ORIGINAL RESEARCH PAPER

Paediatrics

SPECTRUM OF COMPLICATIONS IN HAEMOGLOBINOPATHIES-A STUDY IN CENTRAL INDIA

KEY WORDS:
Haemoglobinopathies, Cardiac complication,Infection.

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ABSTRACT

INTRODUCTION: Thalassemias are hereditary hemolytic anemia with autosomal recessive inheritance characterized by inability to produce one or more globin chains forming hemoglobin molecule.
MATERIAL AND METHODS: Prospective observational study conducted at tertiary care hospital from January 2015 - November 2016.Total187 patients of haemoglobinopathies satisfying the inclusion and exclusion criteria were enrolled. Detailed histories with clinical examination were noted in preformed structural proforma.
RESULTS: Complication rates were significantly higher among thalassemia major patients compared to other haemoglobinopathy. Stunting in thalassemia major group160 (85.5%), sickle cell disease 11(91.6%), splenomegaly was noticed in 141(75.4%).Cardiac complication 16(8.5%), most common complication was Congestive cardiac failure 10 (5.8%) cases, followed by Early transfusion reaction in 9 (5.2%), and infection (sepsis and bronchopneumonia) was seen in 6(3.5%).
CONCLUSION: Complication were Stunting, splenomegaly, Congestive cardiac failure, Early transfusion reaction, and Infection (sepsis and bronchopneumonia) seen.

INTRODUCTION

Haemoglobinopathies are a group of genetic disorders of haemoglobin (Hb). These hereditary disorders of haemoglobin pose a massive health problem in many countries including India [2]. Regular blood transfusion and adequate iron chelation therapy are important factors for treatment and follow up of thalassemia patients. Currently, the most common causes of death in these patients are transfusion-related hemosiderosis-induced heart failure and fatal arrhythmias, increased risk of viral hepatitis, cirrhosis, delayed puberty, growth retardation, developmental delay, infection are the other common complications [3].In this study, complications of ß-thalassemia patients were evaluated prospectively. The frequency of ß- thalassemia in India ranges from 3.5 to 15 % in general population.

AIMS AND OBJECTIVE

To study the complications of haemoglobinopathies and consanguity in Maharashtra, located in the mid part of India

MATERIAL AND METHODS

Design: Prospective observational study.
Setting: Tertiary care center.
Period: January 2015 -November 2016.

INCLUSION CRITERIA:
All the cases of haemoglobinopathies in the age group between 6 month to 12 years diagnosed by High Performance Liquid Chromatography.

EXCLUSION CRITERIA:
All other cases of hemolytic anemia other than haemoglobinopathies.

Approval of institutional ethical committee was obtained no: Pharma/IEC-GMCA/445/2014. Total 187 patients of haemoglobinopathies who were diagnosed by HPLC who were visiting in paediatric O.P.D. and I.P.D. Tertiary Care Hospital and satisfying the inclusion and exclusion criteria were enrolled in the study after obtaining written informed consent from parents. Detailed history with demographic details and clinical examination were noted

Height /Length measurement:
Length in centimeters was measured on calibrated infantometer in less than 2 year old patients. Height in centimeters was measured on calibrated stadiometer in more than 2 years old patients.

Weight measurement:-
Weight was measured by calibrated electronic weighing scale in kilograms.

Growth assessment4, 5:-
Assessment of stunting and wasting was done by growth curves of WHO GROWTH CHARTS for patients age <5 years and growth curve of KHADILKAR IAP GROWTH CHART for patients age >5 years.

Assessment of stunting done by making two groups:-
S1:- height between 3 - 50th percentile of growth curve
S2:- height below 3rd percentile of growth curve

Assessment of wasting done by making two groups:-
W1:- weight between 3rd -50th percentile of growth curve
W2:- weight below 3rd percentile of growth curve.
Spleenomegaly[6]:- Classical clinical splenomegaly criteria.
Mild:- 2cm-4cm
Moderate:- 4cm- 8cm
Massive: - > 8cm.

Cardiac complications: - Cardiomegaly, left ventricular dysfunction, LVEF was assessed by 2 D-Echo PHILIPS iE33 WITH 3D Echo and Trans esophageal echo (TEE).

CBC, Peripheral Smear, Liver Function Test was done. Serum ferritin level done at 6 month interval.

All the collected data was entered in Microsoft Excel sheet. It was then transferred to SPSS version 21 software for statistical analysis. Quantitative data represented as mean and standard deviation. Qualitative data presented as frequency and percentage and compared using chi square test. Results graphically represented where necessary, using MS Excel deemed value of less than 0.05

was considered as level of significance.

RESULTS:

Table no.1: Table showing distribution of growth (height) in haemoglobinopathies

Height	Group						Total
	Thal. Major	SCD	SBT	Thal Inter	Thal Trait	Sickle trait	
N	11 (5.8%)	1 (0.5%)	0	0	0	0	12 (6.4%)
S1	79 (42.2%)	10 (5.3%)	1 (0.5%)	0	0	1 (0.5%)	91 (48.6%)
S2	81 (43.3%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	84 (44.9%)
Total	171 (91.4%)	12 (6.4%)	1 (0.5%)	1 (0.5%)	1 (0.5%)	1 (0.5%)	187 (100%)

(Abbreviations: S1-Height between 3rd-50thpercentile, S2-Height below 3rd percentile)

Table no. 2:-Table showing distribution of growth (weight) in haemoglobinopathies

Weight	Group						Total
	Thal. Major	SCD	SBT	Thal Inter	Thal Trait	Sickle trait	
N	11 (5.8%)	1 (0.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	12 (6.4%)
W1	75 (40.1%)	10 (5.3%)	1 (0.5%)	0 (0%)	0 (0%)	1 (0.5%)	87 (46.5%)
W2	85 (45.4%)	1 (0.5%)	0 (0%)	1 (0.5%)	1 (0.5%)	0 (0%)	88 (47.1%)
Total	171 (91.4%)	12 (6.4%)	1 (0.5%)	1 (0.5%)	1 0.5%)	1 (0.5%)	187 (100%)

(Abbreviations: W1-Weight between 3rd-50thpercentile, W2-Weight below 3percentile)

Table no.3:- Table showing distribution of splenomegaly in haemoglobinopathies

Splenomegaly	Group						Total
	Thal. Major	SCD	SBT	Thal Inter	Thal Trait	Sickle trait	
Massive	33 (17.6%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	33 (17.6%)
Mild	56 (29.9%)	6 (3.2%)	1 (0.5%)	1(0.5%)	0(0%)	0(0%)	64(34.2%0)
Moderate	42 (22.4%)	2 (1%)	0 (0%)	0(0%)	0(0%)	0(0%)	44(23.5%)
Total	171(91.4%)	12 (6.4%)	1(0.5%)	1(0.5%)	1(0.5%)	1(0.5%)	187 (100%)

Table no.4:- Table showing distribution of other complications among cases of thalassemia major

Complications in thalassemia major	Frequency	Percent
None	151	80.7%
Infection(Sepsis,broncho pneaumonia)	6	3.5%
CCF	10	5.8%
Hepatitis C virus	1	0.58%
HIV	1	0.58%
Transfusion reaction	9	5.2%

DISCUSSION:

This is a hospital based prospective observational study carried out in O.P.D. and I.P.D section, Paediatric department of Medical College and Tertiary Referral Centre, Aurangabad. After approval from institutional ethical committee, approval no. Pharma/IEC-GMCA/445/2014, study was conducted between the periodJanuary2014 to November 2016.Patients of haemoglobinopathies fulfilling the inclusion and exclusion criteria were enrolled for study. In our study we observed 187 cases of haemoglobinopathies , most common was beta thalassemia major 171(91.4%) followed by sickle cell disease 12(6.4%) and other haemoglobinopathies sickle beta thalassemia, sickle cell trait, thalassemia intermedia, thalasemia trait had very low percentage 1(0.5%) each presented with us.

Table no 5:- Showing different studies of Presence of Stunting among haemoglobinopathies (Refer table no.1)

Study	No. of subjects	Height affected
Kwan et al[8],1995	68	45 (68%)
Chattopadhyayet al[1],2011	297	70(23%)
Ayhan Yaman et al[9],2013	56	13(19.4%)
Varsha wankhade et al[10]2013	SCD-67	40(55.1%)
Present study	187	S1 91(48.6%) S2 84(44.9%)
	TM - 171(100%)	S1= 79(46.1%) S2= 81(47.3%)
	SCD-	S1=10(83.3%) S2=1(8.3%)
	TI,TT-	S2=1(0.5%)
	SBT, SCT	S1=1(0.5%)

In present study among 187 cases of haemoglobinopathies, 175(93.5%) cases had stunting, from which we observed S1 stunting in 91(48.6%), S2 stunting in 84(44.9%) cases.Thalassemia major (n=171) group stunting was present in 160(93.5%) In which S2 stunting was noticed in 81 (47.3%) while, S1 stunting was noticed in 79 (46.1%) cases. Among 12 sickle cell disease cases, 11(91.6%) had stunting. In which 10 (83.3%) cases had S1 stunting,while S2 stunting was noticed in 1(8.3%) case. In thalassemia major most common cases were of S2, severe stunting. In Sickle cell disease most common cases were S1, moderate stunting. Kwan et al81995 observed stunting below 3rd percentile in 45 (68%) cases.Chattopadhyay et al12012 observed growth retardation in 70(23%) of cases. Ayhan yaman et al92013 observed short stature in 13(19.4%) of cases. Varsha wankhade et al102013 found growth failure in 40(55.1%) patients of Sickle cell disease. One of the most common complications of haemoglobinopathies is growth failure which is multifactorial. Iron deposition is due to recurrent transfusions, which leads to free iron and haemosiderosis induced damage to endocrine glands. Aneamia, under nurishment, lower socio economical status are predisposing factors of growth failure.

We observed growth failure in most of cases. It's because majority of cases 171(91.4%) were of transfusion dependant thalassemia major,anaemic, also large no of cases were from low socio economical status with undernurishment. Hence we observed growth failure as above mentioned studies.

Table no 5 – Showing different studies of Presence of wasting among haemoglobinopathies. (Refer table no.2)

Study	No.of cases	Wasted cases
Amita trehan et al[2],2007	TM-964	257(26%)
Chattopadhyay et al[1],2012	297	70(23%)
Varsha Wankhade et al[10], 2013	SCD-67	40(55.1%)
Present study	187	W1-87(46.5%) W2-88(47.1%)
	TM - 171(100%)	W1-75(43.8%) W2-85(49.7%)
	SCD- 12(100%)	W1-10(83.3%) W2-1(8.33%)
	SBT, SCT	W1-1(0.5%)
	TI,TT	W2-1(0.5%)

In present study among 187 cases of haemoglobinopathies, 175(93.5%) cases had wasting, from which we observed W2stunting in 88(47.1%), W1 wasting in 87(46.5%) cases. Among (N-171) thalassemia major cases, wasting was present in 160(93.5%). From which W2 wasting was noticed in 85(49.7%), while W1 wasting was noticed in 79 (43.8%) cases. Among (N-12) sickle cell disease cases, 11(91.6%) had stunting. In which 10

(83.3%) cases had W1 wasting, W2 wasting was noticed in 1(8.3%) case. In thalassemia major most common cases were of W2, severe stunting. In Sickle cell disease most common cases were W1, moderate stunting.Amita trehan et al2, 2007 observed 964 cases of thalassemia major, she found 257(26%)cases wereunder nourished.Chattopadhyay et al1,2012 studied 297 cases of haemoglobinopathies, he found 70 (23%)cases with growth retardation.Varsha Wankhade et al10,2013 studied 67 cases of sickle cell disease, she found growth failure in 40(55.1%) patients.One of the most common complications of haemoglobinopathies is growth failure which is multifactorial. Iorn deposition is due to recurrent transfusions,which leads to free iorn and haemosiderosis induced damage to endocrine glands. Aneamia, under nurishment, lower socio economical status are predisposing factors of growth failure.

We observed growth failure in most of cases. It's because majority of cases (N-171) were of transfusion dependant thalassemia major, anaemic, also large no of cases were from low socio economical status with undernurishment.

Our observations of growth failure were comparable to growth above mentioned studies.

Table no.6:-Showing different studies of other complications observed in haemoglobinopathies (Refer table no. 5)

Study	No.of patients	Transfusion reaction	Transfusion Related infection	Venoocluse crisis	Splenic sequestration Crisis
Ahyan YAMAN et al[9]2013	67-TM	3(4.4%)	1(1.5%)	_	_
Elliot Vinchinsky et al[12]2012	407-TM	211(52%)	97(24%)	_	_
Dipty Jain et al[11]2012	316-SCD	_	_	166(52.5)	26(8.2%)
Present study	N-187 171 BTM 12 SCD	5.2% _	1% _	_ 10(83.3%)	_ 1(8.3%)

In this study we observed Early transfusion reaction in 9(5.2%) cases and Transfusion related infections in 2(1%) of cases. In sickle cell disease we observed most common presentation was Vasooclusive crisis 10(83.3%) and 1(8.3%) presented as splenic sequestration crisis.Ayhan Yaman et al9,2013 Studied complications in 67 cases of thalassemia major, and observed transfusion reactions in 3(4.5%) and transfusion related infections in 1(1.5%) of cases.Vinchisky et al12,2012 studied 407 cases of thalassemia major, and observed Early transfusion reaction in 211(52%) of patients and transfusion related infections in 97(24%) of cases.Dipty jain et al11,2012 studied 316 cases of sickle cell disease, and observed vasooclusive crisis in 166(52.5%) of patients and splenic sequestration syndrome in 26(8.2%) of cases.Our study showed comparable data with Ahyan et al and Dipty Jain et al.Disparity in the results of above mentioned study was may be due faulty blood collection technique, poor aseptic precautions and variation of samples size.

CONCLUSION:

With the help of timely and appropriate interventions like spleenectomy, iron chelation therapy, hydroxyurea, maintaining mean serum ferritin level below 5000 ng/ml, we can minimize cardiac complications, growth retardation, and recurrent transfusions which will eventually improve quality of life.

REFERENCES

1. Chattopadhyay et al an epidemiological study on the clinico haematological profile of patients of congenital haemolytic anemia in a tertiary care hospital,Kolkata. Indian J. Prev. Soc. Med. Vol. 43 No.4, 2012
2. Amita trehan et alClinicoinvestigational and Demographic Profile of Children with Thalassemia MajorIndian J Hematol Blood Transfus (Jan-Mar 2015) 31(1):121–126 DOI 10.1007/s12288-014-0388-y
3. Cunningham MJ, Sankaran VG, Nathan DG, Orkin SH. The Thalassemias. In: Orkin SH, Nathan DG, Ginsburg D, Look AT. Nathan and Oski's Hematology of Infancy and Childhood, 7th ed. Philadelphia: Sounders Elsevier; 2009:1015-1109
4. IAP Growth charts, http://www.iapindia.org/page.php,id=79.
5. WHO Growth standards. http://www.who.int/childgrowth/standards/en.
6. eMedicineHealth (2011): Enlarged splee. URL-http://www. emedicinehealth. com/ enlarged_spleen_ splenomegaly/article_em.htm
7. chopra et al Spectrum of haemoglobinopathies in tertiary care hospital,armed Chattopadhyay et al an epidemiological study on the clinico haematological profile of patients of congenital haemolytic anemia in a tertiary care hospital,Kolkata. Indian J. Prev. Soc. Med. Vol. 43 No.4, 2012
8. Kwan EY, Lee AC, Li AM, Tam SC, Chan CF, Lau YL, et al. A cross-sectional study of growth, puberty and endocrine function in patients with thalassaemia major in Hong Kong. J Paediatr Child Health. 1995 Apr;31(2):83-7.
9. Ayhan yaman et al Common complications in beta thalasseia patients,international journal of hematology and oncology,turkey;nov3,vol23;2013
10. Varsha wankhade et al,Diverse Clinical manifestations in Sickle Cell Anemia: study in District Amravati, MS India.J Blood dis.trans.2013,4:1
11. Dipty jain et al Efficacy of Fixed Low Dose Hydroxyurea in Indian Children with Sickle Cell Anemia: A Single Centre Experience,Indian paediatrics;2013
12. Vichinsky et al. Causes and outcomes of the acute chest syndrome in sickle cell disease. National Acute Chest Syndrome Study Group. N Engl J Med. 2000;342(25):1855-65. [Erratum appears in N Engl J Med. 2000 Sep 14;343(11):824].
13. F.UR.Khan Frequency of complications in Beta Thalassemia major in D.I.KHANE:/Biomedica/Vol.23Jan Bio-5.-Jun.2007/