Research Article

Frequency of Diabetes Mellitus in Thalassemia Major Patients in Thalassemia Center, Sir Ganga Ram Hospital, Lahore

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Abstract

Background: Diabetes mellitus (DM) represents a significant complication in individuals with thalassemia major (TM),[(1)] yet the underlying mechanisms and risk factors are not yet completely understood. Aim of this study is to investigate the frequency and associated factors of Diabetes Mellitus in Thalassemia Major patients and describing relationship between genetic predisposition, iron overload and metabolic dysfunction.

Objectives: Determining the frequency of Diabetes Mellitus among Thalassemia Major patients presenting at the Thalassemia Center, Sir Ganga Ram Hospital, Lahore. Additionally, the study aims to describe demographic factor, clinical parameters and family history profiles associated with the presence of DM.

Methods: A cross-sectional study was carried out from July 2023 to October 2023, involving data collection from medical records of Thalassemia Major patients over a three-month period. Demographic characteristics, including age and gender; clinical parameters such as the number of blood transfusions; and family history profiles of thalassemia and Diabetes Mellitus were analyzed. Statistical analysis, including chi-square tests, was used to assess associations and significance levels.

Results: The study included 129 Thalassemia Major patients, with a majority falling within the 5-11 years age group (70%) and a slight predominance of males (56%). There wer no significant associations upon analysis between age, gender, or the number of blood transfusions and DM. There was a significant correlation between positive family history of thalassemia ($p = 0.0047$) and Diabetes Mellitus ($p = 0.0026$) with the presence of Diabetes Mellitus among Thalassemia Major patients.

Conclusion: Despite the lack of significant associations with demographic and clinical parameters, the findings emphasize the need for targeted screening and intervention strategies for high-risk individuals. [(2)]

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Keywords | Thalassemia major, diabetes mellitus, prevalence, risk factors, genetic predisposition, iron overload, metabolic dysfunction.

Introduction

Diabetes mellitus (DM) represents a significant health burden globally, with different subtypes. Gestational diabetes, occurring during pregnancy, and other rare diabetes subtypes further establish the heterogeneous nature of this metabolic disorder.[3] In adult population obesity is a prominent risk factor for type 2 diabetes, exacerbating insulin resistance and impairing pancreatic beta cell function. Thalassemia encompasses a diverse spectrum of inherited hemoglobinopathies, presenting as anemia due to aberrant hemoglobin gene function. The severity of thalassemia varies. Characteristic feature of Alpha thalassemia is absent or reduced alpha-globin chain. Beta thalassemia is characterized by mutations in the beta-globin gene. Beta thalassemia major, which is the most severe form, necessitates lifelong blood transfusions for survival.[4,5] Despite improvements in management, individuals with thalassemia major face significant challenges, including iron overload and associated endocrine

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complications.[6]

Recent studies have revealed the intricate relationship between thalassemia major and diabetes mellitus giving evidence of increased susceptibility to diabetes in this population.[7] Iron overload-induced cytotoxicity in the pancreas is considered as a significant contributor to the pathogenesis of diabetes in thalassemia major. This highlights the intricate interplay between iron metabolism and pancreatic function. Moreover, the aging TM population faces multiple risks, as cumulative iron-related damage and natural aging processes act to exacerbate metabolic dysfunction.[8]

Our study aims to investigate the frequency and associated risk factors of diabetes mellitus among individuals diagnosed with thalassemia major seeking medical attention at the Thalassemia Center, Sir Ganga Ram Hospital, Lahore. By conducting a comprehensive analysis of demographic characteristics, family history profiles, and clinical parameters, we seek to describe the complex relationship between genetic predisposition, iron overload, and metabolic dysfunction in the pathogenesis of diabetes mellitus in thalassemia major. Furthermore, our study aims to provide updated data that correlates with existing literature, offering fresh insights and avenues for further research in this critical area.[9] Through rigorous investigation and analysis, we attempt to provide a good understanding of the epidemiology, risk factors, and underlying mechanisms of diabetes mellitus in individuals with thalassemia major, with the ultimate goal of informing targeted preventive strategies and improving clinical outcomes in this vulnerable population.

Methods

A cross-sectional study was carried out from July 2023 to October 2023, at the Thalassemia Center, Sir Ganga Ram Hospital, Lahore, to investigate the frequency and other risk factors associated with diabetes mellitus among individuals diagnosed with thalassemia major (TM). The study duration was three months, during which data were collected from medical records of TM patients who sought medical care at the center. A sample size of 129 participants was determined using a proportionate sampling technique based on previous literature and calculated with a 95% confidence level.

Participants included in the study met the following inclusion criteria: diagnosed with TM and having a disease duration of more than 6 months, aged between 5 and 18 years, registered at the Thalassemia center for a minimum of 6 months, received a minimum of 20-30 blood transfusions, and had serum ferritin levels of at least 1500 mg/dL. Exclusion criteria comprised patients aged less than 6 years, those who had not undergone chelation therapy, and individuals with a family history significant for diabetes.[10] Ethical approval was obtained from the institutional ethical and research committee, and informed consent was obtained from all participants or their guardians before data collection commenced. Demographic characteristics, including age and gender; clinical parameters such as the number of blood transfusions; and family history profiles of thalassemia and Diabetes Mellitus were analyzed. Statistical analysis, including chi-square tests, was used to assess associations and significance levels.

Results

The majority of the study participants fell within the age range of 5-11 years old (70%), with a smaller but significant proportion aged between 12-18 years old (30%). Gender distribution indicated a slight predominance of males (56%) compared to females (44%). According to transfusion history, approximately half of the individuals had received less than 3 blood transfusions (51%), while the remaining half had undergone more than 3 transfusions (49%).

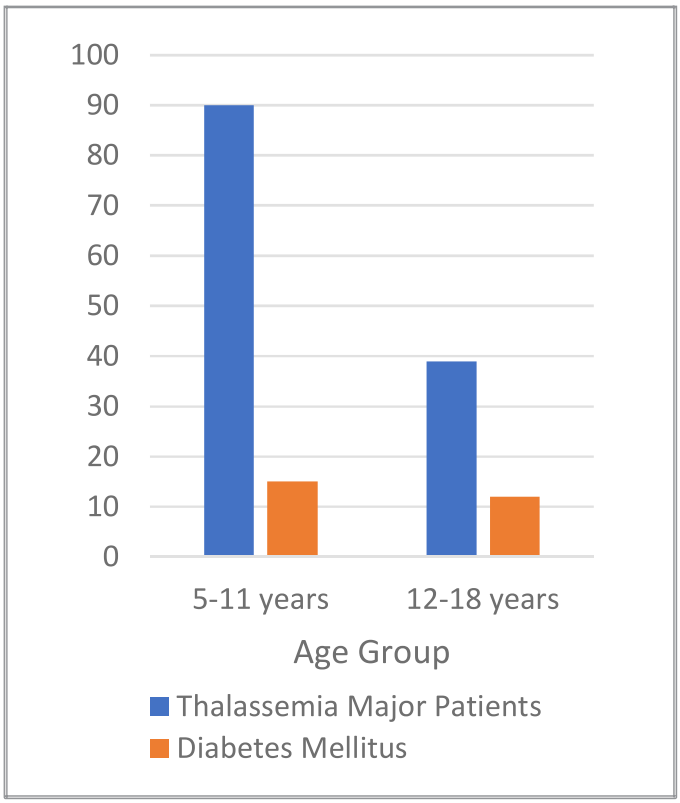

Figure 1: *Distribution of Thalassemia Major Patients and Diabetes Mellitus by Age Group*

Analysis of family history data yielded noteworthy findings. A minimal percentage of participants had a positive family history of thalassemia (1%), while the overwhelming majority had a negative family history (99%). Despite the rarity of positive family history, a significant association was

Table 1: *Demographic Characteristics of Thalassemia Major Patients*

Characteristic	Frequency	Percentage
Age group		
- 5-11 years	90	70%
- 12-18 years	39	30%
Gender		
- Male	72	56%
- Female	57	44%

observed between family history of thalassemia and the presence of DM (p=0.0047), highlighting the role of genetic predisposition in disease development. Similarly, a considerable proportion of individuals had a positive family history of diabetes mellitus (35%), while the majority had a negative family history (65%). Importantly, a significant association was identified between family history of diabetes mellitus and the presence of DM (p = 0.0026), emphasizing the importance of genetic factors in the pathogenesis of DM among TM patients.

Despite the lack of significant associations between age, gender, or the number of blood transfusions with the presence of DM among TM patients in our study, the findings contribute valuable insights into the demographic characteristics and family history profiles of this population. The significant

Table 2: *Associations with Diabetes Mellitus (DM) Presence*

Factor	p-value
Age group and DM	0.56
Gender and DM	0.84
Number of transfusions and DM	0.97
Family history of thalassemia and DM	0.0047
Family history of DM and DM	0.0026

associations between family history of thalassemia and diabetes mellitus with the presence of DM underscore the need for early identification and screening of individuals with a positive family history to facilitate timely interventions and management strategies.[5,8] Further research is warranted to explore additional risk factors and underlying mechanisms contributing to the development of DM in individuals with thalassemia major.

Discussion

The findings of our study shed light on the complex interplay between genetic predisposition and the development of diabetes mellitus (DM) among individuals with thalassemia major (TM). While age, gender, and the number of blood transfusions did not demonstrate significant associations with the presence of DM in our study population, family history emerged as a crucial predictor of disease occurrence.[11] Specifically, our analysis revealed significant associations between both family history of thalassemia and diabetes mellitus with the presence of DM among TM patients. These findings underscore the importance of genetic factors in influencing susceptibility to DM in this population and highlight the need for targeted screening and intervention strategies for individuals with a positive family history of these conditions.[12]

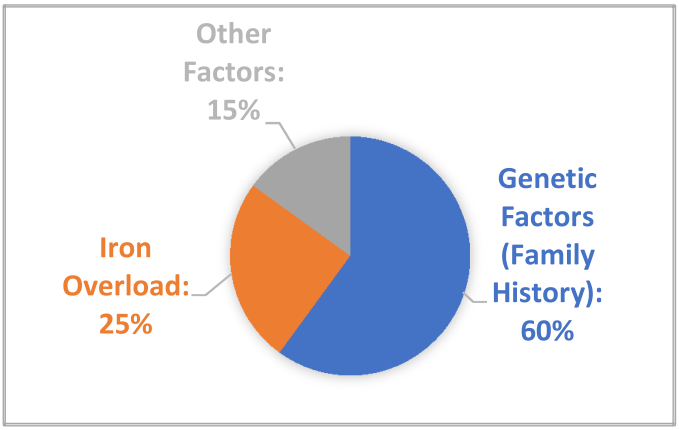

Figure 2: *Factors Contributing to Diabetes Mellitus Among Thalassemia Major Patients*

The lack of significant associations between age, gender, or the number of blood transfusions with the presence of DM suggests that other factors may play a more prominent role in disease development among individuals with TM.

Table 3: *Clinical Parameters and Family History Profiles*

Parameter	Frequency	Percentage
Number of transfusions		
- <3 transfusions	66	51%
- ≥3 transfusions	63	49%
Family history of thalassemia		
- Positive	1	1%
- Negative	128	99%
Family history of diabetes mellitus		

While age-related changes in insulin sensitivity and secretion are well-documented in the general population, the relatively homogeneous age distribution of our study population may have contributed to the lack of significant associations observed. Similarly, the absence of gender disparities in DM prevalence among TM patients contrasts with the observed gender differences in other populations, suggesting that disease pathogenesis in TM may be influenced by unique factors independent of gender.

The absence of a significant association between the number of blood transfusions and the presence of DM is noteworthy, considering the established relationship between iron overload and diabetes complications in TM patients.[13,14,15] While

iron overload-induced cytotoxicity in the pancreas has been proposed as a potential mechanism contributing to DM development, our findings suggest that factors beyond transfusion frequency may modulate this relationship.

The significant associations between family history of thalassemia and diabetes mellitus with the presence of DM highlight the need for comprehensive risk assessment and tailored preventive strategies for TM patients with a positive family history of these conditions. Additionally, our findings underscore the importance of ongoing monitoring and management of iron overload in TM patients to mitigate the risk of diabetes and other complications associated with chronic transfusion therapy.[16,17]

The significant associations observed between family history of thalassemia and diabetes mellitus with the presence of DM underscore the importance of genetic predisposition in disease development.[18,19] Future research efforts should focus on elucidating the underlying mechanisms linking genetic factors, iron overload, and metabolic dysfunction in the pathogenesis of DM among TM patients, with the ultimate goal of informing targeted preventive and therapeutic interventions to improve outcomes in this population.

Conclusion

In conclusion, our study underscores the significant influence of genetic factors, particularly family history of thalassemia and diabetes mellitus, on the development of diabetes mellitus (DM) among individuals with thalassemia major (TM). While age, gender, and the number of blood transfusions did not exhibit significant associations with DM prevalence in our study population, the observed associations with family history highlight the importance of targeted screening and intervention strategies for high-risk individuals. These findings underscore the need for comprehensive risk assessment and tailored preventive measures to mitigate the risk of DM and its complications in TM patients, emphasizing the importance of ongoing monitoring and management of iron overload and metabolic dysfunction in this population.

Conflict of Interest: The authors declare no conflict of interest.

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Ethical Approval: Given

Authors' Contribution

All the authors contributed equally in accordance with ICMJE guidelines.

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