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Mathematical Predictions of Neuropathic Diabetes from Unit Level Data

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Abstract: *The purpose of this study is to examine the factors which determines the neuropathic diabetes. The study considered family background, smoking, alcoholic habits and pattern of exercise influence of neuropathic diabetes. The study adopted association test, mean difference test to make inference about the pattern of relationship existing between the factors under analysis. The study clearly depicts that gender is unbiased factor in terms of having diabetes. There is a strong association between diabetic nature and family background, habits and pattern of exercises. The study concludes that age, food habits and regular exercise are important factors which inhibits the diabetes.*

Keywords: *Neuropathic diabetes - Chi-square test- Determinants- Food habits.*

1. INTRODUCTION

Diabetes is a chronic [1] and one of the dramatically increasing metabolic disorder in the World. It is a global health problem. Recent statistics shows that the number of people living with diabetes is expected to rise from 366 million in 2011 to 552 million by 2030 if no urgent action is taken [2,3]. The prevalence of diabetes in India is increasing at a fast rate. Diabetes is associated with an abnormal increase in the level of glucose in blood, ensued either owing to the inadequate production of insulin by pancreas or the cell failure in the effective response to insulin produced by pancreas. The former is called Type 1 diabetes and the later is Type 2 diabetes[4]. The downside of all this variability in plasma glucose is that it leads to severe damage to many of the body's vital systems especially blood vessels and the nervous system. While it causes are not yet entirely understood, Medical Scientists believe that both genetic factors and environmental triggers are involved therein. However, diabetes used to be most prevalent in adults and once called adult-onset diabetes. It is now widely believed that diabetes mellitus is closely related with the aging process. Diabetes results from the interaction between a genetic predisposition, behavioral and environmental risk factors [5]. Although the genetic basis of type 2 diabetes has yet to be identified, there is strong evidence that such modifiable risk factors as obesity and physical inactivity are the main non-genetic determinants of the disorder [6]. Lifestyle factors linked to the incidence of diabetes or diabetes-related risk factors include physical activity level, dietary habits, adiposity, alcohol consumption, smoking [7-16] and duration of sleep [17,18]. The World Health Organization (WHO) recommends the development of simple strategies to identify those at risk of diabetes and provide them with early lifestyle interventions [19]. It is very important to establish predictive models using those risk factors for interventions relating to the development of diabetes. Previous studies have suggested that anthropometry measurement and adipocyte size can serve as predictors of diabetes incidence using traditional statistical methods [20-23].

To gain a better understanding about neuropathic diabetes and non-neuropathic diabetes to treatment it was analysed for the association between clinical factors such as smoking, alcohol habits, blood pressure, body mass index and previous blood pressure or BMI, need of insulin treatment after diagnosis.

2. MATERIALS AND METHODS

The dataset used in the study has been collected from the Dr. Mohan diabetes specialities centre database. The database containing 1393 records and each record containing several information including demographic particulars of the patients, family history, personal habits and food consumption behaviour were collected. A family history is defined as any member previously have been diagnosed as having diabetes by a physician. Height and weight of the patients were also recorded. BMI was calculated. SPSS version 24 (IBM Corporation) was used for all Statistical analyses. A two sided p-value of 0.05 was considered statistically significant.

2.1 Chi-square test

By definition of the Chi-square random variable with n degrees of freedom is given by

$$\chi^2 = X_1^2 + X_2^2 + \cdots + X_n^2.$$

Where $X_j's$ are all independent and have $N(0,1)$ distributions. Also recall that χ^2 has a gamma distribution with parameters $\theta = \frac{n}{2}$ and $\phi = \frac{1}{2}$.

$$\text{Let } f(x) = \left(\frac{1}{2}\right)^{\frac{n}{2}} \frac{x^{\frac{n}{2}-1} e^{-\theta x}}{\Gamma\left(\frac{n}{2}\right)}$$

Where $\Gamma(t)$ is a gamma function, given by

$$\Gamma(t) = \int_0^\infty x^{t-1} e^{-x} dx, \text{ for } t > 0.$$

Then, we are saying that

$$P\left(\chi^2 \geq \alpha\right) = \int_0^\infty \left(\frac{1}{2}\right)^{\frac{n}{2}} \frac{x^{\frac{n}{2}-1} e^{-\theta x}}{\Gamma\left(\frac{n}{2}\right)} dx$$

Chi-square follows gamma distribution

Theorem 1: For large values of M, the random variable $E = \sum_{i=1}^{n} \frac{(X_i - p_i M)^2}{p_i M}$ has approximately a Chi-square distribution with $n-1$ degrees of freedom.

Theorem 2: Suppose that X and Y are continuous random variables having moment generating functions $M_X(t) = E\left(e^{tX}\right)$ and $M_Y(t) = E\left(e^{tY}\right)$, respectively. Further, suppose that these functions exist for all t in a neighbourhoodof 0 and that they are continuous at $t = 0$. Then

$P(X \leq \alpha) = P(Y \leq \alpha)$ for all $\alpha \Leftrightarrow M_X(t) = M_Y(t)$.

Theorem 3: If χ^2 is a random variable having n degrees of freedom, and if Z is a random variable that obeys a gamma distribution with parameters $\theta = \frac{n}{2}$ and $\phi = \frac{1}{2}$, then we have that

$P\left(\chi^2 \geq \alpha\right) = P(Z \geq \alpha)$.

Now recall that (i) If n is a positive even integer we get that $\Gamma\left(\frac{n}{2}\right) = \left(\frac{n}{2}-1\right)!$, which gives that

$$P\left(\chi^2 \geq \alpha\right) = P(Z \geq \alpha) = \frac{1}{\left(\frac{n}{2}-1\right)!}\left(\frac{1}{2}\right)^{\frac{n}{2}} \int_{\alpha}^{\infty} x^{\frac{n}{2}-1} e^{-\frac{x}{2}} dx \ .$$

Then the right-most expression equals the sum of probabilities of a certain Poisson random variable. If Y is Poisson random variable with parameter $\frac{\alpha}{2}$, then we have that

$$P\left(\chi^2 \geq \alpha\right) = P(Z \geq \alpha) = \sum_{i=1}^{\frac{n}{2}-1} P(Y = i)$$

$$= e^{-\frac{\alpha}{2}} \sum_{i=0}^{\frac{n}{2}-1} \frac{(\alpha/2)^i}{i!}$$

(ii) If n is a positive odd integer we get that $\Gamma\left(\frac{n+1}{2}\right) = \left(\frac{n+1}{2}-1\right)!$, which gives that

$$P\left(\chi^2 \geq \alpha\right) = P(Z \geq \alpha) = \frac{1}{\left(\frac{n+1}{2}-1\right)!}\left(\frac{1}{2}\right)^{\frac{n+1}{2}} \int_{\alpha}^{\infty} x^{\frac{n+1}{2}-1} e^{-\frac{x}{2}} dx,$$

then the Poisson distribution with parameter $\frac{\alpha}{2}$ is

$$P\left(\chi^2 \geq \alpha\right) = P(Z \geq \alpha) = \sum_{i=1}^{\frac{n+1}{2}-1} P(Y = i)$$

$$= e^{-\frac{\alpha}{2}} \sum_{i=0}^{\frac{n+1}{2}-1} \frac{(\alpha/2)^i}{i!}$$

2.2 Mean Comparison Test: Two Sample t test

We now have three dimensional parameter space $\theta = \left\{\left(\mu_1, \mu_2, \sigma^2\right); \mu_1, \mu_2, \sigma^2 \in R\right\}$.

The two-sided test is

$$H_0 : \mu_1 = \mu_2 \text{ and } \mu_1 \neq \mu_2 .$$

The data $X_{1,j}, \cdots\cdots\cdots X_{n_j,j}$ are independent $N(\mu_j, \sigma^2)$ random variables, $j = 1,2$.

The likelihood function is

$$L(\mu_1, \mu_2, \sigma^2 / X_1, X_2) = \frac{1}{(2\pi\sigma^2)^{(n_1+n_2)/2}} \exp - \frac{1}{2\sigma^2}\left(\sum_{i=1}^{n_1}(x_{i,1}-\mu_1)^2 + \sum_{i=1}^{n_2}(x_{i,2}-\mu_2)^2\right).$$

Then, the likelihood ratio,

$$\Lambda(X_1, X_2) = \frac{L(\hat{\mu}, \hat{\mu}, \hat{\sigma}^2 / X_1, X_2)}{L(\hat{\mu}_1, \hat{\mu}_2, \hat{\sigma}_{12}^2 / X_1, X_2)}$$

Write the unbiased estimators for the mean and variance

$$\bar{x}_j = \frac{1}{n_j}\sum_{i=1}^{n_j} x_{i,j} \text{ and } s_j^2 = \frac{1}{n_j - 1}\sum_{i=1}^{n_j}(x_{i,j} - \bar{x}_j)^2,\ j = 1,2$$

Then, the overall maximum likelihood estimators are

$$\hat{\mu}_1 = \hat{x}_1,\ \hat{\mu}_2 = \hat{x}_2, \qquad \hat{\sigma}^2 = \frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2}.$$

The maximum likelihood estimators in the numerator takes place on the set $\mu_1 = \mu_2$.

$$\hat{\mu} = \frac{n_1\bar{x}_1 + n_2\bar{x}_2}{n_1 + n_2}, \qquad \hat{\sigma}_{12}^2 = \frac{1}{n_1 + n_2}\left(\sum_{i=1}^{n_1}(x_{i,1} - \hat{\mu})^2 + \sum_{i=1}^{n_2}(x_{i,2} - \hat{\mu})^2\right)$$

Thus yields the test statistic

$$T(X_1, X_2) = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\left(\frac{1}{n_1} + \frac{1}{n_2}\right)\left(\frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2 - 2}\right)}}$$

From the fact that the likelihood ratio

$$\Lambda(X_1, X_2) = \left(\frac{n_1 + n_2 - 2}{n_1 + n_2 - 2 + T(X_1, X_2)^2}\right)^{2/(n_1 + n_2)}$$

Under the null hypothesis, $T(X_1, X_2)$ has a $t-$distribution with $n_1 + n_2 - 2$ degrees of freedom.

2.3 Results and Discussion

As mentioned earlier, the dataset used in the study was obtained from the Dr. Mohan diabetes specialities centre database. Table 1 produces summary statistics of the variables used in the study. From the baseline survey, it was found that the mean age of the neuropathic diabetes was 64.93 years, 33% were smokers, 24.55% were alcoholic during the first visit of the treatment. Also, it is inferred that mean time staying at hospital for treatment was 14.01 months, height 163 cm, weight 69.9 kg. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2), Waist 26.3 inches, Hip 98.61cms, Diastolic Blood Pressure 81.01 and Systolic Blood pressure 134.33. The following results shows that before(first visit) and after treatment (last visit). HbA1c in first visit was 9.08 and in last visit was 8.23, Cholesterol in first visit was 175.99 and in last visit 149.70, HDL cholesterol in first visit was 40.36 and in last visit 38.30, LDL cholesterol in first visit was 102.5 and in last visit 82.10, Urea in first visit was 26.64 and in the last visit 27.85, Creatinine in first visit was 0.88 and in the last visit 0.93. It is medically proved that if Great toe right or left is greater than are equal to 20 then the patient is called diabetic under neuropathy.

3. TABLES

Table 1. *Statistics Summary*

Variables	N	Mean	S.D
Age	376	64.93	8.096
Dur_dm_no	376	14.01	8.045
Height	376	163	9.11
Weight	376	69.9	13.12
Bmi	376	26.3	4.42
Waist	376	26.3	10.63
Hip	376	98.61	9.57
Dia bp	376	81.01	9.38
Sys_bp	376	134.33	20.41
FV_hba	376	9.08	2.07
LV_hba	376	8.23	1.78
FV_cho	376	175.99	49.51

LV_cho	376	149.70	39.21
FV_tri	376	174.18	228.51
LV_tri	376	148.85	89.68
FV_hdl	376	40.36	10.64
LV_hdl	376	38.30	10.78
FV_ldl	376	102.5	36.02
LV_ldl	376	82.10	31.15
FV_ure	376	26.64	12.22
LV_ure	376	27.85	11.41
FV_cre	376	0.88	0.29
LV_cre	376	0.93	0.38
Gre_toe_RT	376	26.39	7.52
Gre_toe_LT	376	26.13	7.55

F.V-First Visit, L.V-Last Visit.

Table 2. *Association between Demographic factors and diabetes*

Characteristics	Neuropathy N=376	Non-Neuropathy N= 1017	Total N=1393	Pearson Chi-Square	p-value
Gender					
Male	255	645	900	2.321	0.128
Female	121	372	493		
Age					
30-39	0	45	45	225.313	0.000
40-49	13	206	219		
50-59	74	395	469		
60-69	178	297	475		
70-79	93	65	158		
80-89	18	9	27		
Diabetic Father					
Yes	122	443	565	14.061	0.000
No	254	574	828		
Diabetic Mother					
Yes	112	411	523	13.218	0.000
No	264	606	870		
Sibling					
Yes	202	476	678	5.260	0.022
No	174	541	715		
Smoking Habit					
Yes	100	203	303	7.100	0.008
No	276	814	1090		
Alcohol Consuming Habit					
Yes	82	252	334	8.329	0.024
No	294	765	1059		
Exercise					
Exercise	130	331	461	13.69	0.251
No Exercise	246	686	935		

Source: Computed.

The basic objective of the study is to examine the factors determining the nature of neuropathy. The study has applied Chi-square test as the test is best measurement of association between categorical data. Accordingly, Chi-square test has been applied and the results are presented in the table 2.

Hypothesis 1: There is no association between age and prevalence of diabetes.

The computational process of deriving Chi-square and probability value is discussed here. The sample data furnished in table 2 are used for the computation. The Chi-square value for the above table is

$$E = \sum_{i=1}^{n} \frac{(X_i - p_i M)^2}{p_i M}$$

E = 12.25+35.97+21.85+19.34+59.44+15.74+4.49+13.29+2.97+7.15+21.98+5.82

$= 220.19$

The probability value with $n = 5$ degrees of freedom is

$$P\left(\chi^2 \geq 220.19\right) = e^{-220.19/2} \sum_{i=0}^{2} \frac{\left(220.19/2\right)^i}{i!}$$

$$= 9.432160885X10^{-45}$$

$$\approx 0.000$$

From the computation, it is learnt that the computed Chi-square value is greater than the table value (3.84) as well as the computed p - value is less than 0.05, therefore the study rejects the null hypothesis that there is no association between age and prevalence of diabetes. The study based on the statistical results arrives to conclude that the nature of diabetes is dependent on age. It is practically true that as growing age shall invite many health complications. Diabetes is fast growing disorder among the old age people. It is not only the result of age factor it is due to many of the other factors such as food habits, lack of exercise, etc.

Diabetes is Genetical

Genetics play a strong role in the chances of developing both type 1 and type 2 diabetes. Other factors include environment and lifestyle. The risk of developing diabetes is affected by whether your parents or siblings have diabetes. Blood relatives of people with either type 1 or type 2 diabetes also have a higher risk of developing the same type of diabetes as their family member.

Hypothesis 2: There is no association between Family Diabetics History and nature of Diabetes

Based on the above theoretical consideration, the study tries to examine whether there is any association between family diabetic history and nature of diabetes. Here the family history implies that if a patient's father or mother or siblings have diabetes or not. The Chi-square values for the parameter are provided in the Table 2. As it is evident from the table the computed p - value is less than 0.05, the study rejects the null hypothesis and arrives to conclude that family diabetic history plays a significant role in diabetes. As it is evident from many studies that diabetes is a genetic one.

Nature of Habits

Habits determine the well-being of a person. If a person follow good virtue and habit, he/she would enjoy the life and vice- versa. Especially for some epidemic disorder, habits play a crucial role in its determination. In the case of diabetes, smoking and alcoholic habits are prominent factors. Accordingly, the study intends to examine whether there is any association between habits and nature of diabetes.

Hypothesis 3: There is no associationbetweenSmoking, Alcohol consumption and prevalence of diabetes

The Chi-square value and p - value are greater than the table value and less than 0.05 respectively. To reject the null hypothesis that there is no association between smoking, alcohol habit andprevalence of diabetes.In conclusion, a low proportion of type 2 diabetic patients were smokers and alcohol intakedue to lack of proper awareness and education on the effect of smoking andalcohol intake on diabetes, the disorder is spreading widely and silently into other countries in world. In more than half of the patients found that smoking did not give improvement rather than worsens their type 2 diabetes. People with diabetes already have an increased risk of developing diabetic related complications and this will further elevate if they smoke.

Nature of Exercise

Physical activity or Exercise has been shown to be instrumental in preventing diabetes among people at high risk and in helping to manage symptoms in people with the disorder. Abnormal insulin secretion and peripheral insulin resistance are primary factors that influence the acute effects of physical activity on metabolic responses in those with type 2 diabetes. Several factors including muscle fiber composition, low capillary density, obesity and older age require that physical activity be

initiated at lower intensity/duration and be increased gradually to reduce risks and contribute to maintenance of physical activity by those with type 2 diabetes.

Hypothesis 4: There is no association between Exercise and prevalence of diabetes

The Chi-square value and p - value are greater than the table value and less than 0.05 respectively. To reject the null hypothesis that there is no association between exercise and prevalence of diabetes. In conclusion, Physical activity affords significant acute and chronic benefits for those with type 2 diabetes. The benefits of chronic physical activity are more numerous than those of acute physical activity, emphasizing the need for regular participation by those with type 2 diabetes and those at risk for this form of diabetes. It concludes that diet and regular exercise were more effective than one of the most widely prescribed drug treatments for preventing diabetes.

Food Consumption induces Diabetics:

Table 3. *Changes in Food Consumption*

Variables	N	Mean	S.D	Std. Error	't' value
Calorie_FV	376	1259.35	359.24	18.85	-0.86
Calorie_LV	376	1280.08	355.78	18.68	
Protein_FV	376	45.82	11.69	0.613	-0.50
Protein_LV	376	46.21	11.98	0.629	
Carbo_FV	376	204.40	63.38	3.32	-1.14
Carbo_LV	376	209.35	61.45	3.22	
Fat_FV	376	30.43	17.40	0.91	-0.242
Fat_LV	376	30.68	14.21	0.74	
Satfat_FV	376	1.65	4.90	0.25	3.941**
Satfat_LV	376	0.61	1.54	0.08	
Pufa_FV	376	1.29	3.03	0.16	6.298**
Pufa_LV	376	0.31	1.04	0.05	
Fibre_FV	376	4.75	14.51	0.76	-10.40**
Fibre_LV	376	15.43	13.26	0.69	
Sodium_FV	376	143.17	460.74	24.18	3.526**
Sodium_LV	376	58.40	206.02	10.81	
Potas_FV	376	94.08	143.49	7.53	6.940**
Potas_LV	376	34.35	97.21	5.10	

Note: Values are compared with significant level of 0.05, F V- First Visit, L V- Last Visit.

In this study, the significant mean difference is examined through the application of 't' test. The computational methodology is discussed here:

A good diet to control diabetes:

The DASH or Dietary Approaches to Stop Hypertension is a lifelong approach to healthy eating designed to lower or prevent high blood pressure. It encourages dieters to avoid sodium consumption and eat foods high in nutrients such as calcium, potassium and magnesium.In addition to restricting sodium, the DASH diet is low in saturated fat and cholesterol. It includes lots of vegetables, fruits, low-fat dairy products and whole grains.

Hypothesis 5: There is no significant difference between change in calorie intake before and after treatment:

$$T(X_1, X_2) = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\left(\frac{1}{n_1} + \frac{1}{n_2}\right)\left(\frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2 - 2}\right)}}$$

$$= \frac{1259.35 - 1280.08}{\sqrt{\left(\frac{1}{376} + \frac{1}{376}\right)\left(\frac{(376 - 1)(359.24)^2 + (376 - 1)(355.18)^2}{376 + 376 - 2}\right)}}$$

$$= \frac{-20.73}{\sqrt{679.983}}$$

$$\approx -0.80$$

The result clearly demarks that there is no significant changes in the calorie intake before and after treatment.

Hypothesis 6: There is no significant difference between change in Fibre content before and after treatment.

$$T(X_1, X_2) = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\left(\frac{1}{n_1} + \frac{1}{n_2}\right)\left(\frac{(n_1-1)s_1^2 + (n_2-1)s_2^2}{n_1 + n_2 - 2}\right)}}$$

$$= \frac{4.75 - 15.43}{\sqrt{\left(\frac{1}{376} + \frac{1}{376}\right)\left(\frac{(376-1)(14.51)^2 + (376-1)(13.23)^2}{376+376-2}\right)}}$$

$$\approx -10.54$$

This result shows that there is a significant change in Fibre content before and after treatment.

To conclude above the results, Abnormal glucose tolerance is present in more than 60% of adults older than 60 years of age as a result of a decrease in glucose tolerance as a result of decreased insulin sensitivity and impairment of pancreatic beta-cell function. The elderly diabetic population stands to benefit enormously from streamlining and optimizing diet planning in order to enhance longevity, minimize complications, and improve quality of life.

4. CONCLUSION

The Chi-Square test is conducted in order to identify statistical significance of demographic factors, family history and personal habits with respect to diabetes, particularly to explore the association across different age groups and diabetes prevalence. Table 2 shows the results considering a significant level of 0.05. The result demonstrated a highly significant prevalence among age groups and prevalence of diabetes. This means that those with older age had higher likelihood to develop diabetes than those with younger age. It signifies that age is a significant influencing factor for diabetes. Further the test result also shows that diabetes is hereditary and caused by bad habits such as alcoholic and smoking, and, there is no association between exercise and diabetics before visiting to hospital.

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