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Marriage within Bloodline: Assessing the Impact of Consanguinity on Type 2 Diabetes in Karachi, Pakistan

Saif Ullah Shaikh, Saira Hassan Askarey, Zain Amjad, Sana Barkat Ali, Hina Moazzam, Iram Saddiqa

Abstract

Objective: To investigate the association between parental consanguinity and complications of type 2 diabetes mellitus in the Pakistani population.

Study design & Setting: A cross- sectional study was carried out on the participants from the medical outpatient department at PNS Shifa hospital Karachi, diagnosed with type 2 diabetes mellitus of consanguineous and non-consanguineous family backgrounds from 25th August to 24th October 2025.

Methodology: 423 participants were utilized to collect the information about their demographic data, clinical background, diabetes control indicators, complication status, and treatment strategies in the form of medication and lifestyle interventions. Pearson Chi-Square test was used to analyze the relationship between consanguinity, the onset, severity, and treatment outcomes of diabetes.

Results: Participants born to non- consanguineous parents, 0.6% (1) were suffering from cardiovascular disease; 1.7% (3) had hypertension, 1.1% (2) had a visual problem, and 0.6% (1) were reported to have dyslipidemia. Among the progeny of consanguineous parents, 14.5 %(35) were suffering from cardiovascular disease, 4.1% (10) suffered from chronic kidney disease, 21.5 %(52) had hypertension, 38.0% (92) had problems related to vision, and 7.0 %(17) were reported to have dyslipidemia after being diabetic. There is a strong significant association between diabetes and their complications in the offspring of consanguineous couples after being diagnosed as diabetics ($p<0.01$).

Conclusion: Clarifying the role of consanguinity in the prevalence and progression of T2DM can promote understanding of genetic susceptibility among high-risk populations and guide culturally sensitive public health practice and genetic counseling policy in Pakistan.

Keywords: Consanguinity, Type 2 Diabetes Mellitus, Genetic predisposition, Public health.

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INTRODUCTION

Consanguinity is the bond between individuals who have common ancestors, usually by blood or kinship. In a study in Pakistan, 28.13% to 34.1% of the couples were first cousins and hence genetically related.[1?2] It results in an increase in genetic and metabolic disorders, thus leaving the population lacking genetic diversity, by placing the population at a high rate of disease like diabetes and hypertension.[3]

Consanguineous marriages remain a deep-rooted cultural tradition in many parts of South Asia, particularly Pakistan, where social, religious, and familial ties often reinforce these unions. This practice, while socially cohesive, also increases the likelihood of recessive genetic disorders and metabolic syndromes appearing across generations. Thus, there is a dire need to balance cultural acceptability with health awareness in order to solve this problem..

Studies have found that the risk of type 2 diabetes is at least two times higher in individuals with one parent with diabetes and up to four times higher with two parents with diabetes. The rapid expansion of urban sprawl has a long-lasting effect on the lifestyle, leading to unhealthy eating, non-

active lifestyle, more stress, and environmental issues.[4] The worldwide prevalence of Diabetes Mellitus is 10.5% in individuals of 20–79 years. Type 2 Diabetes Mellitus accounts for approximately 98 percent of diabetic diagnosis worldwide.[5, 6]

Modernization and sedentary lifestyles have amplified these genetic risks, creating a dual challenge of inherited predisposition and environmental triggers. The growing burden of obesity, physical inactivity, and poor dietary habits has further accelerated the rise of T2DM in developing countries like Pakistan. Consequently, understanding the combined impact of genetics and lifestyle has become a public health priority.

But the pathophysiology has two main factors i.e., â-cell destruction of the pancreas leading to faulty insulin secretion, and the failure of insulin-sensitive tissues to respond effectively to insulin. The hereditary and dietary factors have a major role to play in the development of this disease.[7] Further, a number of studies confirm that diabetes is more prevalent among the offspring of first-cousin unions than in offspring of second-cousin unions.[8] Globally, the 2021 International Diabetes Federation report states that an estimated 537 million individuals are living with diabetes and account for approximately 10.5% of the world's population. The condition has resulted in health expenditure of $966 billion. Projections predict that by the year 2045, diabetes cases will increase to 783 million, while the cost of healthcare will be more than $1,054 billion.[9]

Recent research has determined that Diabetes Mellitus is associated with a broad spectrum of serious and progressive multisystem complications. Diabetic Kidney Disease (DKD), which can result in chronic kidney failure, is just one type of complication; other complications include Diabetic Retinopathy, which is a leading cause of vision loss and blindness, and Diabetic Neuropathy, which is the result of nerve injury and can cause varying degrees of pain, numbness, and reduced capacity to use the limbs, particularly in the distal extremities. Moreover, metabolic dysfunction associated with diabetes can contribute to Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD), which is characterized by fat deposition and inflammation in the liver. Cardiovascular complications are also widespread, and only Coronary Artery Disease (CAD) and stroke are ranked higher than diabetes as contributors to morbidity and mortality. Furthermore, Peripheral Artery Disease, which affects blood flow to the limbs, usually results from a prolonged period of damage to the vessels due to high levels of blood sugar.[10]

These complications not only result in a social burden but also put a financial burden on the system. The ever-increasing rise of diabetes, coupled with a lack of awareness about preventive care, is a clear indicator of the urgent need for early screening, education, and intervention, especially in areas where consanguinity is extremely high.

During this period of global recession of all resources, it is a tough time for authorities across the world to cope with the impact of Diabetes Mellitus. Type I Diabetes is also a result of consanguinity. A study conducted in Iraq revealed that despite the high rates of consanguinity, type 1 diabetes is the predominant type of diabetes among children. Pathogenic variants caused monogenic diabetes in 83% of neonatal cases and 57% of syndromic cases, which were homozygous, thus indicating the presence of distinct genetic variants.[11]

A new study carried out in Australia emphasizes the significance of taking into account the health effects of consanguineous marriages, such as the prevalence of inherited and genetic disorders. The study emphasizes that if two individuals are closely related by blood, such as first cousins or second cousins, there is a high possibility that their offspring may inherit recessive genetic factors, which may result in various types of recessive genetic diseases, many of which may go unnoticed for many years until two individuals with the same gene mutations have a child.

The evidence from the studies suggests that using genetic testing technologies would provide potential couples with useful information about their genetic compatibility and their risk of transmitting inherited diseases. Consanguinity increases the fraction of an individual's genome that is inherited identically from both parents, a phenomenon termed autozygosity. While it is well established that consanguinity increases the risk of rare single-gene disorders by increasing the chance that an individual will inherit the same rare DNA change in a disease-causing "recessive" gene, its impact on common diseases remains understudied.

The rationale behind this research is to understand the impact of consanguineous marriages, such as cousin marriages, on the incidence of genetic diseases in communities where such marriages are common. By comparing the health hazards in offspring of cousin marriages with and without diabetes, the research aims to highlight the risks associated with these marriages and identify preventive steps to alleviate health problems in children. Ultimately, the goal is to facilitate informed decision-making and prevent genetic diseases, reducing their impact on communities. This is particularly relevant in regions like Pakistan, where cousin marriages are prevalent, and awareness about genetic risks can help mitigate potential health issues.[12]

METHODOLOGY

This cross-sectional study employed a non-probability purposive sampling method to recruit 423 adults with diabetes whose parents had either consanguineous or non-consanguineous marriages. The sample size was calculated using Open Epi-version 7 software, ensuring a 95% confidence level and a 5% margin of error. Conducted between August 25, 2025, and October 24, 2025, it was

approved by Bahria University Health Sciences Campus, Institutional Review Board (Reference BUHS-IRB#187/25).

This study included adults aged 20-75, living in Pakistan, with different educational and professional backgrounds, who knew their HbA1c status within the past six months. We excluded those with pregnancy, mental health issues, genetic conditions, autoimmune diseases, or unclear diabetes status. Every participant gave informed consent, and we ensured their information stayed confidential and participation was voluntary.

In this study we used a comprehensive questionnaire which had four key parts: demographic details of the participants (age, gender, where they're from, and family history of diabetes); their health before diabetes (any existing conditions like high cholesterol, kidney disease, cancer, or high blood pressure); diabetes complications (any new issues like heart disease, kidney problems, or eye issues); and managing their diabetes (lifestyle changes, diet, exercise, medications, and insulin use).

The collected data was then analyzed to evaluate a comparative perspective on outcomes between consanguineous and non-consanguineous marriages. This study aimed to uncover potential correlations of the impact of consanguinity on diabetes management and outcomes. The data was statistically analyzed using the Pearson Chi-Square test, and considered $p < 0.05$ as a sign of significant associations between marriage type and health outcomes.

RESULTS

The study sample included 423 respondents with mean age (49.1) years, majority 72.6% were males and 57.2% (242) have cousin marriage whereas 42.8% (181) have non-cousin relationships of their parents. Table 1 showed, In non-cousin marriages, 0.6%(1) were suffering from dyslipidemia; none were suffering from kidney disease, 1.1%(2) had hypertension, and 0.6%(1) were reported to have cancer as compared to cousin marriages with 15.7% (38) were suffering from dyslipidemia, 1.2%(3) were suffering from chronic kidney disease, 8.3% (20) had hypertension, and 0.4%(1) were reported to have cancer. There is a statistical significant risk of health conditions like dyslipidemia and hypertension in the off springs of consanguineous couples before the diagnosis of diabetes ($p<0.01$).

Table 2 reports the association of diabetes with associated conditions in the offspring of Consanguineous couples as well as non-consanguineous couples after being diagnosed as diabetic.

Among the children's of non-cousin marriage, 0.6%(1) were suffering from cardiovascular disease; none suffered from chronic kidney disease, 1.7% (3) had hypertension, 1.1% (2) had a visual problem, and 0.6% (1)were reported to have dyslipidemia. Among the progeny of cousin marriage, 14.5 %(35) were suffering from cardiovascular disease, 4.1% (10) suffered from chronic kidney disease, 21.5 %(52) had hypertension, 38.0% (92) had problems related to vision, and 7.0 %(17) were reported to have dyslipidemia after being diabetic. Table 2 showed a strong significant association between diabetes and their complications in the offspring of consanguineous couples after being diagnosed as diabetics ($p<0.01$).

Table 3 reports the treatment plan followed by the participants to maintain their blood sugar levels. Among the progeny of non-cousin marriage, 5.5% followed regular physical exercise, 5.0% avoided sugar in their diet, 3.9% injected insulin, and 6.1% used oral medications. Among the progeny of cousin marriage, 80.6% followed physical exercise, 78.9% avoided sugar in the diet, 22.3% injected insulin, and 74.8% used oral medications with statistically significant p-value = 0.01 respectively.

DISCUSSION

This study assessed the impact of parental consanguinity on the prevalence, severity, and complications of Type 2 Diabetes

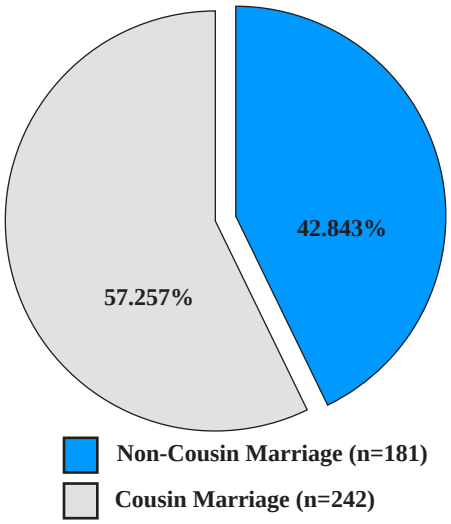

Table 1: Risk of other health conditions in offspring of consanguineous couples

Were you suffering from any other health conditions before the diagnosis of diabetes?		non-cousin marriage		cousin marriage		p-value
		n	%	n	%	
Cholesterol (dyslipidemia)	Yes	1	0.6	38	15.7	<0.01*
	No	180	99.4	204	84.3	
kidney diseases	Yes	0	0.0	3	1.2	0.13
	No	181	100.0	239	98.8	
Hypertension	Yes	2	1.1	20	8.3	<0.01*
	No	179	98.9	222	91.7	
Cancer	Yes	1	0.6	1	0.4	0.83
	No	180	99.4	241	99.6	

*p<0.05 was considered statistically significant using the Pearson Chi-Square test

Table 2: Association of diabetes-related with other health conditions

Have you been diagnosed with any other condition after being diabetic?		*Parents' marriage*				*p-value*
		non-cousin marriage		*cousin marriage*		
		n	*%*	*n*	*%*	
cardiovascular disease	Yes	1	0.6	35	14.5	<0.01*
	N o	180	99.4	207	85.5	
chronic kidney disease	Yes	0	0.0	10	4.1	<0.01*
	N o	181	100.0	232	95.9	
Hypertension	Yes	3	1.7	52	21.5	<0.01*
	N o	178	98.3	190	78.5	
eye problems	Yes	2	1.1	92	38.0	<0.01*
	N o	179	98.9	150	62.0	
Cholesterol	Yes	1	0.6%	17	7.0	<0.01*
	N o	180	99.4%	225	93.0	

*p<0.05 was considered statistically significant using the Pearson Chi-Square test

Table 3: Management strategies followed by the participants

		non-cousin marriage		*cousin marriage*		*p-value*
		n	*%*	*n*	*%*	
Physical exercise	Yes	10	5.5	195	80.6	<0.01*
	No	171	94.5	47	19.4	
Avoiding sugar	Yes	9	5.0	191	78.9	0.13
	No	172	95.0	51	21.1	
Injecting insulin	Yes	7	3.9	54	22.3	<0.01*
	No	174	96.1	188	77.7	
Oral medicines	Yes	11	6.1	181	74.8	0.83
	No	170	93.9	61	25.2	

*p<0.05 was considered statistically significant using the Pearson Chi-Square test

Mellitus (T2DM) among adults in Karachi. The findings of this study clearly show that the offspring of consanguineous marriage are more prone to pre-diabetic states such as hypertension and dyslipidemia and complications arising after the diagnosis of diabetes, such as cardiovascular complications, chronic renal failure, and visual disturbances. For instance, before the diagnosis of diabetes, dyslipidemia was experienced by 15.7% of the patients with consanguineous marriage compared with merely 0.6% of the patients with non-consanguineous marriage. Hypertension was also experienced by 8.3% and 1.1% of the patients with consanguineous and non-consanguineous marriage, respectively. After the diagnosis of diabetes, the differences are more marked with 14.5% of the patients with consanguineous marriage experiencing cardiovascular complications compared with merely 0.6% of the patients with non-consanguineous marriage. These differences are significant at $p < 0.01$.

This is consistent with larger epidemiological trends observed in South Asia. Nielsen et al. had highlighted couple concurrence of diabetes, as well as co-morbidities such as hypertension and dyslipidemia, among urban Indians and Pakistanis, emphasizing socioeconomic and household factors that may contribute to these risks.[13] Our study contributes to their research by adding a new dimension of consanguinity, a genetic factor, to this risk scenario. Another study by Samad et al. had highlighted a high rate of consanguinity among Pakistani diabetics, emphasizing the impact of cultural factors on disease prevalence.[14] The genetic impact of such marriages is critical, where one study had highlighted how populations that result from such inbred marriages have a high prevalence of deleterious recessive alleles, which not only increase risk for monogenic disease states but also for complex metabolic disorders such as T2DM.[15] Our study's observation of a high prevalence of dyslipidemia and hypertension among consanguineous children, even before disease onset, is consistent with this genetic risk.

The genetic pathways that underlie this association are important in understanding the link between consanguinity and metabolic disease. Saeed et al. have identified a high rate of genetic mutations that are associated with severe childhood obesity in an inbred group from Pakistan, which is a significant risk factor for T2DM in children.[16] This study is followed by another study by Niazi et al., in which they have identified genetic mutations that are responsible for obesity in children from Pakistan.[17] Our study extends this understanding by demonstrating that not only are children from a consanguineous marriage more prone to obesity-related conditions such as dyslipidemia and hypertension, but they are also more prone to complications from diabetes such as nephropathy and retinopathy after diagnosis itself. Sami et al. have elaborated on the role of genetics and environmental factors in the development of diabetes and have shown that although our study does not include genetic analysis in it, the high degree of association between consanguinity and disease severity does point to the role of genes and environmental factors that may be exacerbating them.[18]

The impact of consanguinity on the management of diabetes and its complications is of significant public health importance. Shahid et al. found that impaired fasting glucose was strongly related to family history and parental consanguinity, and thus there was a need for screening in these populations early.[19]Our research corroborates this and also illustrates that children of consanguineous parents do more diabetes self-care activities, i.e., physical activity and dietary change, probably because of higher disease load and perception.

Family history of metabolic syndrome was also emphasized by Bener et al. as one of the essential risk factors, especially in very endogamous populations, suggesting targeted education.[20] Chauhan et al. highlighted how consanguinity affects nutritional status,

which is a confounding factor with metabolic risk factors.[21] All these studies highlight that, while designing prevention and control strategies for diabetes, there is a need to take into account genetic counseling and education about the risks of consanguinity.

A research conducted among 94 people in the Bahawalpur area of Pakistan resulted in the conclusion that there is a complex interrelationship existing between the genetic and environmental factors in the development of diabetes among this population group and reiterated the findings of previous research studies conducted in the South Asian population. Moreover, they also stress the need for screening programs and interventions, as well as the continued research in the genetics of diabetes for its effective management among this population.[22]

The above findings have also been reflected in the recent literature. Samad et al. have demonstrated a significant link between consanguinity and the development of Type 2 Diabetes in the Pakistani population. This again reflects the importance of the contribution of genetic factors and the cluster effect of consanguinity.[14] Jan et al. have also demonstrated the presence of novel genetic mutations for T2DM in the Pashtun population. This reflects the importance of the genetic isolation of the population and the increased likelihood of the development of diabetes.[23] Again, a study by Ali et al. has reaffirmed the importance of the above findings by showing that patients with a positive family history of diabetes and consanguinity among the parents had significantly higher levels of fasting blood glucose.[24]

The sociocultural factors also play an important role in the above findings. Hussain.R have shown that the knowledge of the genetic risks of inbreeding is low in the Pakistani population. The social acceptability of marrying cousins is much higher than the health implications.[25] Similarly, Bener et al. and Hussain.R. have shown that not only is there an increase in the prevalence of diabetes, but there is also an increase in the severity of complications through gene-environmental interactions.[20,25] Hamamy emphasized the role of pre-conception counseling and community education in populations where there is a high rate of consanguinity to alleviate the genetic burden of common metabolic disorders.[26 27]

All these studies have highlighted that Type 2 Diabetes in Muslim populations with high rates of consanguinity is a multifactorial problem that incorporates genetic, cultural, and environmental factors. Genetic counseling, screening, and community education can go a long way in alleviating this problem in high-risk populations.

Limitations of the study: It is imperative to note that even with the established associations; there is a need to consider the limitations of the study. The major limitation of the study is the fact that the associations established cannot be used to make any inferences regarding the causation of consanguinity and the risk of acquiring T2DM. This is because the study did not employ a longitudinal design. In addition, the fact that the study did not collect data on genetics and lifestyle factors, including diet, exercise, socioeconomic factors, and environmental factors, is a major limitation. Each of these factors is very important in explaining the mechanisms of each of the factors. They may also explain how genetics and lifestyle factors interact in the progression of T2DM.

To build on the above findings, it is suggested that future longitudinal and molecular studies, including genetic profiling, environmental, and lifestyle assessments, be undertaken. This will assist in clarifying the intricacy of the link between consanguinity, genetic predisposition, and environmental factors in the aetiology of T2DM. However, the above findings will assist in providing evidence to healthcare providers, researchers, and public health officials with regard to public health encouragement, engagement, and education in the community with regard to genetic education and the practice of consanguineous marriage.

CONCLUSION

Thus, in regions where high levels of consanguinity exist, early hypertension, dyslipidemia, and complications of diabetes should be a priority for those with a history of cousin marriage. Genetic counseling integration, both in primary care settings and pre-marital settings, could also help reduce future disease burden. Lastly, appropriate cultural-sensitive public health programs need to be established to address the cumulative effects of consanguinity and lifestyle factors that have led to the epidemic of diabetes in Karachi, etc.

Furthermore, increasing awareness about genetic risks associated with close-kin marriages could prove to be a key factor in future prevention. Primary health care professionals need to be trained to identify high-risk families, providing them with appropriate lifestyle modifications from an early age.

Genetic risk assessment needs to be included in public health programs, which could further help refine prevention strategies, especially in regions where high levels of endogamy exist. Addressing all these factors could help reduce the increasing prevalence of Type 2 Diabetes in Pakistan, creating a better metabolic future for generations to come. Therefore, progress towards sustainability would depend on a concerted effort by health institutions, education systems, and governments to ensure that decisions about marriage, as well as health habits, are made with adequate information. Future studies would thus focus on pinpointing certain genetic factors that increase the risk of metabolic disorders in families with consanguinity, thus helping to address these issues more effectively. Thus, Pakistan would look towards a brighter future with reduced instances of diabetes and other hereditary illnesses.

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Zain Amjad: Manuscript writing & Acquisition of data
Sana Barkat Ali: Manuscript writing & Acquisition of data Worked for important intellectual content
Hina Moazzam: Acquisition of data analysis & Interpretation of data, Revised it Critically for final approval
Iram Saddiqa: Revised it critically for important intellectual content and final approval to be published

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