

Association of Diabetes with History of Inherited Diabetes

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ABSTRACT

Background: Type-II Diabetes is a major global health risk and is often associated with genetic inheritance of diabetes. **Objectives:** The aim of the study was to identify whether an association exists between family history of diabetes and suspected cases of diabetes. **Material and methods:** Cross sectional study conducted in screening camps from 19th till 24th February 2018. **Setting:** 56 public sector health facilities of Faisalabad and Nankana Sahib. **Data collection and Analysis:** 55,080 people of district Faisalabad and Nankana Sahib, age 25 and above were screened for diabetes by blood glucose level test. People with BSR \geq 200mg/dl were labelled screened positive for diabetes. People with BSR $<$ 200mg/dl were categorized as Normal. Family history of any family member having diabetes was taken for all participants. The members of the family only included immediate blood relations like mother, father, brother, sister and grandparents. Data was entered in SPSS v.23 for analysis. Frequency distribution and percentage were calculated for age, gender, screening for diabetes and family history of diabetes. Chi square was used as a test of significance for association between family history and diabetes. **Results:** 55,080 people aged 25 and above were screened for diabetes. 2,855 people were screened positive for diabetes. 67.9% were females and 32.1% were males. Mean age was 43 \pm 12.61 years. In Normal category, 90.3% people had no family history of diabetes in their family while 9.7% reported positive family history. In screened positive for diabetes category, 64.7% people did not report any history of diabetes in their family where as 35.3% reported having positive family history. The association between diabetes and family history was found to be statistically significant. **Conclusion:** Risk of diabetes is associated with a positive family history of diabetes. Screening for early detection should be performed regularly for people with positive genetic risk of diabetes to ensure prevention and control of complications.

Keywords: Diabetes, Family History, Genetics, Early detection.

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INTRODUCTION

Diabetes mellitus (DM), referred commonly to as simply diabetes, is a chronic and debilitating disease that occurs due to autoimmune destruction of pancreatic beta cells (Type-I diabetes), or when the body cannot produce sufficient insulin for its requirements (Type-II Diabetes).¹ This leads to metabolic and cardiovascular disorders due to consistently high blood sugar levels for prolonged time periods.² The International Diabetes Federation (IDF) guidelines classify individuals with glucose values between 100 and 199 mg/dl (5.6–11.0 mmol/L) as pre-diabetics and beyond 200mg/dl as diabetics. Symptoms of consistently high BSR include recurrent urination, intensified thirst and hunger. If left un-treated, diabetes may lead to development of micro-vascular and macro-vascular disorders. Acute complications include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death.³ Serious long-term complications include CVDs, nephrosis, foot ulcers, neuromuscular disorders and loss of vision.^{4,5}

Since 1980s, the number of diabetics has increased from 108 million (4.7%) to 382 million in 2013 and this figure is estimated to rise up to 592 million by the year 2035.⁶ In 2012, diabetes was responsible for approximately 13.5 million deaths directly whereas 2.2 million deaths were indirectly associated with high blood sugar levels. The WHO estimates that the 7th leading cause of death in 2030 shall be attributable to diabetes alone.

According to The Diabetic Association of Pakistan, the prevalence of Type-II Diabetes (T2DM) above the age of 25 years is more than 10%.

Diabetes Mellitus is associated with a number of environmental factors and genetic influences. Environmental risk factors having an impact on development of diabetes include stress, obesity and imbalanced nutrition.⁷ Multiple genes have been identified responsible for development of diabetes indicating a polygenic origin of Type-II diabetes. Maturity onset diabetes of the young (MODY) is ascertained to mutations in more than 6 identified genes encoding the glucose sensor enzyme glucokinase and transcription factors.⁸

The genetic influence on the onset of diabetes is undeniable from strong historical evidence of patterns of diabetes inheritance in families.⁹ Inheritance pattern of diseases and susceptibility of specific ethnic groups towards diabetes is well documented.^{10,11} Population based research indicate genetic transmission of T2DM ranging between 20% - 80%. Evidence for genetic tendency is derived from a multitude of population based, family, and twin sibling's studies.¹² The relative risk of developing T2DM is approximately 3 if person is related to one affected parent or brother/sister in comparison to the general population, and this rises up to ~6 when both the parents are affected.¹³ The results, however, show variation between ethnicity, geographic and environmental factors.

Outcome of medical interventions for management of diabetes mellitus is dependent on earliest diagnosis and prevention of commencing complications. Familial and genetic patterns may predispose a person to early onset of diabetes without their awareness. Current state of knowledge is not complete and scientific basis for most of the inherited risk is limited due to lack of availability of data over diverse ethnic and geographic regions. A holistic approach is required to identify a linkage between the genetic tendencies which leads to diabetes.

Faisalabad and Nankana Sahib are geographical adjacent, major agricultural and industrial districts of Punjab. The objective of the study was to identify association of diabetes in screened positive people (BSR>199mg/dl) with family history of diabetes in public sector healthcare facilities in district Faisalabad and Nankana Sahib.

METHODOLOGY

Study Design: Cross Sectional Study.

Place of Study: 5 THQ, 10 RHC and 30 BHU Hospitals of Faisalabad district, and 1 DHQ, 2 THQ, 3 RHC and 5 BHU Hospitals of Nankana Sahib district.

Duration of Study: Screening camps conducted from 19th till 24th February 2018.

Sample Technique: Multistage purposeful Sampling.

Study Subjects: All members of the population aged ≥ 25 years screened for BSR.

Data Collection: 55,080 people from general population, aged 25 and above were screened for diabetes in screening camps conducted in 56 public sector hospitals of Faisalabad and Nankana Sahib which included DHQH, THQHs, rural centers and basic health units. Of the screened population, 3,992 people had BSR value ≥ 200 mg/dl and were labelled screened positive for diabetes. These screened positive people were inquired about history of any known diabetics in their families. Data was recorded from interviews of the selected cases if any member of their family had any diagnosed and confirmed cases of diabetes. The members of family included only immediate blood relations like mother, father, brother, sister and grandparents. Data was verified for completeness and entered in SPSS Version 23 for analysis.

RESULTS

In current study, 55,080 people aged 25 years and above were screened for diabetes in 56 Primary and secondary care hospitals in district Faisalabad and Nankana Sahib. In district Faisalabad, 43,043 people were screened for diabetes and in Nankana Sahib, 12,307 were screened. 67.9% were females and 32.1% were males. Mean age of the population (limited to 25 years age) was 43.8 ± 12.61 years. In the study population, a total of 2,855 were screened positive for diabetes (BSR ≥ 200 mg/dl).

After screening, members of population with BSR<200mg/dl were categorized as Normal, while those with BSR ≥ 200 mg/dl were categorized as suspected diabetics.

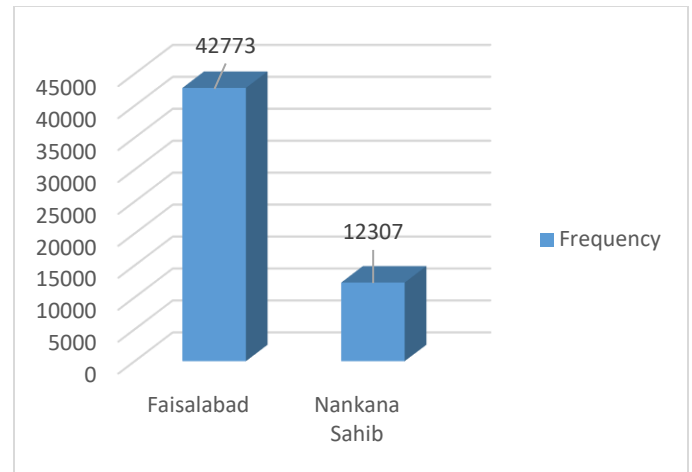


Figure 1: District wise population distribution

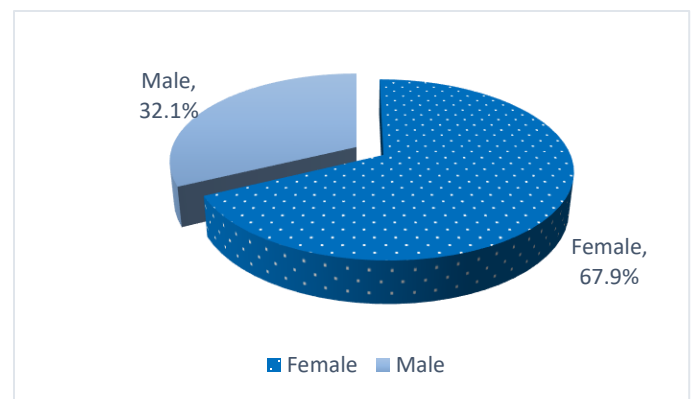


Figure 2: Frequency Distribution of Study Population by Gender

Table 1: Frequency Distribution of Screened Positive for Diabetes in Study Population

| Diabetes | Frequency | Percentage |
|--------------------------------|---------------|--------------|
| Normal | 52,225 | 94.8% |
| Screened Positive for Diabetes | 2,855 | 5.2% |
| Total | 55,080 | 100 % |

Family history of the sample population was taken, where the respondents reported if any member of their immediate blood relations had a confirmed case of diabetes. Only mother, father, brother, sister and grandparents were included in the selectable options to ensure genetic relationship. The answer was recorded in Yes or No.

Table 2: Frequency of Family History of Diabetes in Study Population

| Family History of diabetes | Frequency | Percent |
|----------------------------|---------------|-------------|
| No | 48,988 | 88.9% |
| Yes | 6,092 | 11.1% |
| Total | 55,080 | 100% |

In the group categorized as Normal, 90.3% people had no family history of any diabetics in their family while 9.7% reported having at least one diabetic family member. In the group categorized as screened positive for diabetes, 64.7% people did not report any history of diabetes in their family whereas 35.3% reported having at least one diabetic member in their family.

Table 3: Cross tabulation between Diabetes and Family History of Diabetes

| Screening for Diabetes | Family history | | Total | Pearson's Chi-square |
|--------------------------------|-------------------|------------------|--------|----------------------|
| | No | Yes | | |
| Normal | 47,140 (90.3%) | 5,085 (9.7%) | 52,225 | 0.000 |
| Screened Positive for Diabetes | 1,848 (64.7%) | 1,007 (35.3%) | 2,855 | |
| Total | 48,988 | 6,092 | 55,080 | |

In Faisalabad district, 89.1% of the Normal Category reported no family history of diabetes while 10.1% reported a positive family history of diabetes. In the screened positive category, 61.7% of the people responded No for any diabetic family history whereas 38.3% of the people reported Yes for at least having one diabetic family member. Similarly, in district Nankana Sahib, 94.5% of the Normal category responded with no family history of diabetes while 5.5% reported a positive family history. In the screened positive category, 74.6% of people responded No for any diabetic family member whereas 25.4% of the respondents reported at least having one diabetic family member.

Table 4: District Wise Distribution of Diabetes and Family History of Diabetes in Study Population

| District | Screened Study Population | Family history | | Total | Pearson's Chi-Square |
|---------------|--------------------------------|-------------------|------------------|--------|----------------------|
| | | No | Yes | | |
| Faisalabad | Normal | 36,142 (89.1%) | 4,441 (10.9%) | 40,583 | 0.000 |
| | Screened Positive for Diabetes | 1,352 (61.7%) | 838 (38.3%) | 2,190 | |
| Nankana Sahib | Normal | 10,998 (94.5%) | 644 (5.5%) | 11,642 | 0.000 |
| | Screened Positive for Diabetes | 496 (74.6%) | 169 (25.4%) | 665 | |

The association of screened positive suspected diabetes with family history of diabetes was highly significant with a Pearson's chi square value of 0.000 in both districts Faisalabad and Nankana Sahib.

DISCUSSION

Diabetes is an emerging global epidemic of the 21st century. It is a debilitating disease with a high prevalence. Complications of diabetes are not only incapacitating to the patient, but also a high economic burden on the society and the healthcare

system. Similar to cancers and hypertension, diabetes has a strong genetic component. Faisalabad and Nankana Sahib are relatively developed districts of Punjab with high agricultural and industrial significance. These districts were selected for the study due to their geographic location and demographics. A large study sample was selected for the study to identify the association between diabetes in screened positive people and their family history of any family member who was a diagnosed case of Type-II diabetes. Cases were selected on the criteria having BSR ≥ 200 mg/dl. The global guideline state that the people with random BSR between 140mg/dl and 199mg/dl are also suspected diabetics (pre-diabetes). However, the sample population criteria was set for BSR ≥ 200 mg/dl to ensure the relatively high susceptibility of diabetes in the study population and generalizability of the results.

Our study showed that a significant pattern in people who were screened positive for diabetes also had a family history of at least one family member with diabetes. This coincides with study by Kral et.al who discovered the relationship of family history and risk of Type-II diabetes by ancestry.¹⁴ In a study conducted in immigrants to western countries, it was seen that individuals with three or more siblings and parents with diabetes presented with the lowest levels of insulin secretion in body.¹⁵ Our study showed that risk of development of diabetes is directly associated with a positive family history of diabetes. In a study conducted in Tehran, the Iranian population family tree was mapped for evaluation to identify pattern of transmission of diabetes in suspected cases aged 20 and above. The methodology was similar to the current study. The results showed that there was predominantly familial transmission of diabetes in 53% among siblings and 44% among offspring.¹⁶

CONCLUSION


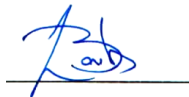
With the rising burden of diabetes and imminent increase in risk of developing complications due to late detection, understanding the familial pattern of diabetes is important to ensure that people who are at high risk should be screened regularly for prevention and control of diabetes. Further research and hereditary investigations are required to improve genetic counselling, proper treatment and familial risk assessment for individuals with diabetes.

REFERENCES

1. Dan L. Longo, Dennis L. Kasper, J. Larry Jameson, Anthony S. Fauci, Stephen L. Hauser JL, editor. Harrison's principles of internal medicine. 18 ed. States of America; 2012.
2. Diabetes programme [Internet]. World Health Organization. 2018 [cited 20 June 2018]. <http://www.who.int/diabetes/en/>
3. Kitabchi A, Umpierrez G, Miles J, Fisher J. Hyperglycemic Crises in Adult Patients with Diabetes: Response to Yasuda et al. Diabetes Care. 2009;32(12):158.
4. Retinopathy and Nephropathy in Patients with Type 1 Diabetes Four Years after a Trial of Intensive Therapy. N Engl J Med. 2000;342(6):381-9.
5. Kumar R. Hepatogenous diabetes: An underestimated problem of liver cirrhosis. Indian J Endocr Metab 2018;22:552-9.

6. Guariguata L, Whiting D, Hambleton I, Beagley J, Linnenkamp U, Shaw J. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res Clin Pract.* 2014;103(2):137-49.
7. Portha B, Fournier A, Ah Kioon M, Mezger V, Movassat J. Early environmental factors, alteration of epigenetic marks and metabolic disease susceptibility. *Biochimie.* 2014;97:1-15.
8. Vaxillaire M, Froguel P. Monogenic Diabetes in the Young, Pharmacogenetics and Relevance to Multifactorial Forms of Type 2 Diabetes. *Endocr Rev.* 2008 May;29(3):254-64.
9. Gottlieb M. Diabetes in offspring and siblings of juvenile and maturity onset type diabetics. *J Chronic Dis.* 1980;33(6):331-9.
10. Zimmet P, Taylor R, Ram P, King H, Sloman G, Raper L et al. Prevalence of Diabetes and Impaired Glucose Tolerance in The Biracial (Melanesian And Indian) Population of Fiji: A Rural-Urban Comparison. *Am J Epidemiol.* 1983;118(5):673-88.
11. Diabetes risk factors and complications. *Diabetic Medicine.* 2018;35:27-9.
12. Poulsen P, Ohm Kyvik K, Vaag A, Beck-Nielsen H. Heritability of Type II (non-insulin-dependent) diabetes mellitus and abnormal glucose tolerance - a population-based twin study. *Diabetologia.* 1999;42(2):139-45.
13. Meigs J, Cupples L, Wilson P. Parental transmission of type 2 diabetes: the Framingham Offspring Study. *Diabetes.* 2000;49(12):2201-7.
14. Kral B, Becker D, Yanek L, Vaidya D, Mathias R, Becker L et al. The relationship of family history and risk of type 2 diabetes differs by ancestry. *Diabetes Metab.* 2018;21. pii: S1262-3636(18)30089-2.
15. Bennet L, Franks P, Zöller B, Groop L. Family history of diabetes and its relationship with insulin secretion and insulin sensitivity in Iraqi immigrants and native Swedes: a population-based cohort study. *Acta Diabetol.* 2018;55(3):233-42.
16. Najafipour F, Najafipour M, Zareizadeh M. Epidemiologic study of familial Type 2 diabetes in Tehran. *J Adv Pharm Technol Res.* 2018;9(2):56-60.

AUTHORSHIP AND CONTRIBUTION DECLARATION

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