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Original Article

# Determinants of Diagnostic and Treatment Delay Among Thalassemia Patients in Sialkot

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**Abstract**

**Objectives:** To find out determinants of diagnostic and treatment delay among patients with thalassemia major in Sialkot.

**Methods:** A cross –sectional analytical study was conducted in Sundas Foundation, Sialkot, from April 2019 to July 2019. A total of 120 patients were selected by convenient sampling and data was collected through semi-structured, pre-tested questionnaire. Important determinants considered were age, gender, literacy of parents, previous knowledge of disease and first health care facility visited. Data was analysed on SPSS version 25.0 and presented in the form of tables and figures. Chi-Square test was applied to study relationships between diagnostic and treatment delays with sociodemographic profile and other factors. P-value < 0.05 considered significant.

**Results:** There was considerable delay of 30-180 days in diagnosis of thalassemia patients (37.5%), 42.7% patients diagnosed in less than 30 days. Treatment delay of 7-21 days in 18% patients seen, 71% started treatment within a week. 30-180 days delay in seeking medical care, was observed in 20.8% patients. Only 24.2%patients visited government health facility for medical care. First facility visited and delay in seeking medical care were significantly associated with diagnostic delay (p value 0.000 and 0.005 respectively). Only 16.7% had previous knowledge about thalassemia and 21.6% parents knew about legislation regarding mandatory pre-marital screening for thalassemia.

**Conclusion:** Among important determinants, first health care facility visited and delay in seeking medical care had significant relationship with diagnostic delay. Better accessibility to healthcare facilities can overcome them.

**Key words:** Diagnostic Delay, Treatment Delay, Thalassemia, Determinants

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## Introduction

Thalassemia is an important public health challenge in both developed and developing countries with an estimated number of 330,000 affected newborns annually.[1,2] About 3% of the world population caries genes for beta thalassemia and it is estimated that every year about 60,000 thalassemia babies are born all over the world[3] and 270 million people are carriers of hemoglobinopathies. Approximately 79% of affected births are in the Asian population. Beta thalassemia is most prevalent in South China, Mediterranean, Arab countries, South East Asia, Africa and Iran with reported ranges from 2-25%.[4] In Pakistan, the prevalence of thalassemia is 6-7% and is present in all ethnic groups. Carrier rate is 5-8% and there are about 9.8 million carriers in total population with around 6000 children diagnosed with beta thalassemia in Pakistan each year[5] where 5% of population has thalassemia minor and disease burden

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estimated to range between 50,000-100,000 patients, which is 5% of patients globally.[6] There were 25,000 children registered with Thalassemia Federation of Pakistan in 2016. However, the actual figure is much higher as 1 lac of the rural population is not registered with Thalassemia Centers.[7]

Only one similar was conducted previously regarding the factors that affect the delay in diagnosis, however, it takes into account all haemoglobinopathies. It was a cross-sectional study conducted in Iran in 2015, where 1002 enrolled patients were taken into account. The diagnostic delay was observed among 64.9% of the patients with a mean of 13.4 months.[8]

This study takes into account two types of delays i.e. diagnostic delay and treatment delay that ultimately contribute to a total delay. Total delay is the time interval from the onset of the illness until the initiation of treatment. Diagnostic delay is defined as the time interval between the onset of symptoms and labeling of the patient as diseased. It may be due to parent's delay in bringing the child to health care or physician's delay in diagnosing the disease, whereas treatment delay is defined as the time interval between disease diagnosis and disease treatment.[8] Delay is important to study in thalassemia as any sort of delay in diagnosis and treatment would result in worsening of prognosis and decreased survival rate. It is also associated with increased complications requiring advanced treatment and increase in morbidity and mortality. Not long ago, children born with thalassemia seldom survived after their first decade of life but nowadays the survival of patients with beta thalassemia major is increasing because of better treatment and supportive measures.[8]

The objective was to study the diagnostic and treatment delay among thalassemia patients in Sialkot and its determinants.

## Methods

It is analytical cross-sectional survey conducted during April to July 2019 at Sundas Foundation, Sialkot, which is a non-government organization providing blood transfusion to registered patients of Thalassemia, Leukaemia and Haemophilia. From amongst the patients suffering from Thalassemia, a sample size of 120 patients taken for this study through convenience sampling, based on feasibility and available resources of the study. A semi-structured questionnaire used for data collection. All male and female patients below or equal to 25 years accompanied by any parent or family member, diagnosed with thalassemia and willing to participate were included. Before data collection, a pre-tested, semi-structured questionnaire devised and translated in local language. A training session for interviewers conducted in effort to conduct the interviews in same tone and duration so that intra-observer bias minimized. A formal permission obtained from the institution and organization. Before starting the interview, patients and parents of patients informed about the objective of study, verbal informed consent taken, and parents assured about the confidentiality of information. The foundation visited during the 6 working days of the week and on average, 8-10 questionnaires were filled daily. Patients' names noted in a separate list and assigned serial numbers, and it made sure that same patients were excluded upon each visit. Upon data entry, only serial numbers used for identification of subjects.

Some of determinants related to delay in thalassemia diagnosis and treatment included: socio-demographic profile including gender, age, type of residence, parental education and income. Patient related determinants such as knowledge, preferences to the type of health facility were included. Similarly, health system related determinants such as accessibility of health facility, counselling of the parents about thalassemia prevention and treatment, number of visits, first contact with health professional and expertise of health care personnel. The frequency of these characteristics calculated by descriptive analysis. Delay was noted on the basis of Healthcare system delay – which included both delay in seeking medical care (the time patients took in seeking healthcare) and diagnostic delay (the time taken by physicians to diagnose the illness), and Treatment delay (the time that was taken in starting the recommended treatment). The collected data was analyzed on SPSS Version 25.0 and presented in the form of tables and figures. The relationship between diagnostic/ treatment delays and age, gender, education of father, education of mother, income of father, type of living, frequency of visit, previous knowledge about thalassemia program and knowledge about legislation was analyzed by cross-tabulation and Chi-Square test was used as a test of significance with $P$ value $< 0.05$ as significant .

All ethical considerations ensured at every step. Anonymity and autonomy of the participants was

taken care along with confidentiality of data. An informed consent was taken from the parent/guardian in case of minors (age less than 15 years).

## Results

The socio-demographic characteristics of the patients and their parents in Sialkot shown in Table 1. Among 120 patients, with mean and median age 9.741 +4.77 SD and 13.5 respectively, 54.2% were male patients, 57.7% lived in rural areas. The fathers of 56.7% patient and mothers of 57.5% patients received formal education. The fathers mean income was 16,166.67 +1000.6 SD and median income of 15,000 showing that 48.3% fathers were having income less than 15000 rupees.

For the determinants of delay, Table-2 shows that out of 120 patients, 75.8% people preferred to visit a private health facility, being accessible was the most common reason of visit for 43.3% people. Out of 120 patients 62 (51.67%) visited fortnightly. Regarding knowledge, 83.33% did not have any previous knowledge about thalassemia, 65.83% mothers did not receive any counselling in the subsequent pregnancies, 76.67% were having no knowledge about the national thalassemia prevention program, and 78.33% were unaware of any legislation regarding thalassemia in Pakistan. Only 42/120 (35%) had history of thalassemia in their family. Table 2 also shows association between different determinants and diagnostic and treatment delay was calculated by applying chi square test ($P < 0.05$ taken as significant). All determinants under study had insignificant association with diagnostic delay except the first health care facility visited

**Table 1:** *Descriptive Statistics of Thalassemia Patients According to their Socio-Demographic Profile (n=120)*

| Characteristics | Frequency | Percentage (%) |
|---|---|---|
| **Age (Years)** | | |
| Less than 5 | 24 | 20.0% |
| 5-9 | 43 | 35.8% |
| 10-15 | 40 | 33.3% |
| Above 15 | 13 | 10.8% |
| **Gender** | | |
| Male | 65 | 54.2% |
| Female | 55 | 45.8% |
| **Type of Living** | | |
| Urban | 51 | 42.5% |
| Rural | 69 | 57.5% |
| **Education of Father** | | |
| Formal education | 68 | 56.7% |
| No formal education | 52 | 43.3% |
| **Income of Father (Pakistani Rupees)** | | |
| <15,000 | 58 | 48.3% |
| 15-20,000 | 25 | 20.8% |
| >20,000 | 37 | 30.8% |
| **Education of Mother** | | |
| Formal education | 69 | 57.5% |
| No formal education | 51 | 42.5% |

**Table 2:** *Descriptive Statistics of Thalassemia Patients According to Determinants of Delay (n=120)*

| Determinants | Frequency | Percentage (%) | P-value Diagnostic Delay[1] Treatment Delay[2] |
|---|---|---|---|
| **First health facility visited for seeking medical care** | | | |
| Private | 91 | 75.83% | 0.000[1*] |
| Govt. hospital | 27 | 22.50% | 0.901[2] |
| Hakeem | 02 | 1.67% | |
| **Reason for consultation with health facility** | | | |
| Accessible | 52 | 43.30% | 0.104[1] |
| Confidence in treatment | 43 | 35.80% | 0.587[2] |
| Referred | 25 | 20.80% | |
| **Frequency of visits to the health facility** | | | |
| Weekly | 38 | 31.67% | 0.709[1] |
| Fortnightly | 62 | 51.67% | 0.647[2] |
| Monthly | 20 | 16.67% | |
| **Previous knowledge about thalassemia** | | | |
| Yes | 20 | 16.67% | 0.674[1] |
| No | 100 | 83.33% | 0.929[2] |
| **Family history of thalassemia** | | | |
| Yes | 42 | 35% | 0.781[1] |
| No | 78 | 65% | 0.742[2] |
| **Counselling for subsequent pregnancy** | | | |
| Yes | 41 | 34.17% | 0.904[1] |
| No | 79 | 65.83% | 0.769[2] |
| **Knowledge about National Thalassemia Prevention Program** | | | |
| Yes | 28 | 23.33% | 0.575[1] |
| No | 92 | 76.67% | 0.714[2] |
| **Knowledge about legislations regarding thalassemia** | | | |
| Yes | 26 | 21.67% | 0.802[1] |
| No | 94 | 78.33% | 0.318[2] |
| **Delay in seeking medical care** | | | |
| Less than 30 days | 89 | 74.2% | 0.005[1*] |
| 30days and above | 25 | 24.8% | 0.215[2] |

*p-value is significant (<0.05)

and delay in seeking medical care diagnostic delay (p value 0.000 and 0.005 respectively).

Taking into account the types of medical delays among Thalassemia patients (TP), Figure 1 shows that 20.8% patients encountered delay in seeking medical care extending from 30-180 days whereas 5% TP delayed seeking care from 181 days to 365 days. The diagnostics delay of 30-180 days was found in 37.5% patients, whereas 14.3% patients had 181-365 days delay and 5.50% had delay in diagnostics for more than 365 days. Only 11% patients delayed their treatment for more than 21 days, 89% patients acquired medical treatment within 3 weeks.

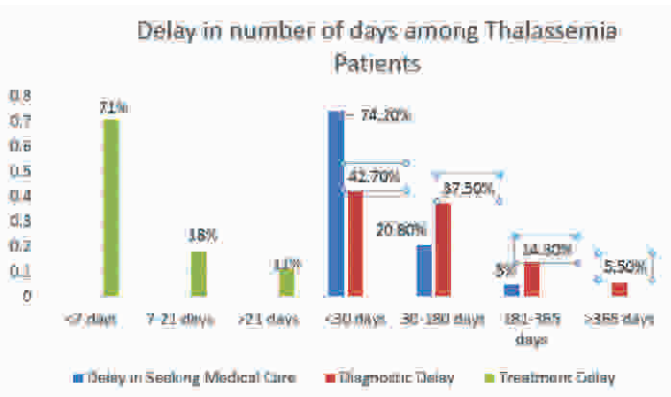


**Fig 1:** *Delay in Number of Days Among Thalassemia Patients (n=120).*

## Discussion

The following study was conducted to study the diagnostic and treatment delays and its determinants among thalassemia patients (TP) in Sialkot. It showed that 51.8% patients had diagnostic delay from 1-12 month and 5.5% patients had delay above one year, 29% had treatment delay more than 7 days and 25.8% delayed seeking medical care. A retrospective study conducted in Iran with the objective of determining diagnostic delay in 1002 thalassemia patients, showed that 64.0% of the patients had diagnostic delay, most of them lying in the category of less than 12 months (44.1%).[8] Wu et al argued that time of diagnosis is crucial for the treatment, complications and survival of the patients. Hassanzadeh et al showed that diagnostic delay in 65.3% of patients was significantly associated with their survival, arguing 25% of deaths could be avoided if delay in diagnosis didn't occur.[9,10] Biswas J and her colleagues argued that treatment delayed is treatment denied with consistent relationship of delayed treatment with poor outcomes,[11] emphasizing the role of treatment delays among patients with chronic ailment. Caocci et al showed that despite the median diagnosis of TP at 8 months, the treatment started at median age of 11 months. Similarly, Mevada showed that delay in diagnosis and start of chelation therapy among TP had negative impact on their quality of life, adding mental health issues and social challenges.[12,13]

In this analytical cross-sectional study having primary data with 120 sample size, two third of the patients were below 15 years with mean age being 9.741years + 4.77; 54.2% being males and most of them from the rural background, and 48.3% belonged to families with income less than 15,000 PKR/month. The sociodemographic profile of this study is comparable with the TP enrolled in study Thailand and Bangladesh[14,15] except that in a study of Bangladesh where 54.3% of their patients were below 5 years with mean age being 6years+3.66[14,15] and 31.4% patients were from the lower income group.[14] Like other studies, in this study, there was male predominance indicating gender disparity similar to other studies.[8,14,15,16] Out of 120 patients, 10.8% patients were above 15 years. The number of <15 years patients is more than above mentioned studies where hardly any patient was < 15 years. Malik et al found that almost 38% of patients were above 15 years arguing that increasing mean age of TP means better survival among thalassemia families in last few decades.[16] Moon et al also showed no such disparity, may be because the socio-cultural set up in modern Korea is different from South Asia.[17] Malik showed that prevention and adherence to treatment affected indirectly by educational level of parent. Out of 120 patients, 68(56.7%) fathers were educated and 57.5% of mothers were educated. The literacy levels in the parents is slightly better than Iranian study but less than Malik's study where 65.2% fathers and 58% mothers had more than primary education.[18]

Studying the association of first visit to health facilities with diagnostic and treatment delay shows that this variable is statistically significant to diagnostic delay with p value 0.000. 75.8% of TP visited private clinic with most common reason was accessibility (43.3%) and confidence in treatment (35.8%). Zeydi et al identified that among others, accessibility is one of the barriers in among TP towards treatment while trust and friendly interaction with health care provi-

ders facilitated adherence it.[18]

Among 120 patients, treatment delay of less than 7 days showed in 71%. No other study on treatment delay among TP is published. The frequency of visit to the health facility was also calculated. 31.7% of the sample visited weekly while 51.7% visited fortnightly. About 16.7% of people visited the health facility on a monthly basis for blood transfusions. TP require at-least one dose of transfusion every fortnightly and up to five doses of iron chelation therapy per week, if needed. Thus, visits to the health facility indirectly indication the regularity and compliance to treatment along with the severity. Similarly, delay in seeking medical care related significantly to delay in diagnosis. Studies show that regular transfusions increase the survival of TP but delay in the onset of complication could lead to discontinuation of the therapy.[19,20,21,22] Caocci et al showed different results where only 22% of the children had regular transfusion support and 78% of the patients had received irregular iron chelation therapy (less than once a week), reducing their health care facility visits for treatment sake.[16]

It is a well-established notion that effectiveness of prevention program especially for thalassemia requires health education, mass screening of the high risk, genetic counseling, prenatal diagnosis and legislation.[16,23] This study showed that 23.3% parents had knowledge about thalassemia prevention program and 83.3% had no previous knowledge, 21.7% people had knowledge about legislation regarding thalassemia. Malik et al and Ishaq et al showed contrasting results where 68.9% and 44.6% of parents had knowledge about thalassemia but Ghafoor et al showed that only 15% of parents were aware of thalassemia previously. High knowledge in the previous two studies could be due to study settings as all these studies conducted in the tertiary hospitals and had large sample sizes. Only 34.1% parents received counselling for subsequent pregnancy in contrast to Malik et al where 64.5% parents received counselling.[16, 23,24] This shows the lack of preventive and management tiers of the programme. Although Pakistan has adopted regulatory approach towards thalassemia for pre-martial screening in 2017,[25] only 21.6% of parents were aware of such efforts. However, Ishaq et al already showed that 87.9% of parents supported such legislation in 2009. It should be kept in mind that in that study,76.5% and 84.3% parents were aware of pre-marital screening and prenatal diagnosis respectively and the study was conducted in a leading Thalassemia Centre of the provincial capital.

The study under discussion is the first study conducted on the topic of diagnostic and treatment delays in patients of thalassemia in Sialkot. It was an attempt to cover all possible determinants of diagnostic delay and treatment delay in thalassemia patients. Face to face interviews were held, and primary data was collected (not secondary which is collected from the previous records of patients).But this study was not without limitations.

Major limitations were small sample size of 120 patients, selected by convenient sampling, using data of patients from single health facility for blood transfusion and resource constraints including time. Inability to cover older patients and other haemoglobinopathies was another limitation. Cohort Study design and subsequent follow up was not feasible. Moreover, Sialkot is just at a distance of two-hour drive from Lahore and people prefer utilizing health facilities of Lahore over Sialkot's. Future multicentre studies on the same subject with a large sample size, can give better picture of the situation in the country. Efforts are required to increase awareness at different strata of public and health care providers so to prevent delay in both diagnosis and treatment.

## Conclusion

In conclusion, the following analytical cross- sectional study is an attempt to determine delays in diagnosis and treatment among thalassemia patients in Sialkot, Pakistan. It was found that 1-12 months were taken by a quarter of thalassemia patients to seek medical care, 51.8% had diagnostic delay from 1-12 months and in 5.5% patients, it extended beyond 1year.The treatment delay was >7days for 29% of the patients. Among important determinants considered for their possible role, no relationship of delay found with socio-demographic profile. Delay in seeking medical care and type of facility visited was related to diagnostic delay. Hurdles like inaccessibility, lack of knowledge about thalassemia and its prevention can only be overcome by vigilant multi-pronged approach that incorporates both patient and health system related delays.

**Conflict of Interest:** None

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## Authors Contribution

**ZT:** Conceptionlization of Project
**PA:** Data Collection
**TF:** Literature Search
**MS:** Statistical Analysis
**KA:** Drafting, Revision
**MN:** Writing of Manuscript