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Genetic Epidemiological Studies of Diabetes Mellitus in Hospital Population of District Bahawalpur

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ABSTRACT

Diabetes is considered a disease that is characterized by high glucose levels in the blood. Diabetes has become a global epidemic disease which is most common in developing countries. The aims are to provide an estimate of diabetes prevalence in the hospital population of district Bahawalpur. The study was carried out on 1000 Diabetic patients, Data was collected by a well-designed Questionnaire. In the statistical analysis, the percentage (%), Standard Error (S.E), mean (M), and Chi-Square tests were used. Out of 1000 Diabetic patients, 39.6% (396) were females and 60.4% (604) were males. The mean age was 51.57 ± 0.50 years in females and for the males, it was 47.99 ± 0.53. A greater number of patients belonged to the urban areas with 70.5% (705/1000) and Minimum belonged to Rural areas with 29.5% (295/1000). BMI recorded in the maximum range of 23-26.9 with 39.9% (399/1000) of the patients while it is recorded minimum the range of ≥27 with 10.1% (101/1000). By family history, much of the diabetic patients belonged to the consanguinity group with 35.7% (357/1000), while it was minimum in the out of cast 7.8 (78/1000). Type II Diabetes mellitus was more common with 64.2% (642/1000) and less common with 35.8% (358/1000). A more fetal onset of Diabetes occurs in the patients with Diabetic family history.

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1. INTRODUCTION

Diabetes mellitus is a disease related to metabolism which is characterized as the rise in the sugar contents level in the body for a long period, Symptoms of this disease include more urination, more thirst, and hunger. Diabetic ketoacidosis, and the hyperosmolar coma. (Kitabchi *et al*., 2009) In history diabetes firstly was described by the Egyptians as a disease that causes a reduction in weight and renal disorder such as polyuria. Multiple Complications which are retinopathy (disease of retina of the eye), nephropathy (disease of kidneys), and last one neuropathy (disease of nerves) occur in diabetes (Nathan, 1993). 80% of diabetics die because of thrombotic death. Almost 75% of deaths are due to cardiovascular complications, and the remainder is due to cerebrovascular events and peripheral vascular complications (Carr, 2001).

The most common disease in developing countries is diabetes mellitus, which rises quickly. In 2013, it is expected that the number of 382 million diabetes patients will rise to 592 million by 2035 (Whiting *et al*., 2011). Recent studies have projected an increase from 4% in 1995 to 6.4% in 2025 in the spread of the disease of diabetes in adults.

Worldwide, diabetes develops. Asia has more cases of diabetes than any other region, with India, China, Pakistan, and Japan reporting 33, 23, 9, and 7 million diabetics respectively. In the Asian population, Diabetes emerges at an earlier age as compared to the white population of the world (Ramachandran *et al*., 2010). Pakistan has a high incidence of diabetes. The surveys are undertaken in the four districts of the Sindh Province, the Baluchistan Province, and the Northwest Frontier Province (NWFP) and it has been concluded that they have 13.9%, 8.6%, and 11.7% cases of diabetes respectively. Punjab diabetes prevalence was almost 12.14% in men and less recorded 9.83% in women (Shera *et al*., 2010).

Risk factors involve lifestyle, obesity, overweight, unhealthy diet, physical inactivity, increasing age, high blood pressure, Ethnicity Impaired glucose tolerance (IGT)*, History of gestational diabetes, Pregnancy Intrauterine environment, Low birth weight, Puberty, Toxicology (consumption of alcohol and illicit drugs), Family history of Diabetes, poor nutrition (Sharma & Kumar, 2010).

Diabetes was identified in hospitalized patients with coronavirus disease 2019 as a significant risk factor for mortality, and rates of progression to ARDS (COVID-19). However, many recent studies on this subject reflect hurried approaches as well as lack a careful design, conduct, and analysis of epidemiology. Features of previous studies have caused difficulty in our understanding of the true contribution to the COVID-19 prognosis of diabetes or other underlying comorbidities (Selvin & Juraschek, 2020).

Diabetes has several types, first Diabetes type 1 second Diabetes type 2. Type 1 diabetes is caused by the autoimmune destruction of the B-cells on the pancreas. B-cells are the cells that are involved in the production of insulin. We can diagnose diabetes at any age, it is a common disease of childhood. The disease goes up to the peak at 5-7 years of age. Although many of the autoimmune diseases attack women, in this case, the disease of type 1 diabetes is more common in boys and men. Type 1 diabetes is associated with the change in seasons and birth months. It has been observed that more cases are in autumn and winter, also the births that occur in spring have much greater chances to inset type 1 diabetes. The development of type 1 diabetes is associated with seasonal changes give us a concept that it is associated with the environmental factors that cause the pathogenicity of disease (Atkinson & Eisenbarth, 2001).

Both Pakistan and India consist of 3.1% of the British population (2001 census). They have more threat of getting type II diabetes as compared to the general population. Another

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problem with them is that they have less efficiency to control glucose levels so they are at the risk of getting diabetes and its associated complications more easily, and 40% higher mortality than the general population of both countries (Lawton *et al*., 2006).

This epidemiological study has been performed to know the incidence and prevalence of Diabetes Mellitus in patients visiting hospitals of Bahawalpur, Punjab.

2. METHODS AND MATERIALS

2.1. Collection of Data

The data of diabetes mellitus patients was collected from the Government Hospital of Bahawalpur which is known as the Bahawal Victoria Hospital, Bahawalpur. For the data collection, a structured questionnaire was used to collect data from 1000 patients. The data covers various aspects such as demographics, dietary habits, history of the family, any allied diseases, physical activity, working environment information, living style, type of control measures, and smoking status. Family history was recorded by asking them directly and seeking permission for further questions for pedigree.

The following points were used:

(i) Gender.
(ii) Age.
(iii) Area.
(iv) BMI.
(v) Exact Diagnose.
(vi) Genetic relationship of Husband and wife.
(vii) Parental Genetic Relationship.
(viii) Allied Diseases.
(ix) Obesity in family.

2.2 Statistical Analysis

The statistical analysis was carried out including percentages, means, standard error & chi-square test. The mean coefficient of inbreeding will also be calculated by following Wright's (1992) formula:

$$F = \frac{IC \times 0.0625}{\text{Total number of each type}} + \frac{I½C \times 0.031}{\text{Total number of each type}} + \frac{2C \times 0.015}{\text{Total number of each type}}$$

3. RESULTS

1000 diabetic patient's data was collected. From all the data 61.4% were males and 39.6% were females. The difference between males and females was highly significant to diabetes. Males were more affected by diabetes. From females and it was also noticed that the ratio of males relative to females was 152.52 to 100n females. The mean age at present was 51.57 ± 0.50 years in females. The age at present in males was 47.99 ± 0.53. The overall mean age of both males and females was 49.24 ± 0.36. The mean age at diagnosing was 41.78 ± 0.48 years in females. The age at diagnosis in males was 39.71 ± 0.56. The overall mean age of both males and females was 40.53 ± 0.39. Maximum diabetic patients have been observed under the age group of 41-60 (see **Table 1** and **Figure 1**).

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Table 1 Distribution of Diabetic patients according to the mean age at present.

Category of patients	No.	Mean age (Mean ± S.E) at present
Male	604	47.99 ± 0.53
Female	396	51.57 ± 0.50
Total	1000	49.24 ± 0.36

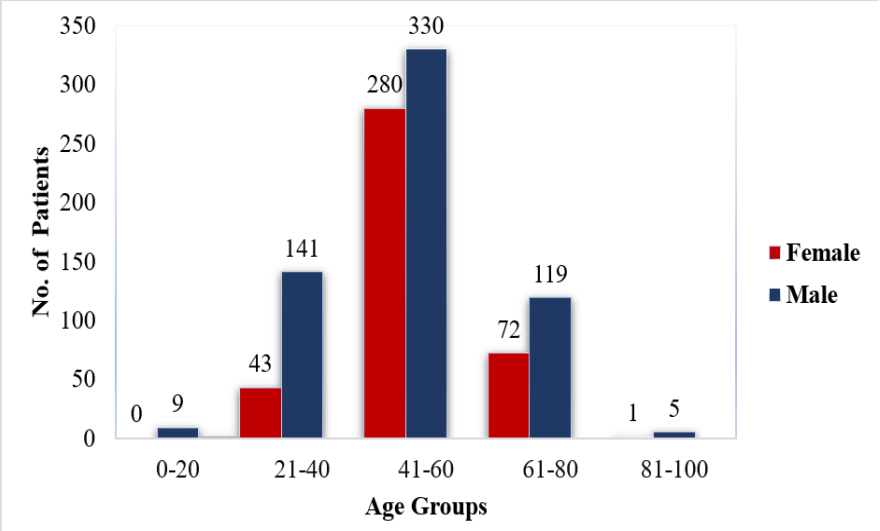

Figure 1 Illustration of distribution of Diabetic patients according to their Age groups.

As the study was conducted in the hospitals of the city so many of the patients belong to the urban areas with a total percentage of 70.5% and least in the rural areas with 29.5%. BMI of the 1000 patients was also recorded and categorized in 4 groups, it was noticed that the maximum of them have a BMI of 23-26.9 with 39.9% which is referred to as overweighed. After that normal weighted patients with 33.9%. The minimum BMI was of obese patients (≥27) with 10.1% (see **Figures 2** and **3**).

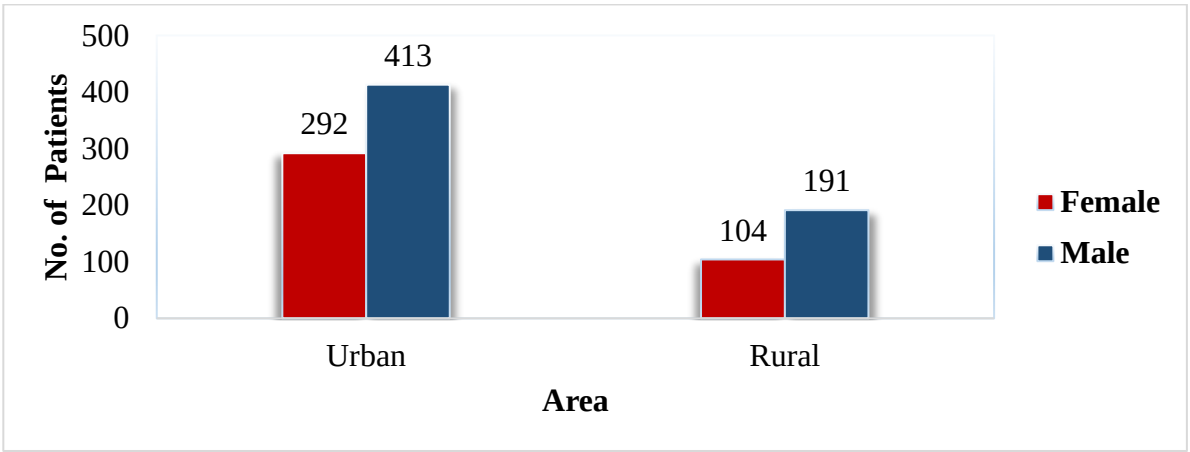

Figure 2. Illustration of distribution of Diabetic patients according to their Area.

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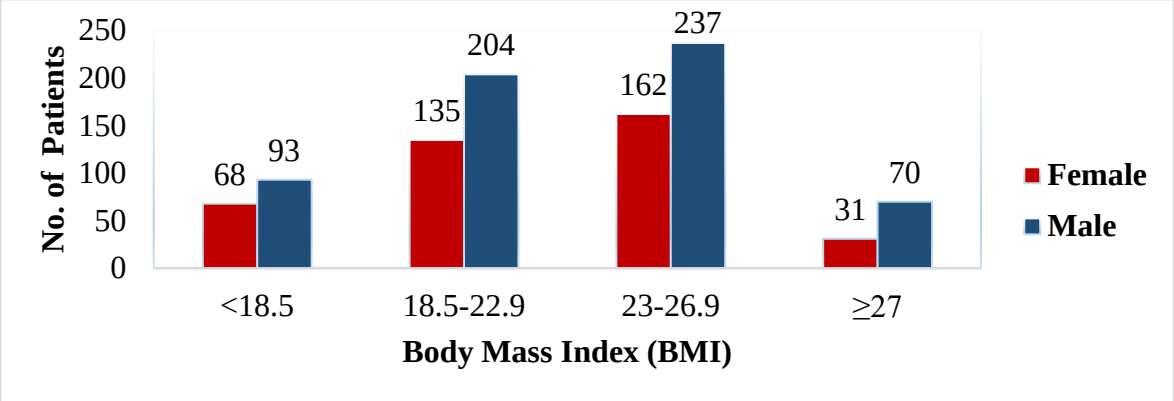

Figure 3. Illustration of distribution of Diabetic patients according to their BMI.

The distribution of diabetic patients according to their husband-wife genetic relationship was recorded. The relationship of patients that were in maximum first cousin (consanguinity) (1C), and then distant relatives, first cousin removed once (1 ½ C), second cousin (2C), baradri and at the end out of the cast. Most of them which have high percentage were in consanguinity with 33.6%, which is then next followed by the distant relatives of 17.8%, the first cousin removed once 15.5%, the second cousin of 15.1%, the first cousin removed once 15.5%, their brotherhood of 11.57% and less of them were observed out of the cast with 6.43% only. The distribution of diabetic patients according to their parental genetic relationship was recorded. The relationship of patients that were in maximum consanguinity (1C), and then, distant relatives, first cousin removed once (1 ½ C), baradri, second cousin (2C), and at the end out of the cast. Most of them which have high percentage were in consanguinity with 35.7%, which is then next followed by the distant relatives 20.0%, the first cousin removed once 13.8%, their brotherhood of 12.6%, the second cousin of 10.1%, and less of them were observed out of the cast with 7.8% only. According to the percentage distribution of 1000 patients, it has been observed that the maximum patients were with type II diabetes with 64.2% and a smaller number of them were with type I diabetes 35.8%. According to the percentage distribution of 100 patients, allied diseases were also observed. The maximum of them included blood pressure patients with 32.2%, followed by both blood pressure and cardiac diseases with 28.3%, cardiac problems 25.1%, and the minimum with kidney problems of 14.4%. According to the data provided by the patients for their obesity status in the family it was observed that maximum patients' family is obese. Out of 1000 patients, 599 (59.9%) families were obese while the remaining 401 (40.1%) belongs to families which were not obese (see **Figure 4** and **Table 2**).

Pedigree of three families with a history of Diabetes mellitus extending at a minimum of three generations with the members who were affected was drawn.

Figure 5 shows three generations consisted of 49 individuals, from the 11 who were dead and 38 were alive when this data was collected. Of 49 individuals 26 having Diabetes mellitus. From the affected individuals 11 were females and 15 were male in the first generation 1 female (I.2) was affected but male (I.3) of first-generation was normal. In the second generation, all the 5 sons (II.1, II.3, II.5, II.7, II.9, II.11) were affected by Diabetes mellitus and they all married to Diabetic females (II.2, II.4, II.6, II.8, II.10, II.12). The first affected male and female from the second generation (II.1, I.2) produced two affected sons (III.1, III.2) and 1 affected daughter (III.8). They also had four normal sons (III.4, III.5, III.6, III,7) and one normal daughter (III.3). Second affected male and female (II.3, II.4) from the second generation produced two affected sons (III.9, III.11) and two affected daughters (III.14, III.15) and three

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normal sons (III.12, III.13, III.14) and one normal daughter (III.10). The third affected male and female (II.5, II.6) from the second generation produced two affected sons (III.17, III.18) and one normal daughter (III.19). Fourth affected male and female (II.7, II.8) from second-generation produced one affected (III.21) and one normal daughter (III.20) and three normal sons (III.20, III.23, III.24). Fifth affected male and female (II.9, II.10) from the second generation produced three affected (III.25, III.26, III.27) and one normal son (III.31) while all three daughters were normal (III.28, III.29, III.30). Sixth affected male and female (II.11, II.12) from the second generation produced three normal sons (III.32, III.33, III.34) and a normal daughter (III.35). The common onset age of diabetes in their family has been observed from 30 to 45 years. The diabetic condition in their family was severe and two of the members lost their legs because of having Peripheral artery disease.

Figure 6 shows the data of the second observed family consisted of 26 individuals. From them 1 was dead and 25 were alive when data of their family were collected. From 26 individuals 15 were affected and 11 were normal. 12 of the 26 individuals were females and 14 were male. In the first generation, both males and females (I.1, I.2) were observed affected. They produced two sons (II.1, II.3), one of them got married to the affected female (II.2) while the other got married to a normal female (II.4) and they also had two daughters both affected (II.5, II.7) and both married to normal males (II.6, II.8). First male and female from second-generation (II.1, II.2) produced two affected sons (III.1, III.2) and one affected daughter (III.4) they also had one normal son (III.3). Second male and female from the second generation (II.3, II,4) produced two affected sons (III.5, III.8) and two affected daughters (III.6, III.9) and they also had one normal daughter (III.7) and one normal son (III.10). The third male and female from the second generation (II.5, II.6) produced two normal sons (III.11, III.12) and one normal daughter (III.13). The last male and female from second-generation (II.7. II.8) produced one affected son (III.14) and two normal daughters (III.15, III.16). The common onset age of diabetes was 12-40 years. One of their recent members was diagnosed at the age of 12.

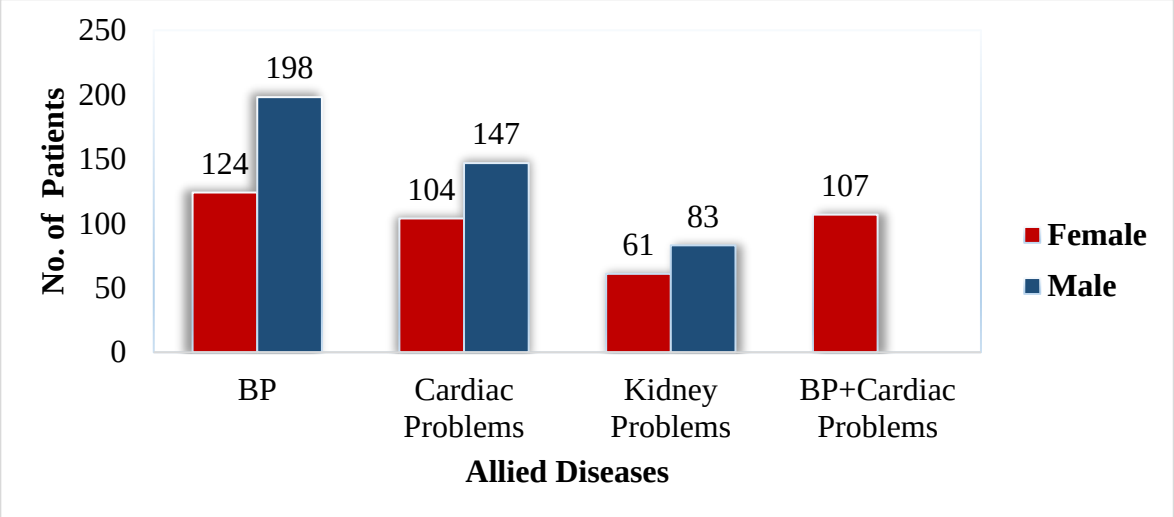

Figure 4 Illustration of Percentage distribution of Diabetic patients according to their Allied diseases.

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Table 2. Baseline characteristics of the study participants.

Sr. No.	Question	Female		Male		No. of patients	Percentage %
		No.	%	No.	%		
1	Gender	396	39.60	604	60.40	1000	100
2	Area						
	Urban	292	73.70	413	68.78	705	70.50
	Rural	104	26.30	191	31.62	295	29.50
3	BMI00						
	<18.5	68	17.17	93	15.40	161	16.10
	18.5-22.9	135	34.10	204	33.77	339	33.90
	23-26.9	162	40.91	237	39.23	399	39.90
	≥27	31	7.82	70	11.60	101	10.10
4	Exact Diagnose						
	Type 1	157	39.65	201	33.28	358	35.80
	Type 2	239	60.35	403	66.72	642	64.20
5	Allied Diseases						
	BP	124	31.30	198	32.80	322	32.20
	Cardiac problems	104	26.30	147	24.34	251	25.10
	Kidney problems	61	15.40	83	13.72	144	14.40
	BP+Cardiac problems	107	27.00	176	29.14	283	28.30
6	Genetic relationship of Husband and wife						
	Consanguinity	127	33.23	195	33.80	322	33.60
	$1^{1/2}$ Cousin	52	13.61	97	16.81	149	15.50
	2^{nd} Cousin	56	14.66	89	15.42	145	15.10
	Distant Relatives	68	17.80	103	17.90	171	17.80
	Baradri	50	13.10	61	10.60	111	11.57
	Out of cast	29	7.60	32	5.55	61	6.43
7	Parental Genetic Relationship						
	Consanguinity	158	39.90	199	32.90	357	35.70
	$1^{1/2}$ Cousin	66	16.70	72	11.90	138	13.80
	2^{nd} Cousin	51	12.90	50	8.30	101	10.10
	Distant Relatives	71	17.90	129	21.40	200	20.00
	Baradri	29	7.30	97	16.10	126	12.60
	Out of cast	21	5.30	57	9.40	78	7.80
8	Obesity in family						
	Yes	213	53.80	386	63.90	599	59.90
	No	183	46.20	218	36.10	401	40.10

Figure 7 shows the third observed family with a Diabetes history. This family consisted of 19 individuals of which 4 were dead and 15 were alive at the time of collection of data. From them, 13 were affected while 6 were normal. The first generation contains one male and one female both were affected (I.1, I.2). They produced two sons (II.1, II.3) and one daughter (II.5) all were affected. Two sons married to affected females (II.2, II.4), and their daughter married to normal male (II.6). The first male and female from the second generation (II.1, II.2) produced two affected (III.1, III.3) and one normal son (III.6) and they also had two affected (III.2, III.4) and one normal daughter (III.5). The second male and female from the second generation (II.3, II.4) produced one affected (III.7) and one normal daughter (III.9) as well as one normal son (III.8). The third male and female from the second generation (II.5, II.6) produced two normal sons (III.10, III.11). In the family, their onset age of diabetes has been observed between 25 to 45 years.

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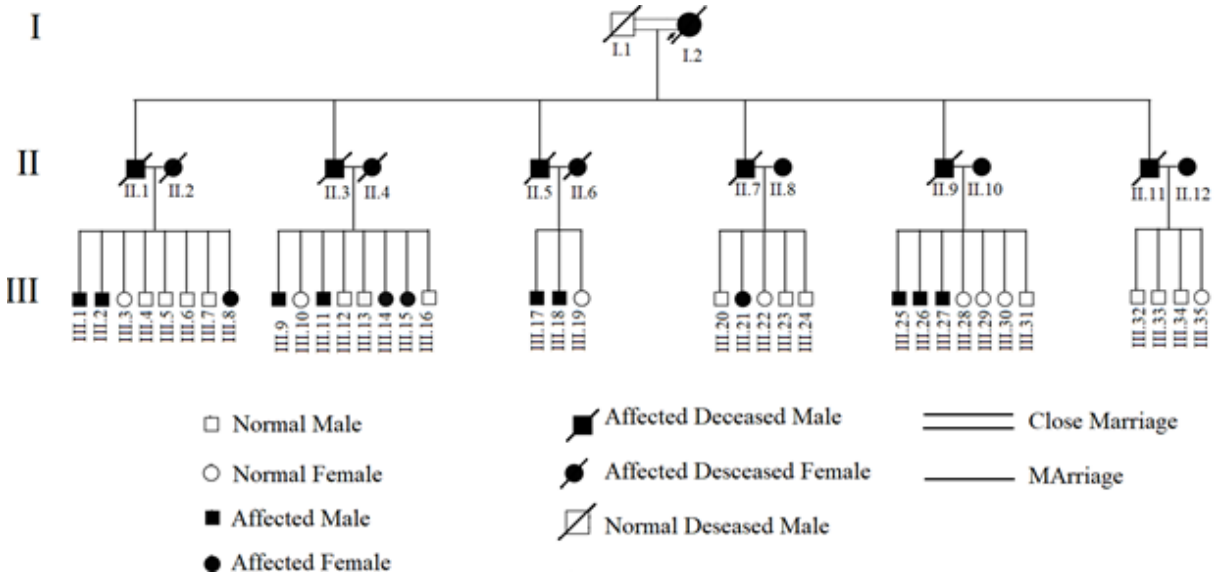

Figure 5. Pedigree of first Diabetic family observed.

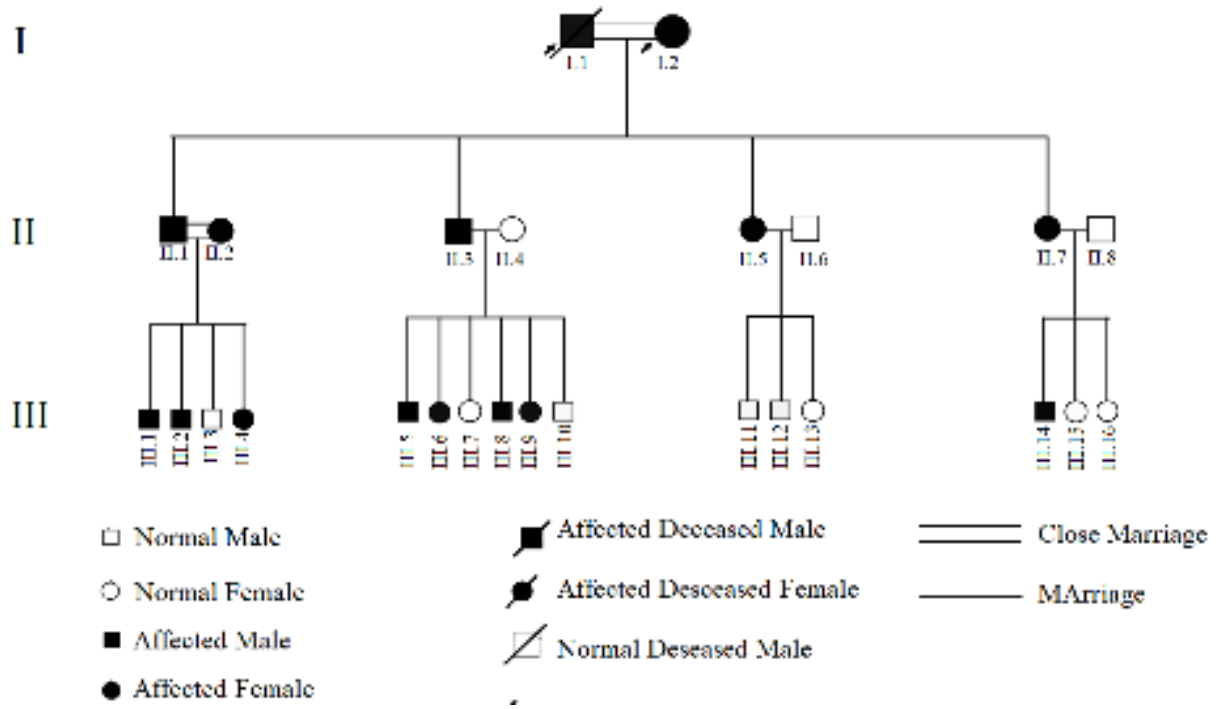

Figure 6. Pedigree of second Diabetic family observed.

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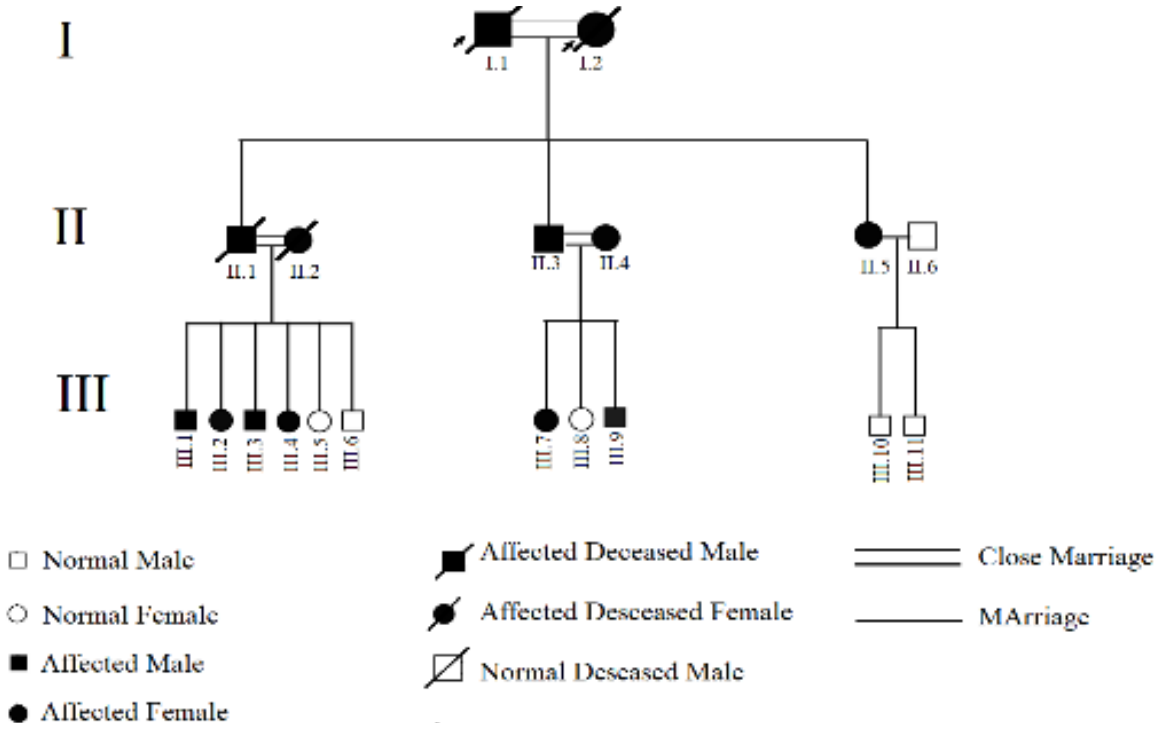

Figure 7. Pedigree of third Diabetic family observed.

4. DISCUSSION

The epidemiological study of diabetes mellitus was carried out to check the genetic epidemiology of diabetes. This study showed that diabetes has become one of the most serious issues. 1000 affected diabetic patient's data were collected and it was recorded that out of 1000 patients 396 (39.6%) were females and 604 (60.4%) were males. The analyzed data results in a P value less than 0.0001 with 1 degree of freedom. The mean and SE value for females and males were recorded at the present age.

For the age groups status of the patients, four groups were designed to check the epidemiology of the disease. The data of the age groups were highly significant in age groups (P<0.0001) and most of the diabetes cases have been found in one age group (41-60) (Becker *et al*., 2002). In this study, the area of the patients was also traced and patients were divided into two categories (Urban and Rural) and much of the patients belongs to the urban areas which were 705 of them with a total percentage of 70.5% and least in the rural areas which were 295 with 29.5%. The same was also concluded by research and they concluded that more diabetic patients belong to the urban areas while less of them belong to rural areas. Type 2 diabetes mellitus prevalence is 11.77% in Pakistan (Meo *et al*., 2016). From the observation, it was recorded that relationship status did not affect the onset of disease. Most of the married patients were found in diabetes because this disease attacks in ages 41-60. This is the age where most people can get diabetes. The study conducted supported these results showing that marital status had no significant relation with diabetes mellitus (p=0.37) (Shojaei *et al*., 2013).

In the case of family history of the patients, the parental relationship of the patients was traced and distribution of diabetic patients according to their parental genetic relationship was recorded. The relationship of patients that were in maximum first cousin (1C), and then, distant relatives, first cousin removed once (1 ½ C), baradri, second cousin (2C), and at the end out of the cast. 357 out of 1000 which have high percentage found in the first cousin with 35.7%, which is then followed by the distant relatives (200) 20.0%, the first cousin removed

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once 138 (13.8%), brotherhood 126 (12.6%), second cousin 101 (10.1%), and less of them were observed out of cast 78 with 7.8% only.

In observed data of females' percentage distribution goes from first cousin 39.9% with total number 158, 71 distant relatives 17.9%, first cousin removed once was 66 (16.7%), second cousin 51 (12.9%), baradri 29 (7.3%), and 21 in out of the cast with 5.3%. In observed data of males' percentage distribution goes from first cousin 32.9% with total number 199, distant relatives (129) 21.4%, baradri (97) 16.1%, first cousin removed once 72 (11.9%), out of the cast with 57 (9.4%) and 50 in the second cousin with 8.3%. The data was highly significant and ($p<0.0001$). And it has been concluded from the study that close parental relationships i.e. first cousin relations are at higher risk of diabetes which shows the genetic aspects of this disease. The research was performed and according to their study, it is evident that parents with diabetic history can transmit this disease to their offspring.

These data show a family impact on diabetes incidence. The excess cases of mothers of the elderly are consistent with genetic and environmental consequences. To check out the risk factors carefully obesity history in the family was also observed from the data provided by the patients for their obesity status in the family it was observed that maximum patient's family is obese (Klein *et al*., 1996). Out of 1000 patients, 599 (59.9%) families were obese while the remaining 401 (40.1%) belongs to families which were not obese. It was recorded that maximum females and males were from obese family history with 53.8% and 63.9% in males and females respectively. While those who belong to families without obesity were 46.2 females and 36.1% were males. The data was highly significant and ($p<0.0001$). The research conducted by Portha *et al*. (2019) supports these results, according to them the paternal and maternal lines are not only responsible for their genetically encoded data. Many recent laboratory experiments have shown convincingly that a father's obesity or diabetes leads to sperm epigenetic changes that can be inherited over several generations, yet epigenetic traces in somatic tissue are gradually affected (Portha *et al*., 2019).

BMI of the 1000 patients was also recorded and categorized in 4 groups, it was noticed that 399 out of 1000 of them having a BMI of 23-26.9 with 39.9% which is referred to as overweighted. 339 belongs to normal weighted patients with 33.9%. The minimum BMI was of obese 101 patients (≥27) with 10.1%. In female patients, 162 out 396 BMI was also with maximum range 23-26.9 with 40.91%, which is referred to as overweighted. After that, it is followed by 135 patients with a normal weight BMI (18.5-22.9) (34.1%). The minimum BMI of female patients was 31 from the obese group (≥27) with 7.28%. In male patients, 237 out of 604 BMI was recorded with a maximum range of 23-26.9 with 39.23%, which is referred to as overweighted. After that, it is followed by the BMI normal weight 204 patients (18.5-22.9) with 33.77%. The minimum BMI male 70 patients were from the obese group (≥27) with 11.6%. The data was highly significant and ($p<0.0001$). According to them, any BMI rise over average weight rates has an elevated chance of the development of diabetes mellitus complications. For men, the probability of such complications was higher than for women at BMI rates. Ocular complications occurred in both men and women at higher BMI rates than other forms of complications.

5. CONCLUSION

The objectives are to provide an estimate of diabetes prevalence in the hospital population of district Bahawalpur. The study was carried out on 1000 Diabetic patients, Data was collected by a well-designed Questionnaire. In the statistical analysis, the percentage (%), Standard Error (S.E), mean (M), and Chi-Square tests were used. Out of 1000 Diabetic patients, 39.6% (396) were females and 60.4% (604) were males. The mean age was 51.57 ±

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0.50 years in females and for the males, it was 47.99 ± 0.53. A greater number of patients belonged to the urban areas with 70.5% (705/1000) and Minimum belonged to Rural areas with 29.5% (295/1000). BMI recorded in the maximum range of 23-26.9 with 39.9% (399/1000) of the patients while it is recorded minimum the range of ≥27 with 10.1% (101/1000). By family history, much of the diabetic patients belonged to the consanguinity group with 35.7% (357/1000) while it was minimum in the out of cast 7.8 (78/1000). Type II Diabetes mellitus was more common with 64.2% (642/1000) and less common with 35.8% (358/1000). A more fetal onset of Diabetes occurs in the patients with Diabetic family history, so genetics have a major role with other risk factors which cannot be ignored.

6. AUTHORS' NOTE

The authors declare that there is no conflict of interest regarding the publication of this article. The authors confirmed that the paper was free of plagiarism.

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