

# CLINICAL SPECTRUM OF PATIENTS WITH BETA THALASSAEMIA: A REVIEW OF FIFTY-FOUR PATIENTS

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## ABSTRACT

**Background:** Beta thalassaemia is a common haematological disorder presenting as anaemia through out the world including Pakistan. Although nutritional anaemias and anaemias due to worm infestation are the leading cause of anaemia in our children but thalassaemia is also an important cause of increased morbidity and mortality in children belonging to this part of the world. This study was undertaken to know the clinical aspects of this disease.

**Material & Methods:** This study was carried out in children Centre, Military Hospital, Rawalpindi during one year period from October 2000 to September 2001. A total of 54 cases of  $\beta$  thalassaemia were included in the study. Out of these, eight patients were referred for the first time and were newly diagnosed while others were already diagnosed. In all these cases history was taken and detailed clinical examination carried out. Blood picture and haemoglobin level of the patients and parents were performed along with other necessary laboratory investigations.

**Results:** Majority of these patients were from the rural areas of Rawalpindi, belonging to Rajput, Awan and Mughal families. Age range was from one month to three years. Male to female ratio was 2.4 : 1.0. All these patients were having severe anaemia and hepatosplenomegaly. Seventy-seven percent cases were below third centile for height and weight. Fetal haemoglobin was raised in all these cases ranging from 70 to 90 percent. Seventy six percent of the parents were heterozygous for this disease.

**Conclusion:** In all these patients, there was poor compliance for blood transfusion and chelation therapy. The life expectancy in our patients is low as compared to western population.

**Key words:** Thalassaemia, Anaemia, Haemoglobin F, Hepatosplenomegaly. Blood transfusion.

## INTRODUCTION

Anaemia is one of the most common presenting feature in children suffering from haematological disorders and in fact is one of the leading cause of death in childhood. Although still nutritional anaemias are very common but thalassaemia is the most common inherited disorder in Pakistan, resulting in considerable morbidity and Mortality.<sup>1</sup> The factors like poverty and ignorance prevailing in the thalassaemia belt of Asia, aggravate the miseries of these thalassaemics.<sup>2</sup> Accordingly, a better understanding of molecular genetics, clinical presentation, diagnostic approach and up to date management of this disease is required to meet these challenges.<sup>3</sup>

The thalassaemia syndromes consist of a group of disorders in which there is an inherited abnormality of the structure and rate of synthesis of the globin chains.<sup>4</sup> In  $\beta$  thalassaemia absent or inadequate production of  $\beta$  globin chains leads to ho-

mozygous or heterozygous beta thalassaemia. Homozygous beta thalassaemia also called Cooley's anaemia is one of the fatal disease of childhood.<sup>5</sup> Predominantly this disease occur in Mediterranean countries such as Cyprus, Italy, Greece, Turkey, the Middle and Far East: Pakistan, India and Bangladesh have also a large population of thalassaemics.

Thalassaemia is said to be more common in the areas endemic for plasmodium falciparum. It seems that plasmodium causes mutation at the genetic level leading to protection against falciparum malaria.<sup>6</sup> The carrier rate approached to 20% in Turkey & Greece, 10% in Sicily and 4% in Southern Italy. There is also high incidence in Burma and Thailand.<sup>7</sup> In Pakistan the incidence is also high, 4% in Pathans and 1.5% in Karachites.<sup>8</sup> The higher incidence in Pathans is related to Alexander's Arrival in the subcontinent through Khyber Pass whose army brought this disease from their native place "Greece".

Since thalassaemia is a very serious problem in our children it requires attention not only for the proper management but also for preventive measures by screening, genetic counselling and prenatal diagnosis of this disease. This can be achieved by involving the Government, NGO's and general population as a whole.

## MATERIAL & METHODS

The present study was carried out at children Centre, Military Hospital Rawalpindi. All the children coming to out door department and presenting with pallor along with hepatosplenomegaly were included in this study. Special Performa prepared for the purpose was filled along with informed consent of the parents. In all these cases proper history including present, past, family socioeconomic and drug history was taken. A thorough clinical examination was also carried out. Blood complete picture and haemoglobin F level of patients and parents were performed along with other necessary laboratory investigations. X-ray skull, chest and both hands were carried out in selective cases. The selection criteria for identification was microcytic hypochromic anaemia with hepatosplenomegaly, specific radiological changes and raised haemoglobin F level.

## RESULTS

In this study we have analyzed the clinical profile of thalassaemia in a heterogeneous population consisting of people from all provinces of Pakistan including Jammu and Kashmir. Data of various parameters obtained have been analyzed as follows:

Age range was 1-36 months. Male to female ratio was 2.4: 1.0. Patients came from different geographical areas. (Table-1)

The consanguinity and ethnicity of the parents showed that 38 (70%) parents were first cousins 4 (7.4%) were second cousins, 2 (3.7%) were different relatives, while 10 (18.5%) parents were not related. (Table-2)

Out of these 54 cases, 40 (74%) belonged to rural areas while 14 (26%) were from urban areas. Majority of patients from Rawalpindi, belonging to Rajput, Awan and Mughal families. Rural to urban ratio was 3:1. As far as their economic status is concerned 2 cases (3.7%) belonged to the upper class, 6 (11%) were from upper middle class, 20 (37%) were from lower middle class while 26 (48%) were from lower class. Poor to rich ratio was 5:1.

**Table-1: Age, sex and geographical distribution.**

Age Group	No. of cases	%age	Sex	Number	%age	Geographical area	Number	%age
1-3 Months	20	37.0	Male	37	69.50	Punjab	38	70.4
4-6 Months	22	40.7	Female	17	31.50	N.W.F.P	08	14.8
7-11 Months	11	20.4	–	–	–	A.J.K	08	14.8
1-3 Years	01	1.9	–	–	–	–	–	–

**Table-2: Ethnicity and consanguinity distribution.**

Cast	Number	%age	Consanguinity Relationship	Number	%age
Rajput	20	37	First Cousin	38	70.4
Awan	14	26	Second Cousin	04	7.4
Mughal	06	11	Distant Relative	02	3.7
Jat	04	07	Non-relatives	10	18.5
Abbasi	02	04	–	–	–
Syed	01	02	–	–	–
Pathans	05	09	–	–	–
Niazi	01	02	–	–	–
Sheikh	01	02	--	–	–

Anthropometric examination of these children revealed that out of 54 children, 42 cases (77.7) were below third centile for weight while 8 (14.8%) were between 25<sup>th</sup> centile and only 4 cases (7.4%) were between 25<sup>th</sup> and 50<sup>th</sup> centile. Centile chart for height showed that 39 cases (72%) were below 3<sup>rd</sup> centile, 10 cases (18%) were between 3<sup>rd</sup> and 25<sup>th</sup> centile while 5 cases (9.2%) were between 25<sup>th</sup> and 50<sup>th</sup> centile. Head circumference was normal or increased in most of the cases.

Most of the cases above 2 years were having bony changes with typical Mongoloid facies. Radiological examination was performed in 30 cases (55.2%). Early changes were noted in 25 cases (46%), while typical "hair on end" appearance was noted in 5 cases (9.2%). All 54 cases were having enlarged liver and spleen. Liver was massively enlarged in 3 (5.5%) cases (6, 7 and 8 years old). Moderate enlargement of the spleen was found in 40 cases (74%) while 9 cases (16.6%) were having mild enlargement. Out of these 1 patient (1.8%) was splenectomized two years ago due to hypersplenism.

Haematological parameters showed 46 cases (85%) having severe anaemia. Minimum Hb level was 1.5 while maximum level was 9.5 g/dl. All patients had nucleated RBC's in their peripheral blood. Moderate leukocytosis was present in most cases. The Hb F was increased in all the cases.

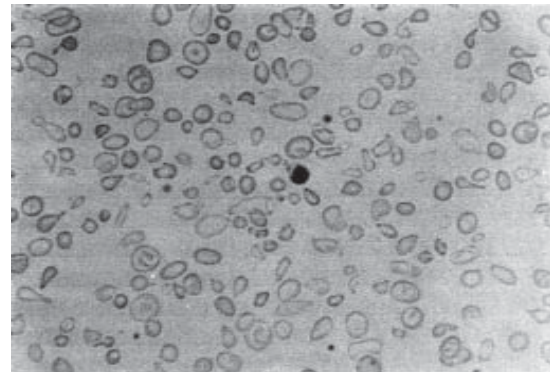
The detail is given in table 3.

**Table-3: Hemoglobin and Hemoglobin F level in the patients.**

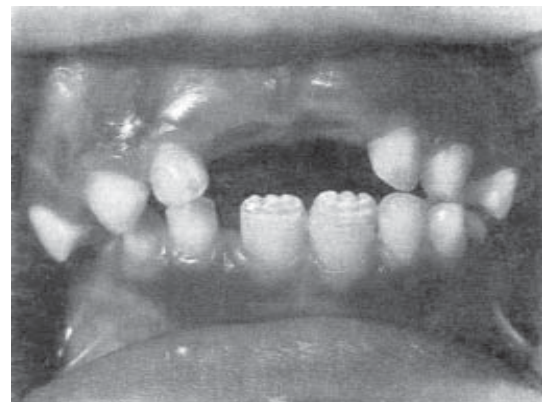
Parameter	Number	%age
<b>Hb g/dl</b>		
1.5	22	40.7
5.0	24	44.5
7.0	6	11.0
9.5	2	3.7
<b>Hb F</b>		
90%	17	31.5
70-90	17	31.5
70%	20	37.0



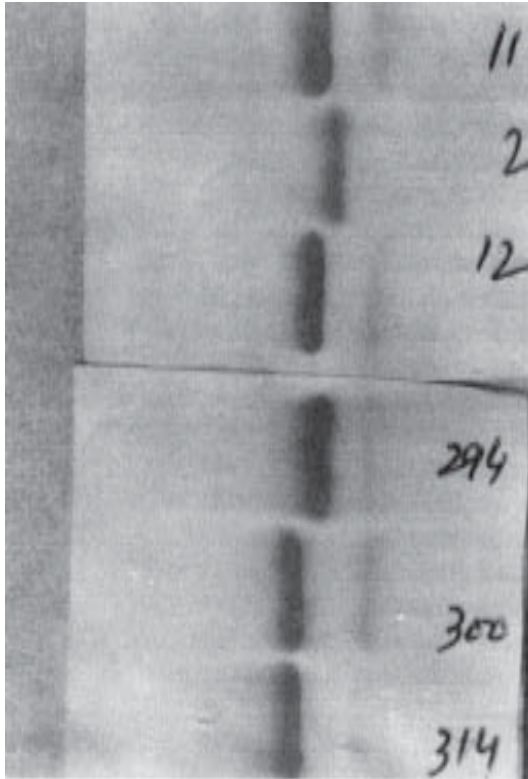
Seven years old child suffering from Thalassaemia. Showing hepato-splnomegaly.



Peripheral Blood Film in Thalassaemia. Showing hypochromic microcytic picture.



Dental Abnormalities in Thalassaemia. Showing gum hypertrophy.



Haemoglobin Electrophoresis in Beta Thalassaemia. Showing HbF bands.

**DISCUSSION**

Beta thalassaemia major is one of the most common inherited hematological disorders through out the world, causing thousands of deaths every year. This disease is also common in our population. A study carried out by Ahmed and his co-workers has shown that more than 4 thousands homozygotes are born each year in Pakistan. Age at the time of presentation in all these cases studied at the Military Hospital Rawalpindi, during one year time showed that most of these cases presented before the age of 6<sup>th</sup> months. The youngest patient was 1 month old, while the oldest was 3 years old. The disease is more common in males than females. Almost similar observations were made by Saleem and his Associates.<sup>8</sup>

Most of these cases belonged to northern area of Punjab, particularly Rawalpindi and its suburbs; this was probably due to their easy accessibility to this hospital and not because of the high prevalence of thalassaemia in this part of the country. The low incidence of thalassaemia shown in North West Frontier Province NWFP is not contrary to the study of Imran and Associates (1986) which was showing high prevalence of thalassaemia in Pathans.<sup>9</sup> This is probably due to the reason that every patient reports to his nearest referral center which is Peshawar for NWFP people.



Radiological changes in Beta Thalassaemia. Skull showing hair on end picture.



Radiological changes in Beta Thalassaemia. Upper limb showing thin cortex and expanded marrow.

Study of ethnic group showed that this disease is common in Rajputs and Awans. From consanguinity analysis 42 parents were found to be closely related while 12 were distantly related or not related at all. This figure shows very high incidence of consanguineous marriage in our society. Socio-economic analysis of these patients revealed a rural to urban ratio of about 3:1 which depicts the higher proportion of rural than urban populations while a poor to rich ratio was 5:1 which is again in accordance with normal socioeconomic status in our society.

On anthropometric examination, 78% of these cases were below the 3<sup>rd</sup> centile for sex, height and weight as compared to Roth and co-workers study which showed only one patient with short stature. The difference indicates the poor management of these thalassaemia cases in our society<sup>10</sup>.

All these cases were having hepatosplenomegaly. Massive splenomegaly was noticed in 3 cases while spleen was moderately enlarged in 75% of these cases and mild splenomegaly was found in 17% of these cases.<sup>11,12,13</sup>

The maximum Hb noted was 9.3 g/dl in only one case. While 85% of the cases were having Hb level below 5 g/dl with a minimum level of 1.5 g/dl. Saleem and co-worker study also coincides with this study where minimum Hb was 1.5 g/dl and maximum 9 g/dl with a mean level of 4.6 g/dl.<sup>9</sup> Out of these severely anemic children 5 cases presented with congestive cardiac failure (CCF). The compliance of these patients was far from satisfactory. Transfusion was not regular in most of these cases. These cases report to the hospital when Hb level used to fall significantly. Being a military hospital and the availability of better facilities for transfusion at Armed Forces Institute of Transfusion at Rawalpindi, the entitled children do not face much problem to get the blood but due to non-availability of a male member at home most of these children fail to receive blood transfusion regularly at proper time.

Genetic implication were discussed with all the parents and almost all the parents accepted it as inherited disease and agreed to avoid the inter marriages but regarding the precautionary measures for family planning, 39 parents refused because they were not having any healthy issue in the family.

Prognosis of these cases have very much improved in western society. In 1963, 25-years survival rate was only 25% which increased to 95% in 1982.<sup>11,12</sup> Most of these thalassaemics lead a normal life till the age of forty. But unfortunately most of our children die at an earlier age. In the present study

only one child was 14 years old; all others were below 10 years age. This worse prognosis is due to the poor management of these cases in this part of the world.

## CONCLUSION

Most of these children are severely anaemic but inadequately and irregularly transfused without chelation therapy. Consanguineous marriage is more frequent among the parents of these patients. The life expectancy in our thalassaemics is low as compared to the western population.

A screening program at secondary school level for detection of heterozygous state is recommended. Consanguineous marriages should be stopped in such cases and proper genetic counselling provided. There is an urgent need of Thalassaemia society in every big city of Pakistan to provide information, economic support and arrange blood and chelating agents for these children.

In every small hospital blood transfusion facilities along with subcutaneous desferol pump facilities should be made available.

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