorder is commonly come about in parents and siblings of schizophrenia patients [9]. There was relationship between perceived quality of life (QOL) and subjective quality of sleep among schizophrenia patients and its relation to symptom severity, side effects and emotional distress. One hundred and forty five schizophrenia patients were comprehensively evaluated with standardized measures of symptom severity, adverse effects, emotional distress, Quality of life (QOL) and sleep quality. Partial correlation and multiple regression analyses were performed. There is a negative relationship

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between complaints of poor sleep quality and QOL [10]. The association between risk of schizophrenia and urban city is well established. The occurrence of schizophrenia has been seen to increase in line with growing levels of town, as calculated in terms of population size. A linear association was observed among the logarithm of the odds of urban city and risk for schizophrenia. The risk for schizophrenia at the most urban environment was estimated to be 2.37 times higher than in the most rural environment [11].

Methods: A case-control study was conducted and data was collected through a structured questionnaire and personal interview. The cases were patients who were diagnosed with schizophrenia. The controls were healthy people never diagnosed with Schizophrenia. A sample of 130 cases and 260 controls was chosen for this study. Inverse sampling was used to collect the patient data. Data was collected in 1:2. Data was collected for patients from PIMS, General Hospital. Descriptive statistic was analyzed and interpreted. The dependent variable was binary having value '0' for patient with no schizophrenia and value '1' for patient with schizophrenia. Through Questionnaire collected the information about age of the respondents, area of residence, marital status, income level, low birth weight, seasonal birth, heredity factor, twin babies, left hander, paternal age, childhood abuses, substance abuse, suicide attempt, viral inefficient, famine, maternal BP, lack of oxygen, sleeping disturbance, neurological problem, ellipse, OCD, depression, early parents loss. Chi-squared test of independence was applied to check the individual significance of the risk factors. Linear regression was not useful any more as dichotomous dependent variable was involve in the analysis therefore binary logistic regression was applied to check the significance of overall model. Only those variables were included in the logistic regression model which showed significance by chi-squared test of independence. Receiving operative characteristic curve was applied to check the fit of model predictions. Stepwise binary logistic regression by backward elimination was also used. Model comparison was also done.

RESULTS

Income Descriptive statistics was calculated for the cases and controls about the demographic factor. The most patients (n=62) are diagnosed within the age period of 25-32 years and controls (n=115) for this age group. It also demonstrated that patients of the age group 17-24 years were second familiar group of patients (n=58) having schizophrenia and controls (n=120) lie within this age group.10 out of 130 patients with schizophrenia were placed in the age range of 33-40 years and controls(n=25) for this age group. Patients (n=72) lie within the income range of 12,000Rs-21,000Rs and controls (n=103) lie within same income level. The second most common income level of the patients was (n=48) which was paced within 22,000Rs-31,000Rs per month and controls (n=113) for this income level. Only 10 schizophrenic patients were positioned in the range of 32,000Rs- over and controls (n=44) for this income level. The gender distribution among schizophrenic patients and controls. The results illustrated that females were more prone to the schizophrenia (n=69) as compared to males (n=61) and females of control group were (n=169) and male were (n=91). Results showed the type of residential area of schizophrenic patients and controls. Results revealed that 42 percent (n=55) patients belonged to rural area where as 58 percent (n=75) lived in urban area and for control group 32 percent (n=84) lived in rural area where as 68 percent (n=176) lived in urban area. The average age of the onset of schizophrenia was 25 years old with the standard deviation of 4.86. The average income of the schizophrenic patient was 21,000Rs per month with minimum level was 6000 and the maximum income level was 45000.

The 56.2 percent (n=73) of the patient with schizophrenia responded on low birth weight while 43.8 percent (n=57) respond on normal birth weight and controls (n=110) responded on low birth weight while (n=150) respondent on normal weight. The patients (n=76) were born in winter season while patients (n=54) were born in other seasons and controls (n=119) were born in winter season while (n=141) were born in other season. The patients (n=75) respond on positive family history of schizophrenia while (n=55) respond on negative heredity of schizophrenia and controls (n=72) respond on positive family history and (n=188) respond for negative family history. The respond (n=20) have twin sibling with schizophrenia and (n=110) respond that they do not have twin siblings with schizophrenia and controls (n=49) respond on twin siblings and (n=211) respond having not twins siblings. The patients (n=43) were left hander while (n= 87) were right hander and controls (n=82) were left handed and (n=178) were right handed. The (n=55) were with father age above 45 while other patients (n=75) respond that their father age at the time of their birth was less than 45 and controls (n=85) were with father age

above 45 while other patients and (n=175) respond that their father age at the time of their birth was less than 45.The patients (n=72) respond that they suffered from physical abuse in childhood while patients (n=58) respond vice versa and controls (n=78) respond that they suffered from physical abuse in childhood and (n=182) respond vice versa. The (n=80) were chronic drug abuser while (n=50) patients were not substance abuser and controls (n=96) were chronic drug abuser and (n=164) were not substance abuser. The (n=60) attempted suicides and (n=70) did not attempt suicide and controls (n=62) attempted suicides and (n=198) did not attempt suicide. The (n=57) suffered with maternal viral infection and mother of (n=63) patients were not infected with virus and controls (n=74) suffered with maternal viral infection and (n=186) were ot infected with virus. The patients (n=81) go through famine in childhood while (n=49) did not go through famine and controls (n=98) go through famine in childhood and (n=162). Patients (n=74) reported that their mother were sufferer of blood pressure while (n=56) reported no maternal blood pressure and controls (n=109) reported that their mother were sufferer of blood pressure and(n=151). Patients (n=100) reported that they have sleep disturbances and patients (n=38) reported that do not have sleep disturbance and controls (n=132) they have sleep disturbances and (n=128) reported that do not have sleep disturbance. The (n=70) suffered from lack of oxygen and patients (n=60) were not suffered with oxygen deficiency and controls (n=91) suffered from lack of oxygen and (n=169) were not suffered with oxygen deficiency. The Patients (n=70) reported that that have neurological problems and patients (n=60) reported that they do not have neurological problems and controls (n=75) reported that that have neurological problems and (n=185).Patients (n=71) reported that they have family history of epilepsy and patients (n= 59) did not have family history of schizophrenia and controls (n=83) reported that they have family history of epilepsy and (n=177) reported that they have family history of epilepsy. Patients (n=64) respond that they had OCD Problem and patents (n=66) respond that they did not have OCD and controls (n=87) respond that they had OCD Problem and (n=173) respond that they did not have OCD Problem. Patients (n=105) while patients (n=25) and controls (n=135) have the history of depression and (n=125) do not have the history of depression. Patients (n=86) lost their parents in early age while patients (n=44) did not loss their patients in early age and controls (n=69) lost their parents in early age and (n=191) did not loss their patients in early age.

Chi square was applied to compute the variation between cases and controls. Lower birth weight was significant with P-value=.013.The P-value =.022 showed the significant result of winter birth. Through the p-value=.0022 of viral inefficient cleared that the viral inefficient also significant-value=.002 of OCD showed the significant result of OCD problem. Neurological Problem, Maternal BP, Paternal age was also significant. The variables positive family history of schizophrenia, Childhood abuses, Substances abuses, suicide attempt, famine, sleeping disturbance, epilepsy, depression were found statistically significant in this study of schizophrenia with p-value. 000. The risk factor of twin babies was non significant with p-value=.398.The risk factor left handed was also non significant with p-value=.701. P-value =.940 of lack of O2 showed that non significant result. Early parental loss was also non significant with p-value=.380.

The results of odd ratio and marginal effects showed that with one unit increase in low birth weight, the odds of being Schizophrenia patient (versus control) increase by a factor of 1.72 and one unit increase in seasonal birth increases the odds of being schizophrenia patient (versus control) by a factor of 1.64. The findings also demonstrated that with one unit increase in Heredity, the odds of being schizophrenia patient (versus control) increase by a factor of 3.67. The odd ratio of childhood abuses explained one unit increase in this factor will increase the odds of being schizophrenia patient (versus control) by a factor of 2.95. The results for substance abuse showed that the odds of being schizophrenia patient (versus control) increase by a factor of 2.7 with one unit increase in this variable. The findings illustrated that one unit change in suicide attempt will increase odds of being schizophrenia patient (versus control) by a factor of 2.68. By one unit increase in viral inefficient increases the odds of being schizophrenia patient (versus control) increase by a factor of 2.00. The results also indicated that one unit increase in famine increases the odds of schizophrenia patient (versus control) increase by a factor of 2.73. One unit increase in maternal BP increases the odds of being schizophrenia patient (versus control) increase by a factor of 1.86. The one unit increase in sleeping disturbance increases the odds of being schizophrenia patient (versus control) by a factor of 3.23. The findings also demonstrated that with one unit increase neurological problem, the odds of being schizophrenia patient (versus control) increase by a factor of 2.87. The odd ratio of epilepsy explained one unit increase in this factor will increase the odds of being schizophrenia patient (versus control) by a factor of 2.48.

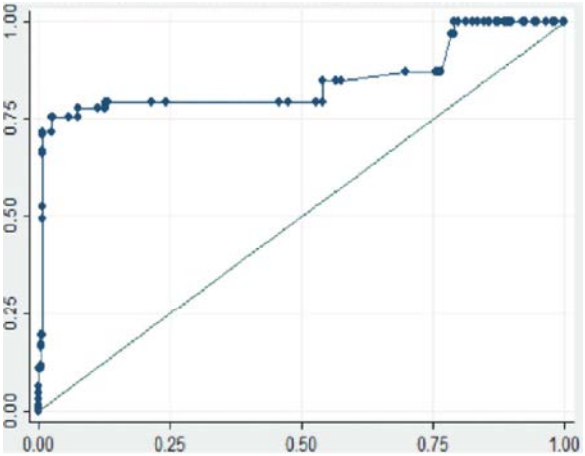

Fig. 1: Area under ROC curve for enter method/step 1

The odd ratio of OCD explained one unit increase in this factor will increase the odds of being schizophrenia patient (versus control) by a factor of 1.98. The odd ratio of depression explained one unit increase in this factor will increase the odds of being schizophrenia patient (versus control) by a factor of 3.88. Apply the logistic regression on all the independent variables together. In table 1 the variables Heredity, Seasonal Birth, Maternal BP, Sleeping Disturbance, Neurological, OCD, Ellipse, Famine and Depression were significant. These significant estimates showed that amount of change in predicted log odds of schizophrenia that would be predicted by a one unit increase in the independent variable, holding all other independent variables constant. By the enter method, some factors became non significant. Those non significant variables were converted into odd ratio. Depression was higher odd ratio after the enter method. Heredity, sleeping problem, Childhood Abuses, Neurological problem, Substance Abuses, Suicide Attempt, Famine, Viral Inefficient, OCD, Maternal BP, Low b birth weight, seasonal birth were in ordered. The value of roc curve was. 8469 which showed that the model was best fitted.ROC was used goodness of model so that value of ROC showed that model was good fitted.

For overall model, the value of Cox and Snell R^2 was. 424 and Negelkerke R^2 was. 589. Through the value of Negelkerke R^2 estimated that only 59% of variation in the data was explained by the overall model.

After the binary logistic regression, apply the stepwise binary logistic regression, in which Backward LR was used.

Table 1: Comparison of Models

	ROC Curve
Model 1	0.8469
Model 2	
Step	
1	0.8469
2	0.8471
3	0.8457
4	0.8457
5	0.8456
6	0.8456
7	0.8454

In second step, all the factors were included in the model and ROC curve value was. 8469. In step two, the factor substances abuse was removed from the model and the value of ROC curve become 0.8471 In third step, the factor viral inefficient was removed with substance abuse. The value of ROC Curve became. 0.8457.

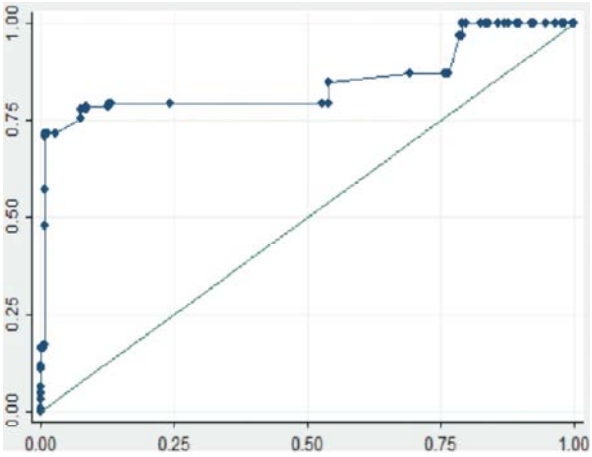

Fig. 2: Area under ROC curve for step 2

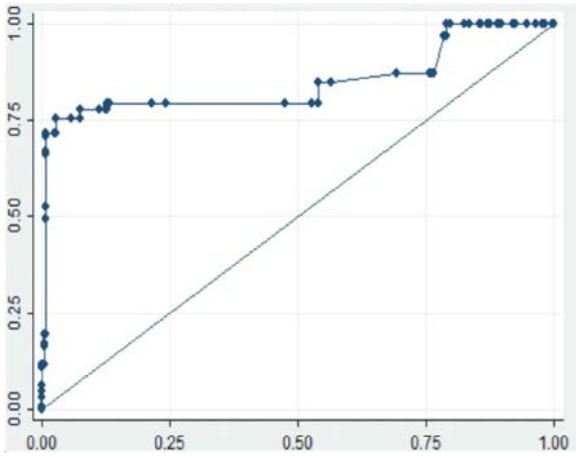

Fig. 3: Area under ROC curve for step 3

In fourth step, viral inefficient, substance abusers and suicide attempt were removed and the value of ROC Curve became 0.8457 as shown below:

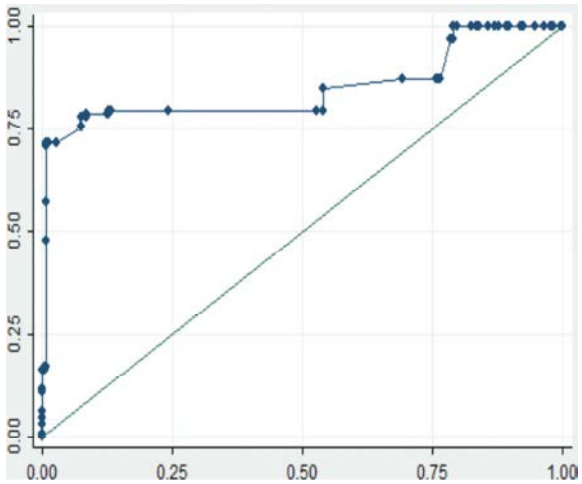

Fig. 4: Area under ROC curve for step 4

In step five, the viral infection, substance abuse, suicide attempt and maternal BP were removed. The value of ROC Curve became 0.8456.

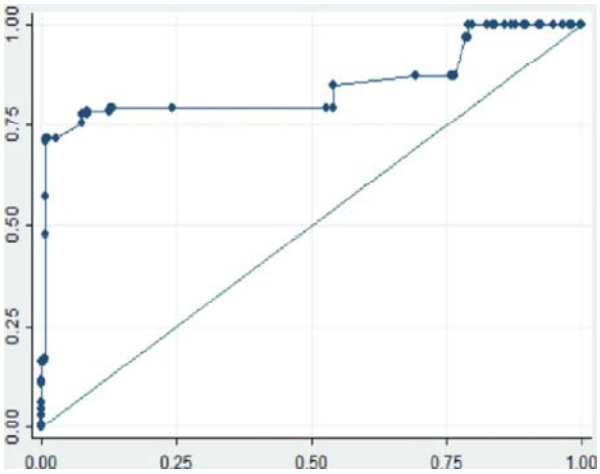

Fig 5: Area under ROC curve for step 5

In step six, the viral inefficient, substance abuse, suicide attempt, maternal BP and Neurological problem were removed from the model. The value of ROC Curve became 0.8456.

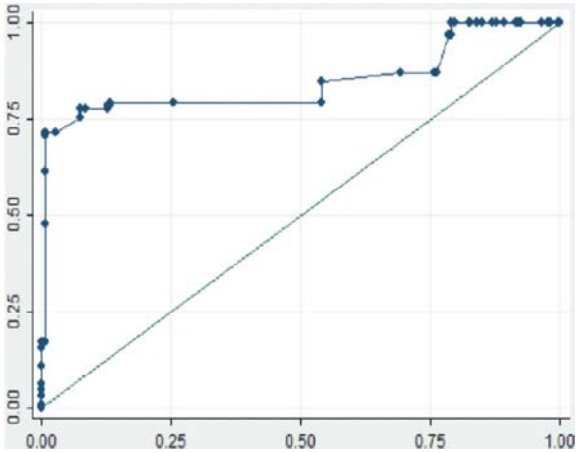

Fig. 6: Area under ROC curve for step 6

In step seven, the viral inefficient, substance abuse, suicide attempt, maternal BP, Neurological problem and childhood abuses were removed and the value of ROC Curve became 0.8454.

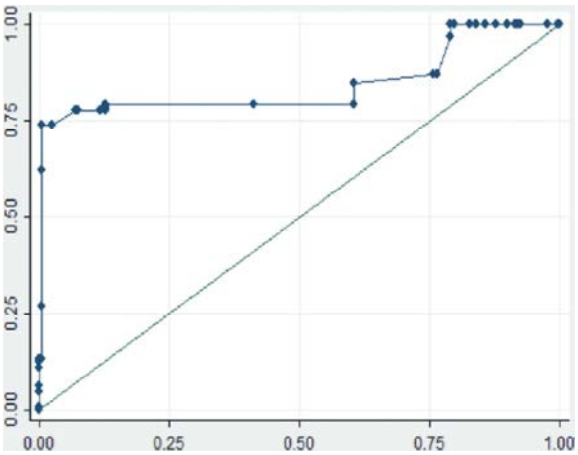

Fig. 7: Area under ROC curve for step 7

Through all the steps, The ROC Curve value of step two showed that on step two models were the best fitted. There was little bit variation all above these steps.

There were two models, model one was made by enter method and second model was by backward LR. Through the ROC Curve value it was showed that in model two, the step two was most best fitted model. In Table 2, the ROC Curve value showed the area under the curve, soon the base of ROC Curve step two was best fitted model.

DISCUSSION

Logistic Regression Technique is commonly used for analysis of epidemiological studies [13]. In this case-control study Logistic Regression Technique was applied. Results were divided into three main sections. In first section it was found the frequency of demographic factors and variables of cases. There were four demographic factors, gender, age, income level and residency [14]. Results showed that male patients were more prone to develop schizophrenia as compared to females and the average age of the patients was 25 years old. The average income level of patients was 21,000 Rupees per month and people living in urban areas are more chances to develop schizophrenia as compare to people living in rural areas. In second section, Chi-Square Test was on overall sample (390) to check the significance of variables of the study through SPSS. There were twenty variables in questionnaire which were related to the risk factors of schizophrenia. Out of twenty variables fifteen variables were significant and five variables were non significant. In the set of fifteen significant variables, four variables (low birth weight, winter birth, OCD, Paternal age) were significant and twelve variables (heredity, childhood abuse, substance uses, suicide attempts, viral infection, famine, maternal BP, sleeping disturbances, neurological problems, epilepsy and depression) were highly significant. In third section Binary Logistic Regression was applied through STATA on fifteen significant variables. Co-coefficients of variables, odd ratios, marginal effects and ROC curve of all significant variables were analyzed. Results presented that Depression has the higher risk of having schizophrenia among all the factors. Heredity, Sleeping Problem is also showed the remarkable association to develop the schizophrenia. Childhood abuses, Neurological Problem, Substances abuses, Famine, Suicide attempt and viral inefficient has showed the average association to develop the schizophrenia. Paternal age, Low birth weight, Seasonal birth and OCD are showed the less association to develop the schizophrenia. In fourth section Iwe applied the enter method on all the variables and make model one. Calculate the ROC Curve value of model one. After that apply the stepwise binary logistic regression by backward elimination and make model two. Backward elimination is completed in seven steps and calculates the ROC Curve value for all these steps. ROC Curve value of model two on step two showed that highest area under the curve as compare the model one and step two f model one good fitted. There is little bit variation in the result of ROC Curve in the model Comparison.

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