

ORIGINAL RESEARCH

OPEN ACCESS

Familial Aggregation and Poor Childhood Survival in Thalassemia Despite Early Diagnosis: A Longitudinal Study From Balochistan, Pakistan

Azmatullah Khan¹  | Wardha Shamim Lodhi² | Muhammad Qasim Khan¹ | Syeda Farwa Naqvi¹ | Saima Iram² | Naseebullah Kakar³ | Yousaf Khan⁴  | Sajid Malik¹ 

¹Human Genetics Program, Department of Zoology, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan | ²Sandeman Provincial Hospital Quetta, Quetta, Balochistan, Pakistan | ³Institute of Human Genetics, University of Regensburg & Universitätsklinikum Regensburg, Regensburg, Germany | ⁴Department of Chemistry, COMSATS University Islamabad, Islamabad, Pakistan

Correspondence: Naseebullah Kakar (naseebkhan_kakar2003@yahoo.com) | Yousaf Khan (yousaf7n@gmail.com) | Sajid Malik (malik7@qau.edu.pk)

Received: 25 June 2025 | **Revised:** 20 April 2026 | **Accepted:** 27 April 2026

Keywords: consanguinity | descriptive epidemiology | mortality | survival analyses | transfusion

ABSTRACT

Background and Aims: Thalassemia remains a major public health concern in Pakistan, particularly in under-resourced regions such as Balochistan, where limited healthcare access and high rates of consanguinity may influence disease burden and outcomes. This study aimed to describe the demographic, clinical, familial, and survival characteristics of thalassemia patients across Balochistan.

Methods: A total of 459 transfusion-dependent patients with hemoglobinopathies were recruited from various thalassemia centers across Balochistan during 2015–2022 and followed for 8 years. Detailed clinical and demographic characteristics, familial patterns, and treatment outcomes were documented. Pedigree analyses were performed to identify affected individuals within families. Descriptive statistics, chi-square and Fisher's exact tests, Kaplan–Meier survival analysis, and Cox proportional hazards models were applied.

Results: The multicenter cohort consisted of 60% males and 40% females. Most subjects were from Quetta (46%) and the rural outskirts of the Loralai, Zhob, and Pishin districts (33%). Over half (53%) belonged to low or poor socioeconomic backgrounds. β -thalassemia major was diagnosed in 94% of cases, while β -thalassemia intermedia, β -thalassemia minor, and sickle cell- β -thalassemia each accounted for 2%. Patients aged up to 10 years made up 75% of the sample, with only 4% over 20 years old. Hepatomegaly and splenomegaly were observed in 14% and 13% of patients, respectively. Parental consanguinity was reported in 60% of cases, and 59% had a family history of thalassemia. In total, 1485 individuals across all families were affected, with a higher proportion of males (57%). There were 582 thalassemia-related deaths. The average age at death was 19.42 ± 6.02 years, with males exhibiting a shorter life expectancy compared to females. The survival rate declined as the distance from the thalassemia centers increased by more than 100 km.

Conclusions: These results demonstrate a very high morbidity and mortality burden from thalassemia and highlight the need for a comprehensive intervention program to reduce its preventable impact.

1 | Introduction

Thalassemia is a major hereditary blood disorder and poses a significant global health challenge, particularly in South Asia,

including Pakistan [1, 2]. It is characterized by abnormal hemoglobin production, leading to ineffective erythropoiesis, chronic anemia, increased hemolysis, and disrupted iron regulation [2, 3]. The disorder has two main forms: alpha and beta,

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2026 The Author(s). *Health Science Reports* published by Wiley Periodicals LLC.

resulting from mutations in the alpha globin and beta globin genes, respectively. Patients with severe β -thalassemia require lifelong blood transfusions and iron chelation therapy to prevent iron overload, which can cause hormonal imbalances, organ damage, and growth delays [4]. Among these, β -thalassemia is the most common and severe variant, necessitating regular transfusions and iron chelation therapy to ensure survival [5]. Transfusion-dependent patients remain at high risk of acquiring various chronic infections, which can further exacerbate their symptoms [6, 7].

The global prevalence of β -thalassemia is approximately 40,000 cases annually, predominantly in low- and middle-income countries [8]. Thalassemia is the most common monogenic disorder in China, the Mediterranean region, Indonesia, and other parts of Asia [2]. Worldwide, the life expectancy for patients with β -thalassemia has significantly increased due to effective iron chelation therapy, earlier diagnosis, improved patient compliance, and enhanced transfusion protocols [3, 9].

In Pakistan, the prevalence of the β -thalassemia trait is estimated to range between 5.0% and 7.0%, with approximately 50,000–100,000 people suffering from β -thalassemia major, and around 5000–6000 new cases occurring annually [1, 10]. There are about 9.8 million β -thalassemia carriers, reflecting a 5%–7% prevalence of the gene in the country [11]. Despite improvements in medical treatments, the life expectancy of individuals with thalassemia remains significantly lower than that of the general population, particularly in regions like Balochistan, one of Pakistan's five provinces. As the largest and most underdeveloped province, Balochistan bears a disproportionately high burden of thalassemia cases. Between March 2017 and June 2018, 2000 confirmed β -thalassemia patients were enrolled at two centers—Bolan Medical College Hospital (BMCH) and Civil Hospital Quetta (CHQ) [6]. The remote geography of Balochistan, coupled with widespread poverty and socio-economic difficulties, exacerbates the challenges patients face in accessing essential medical care [1, 12].

To this end, this study aimed to evaluate the burden of thalassemia in Balochistan, Pakistan, by examining socio-demographic factors, familial characteristics, life expectancy, and mortality rates among patients with haemoglobinopathies.

2 | Materials and Methods

2.1 | Ethical Considerations and Study Design

The study was approved in writing by the Ethics Committee of Quaid-i-Azam University Islamabad, Pakistan (June 3, 2015). The committee did not provide only verbal approval, nor did it waive explicit participant consent. All participants gave written informed consent. All procedures were performed in accordance with the Declaration of Helsinki. Children included in the study were already registered and receiving care at the collaborating thalassemia centers, where parents or legal guardians had previously provided consent for clinical care and use of anonymized data. For the present study, the aims and procedures were explained to parents, families, and adult patients in simple local (vernacular) languages, and additional verbal informed consent was obtained from parents or legal guardians

(or from adult patients themselves) before collecting pedigree and clinical information for research purposes.

2.2 | Study Design and Setting

This study was a cross-sectional observational study conducted to assess survival patterns and mortality among patients with thalassemia. The patients included in this study were receiving treatment and blood transfusions at major referral centers across Balochistan, specifically in Quetta, Loralai, Zhob, Pishin, and the Thalassemia Care Centre at Civil Hospital Quetta. The study spanned from 2015 to 2022, enabling a comprehensive assessment of the clinical outcomes, with longitudinal follow-up of affected families over 8 years period for the survival and mortality assessment.

2.3 | Study Population and Inclusion/Exclusion Criteria

The study population included patients of all ages diagnosed with hemoglobinopathies. A total of 459 independent families were included, and one index case from each family was recruited for detailed clinical and demographic assessment. Diagnostic assessments involved complete blood count, hemoglobin electrophoresis, and high-performance liquid chromatography. Inclusion criteria stipulated that patients must have had at least three documented visits to the study centers during the study period. Patients who had not attended these centers in the 2 years prior to the study or who had incomplete medical records were excluded. Furthermore, patients diagnosed with conditions other than hemoglobinopathies were excluded from the analysis.

2.4 | Sample Size and Sampling Technique

The sample size was determined based on feasibility and the rarity of the disorder, with a minimum threshold of > 80 participants considered adequate to ensure meaningful statistical analysis and representation of thalassemia patients in the study setting. A consecutive sampling technique was employed, whereby all eligible thalassemia patients presenting to the study center during the specified study period were included. This approach minimized selection bias and ensured comprehensive inclusion of available cases within the defined timeframe.

Data were collected using a structured questionnaire. The information gathered included demographic variables, clinical details, transfusion history, outcomes (such as last follow-up, morbidity, and mortality), and distances from thalassemia centers. Detailed pedigrees were constructed for each case, including parental consanguinity, number of affected individuals, and thalassemia-related mortalities.

2.5 | Statistical Analyses

Descriptive summaries and cross-tabulation of key variables were generated using MS-Excel. The association of categorical

variables was assessed with Chi-square tests and Fisher's exact test. A *p*-value of < 0.05 was considered statistically significant.

2.6 | Survival Analyses

Survival analysis was performed to estimate life expectancy and survival patterns among thalassemia patients. The time-to-event variable was defined as the duration (in years) from the date of diagnosis to the date of death or last follow-up. Patients were followed from the time of diagnosis until death or the end of the study period (2022), whichever occurred first. Individuals who were alive at the end of follow-up or lost to follow-up were treated as censored observations. Censoring was defined as the patients alive at the end of the study period, and patients lost to follow-up (no contact or record for ≥ 12 months prior to study end). Patients were followed through hospital records, transfusion registries, and, where available, telephonic contact with families. The date of last transfusion, clinic visit, or confirmed contact was considered the last follow-up date. Survival probabilities were estimated using the Kaplan–Meier method, and differences between groups (e.g., gender, thalassemia type, and

geographic distance) were assessed using the log-rank test. Mean and median survival times, along with standard deviations and 95% confidence intervals, were calculated. These analyses were conducted using R Statistical Software (version 3.5.x) and Stata (Release 11, StataCorp, LLC).

3 | Results

The overall study flow, patient selection process, and outcome assessment are presented in the form of a PRISMA diagram (Figure 1).

3.1 | Sample Characteristics

A total of 459 patients (60% males; 40% females) were recruited during the study period (Table 1). The majority of patients were under the age of 10 years (75%), with a mean age of 8.06 ± 6.05 years (standard deviation). Patients aged over 20 years accounted for only 4% of the sample. Most originated from Quetta (46%) and Loralai districts (22%), belonged to the

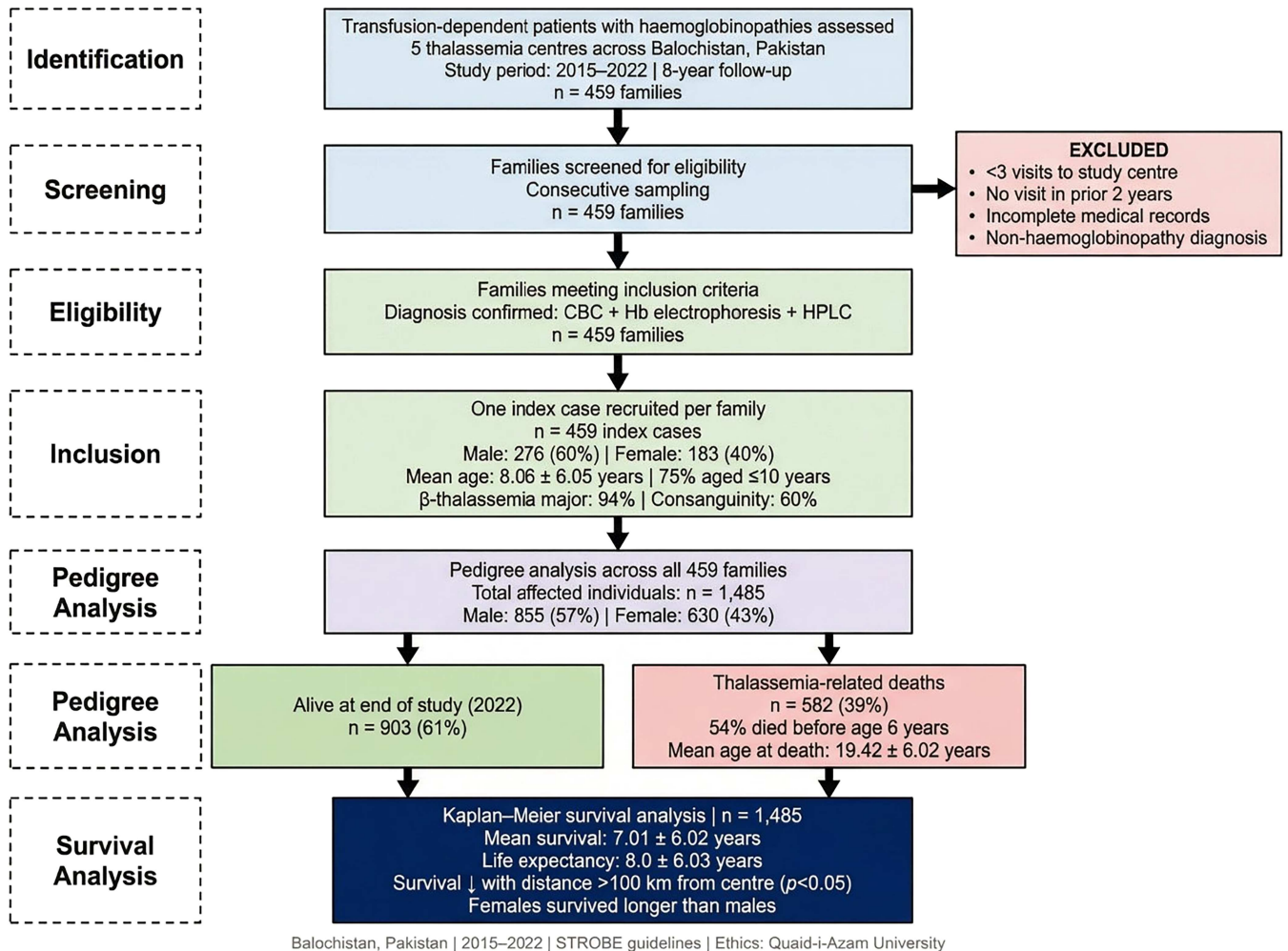


FIGURE 1 | PRISMA flow diagram demonstrating the study design, patient identification, screening, eligibility assessment, inclusion criteria, pedigree analysis, and survival outcomes of transfusion-dependent patients with haemoglobinopathies recruited from five thalassemia centers across Balochistan, Pakistan (2015–2022). A total of 459 families were assessed; 1485 affected individuals were identified through pedigree analysis, of whom 903 (61%) were alive at study end, and 582 (39%) had died. Kaplan–Meier survival analysis was performed on the entire cohort of 1485 individuals. HPLC, high-performance liquid chromatography; CBC, complete blood count; Hb, hemoglobin.

TABLE 1 | Demographic attributes of patients.

Variables [#]	Male, n (%)	Female, n (%)	Total, n (%)
Age categories (years)			
Up to 5	102 (37)	80 (44)	182 (40)
> 5–10	97 (35)	62 (34)	159 (35)
> 10–15	41 (15)	23 (13)	64 (14)
> 15–20	23 (8)	13 (7)	36 (8)
> 20	13 (5)	5 (3)	18 (4)
Sum	276 (60)	183 (40)	459 (100)
District			
Quetta	118 (44)	85 (49)	203 (46)
Loralai	70 (26)	28 (16)	98 (22)
Zhob	18 (7)	8 (5)	26 (6)
Pishin	16 (6)	9 (5)	25 (5)
Ziarat	10 (4)	12 (7)	22 (5)
Others	37 (14)	33 (19)	70 (16)
Caste-system			
Kakar	61 (22)	41 (22)	102 (22)
Syed	16 (6)	10 (5)	26 (6)
Tareen	17 (6)	8 (4)	25 (5)
Barech	10 (4)	9 (5)	19 (4)
Achakzai	10 (4)	8 (4)	18 (4)
Khilji	11 (4)	6 (3)	17 (4)
Others	151 (55)	101 (55)	252 (55)
Socio-economic quartile			
Poor	55 (22)	37 (25)	92 (23)
Low	79 (32)	42 (28)	121 (30)
Low-middle	101 (40)	56 (38)	157 (40)
Mid-high	14 (6)	13 (9)	27 (7)

[#]Differences in the distributions were statistically not significant ($p > 0.05$).

Kakar caste system (22%), and were from the poor and low socio-economic quartile (53%).

3.2 | Hemoglobinopathies and Clinical Complications

β -thalassemia major (BTM) was diagnosed in 94% of patients, followed by β -thalassemia intermedia (2%), β -thalassemia minor (2%), and sickle cell- β -thalassemia (2%) (Table 2). The differences in the distribution of haemoglobinopathies between male and female patients were not statistically significant. Most patients were diagnosed by the age of 6 months (51%), with a further 28% diagnosed between 6 and 12 months. Male patients showed a significantly earlier age at diagnosis compared to females ($p = 0.0397$) (Table 2). Hepatomegaly and splenomegaly were observed in 14% and 13% of patients, respectively. Hepatomegaly and splenomegaly were significantly more frequent among female patients ($p < 0.001$).

TABLE 2 | Hemoglobinopathies, clinical complications, and serological variables in patients.

Variable	Male, n (%)	Female, n (%)	Total, n (%)
Thalassemia (Th.) type			
β -Th. major	259 (94)	172 (94)	431 (94)
β -Th. intermedia	8 (3)	3 (2)	11 (2)
β -Th. minor	5 (2)	5 (3)	10 (2)
Sickle cell- thalassemia	4 (1)	3 (2)	7 (2)
Sum	276 (60)	183 (40)	459 (100)
Age at diagnosis (months)*			
Up to 6	154 (56)	79 (44)	233 (51)
> 6–12	72 (26)	57 (31)	129 (28)
> 12–24	26 (9)	30 (16)	56 (12)
> 24	24 (9)	17 (9)	41 (9)
Hepatomegaly**			
Yes	26 (9)	38 (21)	64 (14)
No	251 (91)	146 (79)	397 (86)
Splenomegaly***			
Yes	26 (9)	36 (20)	62 (13)
No	251 (91)	146 (80)	397 (87)
Blood groups			
B	55 (30)	50 (35)	105 (33)
A	59 (33)	39 (27)	98 (30)
O	50 (28)	44 (31)	94 (29)
AB	17 (9)	9 (6)	26 (8)
Rh factor			
Rh+	162 (90)	135 (95)	297 (92)
Rh–	19 (10)	7 (5)	26 (8)

* $p = 0.0397$; ** $p = 0.0009$; *** $p < 0.0001$.

3.3 | Parental Consanguinity and Familial Characteristics

Sixty percent of patients had parental consanguinity; however, there were no differences between male and female patients in the rate of parental consanguinity (Table 3). The majority of patients belonged to the first parity group (28%), followed by the second parity group (23%).

Pedigree analyses revealed that 59% of patients had a familial occurrence of thalassemia, and in most cases, the disease segregated within one generation (91%), with one sibship affected in the majority of cases (82%).

3.4 | Total Number of Mortalities

Pedigree analysis identified a total of 1485 affected individuals across the 459 families, of whom 582 died during the follow-up

TABLE 3 | Parental consanguinity and familial attributes of patients.

Variable	Male, <i>n</i> (%)	Female, <i>n</i> (%)	Total, <i>n</i> (%)
Parental consanguinity			
Yes	150 (60)	90 (61)	240 (60)
No	99 (40)	58 (39)	157 (40)
Sum	249 (63)	148 (37)	397 (100)
Parity			
1	55 (28)	32 (28)	87 (28)
2	42 (22)	27 (24)	69 (23)
3	43 (22)	20 (18)	63 (21)
4	29 (15)	19 (17)	48 (16)
> 4	24 (12)	15 (13)	39 (13)
Familial/sporadic nature			
Familial	144 (58)	92 (60)	236 (59)
Sporadic	105 (42)	62 (40)	167 (41)
Disease segregating generations (in familial cases)			
1	125 (87%)	79 (86%)	204 (86%)
2	18 (13%)	13 (14%)	31 (13%)
3	1 (1%)	0 (0%)	1 (0%)
Sibship with disease (in familial cases)			
1	98 (68%)	61 (66%)	159 (67%)
2	41 (28%)	20 (22%)	61 (26%)
3	3 (2%)	4 (4%)	6 (3%)
Total affected in all families*			
Index male	442 (79)	113 (33)	555 (61)
Index female	121 (21)	227 (67)	348 (39)
All (surviving)	563 (62)	340 (38)	903 (100)
Deceased individuals*	334 (57)	248 (43)	582 (100)

**p* < 0.0001.

period, while 903 affected individuals were alive at the time of data collection.

Mortalities in male patients were higher (57%) than in females (43%) (Table 4).

Fifty-one percent of patients were diagnosed within the first 6 months and 79% within the first year (Table 4). The survival remained poor, despite early diagnosis. An estimated 54% of deaths occurred before 6 years of age, whereas between six and twelve years, an additional 36% occurred. A very small proportion of patients survived after twelve years, highlighting a reduced survival rate.

Overall, 582 thalassemia-related deaths were recorded among 1485 patients. Of these, BTM contributed to 548 deaths (94%). Generally, male patients experienced higher mortality (334 males, 57%) than females (248 females, 43%). Mortality data stratified by age showed that most deaths occurred before the age of six (297; 54%).

3.5 | Survival Analyses Related to Thalassemia

To evaluate life expectancy, a survival analysis was conducted. The total number of affected individuals (*n* = 1485) across all

families was considered and grouped into year-wise intervals (2015–2022).

Survival analysis using the Kaplan–Meier method demonstrated a mean survival time of 7.01 ± 6.02 years. The estimated life expectancy was 8.0 ± 6.03 years (Figure 2A). Patients who were alive at the end of the study period were censored in the analysis. The majority of deaths occurred before 6 years of age (54%), with an additional 36% occurring between 6 and 12 years. Survival beyond 12 years was uncommon.

Stratified analysis showed that patients with β -thalassemia major had significantly lower survival compared to other types (*p* < 0.05; Figure 2B). Female patients exhibited relatively better survival compared to males (Figure 2C). Additionally, survival probability decreased with increasing distance (> 100 km) from the treatment center (log-rank *p* < 0.05; Figure 2D).

4 | Discussion

This study offers a comprehensive analysis of the demographic and clinical features, familial patterns, and healthcare inequalities faced by transfusion-dependent thalassemia patients in Balochistan, Pakistan. The results highlight significant

TABLE 4 | Age at diagnosis and mortality across thalassemia types.

Variable	β -Th. major	β -Th. Intermedia	β -Th. minor	Sickle cell-th.	Total
Age at diagnosis (months)					
Up to 6	221 (50%)	5 (45%)	5 (50%)	2 (29%)	233 (51%)
> 6–12	122 (28%)	4 (36%)	2 (20%)	1 (14%)	129 (28%)
> 12–24	52 (12%)	1 (9%)	1 (10%)	2 (29%)	56 (12%)
> 24	36 (8%)	1 (9%)	2 (20%)	2 (29%)	41 (9%)
Sum	431 (94)	11 (2)	10 (2)	7 (2%)	459 (100)
Age at mortality (years)*					
Up to 6	282 (51%)	13 (2%)	0	2 (0%)	297 (54%)
> 6–12	184 (34%)	9 (2%)	0	5 (1%)	198 (36%)
> 12	82 (15%)	0	0	5 (1%)	87 (15%)
Sum	548 (94%)	22 (4%)	0	12 (2%)	582 (100%)
All mortalities					
Male	312 (57)	16 (73)		6 (50)	334 (57%)
Female	236 (43)	6 (27)		6 (50)	248 (43%)
Sum	548 (94)	22 (4)		12 (2)	582 (100%)

Abbreviation: Th, Thalassemia.

* $p = 0.0288$.

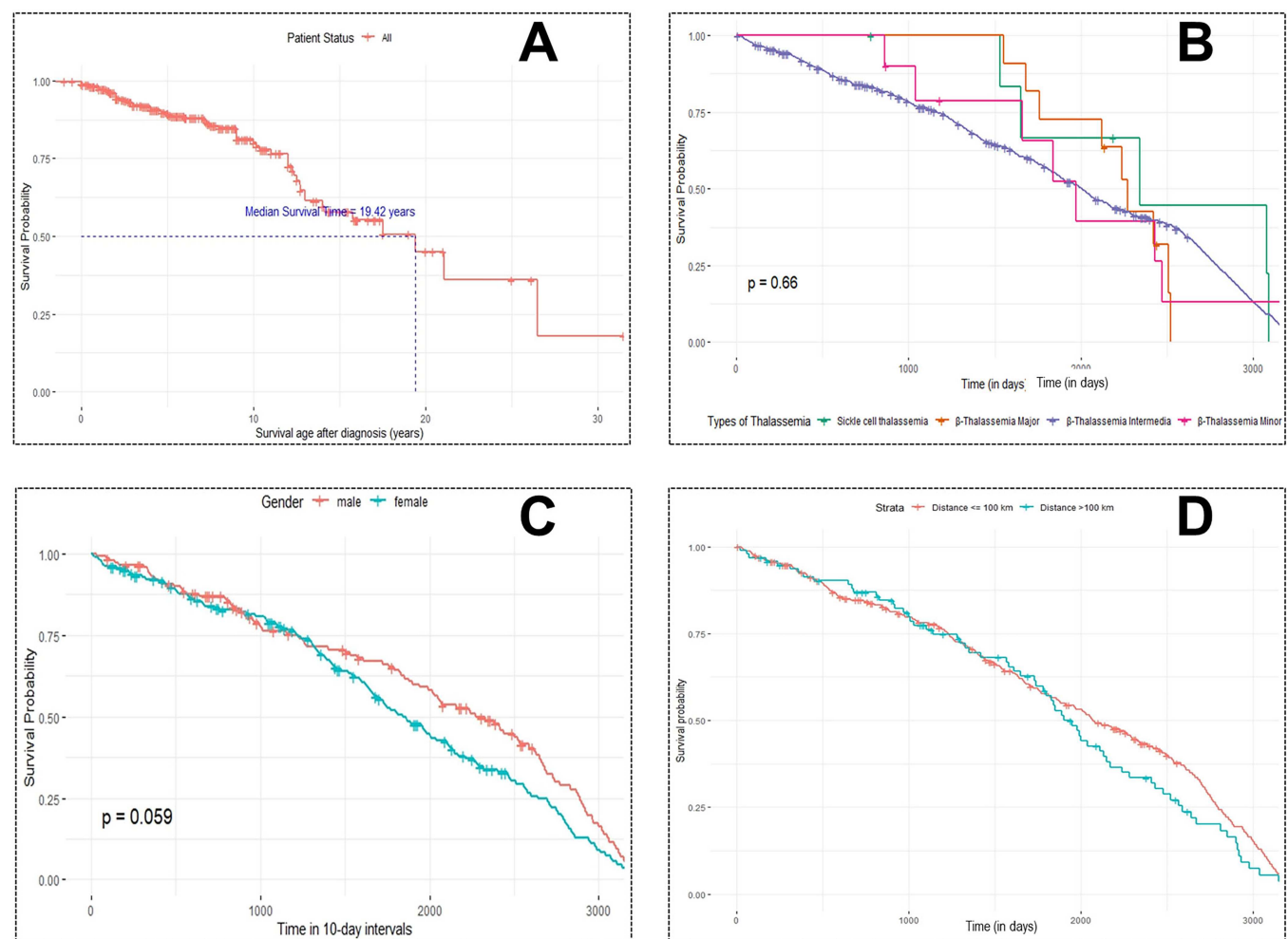


FIGURE 2 | (A) Overall survival curve of 1485 transfusion dependent patients with thalassemia. (B) Survival based on thalassemia types. (C) Survival age with respect to the distance from the thalassemia center. (D) Survival differentials among the male and female patients.

gaps in early diagnosis, access to treatment, and survival rates, providing vital insights for developing better care strategies.

In this study, 75% of the patients were diagnosed by the age of 10 years, with 40% diagnosed before the age of five. This age at diagnosis is significantly later compared to other studies [13]. Delayed diagnosis is linked to high morbidity and mortality in thalassemia [5]. The timing of transfusions also plays a crucial role in patient outcomes. More than half (56%) of the patients in our study received transfusions relatively late due to inadequate and untimely diagnosis, which highlights the systemic barriers to prompt care. These trends differ from findings in Pakistan's Sindh and Punjab provinces [14]. Addressing these treatment gaps is essential to prevent severe anemia and related complications.

This study highlights the critical gap between early diagnosis and effective long-term disease management. Although most patients in this study were identified within the first year of life, more than half died before reaching 6 years of age. This low survival rate reflects limited access to chelation therapy, inadequate transfusion support, a weak health system, and poor socioeconomic conditions. Childhood mortality remains alarmingly high in Balochistan compared to high-income regions, where patients with thalassemia major survive into adulthood.

Furthermore, the clustering of cases in rural districts and among Pashtun-dominant ethnic groups suggests a genetic predisposition likely intensified by high rates of consanguineous marriages, a trend extensively documented in previous studies from South Asia [15]. A prior study reported consanguinity rates of 70% in first-degree relatives among thalassemia patients in Balochistan, Pakistan [16]. The concentration of cases within families, particularly in early parities, emphasizes the importance of community-based genetic counseling and family screening programs. Similar initiatives in Iran have proven successful in reducing the incidence of thalassemia through public education and premarital screening [13].

The mortality rate among thalassemia patients in Balochistan is alarmingly high, with β -thalassemia major (BTM) accounting for over 94% of deaths. Most of these deaths (54%) occur before the age of six. The survival analysis paints a concerning picture, with a mean survival time of 5.8 years, and the majority of deaths occurring before age six. This starkly contrasts with developed countries, where thalassemia patients typically live beyond 40 years with proper care [17]. Such a high rate of early death emphasizes the urgent need for early diagnosis, intervention, and follow-up [18]. The reduced life expectancy in our cohort, with many patients not surviving past childhood, highlights the severe limitations of the healthcare infrastructure in Balochistan. These findings are consistent with previous studies indicating significantly lower life expectancy for thalassemia patients in Pakistan compared to global averages [19, 20].

Additionally, patients living more than 100 km from Quetta had lower survival rates, showing that geographical barriers greatly influence health outcomes. Similar trends have been observed in rural India, where patients from remote regions face higher

mortality rates due to limited access to specialized care [18]. Our study highlights the urgent need for improved healthcare services, including the development of more thalassemia centers and the availability of affordable, accessible treatment options.

Thalassemia patients in Pakistan, especially in Balochistan, have limited access to regular blood transfusions, iron chelation therapy, and other essential medical treatments [21]. The high cost of care, combined with the often-significant distance from thalassemia centers, means many patients do not receive the necessary treatments [22, 23]. In Balochistan, these problems are worsened by widespread poverty, low literacy levels, and reliance on remote medical dispensers, which frequently leads to misdiagnosis and a subsequent reduction in life expectancy.

This study may have several limitations. First, since most of the patients were recruited through multi-center public sector hospitals, there is a high representation of rural and poor families, while a strength for internal analysis, limits the generalizability of findings to urban or higher-income populations. Secondly, hospital-based recruitment may introduce survivorship bias, potentially underestimating disease burden in the most remote communities where patients are lost to follow-up or deceased. Finally, there is potential for recall and social desirability bias, particularly regarding self-reported adherence and financial strain.

5 | Conclusion

Our findings highlight the urgent need for targeted public health interventions to improve survival outcomes for thalassemia patients in Balochistan. Decentralized thalassemia centers, mobile health units, and expanded blood banks are crucial to ensure timely access to care, especially in remote areas. Additionally, prenatal screening and genetic counseling programs should be prioritized to reduce the incidence of thalassemia in future generations.

Author Contributions

Azmatullah Khan: data collection, curation, analyses, drafting. **Wardha Shamim Lodhi, Muhammad Qasim Khan, Syeda Farwa Naqvi, Saima Iram, Naseebullah Kakar, Yousaf Khan:** patient recruitment and clinical examination, drafting, discussion, and final review. **Sajid Malik:** conceived and designed the study, analyses, drafting.

Acknowledgments

The authors greatly appreciate the voluntary participation of subjects/families. We also highly acknowledge the support of the medical staff at Thalassemia Center, Sandman Provincial Hospital and Pakhtunkhwa Blood Bank, Quetta, in data collection. All authors meet the authorship criteria and have read and approved the final manuscript. The corresponding authors, Dr. Sajid Malik and Dr. Yousaf Khan, had full access to all study data and take responsibility for the integrity of the data and the accuracy of the analysis.

Funding

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data utilized in this study is available upon suitable request to the corresponding author.

Transparency Statement

The lead author Yousaf Khan and Sajid Malik affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

References

1. S. Khaliq, "Thalassemia in Pakistan," *Hemoglobin* 46, no. 1 (2022): 12–14, <https://doi.org/10.1080/03630269.2022.2059670>.
2. Y. Tuo, Y. Li, Y. Li, et al., "Global, Regional, and National Burden of Thalassemia, 1990–2021: A Systematic Analysis for the Global Burden of Disease Study 2021," *EclinicalMedicine* 72 (2024): 102619, <https://doi.org/10.1016/j.eclinm.2024>.
3. C. Fragodimitri, V. Schiza, A. Giakoumis, et al., "Successful Chelation in Beta-Thalassemia Major in the 21st Century," *Medicine* 102 (2023): e35455, <https://doi.org/10.1097/MD.00000000000035455>.
4. P. K. Yadav and A. K. Singh, "A Review of Iron Overload in Beta-Thalassemia Major, and a Discussion on Alternative Potent Iron Chelation Targets," *Plasmatology* 16 (2022), <https://doi.org/10.1177/26348535221103560>.
5. M. Hamidreza, S. Ali, and K. Zahra, "Challenges and Advancements in Thalassemia Treatment: A Review," *Blood Disorder Review* 30, no. 1 (2018): 45–53.
6. S. Ahmed, M. Ayub, M. Naeem, et al., "Thalassemia Patients From Baluchistan in Pakistan Are Infected With Multiple Hepatitis B or C Virus Strains," *American Journal of Tropical Medicine and Hygiene* 104, no. 4 (2021): 1569–1576, <https://doi.org/10.4269/ajtmh.20-0740>.
7. G. Din, S. Malik, I. Ali, S. Ahmed, and J. I. Dasti, "Prevalence of Hepatitis C Virus Infection Among Thalassemia Patients: A Perspective From a Multi-Ethnic Population of Pakistan," *Asian Pacific Journal of Tropical Medicine* 7 (2014): S127–S133, [https://doi.org/10.1016/S1995-7645\(14\)60218-2](https://doi.org/10.1016/S1995-7645(14)60218-2).
8. A. T. Taher, K. M. Musallam, and M. D. Cappellini, "B-Thalassemias," *New England Journal of Medicine* 384, no. 8 (2021): 727–743, <https://doi.org/10.1056/NEJMra2021838>.
9. G. L. Forni, B. Ganesin, K. M. Musallam, et al., "Overall and Complication-Free Survival in a Large Cohort of Patients With β -thalassemia Major Followed Over 50 Years," *American Journal of Hematology* 98, no. 3 (2023): 381–387, <https://doi.org/10.1002/ajh.26798>.
10. A. Ahmed, R. Khan, S. Naz, M. Chaudhry, and S. Malik, "Descriptive Epidemiology and Clinical Attributes of Beta-Thalassemia In Upper Sindh Region of Pakistan," *Journal of Rawalpindi Medical College* 29, no. 1 (2025): 113–120, 74 <https://doi.org/10.37939/jrmc.v29i1.27>.
11. N. Saleem, A. Anwar, N. U. A. Shahid, et al., "Perception of Parents of Thalassemic Child to Thalassemia in Pakistan," *Cureus* 13, no. 8 (2021): e17615, <https://doi.org/10.7759/cureus.17615>.
12. A. A. Ghani, A. U. Kakar, Z. Ullah, et al., "Hematological and Biochemical Status of Beta Thalassemia in Pakistani and Afghani Patients of Quetta City, Pakistan," *International Journal of Biosciences* 15, no. 6 (2019): 283–289, <https://doi.org/10.12692/ijb/15.6.283-289>.
13. A. Kattamis, G. L. Forni, Y. Aydinok, and V. Viprakasit, "Changing Patterns in the Epidemiology of B-Thalassemia," *European Journal of Haematology* 105, no. 6 (2020): 692–703, <https://doi.org/10.1111/ejh.13512>.
14. A. Khalid, A. M. Khalil Butt, R. Shahid, and A. Hoor, "Thalassemia: Current Situation in Pakistan," *Lahore Garrison University Journal of Life Sciences* 4, no. 4 (2020): 309–318.
15. S. Malik, A. Bibi, R. Farid, S. Khan, J. Awan, and A. U. Rehman, "Consanguinity in Northwest Pakistan: Evidence of Temporal Decline," *Journal of Biosocial Science* 56, no. 3 (2024): 445–458, <https://doi.org/10.1017/S0021932024000026>.
16. S. O. Akhtar, A. A. Raza, Y. Abdullah, and A. Samadi, "Exploring the Role of Consanguinity in Thalassemia Prevalence in Pakistan: An In-Depth Analysis of Genetic and Cultural Factors Affecting Public Health," *Annals of Medicine & Surgery* 87, no. 7 (2025): 4222–4228, <https://doi.org/10.1097/MS9.0000000000003404>.
17. V. Ladis, G. Chouliaras, V. Berdoukas, et al., "Survival in a Large Cohort of Greek Patients With Transfusion-Dependent Beta Thalassemia and Mortality Ratios Compared to the General Population," *European Journal of Haematology* 86, no. 4 (2011): 332–338, <https://doi.org/10.1111/j.1600-0609.2011.01582.x>.
18. R. Dhanya, A. Sedai, K. Ankita, et al., "Life Expectancy and Risk Factors for Early Death in Patients With Severe Thalassemia Syndromes in South India," *Blood Advances* 4, no. 7 (2020): 1448–1457, <https://doi.org/10.1182/bloodadvances.2019000760>.
19. K. Sumaira, M. Ali, and Z. Waheed, "The Impact of Consanguinity on the Prevalence and Outcomes of Thalassemia in South Asia," *Journal of Genetic Medicine* 28, no. 4 (2022): 354–362.
20. H. A. Zaheer, U. Waheed, Y. E. Abdella, and F. Konings, "Thalassemia in Pakistan: A Forward-Looking Solution to a Serious Health Issue," *International Journal of Clinical Transfusion Medicine* 5, no. 1 (2020): 108–110, https://doi.org/10.4103/GJTM.GJTM_72_19.
21. T. Sumaira, A. Muhammad, S. Hajra, and F. K. Sadia, "Effect of Educational Intervention on Nursing Care in Patients Diagnosed With Thalassemia Major," *Pakistan Journal of Health Science* 3, no. 6 (2022): 357, <https://doi.org/10.54393/pjhs.v3i06.357>.
22. A. Khalid, M. Rashid, and N. Faiza, "Socioeconomic Disparities in the Management of Thalassemia in Pakistan," *International Journal of Public Health* 65, no. 3 (2020): 231–238.
23. L. Muhammad, K. K. Wajid, I. Afridi, S. Ullah, A. Khan, and A. Muhammad, "Awareness Among Educated and Uneducated Parents of Beta-Thalassemia Major Patients about Antenatal Screening," *Cureus* 14, no. 8 (2022): e28561, <https://doi.org/10.7759/cureus.28561>.