PREVALENCE OF THALASSEMIA ASSOCIATED WITH VARIOUS DEMOGRAPHIC FACTORS AMONG THE LOCAL POPULATION OF DISTRICT BAJAUR, PAKISTAN

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ABSTRACT

Thalassemia is one of the hereditary disorders related to the reduction in rate of synthesis of the globin chains of hemoglobin. Depending upon the genetic defects or deletion the body doesn't produce enough of the proteins; the red blood cells become defective and cannot carry sufficient oxygen. The present research study was conducted to find out the prevalence and distribution of thalassemia in human population of District Bajaur. This study was also aimed to determine, Tehsil-wise and sex-wise distribution of thalassemia, and to raise the level of public awareness about this genetic disorder.

The questionnaires were distributed and collected among 1200 individuals on monthly bases from December, 2020 to September, 2021. The data were collected from different areas of Bajaur and finally analyzed by descriptive statistics and parentage method by using Microsoft excel.

In current study a total of 1200 individuals were surveyed for the said genetic disorder of Thalassemia, out of which 80 individuals were found infected with a prevalence rate of 6.67. Similarly, highest prevalence of 7.20 (49x100/680) was reported in Childs than adults 5.96 (31x100/520). Likewise, highest prevalence of 8.78 (29x100/330) was recorded in female than male 5.71(20x100/350). Similarly, in tehsils wise distribution of Thalassemia, highest prevalence of 13.19 (31x100/235) was recorded in tehsil Salarzo while lowest prevalence of 1.87 (3x100/160) was reported in tehsil Nawagai.

T1. INTRODUCTION

Thalassemia is a complex of various hereditary disorders of hemoglobin combination featuring insufficient production of at least one of the globin chains pouring imbalanced globin-chain production; damaged hemoglobin eventually causes anemia (Cappellini *et al*., 2014). In 1932, Whipple and Bradford explained the pathology of the disease for the first time, and as most of the patients were found to be native to the Mediterranean range, they termed the condition as "thalassemia" (Rachmilewitz and Giardina, 2011). The thalassemia is a group of autosomal recessive disorders caused by reduction or absent production of one or more of the globin chains that make up the hemoglobin (Hb) tetramers. According to the type of globin chain involved, two main types, i.e., the a- and b-thalassemias can be distinguished. In addition, complex thalassemias resulting from defective production of two to four different goblin chains (db-, gdb-, and 1 gdb-thalassemia) are recognized *(*Weatherall and Clegg 2001*)*. Abnormal hemoglobin occurs due to mutated and deleted segments of α- or β-globin genes. Thalassemia is caused due to defects in the globin genes, which results in Hb synthesis disorders i.e., under or overproduction of globin chains. Thalassemias are arranged into alpha (α) or beta (β) types. The β thalassemia is found throughout the world while α thalassemia is more prevalent in the Mediterranean region, (Lippi and Mattiuzzi, 2020, De Sanctis *et al*., 2017) and China (Qin and Wu, 2009; Muncie Junior and Campbell, 2009).

1.1.Alpha Thalassemia

There are 2 copies of the alpha-globins' gene in the human genome both located on chromosome 16, therefore in a normal diploid cell, 4 copies of the gene are available, to produce the protein. Alpha-thalassemia is caused by an underproduction of α-globin proteins due to mutation or deletion of one of the four α globin genes (Leung and Lao, 2012).

1.1.1 Alpha thalassemia minor

It is an asymptomatic carrier condition that occurs due to the deletion of the one α- globin gene. This condition usually causes no symptoms or signs of anemia and does not need treatment due to negligible alpha protein deficiency; therefore, the hemoglobin appears to be normal (Leung and Lao, 2012) .it is also called silent carrier (Camacho *et al*., 1999).

1.1.2. Alpha thalassemia trait

The trait is also known as mild alpha-thalassemia. The patients are deficient in two alpha-globin genes. The affected individuals have RBCs smaller than usual and are mildly anemic but do not show any symptoms and may only be diagnosed by routine tests (Leung and Lao, 2012).

1.1.3. Alpha thalassemia intermedia

Also, it is known as hemoglobin H disease. Individuals lacking three alpha globin genes become severely anemic and mostly cannot survive without blood transfusion. As hemolysis occurs in this type of anemia the tendency to develop respiratory infections, gallstones, and leg ulcers increases. Bone deformities are not usually found in hemoglobin H disease (Lee *et al*., 2010

1.1.4. Alpha thalassemia major

"Hydrops fetalis" or alpha thalassemia major is a condition in which no alpha genes are found in the patients' genome, resulting in four gamma-globin chains produced by the fetus that produces malfunctioning hemoglobin known as hemoglobin Bart's. Most affected individuals having Hemoglobin Bart's cannot survive or otherwise die in just a few hours after birth (Lee *et al*., 2010).

1.2.1. Beta Thalassemia

The β thalassemia is found throughout the world while α thalassemia is more prevalent in the Mediterranean region, (Lippi and Mattiuzzi, 2020, De Sanctis *et al*., 2017). β-thalassemia occurs due to mutations that influence all stages of beta-globin protein synthesis including transcription, translation, and beta-globin production stability.

1.2.2. Beta thalassemia minor

Also known as thalassemia trait due to one of malfunctioning beta-globin genes, but this generally causes no significant problem in the proper functioning of hemoglobin protein (Hay and Weatherall, 2017). The Affected individuals have a 1:1 chance to pass the thalassemia minor trait to their child (Memon, *et al*., 2017).

1.2.3. Beta thalassemia intermedia

A condition where the absence of beta polypeptide in the hemoglobin is sufficient to bring about more extreme anemia and serious medical issues, including shortness of breath, bone disfigurements, mild jaundice, and an enlarged spleen. The condition is characterized by having two abnormal genes in affected individuals while still producing some beta-globin. Depending on the level and functional competence of beta-Globin is a broad range in the clinical severity of this disease (Hay and Weatherall, 2017).

1.2.4. Beta thalassemia major

It is also known as "Cooley's anemia" and is the most severe form of beta-thalassemia with absent beta-globin synthesis thus preventing the production of significant amounts of Hb.The severe anemia results in hypoxia and the resulting EPO causes hyperplasia in the bone marrow and will lead to extramedullary hematopoiesis (Cunningham, 2010).

1. METHOD AND MATERIAL

1.1. STUDY AREA:

This study was conducted from December, 2020 to September, 2021. This is a descriptive cross sectional study on distribution and prevalence of Thalassemia among the people of District Bajaur. The study was carried out in Bajaur region which lies between 34^{o} – 30^{o} and 34^{o} – 58^{o} north latitudes and 71^{o} – 11^{o} and 71^{o} – 58^{o} east longitude.

The Area of District Bajaur is about 1,290 Sq KM and its Population is about 1,093,684 according to 2017 census. It has Seven Tehsils and the Number of Village Councils are120, while Number of Neighborhood Councils are 7. District Bajaur is the newly merged District of Khyber Pukhtankhwa. Previously known Federally Administrated Tribal Areas (FATA).

MAP OF BAJAUR

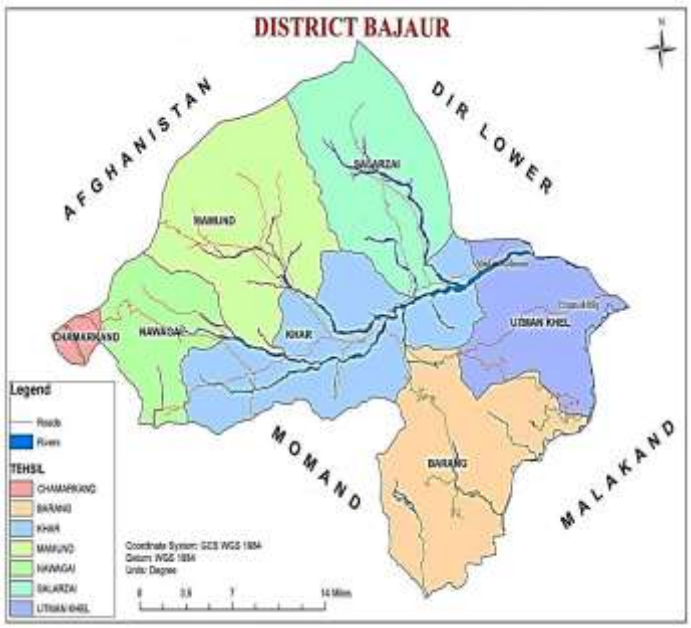

Fig.2.1.Map of District Bajaur (Arif,M *et al*., 2022)

1.1. Data Collection criteria

Random sampling was made from local population of district Bajaur and data was collected through a questionnaire.

1.2. Ethical Approval and Informed Consent

Patients who were agreed to participate in the study were explained the aims and objectives lying behind the study and their informed consent were formally obtained. Patients who were underage, informed consent was obtained from their parents/guardians.

1.3. The Questionnaire and data analysis

A close-ended questionnaire was used to collect data from the study participants. The questionnaire was designed according to the existed literature and various demographic information related questions were included in it. The data was summarized and analyzed by using various descriptive statistics, statistix9 software and Microsoft Excel.

3. RESULTS

Thalassemia is disease affecting millions of people worldwide. In current study data was collected from 1200 persons through questionnaire, out of which, 80 cases were reported from December 2020 to September 2021. The disease was more prevalent in female than male and was especially prominent in children and teenager (6-10) and lower in adults.

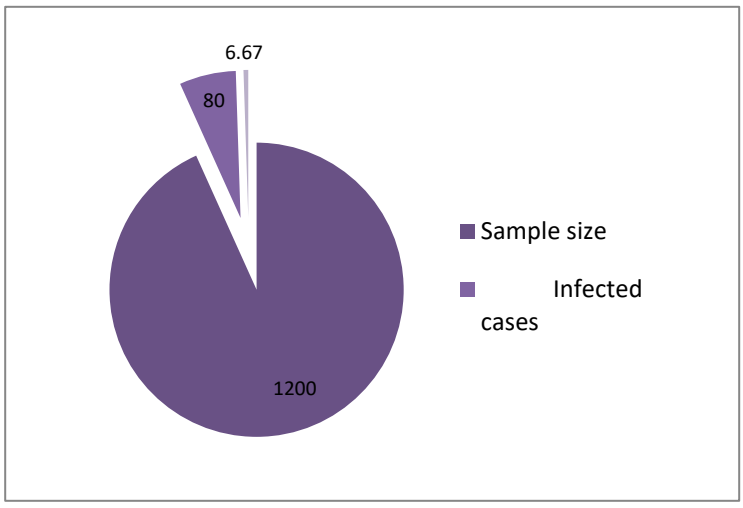

Fig. 3.1 Overall Prevalence of Thalassemia in District Bajaur

The above figure 3.1 shows that overall prevalence of Thalassemia in District Bajaur is 6.67 according to the prevalence formula (80X100/1200).

3.1. Prevalence of thalassemia among different age groups

Figure 3.2 shows prevalence of thalassemia in children and adults of District Bajaur. Highest prevalence is 7.20 (49x100/680) in children while lowest prevalence is 5.96 (31X100/520) were recorded in adults.

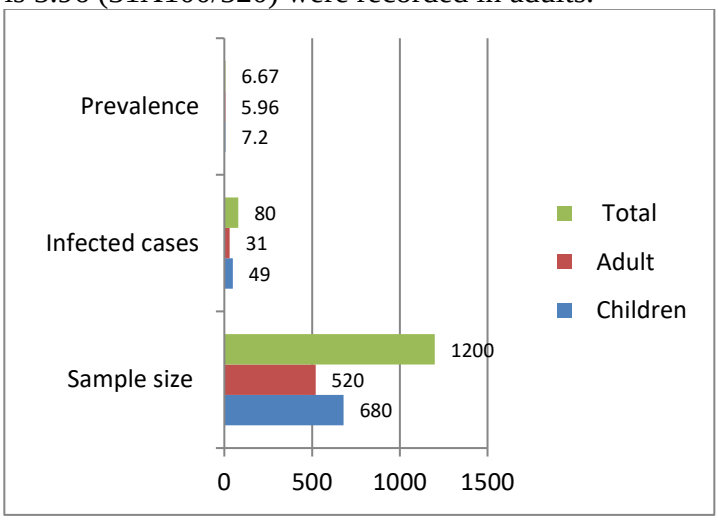

Fig. 3.2: Prevalence of Thalassemia in Adult and Child of District Bajaur

3.2. Gender wise prevalence of thalassemia in local population of District Bajaur

The data was divided into two sex groups. Figure 3.3 shows sex wise prevalence of thalassemia among local population of District Bajaur. The prevalence of thalassemia was higher in females, which was 7.80 (44x100/580), while prevalence of thalassemia was lower in male, which was 5.80 (36x100/620).

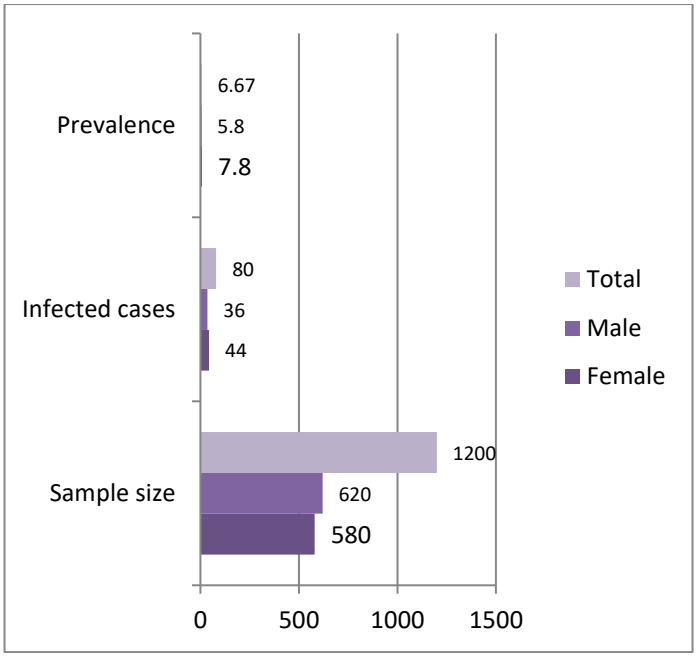

Fig. 3.3: Gender-wise prevalence of thalassemia in locals of District Bajaur

3.3. Gender-wise prevalence of thalassemia in children of District Bajaur

Figure 3.4 shows sex wise prevalence of Thalassemia in children of District Bajaur. The prevalence was 8.78 (29x100/330) in female children while lower prevalence was recorded in male children, which were 5.71 (20x100/350) as shown in figures below.

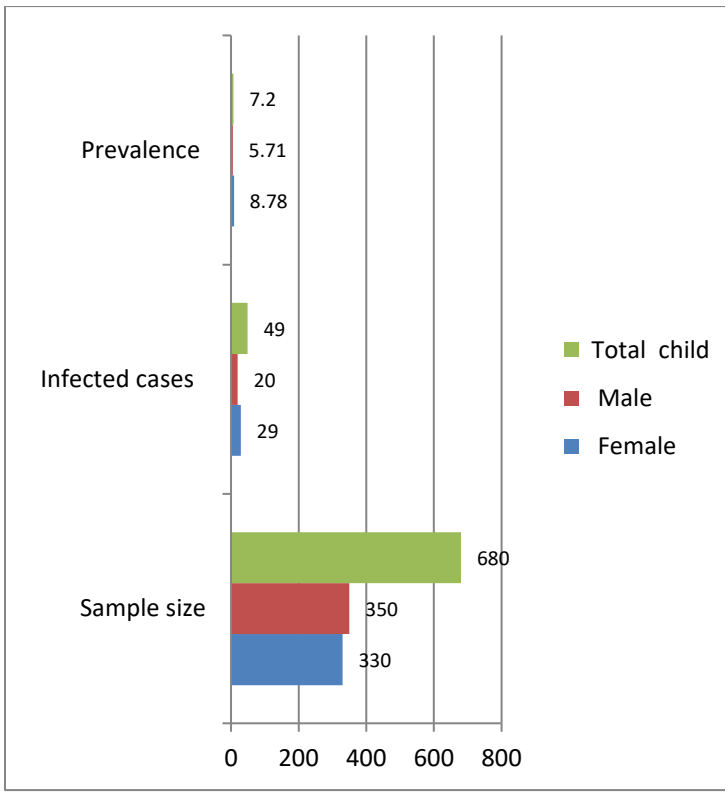

Fig. 3.4: Sex-wise prevalence of Thalassemia in children of District Bajaur

3.4. Gender-wise prevalence of thalassemia in adults of District Bajaur

Figure 3.5 shows sex wise prevalence of thalassemia in adult of District Bajaur. The prevalence of thalassemia was 6.00 (15x100/250) in female adults, which were higher than male adults, while it was 5.92 (16x100/270) in male adults as shown in figure.

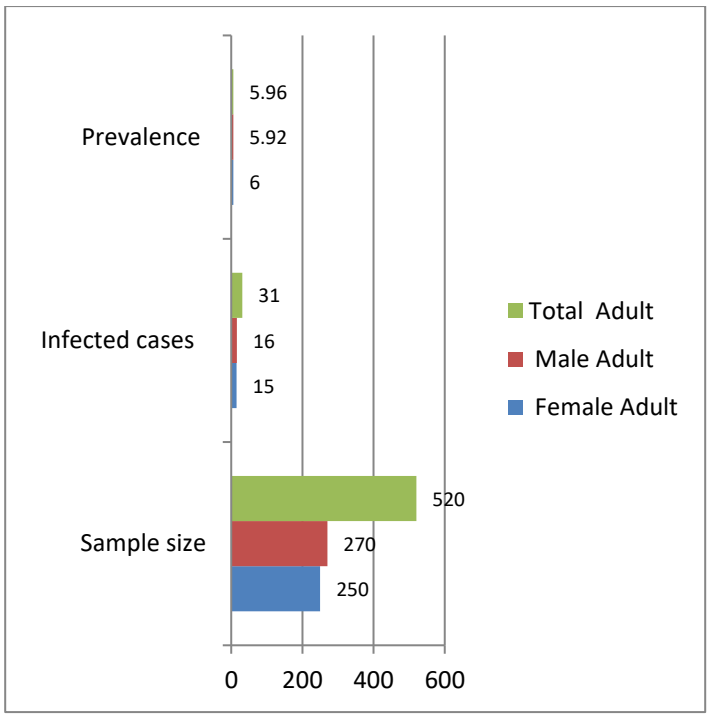

Fig 3.5: Sex Wise Prevalence of Thalassemia in Adult of District Bajaur

3.5. Tehsil-wise prevalence of thalassemia in District Bajaur

Figure 3.6 shows the prevalence of thalassemia in different administrative areas (Tehsils) of

District Bajaur. Highest prevalence of 13.19 (31x100/235) was reported from Tehsil Salarzo, followed by 6.82 (14x100/205) in Tehsil Utman khel, 6.66 (14x100/210) in Tehsil Khar, 6.34 (13x100/205) in tehsil Mamundo and 2.70 (5x100/185) in Tehsil Barang while the lowest prevalence of 1.87 (3x100/160) were recorded in Tehsil Nawagai.

Tahsils	Gender	Sample size	Infected Cases	Prevalence
Salarzo	Male		14	5.95
	Female	235	17	7.23
Utman Khel	Male	205	6	2.92
	Female		8	3.9
Khar	Male	210	8	3.8
	Female		6	2.85
Mamundo	Male	205	6	2.92
	Female		7	3.41
Barang	Male	125	2	1.6
	Female		3	2.4
Nawagai	Male	160	1	0.62
	Female		2	1.25

Table 3.1 Sex Wise Prevalence of Thalassemia in each Tehsil of District Bajaur

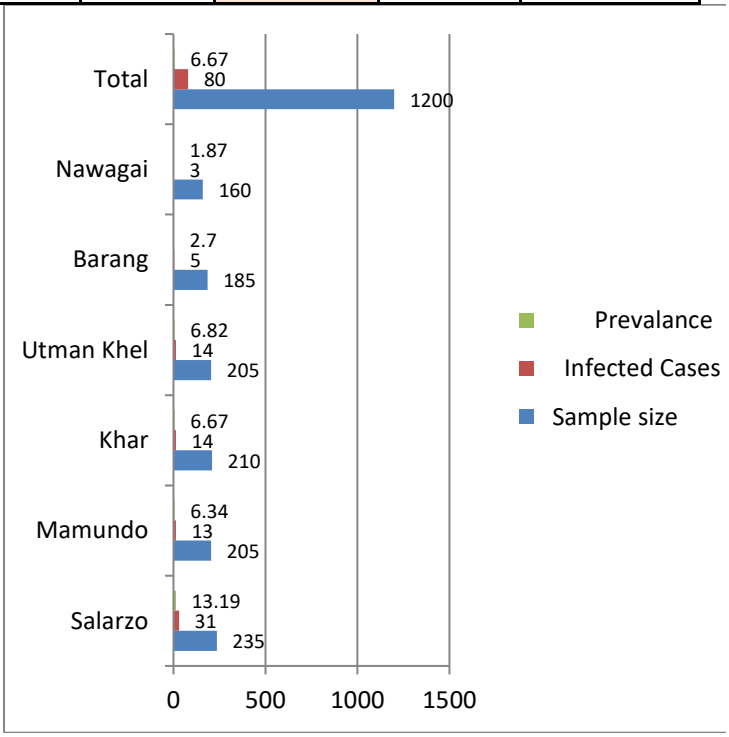

Fig. 3.6: Tehsils Wise Prevalence of Thalassemia in District Bajaur

3.6. Gender-wise prevalence of thalassemia in different Tehsils of District Bajaur

Table 3.1 shows gender-wise prevalence of thalassemia aong local population residing in different Tehsils of District Bajaur. The Highest prevalence of 7.23 (17x100/235) was recorded in female of Tehsil Salarzo,followed by 3.90 (8x100/205) in female of Tehsil Utman khel, 2.85 (6x100/210) in Tehsil khar, 3.41 (7x100/205) in Tehsil Mamundo and 1.62 (3x100/125) in Tehsil Barang while the lowest prevalence was 1.25 (2x100/160) recorded in female of Tehsil Nawagai. Similarly among males of different Tehsils; highest prevalence of 5.95 (14x100/235) was recorded in Tehsil salarzo, 3.80 (8x100/210) in Tehsil Khar, 2.92 in Tehsil Utman Khel and Tehsil Mamundo,1.08 in Tehsil Barang and 0.62 in Tehsil Nawagai.

3.7. Prevalence of thalassemia based on cousin and non-cousin marriages in District Bajaur.

Table 3.2: Prevalence of thalassemia based on cousin and non-cousin marriages in District Bajaur.

The table 3.2 shows the prevalence of thalassemia on the basis of Blood relation in District Bajaur. Highest prevalence of thalassemia was 7.53 (49x100/650) noted in cases of cousin marriages, while the lowest prevalence of thalassemia was 5.63 (31x100/550) recorded in case of non-cousin marriages.

3.8. Prevalence of thalassemia in live and dead children of District Bajaur

Table 3.3 shows the prevalence of thalassemia in children status (live/dead) of District Bajaur. Highest prevalence of thalassemia was 71.42 (35x100/49) in live children, while the lowest prevalence of thalassemia was 28.57 (14x100/49) recorded in dead children.

Table 3.3: Prevalence of Thalassemia on the Basis of Children Status in District Bajaur.

Children status	Sample size	Infected cases	Prevalence
Live	49	35	71.42
Death		14	28.57

3.9. Prevalence of thalassemia in live and dead adults of District Bajaur

The table 3.4 shows the prevalence of thalassemia on the basis of adult status (live/dead) in District Bajaur. Highest prevalence of thalassemia was 51.61 (16x100/31) in live adult, while the lowest prevalence of thalassemia was 48.38 (15x100/31), recorded in dead adults.

Table 3.4: Prevalence of Thalassemia on the Basis of adult status in District Bajaur

Blood relation	Sample size	Infected cases	Prevalence
Cousin Marriage	650	49	7.53
Non Cousin Marriage	550	31	5.63
Total	1200	80	6.67

Adult status	Sample size	Infected cases	Prevalence
Live Adult	31	16	51.61
Dead Adult		15	48.38

3.10. Prevalence of thalassemia among individuals with different ABO blood groups of District Bajaur

Figure 3.7 shows the prevalence of thalassemia among individuals with different blood groups (A, B, AB, O) in District Bajaur. The result shows that highest prevalence was 9.14 (26x100/350) noted in individuals with blood group A, while prevalence of thalassemia was 7.87 (26x100/330) in individuals with O blood group. Prevalence of thalassemia was 7.77(21x100/270) in individuals with blood group B, while the lowest prevalence was 2.8 (7x100/250), recorded in individuals with blood group AB.

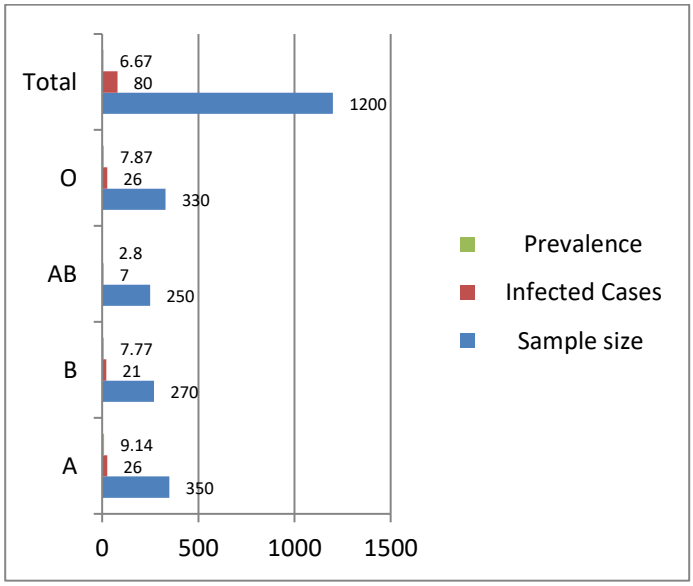

Figure 3.7: Prevalence of thalassemia among individuals with different ABO blood groups of District Bajaur

3.11. Prevalence of thalassemia among males and females with different ABO blood groups of District Bajaur

Figure 3.8 and 3.9 shows the prevalence of thalassemia among male and female with different blood groups respectively. Highest prevalence was 8.88 (12x100/135), recorded in males with blood group O' followed by 8.46 (11x100/130) in blood group A, 8.33 (10x100/120) in blood Group B, while the lowest prevalence was 3.80 (4x100/105), recorded in blood group AB.

Highest prevalence among females was 8.33 (15x100/180), recorded in blood Group A, then

followed by 7.44 (14x100/188 in blood group O, 6.28 (11x100/175) in blood group B, while the lowest prevalence was 1.79 (3x100/167), recorded in blood group AB as shown in figure 3.9.

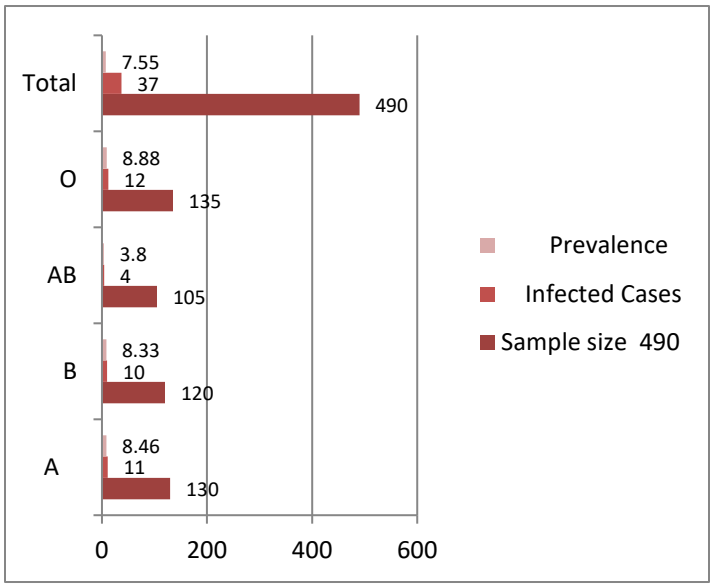

Fig. 3.8: Prevalence of thalassemia among males with different ABO blood groups of District Bajaur

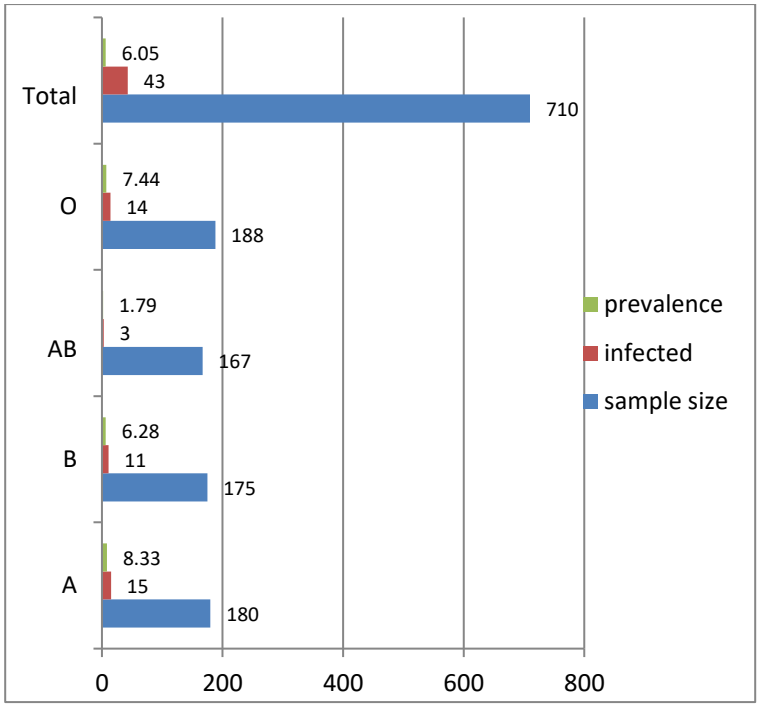

Fig. 3.8: Prevalence of thalassemia among females with different ABO blood groups of District Bajaur

4.DISCUSSION

This study was conducted from December, 2020 to September, 2021 to determine the prevalence of thalassemia in District Bajaur, located towards the north of Pakistan. Prevalence of thalassemia was found to be quite high in this area. In current study total of 1200 samples were collected from the population of six Tehsils of District Bajaur like, Tehsil salarzo, Tehsil Mamund, Tehsil khar, Tehsil Utman Khel, Tehsile Barang and Tehsil Nawagai. The collected data were observed for the prevalence of thalassemia. After observation of the data, there were 80 infected cases of thalassemia out of 1200 with a total prevalence of 6.67 % (80X100/1200).

Thalassemia is an inherited disorder which means they are passed from parents to their children in infected families. In present study highest prevalence of 7.20 (49x100/680) were reported in children, while lowest prevalence of 5.96 (31X100/520) were recorded for adults in the population of Bajaur. The reported data

shows that the children thalassemia ratio is greater than the adult's thalassemia ratio in district Bajaur.

5.CONCULSION

It is concluded that thalassemia is a dangerous disorder which is spreading worldwide; it is not only an important public health problem but also a socio-economic problem of many countries. The lack of awareness about the nature of Thalassemia in general public in combination with the cultural and cousin marriages affects the attitude and practices of people of district Bajaur negatively in relation to Thalassemia prevention.

This study is significant endeavor in promoting awareness about the severe Thalassemia genetic disorder. Presently this problem is continuing to increase gradually and might be a more severe problem in the future, beside the other disease. This study will be beneficial for the study areas people, doctor's health policy makers and affected families to observe the reality of this highly spreading disease

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