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FREQUENCY OF CONSANGUINEOUS MARRIAGES AMONG PARENTS OF THALASSEMIC PATIENTS IN BAHAWALPUR

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Abstract:

Introduction: *Thalassemia is a blood disorder characterized by defective alpha or beta chain synthesis that occurs as a result of mutated globin genes (i.e. alpha & beta). Out of many reasons behind the etiology of the disease, consanguineous marriage is the leading one. The frequency of cousin marriage in Pakistan comes out to be 74% of all marriages.*

Objective: *The study aims at finding out the frequency of consanguinity among parents of thalassemic children coming to Thalassemia Unit, BVH, BWP so that using local data, attention of health authorities can be drawn towards this major health issue in Bahawalpur.*

Study design: *Descriptive type of cross sectional study.*

Study Setting: *The study was carried out in Thalassemia Unit Bahawal Victoria Hospital, Bahawalpur.*

Duration: *The duration of our study was one month with the study period from April 2019 to May 2019.*

Sample size: *Our sample was of 100 parents of thalassemic children.*

Data Collection: *After taking informed consent from the respondents, data was collected through a preformed questionnaire having two separate sections. Section 1 included the demographic details of the respondents whilst Section 2 was based on a total of 14 close ended questions regarding consanguinity, family values, its traditional compulsion, relation of thalassemia with the blood group and personal opinion about premarital screening.*

Data Analysis: *Data was encoded and entered into SPSS version 20. All the interpreted results have been presented in the figures and tabular format.*

Results: *Our study conducted on 100 parents of thalassemic children showed that 89% of the parents whom thalassemic children were born to, had been married within their families. Out of which, 66% were 1st cousins, 12% were 2nd cousins while 11% were far relatives. The remaining 11% were unrelated. O +ve blood group was 39% (highest) among all the patients.*

More than 50% of consanguineous marriages were the result of family tradition. 67 out of 100 respondents were aware of the treatment of the disease. 81% showed up with the view of terminating the pregnancy if they had known about the disease beforehand. 67% agreed on counter advice on consanguineous marriages while 13% showed no interest to answer due to religious reasons.

Conclusions: *It was concluded that most of the thalassemic children were born to consanguineous parents, cousin marriage being a family tradition. The number of parents with no consanguinity was insignificant.*

Keywords: *Thalassemia, Consanguineous Marriages, Family Marriages, Blood Group, Thalassemia Unit.*

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INTRODUCTION:

The word thalassemia is derived from Greek word "Thalassa" means sea and "Haemia" means blood because of pervasiveness of this blood disorder in territory of Mediterranean sea. [1] It is a Haematological disorder stemming from defect in synthesis of haemoglobin chains alpha and beta Hb chains, resulting in paucity of the respective chain and accumulation of beta and alpha chain respectively. Normally one alpha chain is encoded by two alpha globin genes positioned on chromosome 16 whereas beta chain is encoded by a single beta globin gene located on chromosome 11. Any mutation in these end up in thalassemia which is inherited as single gene autosomal recessive disorder. Depending upon the chain affected, thalassemia is of two categories, alpha thalassemia and beta thalassemia. [2]

Thalassemic patient can present with anaemia, pallor, fatigue, bone pain, skeletal abnormalities, stunted growth, delayed puberty, splenomegaly, shortness of breath, abdominal distention and iron overload. Hb electrophoresis, CBC and DNA testing play crucial role in diagnosis of thalassemia. With advancement in diagnostic field of medicine, in utero diagnosis of this disease is no longer a covet. It is possible by amniocentesis, chorionic villus sampling, fetal cell analysis in maternal blood and fetal blood analysis. [2]

Currently two treatment options of thalassemia are available. One is symptomatic treatment, which includes blood transfusion 2 - 4 times weekly depending upon severity of disease and medical care including iron chelation therapy. The second and eventual treatment is the bone marrow transplantation. [3] As thalassemia is preventable, lifelong transfusion dependant disease, many efforts have been made for its prevention by devising various prevention strategies like mass education, mass screening, premarital screening, prenatal diagnosis and termination of pregnancy. [4]

Although high prevalence of genetic disorders can be attributed to many factors, the most vital one is consanguineous marriages which increase the expression of autosomal recessive disorders, most importantly thalassemia so drastically that annually 200000 homozygous and 240 million heterozygous thalassemic children are born worldwide as the prevalence of consanguineous marriages range from 20 -50 %of all marriages worldwide. [5] Hence, cousin marriages play a crucial role in spread of thalassemia in the entire world particularly in Muslim countries like Saudi Arabia, western part of Tunisia and Lebanon where prevalence of this type of marriages among parents of thalassemic children is found to be relatively high, 88%, 75.3% and 63% respectively. [6-7]

It is worth mentioning that the closer the relationship among parents, the higher are the chances of thalassemia among their children as was observed in Muslim countries like Yemen where positive parent consanguinity among thalassemic children came out to be as high as 74.21%, out of which the percentage of 1st degree relatives was 64.2% and that of 2nd degree was 10.1%. [7]

In Pakistan where cousin marriage is followed as a tradition, the prevalence of this type of marriage is very high. Sixty two percent of all marriages are consanguineous, out of which 50% are 1st cousin marriages. The prevalence of thalassemia is very high in Pakistan especially in KPK and Punjab as annually 5000 children with thalassemia major are born in Pakistan and 6% of its population is heterozygous carrier and is a potential source of spread of thalassemia major[5]. The frequency of consanguineous marriages among parents of thalassemic children in Pakistan has been reported to be 74%[4]. All these statistics indicate consanguinity is the distinguishing feature of thalassemia.

Thalassemia is a portentous disease due to its high prevalence, short and miserable life of patient with high mortality rate and interfamilial marriages. Although many studies have been conducted to reveal consanguinity ratio in thalassemic patients worldwide and in some areas of Pakistan but there is no such study conducted in Southern Punjab especially Bahawalpur which is one of the largest and populated cities of Pakistan with increasing prevalence of thalassemia because of increasing inclination of people toward family marriages due to family tradition and religious issues. The aim of our study was to find out the frequency of consanguineous marriages among parents of thalassemic children so that attention of health authorities can be drawn towards this major health issue of Bahawalpur population using the local data. Furthermore, different population strategies can be made in order to bring a decline in the increase of Thalassemia in this region.

Study Objectives:

The objectives of the study were:-

1. To determine the frequency of consanguineous marriages in the available parents of thalassemic patients attending Thalassemia Unit, Bahawal Victoria Hospital, Bahawalpur.
2. To investigate any correlation between consanguineous marriages and the occurrence of thalassemia.
3. To investigate any relation of thalassemia with ABO and Rh blood group type in thalassemic patients.

Literature Review:

Thalassemia, like its name, is a disorder that has spread so vast throughout the world and has been recognized as the most prevalent monogenic disorder of the humans. Children worldwide are seen drowned in this sea of blood but only blood from outside can save them from swamping. They float on the surface for a short period of time looking to their saviors to come and save them again.

Owing to the gravity of this disorder, a cross-sectional study was conducted on a group of 100 close relatives of the patients of thalassemia from January 2015 to December 2015 to find out the frequency and awareness of thalassemia in families with cousin marriages by the students of Dow University of Health Sciences, Karachi. [3] It was seen that out of 100 consanguineous marriages, 56 people were married within families due to a strong family tradition which could not be gone against. [3] Hence, it depicts the mindset of majority of the population towards sticking to the worn-out traditions at the cost of human lives. The researchers suggested that there should be awareness and promotion of screening before marriages to prevent such lifelong diseases.

In a cross-sectional study performed in Maharashtra, India from August 2016 to October 2016 regarding blood group distribution in β-thalassemia patients, it was seen that the highest prevalence of the disorder was among the patients of O +ve blood group (39%), followed by B+ve blood group (29%), with the third highest prevalence seen in A+ve blood group (17%). AB-ve and O-ve were the least prevalent blood groups among the patients of β-thalassemia. [3]

A retrospective cohort study was performed in Hamadan province of Iran during the years 1997 to 2013 on 133 patients. [8] It was revealed that 45 patients (33.8%) were 1st cousins, 53 (39.9%) were 2nd cousins while 35 (26.3 %) had no blood relation with each other before marriage[8]. In this study, blood group A was the most prevalent among thalassemia patients.

From June 2013 to July 2014, a cross-sectional study was performed on 180 subjects at various hospitals of district Bannu in the KPK province of Pakistan. There came out to be 74% cases of consanguinity, while 26% of the parents were unrelated. The researchers suggested for the development of special centers for thalassemia in order to create awareness for its prevention. [4]

In another study conducted in four thalassemia centers situated in Lahore, Pakistan, it was brought to light that out of 500 total respondents. 306 (61.2%) were married to their first cousins, 91 (18.2%) were married to their second cousins, 34 (6.8%) were married to their distant relatives while 69 (13.8%) were married out of their families. [9] It shows that the marriages among cousins lead to a higher incidence of thalassemia in the offspring.

In a study conducted at various hospitals in Faisalabad city involving 300 patients, that the incidence of β-thalassemia was the highest among the children of those parents who were married to their first cousins i.e. 69.66% and the second highest among second-cousin marriage cases i.e. 5.66% whereas in the unrelated parents, it was 22%. [10] Thus, it signifies the role of consanguinity in giving rise to thalassemia.

METHODOLOGY:

Study Design:

It was a descriptive cross sectional epidemiological study.

Study Place:

The study was conducted in the thalassemia unit of BVH, Bahawalpur.

Duration of Study:

The duration of our study was two months i.e form April 2019 to May 2019.

Study Population:

The study was conducted on the parents of the thalassemic children in the thalassemia unit of BVH, Bahawalpur.

Ethical issue:

Informed consent was taken from all the participants.

Sample Size:

According to the availability of time and resources, it was decided to take a sample of 100 parents including both males and females.

Eligibility Criteria

Inclusion criteria:

Parents of thalassemic children.

Exclusion criteria:

- Guardians other than parents
- Unwilling parents

Data collection:

After taking informed consent from the respondents, data was collected through a preformed questionnaire having two separate sections. Section 1 included the demographic details of the respondents whilst Section 2 was based on a total of 14 close ended questions regarding consanguinity, family values, its traditional compulsion, relation of thalassemia with the blood group and personal opinion about premarital screening.

Data analysis:

The data was analyzed using SPSS software; version 20.The frequency was calculated. Tables and Figures have been made.

RESULTS:

During the one month study period, a total of 100 parents of the thalassemic patients were inquired about their marriages through questionnaires to find out the frequency of consanguineous marriages among them. The respondents were selected by random sampling in the Thalassemia Unit of Bahawal Victoria Hospital (BVH), Bahawalpur.

Out of the 100 respondents, 66 were females being mothers of the patients and 34 were males who were the fathers of the thalassemic patients **(Table 1)**. The highest number of patients coming to the thalassemia unit of BVH, Bahawalpur were from Bahawalpur itself (N=53), followed by 28% patients from Lodhran district; the remaining being from nearby areas **(Figure 2)**. Majority (66%) of the parents had 2-4 children, the extremes ranging from 1 to 8.

As per the main objective of the study, it was ascertained that 89% of the parents to whom thalassemic children were born had been married within their families **(Table 2)**, out of which 66% were first cousins; 12% were second cousins while 11% were far relatives. The remaining 11% were unrelated **(Table 3)**.

The trend of people visiting private doctors for the confirmation of the disease was higher (62%) than those visiting government hospitals (38%) **(Figure 3)**. It was divulged that in this region of study, 100% cases were those of β-thalassemia with no prevalence of α-thalassemia.

O+ve blood group was found to be the highest in frequency (39%) among all the thalassemic patients, B+ve being the second most frequent blood group (23%), followed by A+ve (21%), AB+ve (8%), O-ve (5%), B-ve (3%) and A-ve (1%) with no cases among AB-ve blood group patients **(Figure 1)**.

A small proportion of the parents (31%) also had other children suffering from thalassemia than the one they had brought for the treatment. The deaths due to thalassemia among the families of the patients was reported by 48% of the respondents **(Table 4)**.

Family tradition came out to be the cause of more than half of the consanguineous marriages (56%) whereas 17% had married within their families out of their own wish **(Table 6)**.

A substantial number of the respondents i.e. 67 out of 100 was aware of the treatment of thalassemia. Half of the subjects were found to be visiting the hospital once a month for the treatment of their children (N=50) while 43% visited twice a month. A small proportion had to visit the hospital thrice a month (4%) or on weekly basis (3%) **(Table 5)**. Quite a large proportion of the respondents rated the access to the thalassemia unit as difficult (N=61) **(Figure 4)**.

People were not apprehensive of getting a screening test performed for thalassemia before marriage at all; while on the contrary 81% of them held the view that they would have terminated their pregnancy if they knew about their child's condition beforehand. Purposefully, 67% of the respondents agreed on counter advice to consanguineous marriages while 13% did not consent to answer this question due to emotional and religious reasons.

DISCUSSION:

Genetic heritable disorders have always been the main focus of interest for geneticists and physicians. Biologists and scientists are working day by day to find out the main reasons behind these genetic heritable disorders. Mutation in genes is the known cause of these disorders but living with these mutations and passing these mutations to the next generation is the problem of generations to be noted and solved. Geneticists are working to find out the cause of mutation in genes and physicians are working to stop progression of these already mutated genes. Genes once mutated travel in families with consanguinity among them. The present study was actually to find out the frequency of consanguinity among the parents of thalassemic children.

Our study revealed that 89% of the parents were married within their family and were found to have thalassemia in their children. While 11% of the parents were those who were not married in their family and had no consanguinity among them before marriage but still their children were suffering from thalassemia. This is absolutely an indication that consanguinity plays an important role in the progression of genetic disorders i.e thalassemia in our case. A similar study was conducted in Pediatric Unit 1, DOW University Karachi, Pakistan to find out awareness of thalassemia among parents of thalassemic children revealing that consanguinity was positive in 82.5% of the parents with extended family history of thalassemia. [11] Another descriptive study was conducted in the Thalassemia Centre, Sir Ganga Ram Hospital, Lahore, Pakistan showing that 81.7% of the parents with thalassemia in their family had consanguineous marriages. Similar results were found in another cross sectional study conducted in various hospitals of District Bannu in the North Western Khyber Pakhtunkhwa (KPK), Pakistan showing that 73.8% parents of Beta thalassemic patients were cousins while 26.2% parents were Non consanguineous. [4] Our results were more positive for consanguinity among parents of thalassemic children. This may be due to the fact that most of the respondents were coming from rural areas or areas which are underprivileged. Most of the people had tradition of family marriages (50% in our case). Most of the people living in rural areas of Bahawalpur don't marry outside their *Biradari*. A tradition of family marriages is still there even after genetic problems in the families.

According to the study that we conducted the Parents with 1st cousin relations, 2nd cousin relations, far relations were found to be 66%, 12% and 11% respectively. A descriptive study conducted in 4 different Thalassemia Centres of Lahore, Pakistan where the parents of thalassemic children were interviewed, it was found that 61.2%, 18.2% and 6.8% couples were married with their 1st cousins, 2nd cousins and distant relatives respectively. [9] Another similar cross sectional study conducted in Faisalabad, Pakistan on parents of thalassemic patients showed similar results as, 69.66% of the parents were 1st cousins, 5.66% were 2nd cousins, 1% were distant relatives and 1.66% were from same *Biradri*. [10]
We have observed that most of the thalassemic patients, coming to thalassemia unit of BVH, had blood group O+ (39%) followed by B+ (23%) and A+ (21%) respectively. Rest of the patients with other blood groups were not significant enough. These are in collaboration with comparable outcomes from the research conducted on the sample group O+ 39%, B+ 29% and A+ 17% by Sinha PA et al. at St. George's Hospital, Mumbai, Maharasthra, and India. [2]

Our research proposed that 48% of the families of patients who came to the Thalassemia Unit BVH had frequent deaths from thalassemia, 51% did not have a similar family record whereas 1% had no knowledge of family deaths. A cross-sectional study on thalassemia patients in Karachi, Pakistan revealed that thalassemic patients had 28% family deaths due to thalassemia. [3]

In our research, 50% of patients of thalassemia visited blood transfusion Centre once a month, and 43%, 4% and 3% visited it twice a month, thrice a month and once a week respectively. This implies that majority of the patients visited hospital once for blood transfusion. In partnership with virtually comparable studies by Uddin et al. in Karachi, Pakistan, 51% of the thalassemic patients visited hospital every month, 36% visited hospital twice a month, 12% visited three times in a month and only 1% came weekly for the blood transfusion. [3]

Our study reported that 81% of parents did not want to continue pregnancy if their child would have been known to be thalassemic during pregnancy. While 19% were those who would accept the reality and would not undergo abortion even when they knew the situation. In other research by Uddin et al, it was observed that in comparable cases 66% would abort and 23% would still remain pregnant during this condition while 11% of their respondents did not reply at all. [3]

In the current research, 67% of participants did not advise others to marry within their families, while 20% were those with thalassemic children who would still advise others to marry within their families. In 2013,

Uddin et al. in their study found that 51% of their study population would not advise others to marry in their family. While 28% of their study population having thalassemic children recommended others to marry in their family. [3] This small percentage of parents advising others to marry in their families may be due to the fact that they may not know anything about genetically modified diseases and screening tests. Before marriage, screening for the avoidance of genetically modified genetic illnesses is an excellent option even if there is any tradition of family marriages.

This study provides limited data as there is a lack of specifications regarding age group, socio-economic status, life style etc. The limitations of this research are the type of study, small sample size and incomplete demographic history including lifestyle, socioeconomic status etc. For definite results and assessment of causal factors and determinants; large sample size, proper matching and probability sampling are dire needs. Because mainly the data is obtained from thalassemia Centre BVH and the people visiting it are not the representative of the whole population of Bahawalpur. Critically thinking, application of inferences from a probably diseased population on the general population is not justifiable. Further studies on the subject can be improved by keeping these factors in mind.

This study may also serve as a reference and a guide for students and teachers undertaking similar studies. Parents can use this information and take appropriate measures to prevent the chances of thalassemia in their children. This research can also be implemented in practical life and can be helpful in devising strategies to overcome this problem.

CONCLUSION:

The study concluded that most of the thalassemic children were born to the parents with consanguineous marriages, which result in increased risk of genetic mutations. Awareness of the parents was inadequate but this can be improved by educating the general public, parents and families of the patients in this regard.

On analysis, O+ve blood group was found to be the most commonly affected blood-type by the disease. It may be concluded that there are some factors in this blood group that are favoring mutation or promoting thalassemia.

Managing a thalassemia patient is a lengthy process and is tedious for the parents to comply with the treatment plan; blood transfusions being the major ones.

Recommendations:

In view of the demonstrated frequency of consanguineous marriages in thalassemia unit in our study, it is suggested that policy makers urgently develop initiatives to address the following:

- An important step in the prevention of thalassemia is premarital screening. Marrying couples whether consanguineous or not should be made to undergo thalassemia screening tests before marriage. It should be a mandatory criteria for marrying.
- High risk couples i.e. those with a positive family history of thalassemia or already having a thalassemic child should be counselled about chorionic villus sampling.
- People should be educated about the high risks of hereditary disorders specially thalassemia in consanguineous marriages through mass awareness program.
- The only thing we are supposed to do as a part of this society and citizen of the world is to promote screening before marriage whether it is between the cousins or not, to prevent our next generations from this debilitating disease.
- Couples should be counselled about thalassemia screening when they visit the health care providers before conception.
- The termination of pregnancy is a social stigma in our society. People should be counselled on the benefits of terminating a fetus if found positive for thalassemia.
- There is an urgent need to understand the density of the problem, educate the general public and create awareness amongst thalassemic families in order to reduce the burden of disease in Pakistan, particularly in Bahawalpur.
- Special centres should be made for easy provision of information about thalassemia.

Table 1 Gender Wise Distribution of the Respondents

Gender	Frequency	Percentage (%)
Female	66	66
Male	34	34
Total	100	100

Table 2 Frequency of Family Marriages among Parents of the Thalassemic Patients

Family Marriages	Frequency	Percentage (%)
Yes	89	89
No	11	11
Total	100	100

Table 3 Relation of the Respondents with the Spouse before Marriage

Relationship	Frequency	Percentage (%)
1st cousins	66	66
2nd cousins	12	12
Far relatives	11	11
Not applicable	11	11
Total	100	100

Table 4 Frequency of Deaths in the Family due to Thalassemia

Deaths due to Thalassemia	Frequency	Percentage (%)
No	51	51
Yes	48	48
Don't Know	1	1
Total	100	100

Table 5 Frequency of Hospital Visits for Transfusion

Hospitalization	Frequency	Percentage (%)
Once	50	50
Twice	43	43
Thrice	4	4
Weekly	3	3
Total	100	100

Table 6 Reasons of Family Marriages among Respondents

Reasons	Frequency	Percent
Family tradition	50	50
Not necessary	34	34
Own wish	15	15
Religious reasons	1	1
Total	100	100

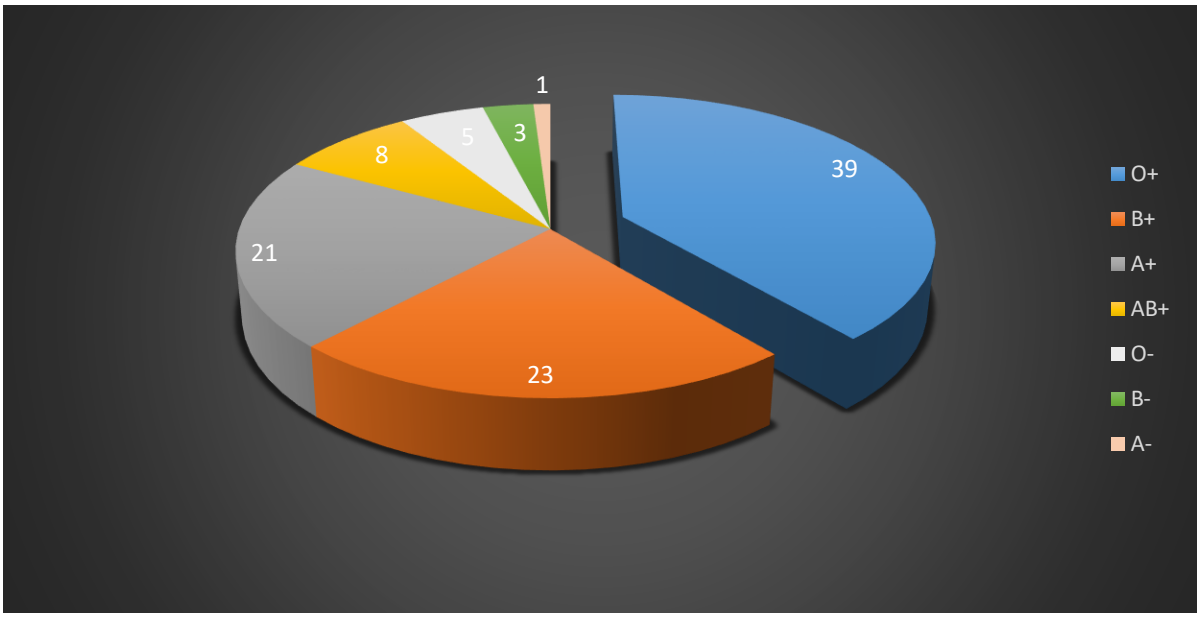

Figure 1 Frequency of ABO & Rh Blood Groups among Thalassemic Patients

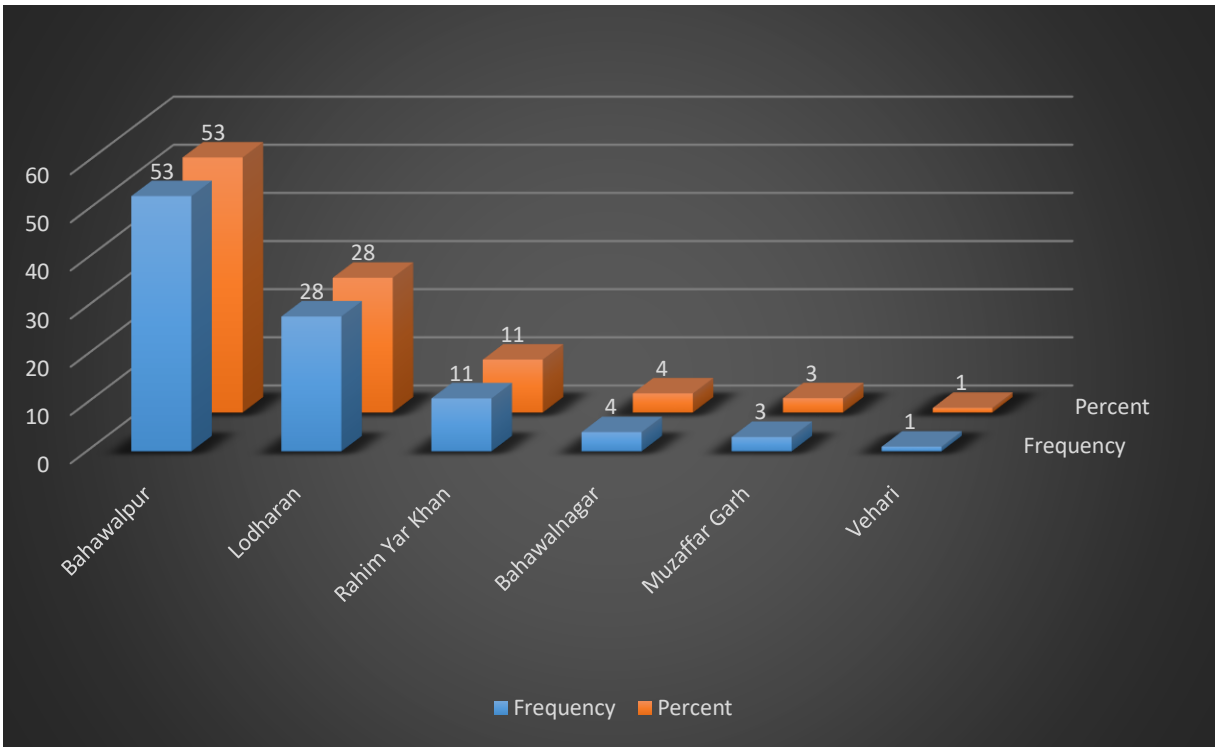

Figure 2 District Wise Distribution of the Respondents

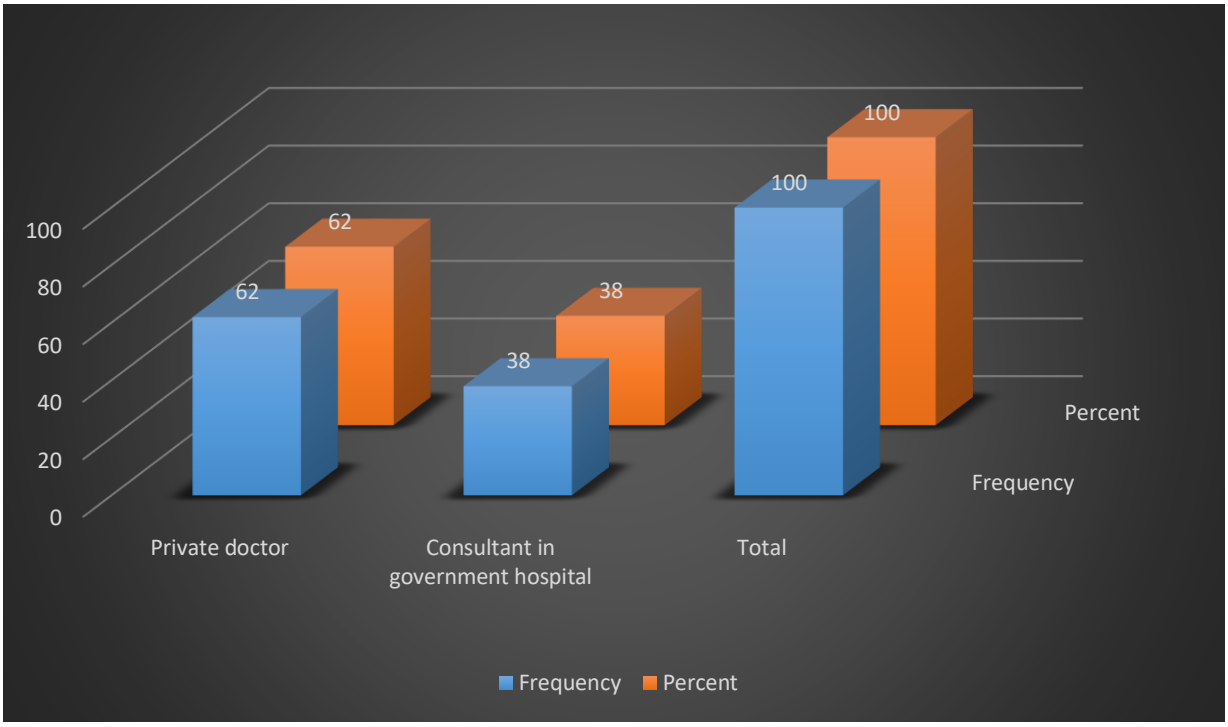

Figure 3 Confirmation of Thalassemia among The Patients

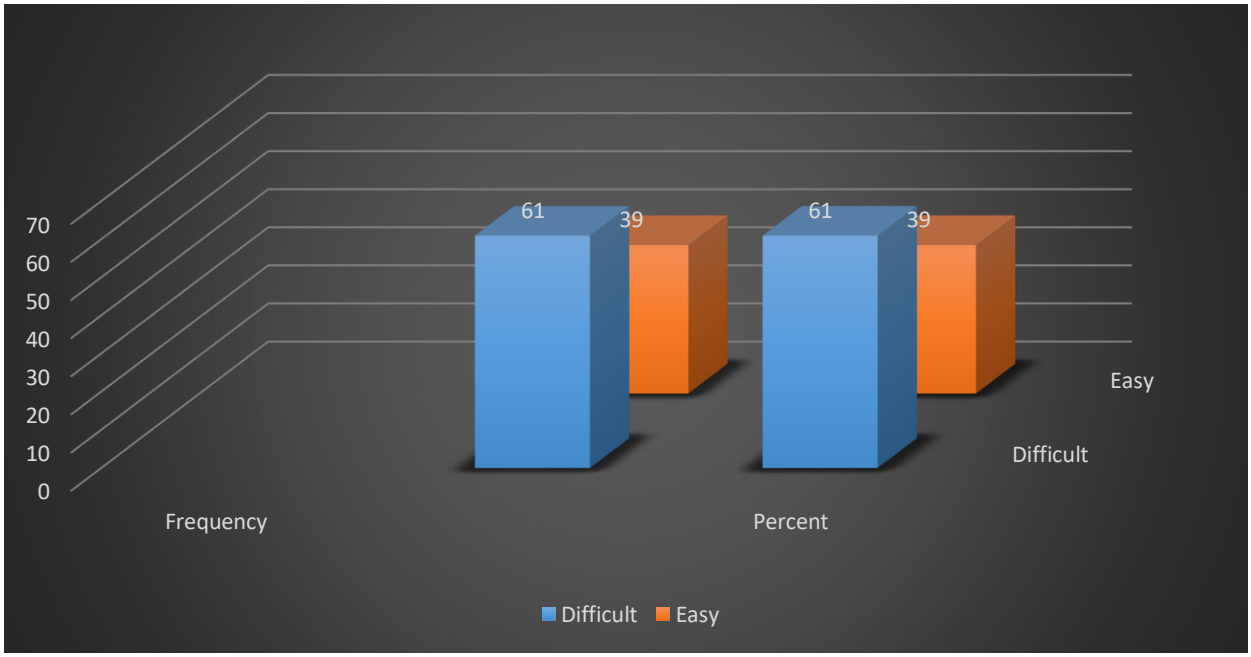

Figure 4 Quality of Access to the Treatment Center

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List of Abbreviations

Serial No.	Abbreviation	Stands for
1	QMC	QUAID-E-AZAM MEDICAL COLLEGE
2	BVH	BAHAWAL VICTORIA HOSPITAL
3	BWP	BAHAWALPUR
4	CBC	COMPLETE BLOOD COUNT
5	KPK	KHYBER PAKHTUNKHWA

ANEXURES

FREQUENCY OF CONSANGUINEOUS MARRIAGES AMONG PARENTS OF THALASSEMIC PATIENTS COMING TO THALASSEMIA UNIT BVH BAHAWALPUR

Name: _____ Age: _____
Sex: ✖ Male ✖ Female District: _____
Occupation: _____ Number of children: _____
Relation with patient: _____

1. Are you married within your family? ✖ **Yes** ✖ **No**
2. If yes, what was your relation with your spouse before marriage?
✖ **1st cousins** ✖ **2nd cousins** ✖ **Far relatives** ✖ **Not applicable**
3. Who confirmed thalassemia in your child?
✖ **Private Doctor** ✖ **Consultant in government hospital** ✖ **Medical camp**
4. Which type of thalassemia is patient suffering from?
✖ **Alpha thalassemia** ✖ **Beta thalassemia**
5. What is the blood group of the patient?
✖ **A+** ✖ **A-** ✖ **B+** ✖ **B-**
✖ **O+** ✖ **O-** ✖ **AB+** ✖ **AB-**
6. Is your any other child suffering from thalassemia? If yes, how many?
✖ **No** ✖ **1** ✖ **2** ✖ **3**
7. Did anyone in your family die from thalassemia?
✖ **Yes** ✖ **No** ✖ **Don't know**
8. Is cousin marriage necessary/prevalent in your family? If yes, why?
✖ **Not necessary** ✖ **Yes-religious reasons** ✖ **Yes-family tradition** ✖ **Own wish**
9. Are you aware of the treatment of thalassemia?
✖ **Yes** ✖ **No**
10. How many times in a month do you take your child to the hospital for transfusion?
✖ **Once** ✖ **Twice** ✖ **Thrice** ✖ **Weekly**
11. How do you rate access to the treatment center?
✖ **Easy** ✖ **Difficult**
12. Was screening test performed on both of you before marriage?
✖ **Yes** ✖ **No** ✖ **On one parent**
13. If during pregnancy you come to know that your child is suffering from thalassemia, will you continue with the pregnancy? ✖ **Yes** ✖ **No**
14. Will you advice others to get married in family?
✖ **Yes** ✖ **No**