22th Years of glorious venture

ISSN 1606-9722

The ORION Medical Journal

2021

March 2021, Volume 22, Issue 1, No. 48

The ORION Medical Journal 2021 March;22-1(48): p08-13

Pattern and epidemiology of hemoglobinopathies in northern Bangladesh.

ABSTRACT

Introduction

Inherited genetic hemoglobin disorders are emerging global public health concern all over the world. It is reported that almost 5.2% of the world population (over 360 million) carry a significant hemoglobin variant. Along with 100 million beta thalassemia carriers with a global frequency of 1.5% . The inherited beta thalassemia, sickle cell disease and hemoglobin E (HbE) disorders are the most common single gene disorders globally . In many Asian countries, the most common form of hemoglobinopathies are beta thalassemia and HbE disorder. In the eastern parts of Indian subcontinent, Bangladesh and other Southeast Asian countries, HbE is the most prevalent hemoglobin variant. So thalassemia and other hemoglobinopathies are a significant disease burden for a developing country like Bangladesh.

Objective

Bangladesh lies in the world thalassaemia belt. Despite this fact there is a huge lack of evidence about the epidemiology and clinical aspects of the disease. Our study to identify the pattern and epidemiology of hemoglobinothy and also evaluation of the hematological features in northern Bangladesh.

Methods

This was a cross sectional study conducted between July 2018 to June 2019 in department of hematology, Rajshahi Medical College Hospital, different hospitals and private physicians chamber. Patients were suspected of suffering from anaemia. Blood sample were collected for complete blood count and hemoglobin electrophoresis.

Result

A total of 1320 patients mean age were 22.6 years and 70% of the participants were female. Among the enrolled patients, 389 (29.5%) had hemoglobinopathies. Hb E Trait was the most prevalent hemoglobinopathy (12%) followed by E-β-thalassemia (7.3%), β-thalassemia minor (6.6%) and Hb E disease (2.6%). Other hemoglobinopathies like α and β-thalassemia major, sickle cell disease etc. were quite rare. β-Thalassemia major and E-β-Thalassemia had most severe level of anemia while Hb E trait, Hb E disease and Sickle cell disease had mild to moderate level of anemia.

Conclusion

Understanding the pattern and epidemiology of these diseases can help in policy making to prevent the diseases.

KEYWORDS: Hemoglobinopathy, Northern Bangladesh.

Author

M. Morsed Zaman Miah
Email: drzaman04@gmail.com
Md. Abdur Rafi
Email: abdurrafi007@gmail.com

Correspondence

Dr. M.Morsed Zaman Miah
Assistant Professor of Hematology
Rajshahi Medical College, Rajshahi-6000, Bangladesh.
Email: drzaman04@gmail.com

INTRODUCTION

Inherited genetic hemoglobin disorders are emerging global public health concern all over the world. It is reported that almost 5.2% of the world population (over 360 million) carry a significant hemoglobin variant along with 100 million beta thalassemia carriers with a global frequency of 1.5% (1). An estimated 320,000 babies are born each year globally with a clinically significant hemoglobin disorders. Among them more than 50,000 new patients are born with a severe form of thalassemia (beta-thalassemia major and HbE beta thalassemia) (1). Largest portion of these births occur in underdeveloped and developing countries.

The inherited beta thalassemia, sickle cell disease and hemoglobin E (HbE) disorders are the most common single gene disorders globally (1). Hemoglobinopathies are most prevalent in Africa, all Mediterranean countries, the Middle East, the Indian subcontinent and Southeast Asia. In many Asian countries, the most common form of hemoglobinopathiesare beta thalassemia and HbE disorder. In the eastern parts of Indian subcontinent, Bangladesh and other Southeast Asian countries, HbE is the most prevalent hemoglobin variant (2,3).

Bangladesh lies in the world's thalassemia belt. Despite this fact there is a huge lack of evidence about the epidemiology and clinical aspects of this disease. According to a recent review, the estimated prevalence of beta-thalassemia carriers ranges from 3 to 6% and HbE carriers ranges from 3 to 4% in Bangladesh (3). Another country-wide population based study reported the prevalence of beta-thalassemia trait as 4.1% and HbE trait as 6.1% among (n = 735) school children in Bangladesh (4).Evidence on pattern of clinically suspected hemoglobinopathiesare very few in Bangladesh. A study in this context reported that the most common form of hemoglobin (Hb) disorder is β-thalassemia minor (21.3%) along with E-β-Thalassemia and HbE trait. Other forms of hemoglobin disorders are HbE disease, Hb D/S trait, β-thalassemia major, and δ-β-thalassemia (5).

To date, no productive treatment for patients with beta thalassemia major has been found, except bone marrow transplantation. It is a fact that most children with severe forms of thalassemia (such as thalassemia major) usually die under 5 years of age and the average life expectancy of patients suffering from thalassemias is about 30 years, particularly in heavily resource constrained countries (1,2). So thalassemia and other hemoglobinopathies are a significant disease burden for a developing country like Bangladesh. Understanding the pattern and epidemiology of these diseases can help in policy making to prevent the diseases.

The present study aims to identify the pattern and epidemiology of hemoglobinopathies in Northern Bangladesh.

MATERIALS AND METHODS

This cross sectional study was conducted in the department of hematology of Rajshahi Medical College Hospital (RMCH) from July 2018 to June 2020. All the patients suffering from anemia who visited to the hematology department of RMCH were the study population.The sample size was calculated from the prevalence estimate using the formula: $n=\frac{z^2 pq}{d^2}$, where, where n = number of the sample; z = 1.96 for 95% confidence interval (CI), p = "best guess" for prevalence and d = precision of the prevalence estimate.A recent study has indicated that about 28% of assessed rural women have beta thalassemia or HbE (7). This data provided that 988 samples would be enough for the study. However, assuming non-responding participants we included 1380 patients. Convenient sampling technique according to inclusion and exclusion criteria was used to include patients. Only proven anemic patients (Hb<12g/dL) were included in the study. Pregnant women and anemic patients due to chronic diseases (e.g. CKD, malignancy, etc.) were excluded.

2 ml intravenous blood samples were collected after obtaining informed consent using EDTA (ethylene diamine tetra acetic acid) as anticoagulants by disposable syringes and needles from each individual free of blood transfusions. The Sysmex XE-2100 system Hematology analyzer (Sysmex Corporation, Kobe, Japan) was used to determine peripheral cell count and red blood cell indices (RBC, Hb%, HCT, MCV, MCH, and MCHC) using standard procedure (6) that employed RF/DC detection method, hydrodynamic focusing, flow cytometry method and SLS-haemoglobin method.

Hemoglobin electrophoresis was carried out on CAPILLARYS 2 FLEX-PIERCING instrument uses the principle of capillary electrophoresis in free solution. With this technique, charged molecules are separated by their electrophoretic mobility in an alkaline buffer with a specific pH. Separation also occurs according to the electrolyte pH and electroosmotic flow (6).

All statistical analyses were carried out using SPSS statistical package (version 22.0). Analysis of variance (ANOVA) of the data was used to detect overall difference in group means. Differences among group means were assessed using least significant difference (LSD), p value <0.05.

RESULTS

A total of 1320 patients were included in the study. Their mean age was 22.6 (SD 13.5) years and 70% of the participants were female (Table 1).

Table 1: Age and sex distribution of the patients

Characteristics	N	%
Age (years)		
0-5	27	2.0
6-12	171	13.0
12-17	204	15.5
18-30	613	46.4
31-40	204	15.5
41-50	73	5.5
51-60	11	0.8
>60	17	1.3
Sex		
Male	395	29.9
Female	925	70.1

Among the enrolled patients, 389 (29.5%) had hemoglobinopathies. Hb E Trait was the most prevalent hemoglobinopathy (12%) followed by E-β-thalassemia (7.3%), β-thalassemia minor (6.6%) and Hb E disease (2.6%). Other hemoglobinopathies like α and β-thalassemia major, sickle cell disease etc. were quite rare (Table 2).

Table 2: Pattern of hemoglobinopathies among patients

Characteristics	N	%
No hemoglobinopathy	931	70.5
α-Thalassemia	1	0.1
β-Thalassemia major	1	0.1
β-Thalassemia minor	87	6.6
E-β-Thalassemia	96	7.3
E-β-Thalassemia trait	6	0.5
Hb E disease	34	2.6
Hb E trait	157	11.9
Hb Bart	1	0.1
Hb D	1	0.1
Sickle cell disease	4	0.3
Sickle cell trait	1	0.1

Patients with β-Thalassemia major and E-β-Thalassemia had most severe level of anemia (mean Hb level 6 g/dL and 6.96 g/dL respectively) while Hb E trait, Hb E disease and Sickle cell disease had mild to moderate level of anemia. Descriptions of different Hemoglobin band RBC related parameters are shown in Table 3 and Table 4 respectively.

Table 3: Hemoglobin types among different types of hemoglobinopathies

Hemoglobinopathy	Hb (g/dL)	Hb A (%)	Hb A2 (%)	Hb E (%)	Hb F (%)	Others (%)
No hemoglobinopathy	9.95 (2.60)	96.91 (6.98)	2.39 (1.14)	0.42 (4.48)	0.27 (2.52)	0.01 (0.25)
α-Thalassemia	10.00	48.00	1.00	0.00	51.00	0.00
β-Thalassemia major	6.00	4.00	4.00	0.00	93.00	0.00
β-Thalassemia minor	9.91 (2.11)	93.23 (9.94)	4.95 (0.83)	0.91 (6.11)	0.92 (4.16)	0.00 (0.00)
E-β-Thalassemia	6.96 (2.15)	16.73 (22.03)	4.68 (1.75)	50.2 (19.48)	28.17 (19.05)	0.11 (0.92)
E-β-Thalassemia trait	8.17 (4.07)	72.67 (37.13)	5.17 (0.75)	7.33 (17.96)	15.00 (22.61)	0.00 (0.00)
Hb E disease	9.88 (1.92)	9.15 (27.29)	5.00 (0.95)	83.6 (26.66)	2.15 (2.03)	0.06 (0.23)
Hb E trait	10.87 (2.14)	74.14 (9.41)	2.75 (0.66)	22.7 (9.33)	0.37 (2.01)	0.00 (0.00)
Hb Bart	9.00	98.00	2.00	0.00	0.00	0.00
Hb D	9.00	63.00	4.00	0.00	0.00	34.00
Sickle cell disease	9.75 (2.98)	0.25 (0.50)	2.50 (1.73)	14.7 (14.31)	3.75 (3.59)	79.00 (13.44)
Sickle cell trait	6.00	59.00	5.00	0.00	6.00	30.00

Table 4: RBC parameters among different types of hemoglobinopathies

Hemoglobinopathy	RBC	HCT	MCV	MCH	MCHC	RDW-SD	RDW-CD
No hemoglobinopathy	4.50 (0.74)	35.85 (7.00)	79.52 (11.45)	24.76 (5.46)	30.64 (3.28)	49.43 (167.74)	15.94 (4.36)
α-Thalassemia	3.00	29.00	98.00	32.00	32.00	66.00	19.00
β-Thalassemia major	3.00	27.00	97.00	33.00	34.00	54.00	15.00
β-Thalassemia minor	5.17 (1.11)	34.30 (6.65)	66.32 (11.59)	20.33 (3.84)	30.28 (3.08)	39.02 (8.12)	17.79 (3.61)
E-β-Thalassemia	3.70 (1.02)	23.83 (6.94)	64.14 (10.92)	19.14 (3.14)	29.60 (2.60)	50.54 (18.28)	28.32 (6.33)
E-β-Thalassemia trait	4.17 (2.40)	28.83 (13.43)	73.67 (19.06)	20.67 (3.93)	28.50 (3.14)	48.20 (16.67)	22.17 (7.65)
Hb E disease	5.38 (0.92)	31.26	59.71 (7.16)	18.56 (2.25)	31.03 (1.24)	35.00 (7.92)	19.76 (3.49)
Hb E trait	4.94 (0.86)	35.53 (6.01)	72.67 (8.66)	23.49 (6.28)	30.96 (1.86)	43.36 (30.90)	17.56 (12.45)
Hb Bart	4.00	30.00	82.00	26.00	32.00	40.00	13.00
Hb D	3.00	31.00	98.00	28.00	30.00	48.00	13.00
Sickle cell disease	4.25 (1.50)	30.25 (8.18)	75.25 (12.89)	23.75 (4.03)	32.00 (1.82)	47.50 (20.74)	17.50 (4.35)
Sickle cell trait	4.00	26.00	60.00	14.00	23.00	53.00	27.00

DISCUSSION

The prevalence of hemoglobinopathies among them was almost 30%.This finding corroborates with a study conducted among anemic patients in a hospital of Dhaka city which reported that 57.8% anemic patients had hemoglobinopathies(5). Another study has indicated that about 28% of assessed rural women of Bangladesh were sufferers or carriers of beta thalassemia or hemoglobin E disorders(7). Similar finding was reported by a population based study which reported that 11.89% of the adult population had β-globin gene mutations(8). An outpatient based study from neighboring India reported that 22% of the anemic children had some sort of hemoglobinopathies(9).

Hb E Trait was the most prevalent hemoglobinopathy (12%) followed by E-β-thalassemia (7.3%), β-thalassemia minor (6.6%) and Hb E disease (2.6%). Other hemoglobinopathies like α and β-thalassemia major, sickle cell disease etc. were quite rare among our included patients. A study conductedamong the anemic patients reported that the most common form of hemoglobin disorder was β-thalassemia minor (21.3%) along with E-β-Thalassemia and hemoglobin E trait. Other forms of hemoglobin disorders are hemoglobin E disease, hemoglobin D/S trait, β-thalassemia major, and δ-β-thalassemia (5).In West Bengal, the neighboring state of India, E- -Thalassemia, hemoglobin E trait and -Thalassemia were most prevalent hemoglobinopathies(9).

Patients with E-β-Thalassemia and β-Thalassemia major of our study were mostly suffering from severe form of anemia while patients with hemoglobin E trait and β-Thalassemia minor were mostly suffering from mild anemia. As E-β-Thalassemia and β-Thalassemia major are homozygotic disorders of β-chain of hemoglobin, production of hemoglobin is extremely low, resulting in severe anemia. On the other hand, the patients suffering from hemoglobin E trait and β-Thalassemia minor inherit one gene of β-thalassemia, they are manifested as either asymptomatic or mild to moderate anemia. Similar pattern of anemia was reported among thalassemia patients of Bangladesh in different studies (4,10,11).

Our study has several limitations. The study was a facility based study that included only the anemic patients visiting the study center, mostly for treatment of anemia. As a result, the anemia status and prevalence of hemoglobinopathies do not represent the community picture. Moreover, detailed socio-demographic, clinical and laboratory parameter data of the patients was not available.

CONCLUSION

The present study provides a bird's eye view about the prevalence and pattern of thalassemia and hemoglobinopathies among anemic patients of northern Bangladesh. Almost one third of the anemic patients were suffering from at least one type of hemoglobin disorder. Hb E Trait, E-β-thalassemia, β-thalassemia minor, and Hb E disease were the most prevalent

hemoglobinopathies.Further community based studies including detailed socio-demographic and clinical factors is suggested for the better understanding of the epidemiology of hemoglobinopathies in the respective region.

REFERENCES

1. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators [Internet]. Vol. 86, Bulletin of the World Health Organization. Bull World Health Organ; 2008 [cited 2020 Nov 16]. p. 480–7. Available from: https://pubmed.ncbi.nlm.nih.gov/18568278/

2. Weatherall DJ. The inherited diseases of hemoglobin are an emerging global health burden [Internet]. Vol. 115, Blood. Blood; 2010 [cited 2020 Nov 16]. p. 4331–6. Available from: https://pubmed.ncbi.nlm.nih.gov/20233970/

3. Hossain MS, Raheem E, Sultana TA, Ferdous S, Nahar N, Islam S, et al. Thalassemias in South Asia: clinical lessons learnt from Bangladesh [Internet]. Vol. 12, Orphanet Journal of Rare Diseases. BioMed Central Ltd.; 2017 [cited 2020 Nov 16]. p. 93. Available from: http://ojrd.biomedcentral.com/articles/10.1186/s13023-017-0643-z

4. Khan W, Khan WA, Banu B, Amin SK, Selimuzzaman M, Rahman M, et al. Prevalence of Beta thalassaemia trait and Hb E trait in Bangladeshi school children and health burden of thalassaemia in our population. Xmn polymorphisms in Bangladeshi thalassaemia patients View project Gestalt Diagnosis of Children with Intellectual disability with Dysmorphism-Necessity for Establishing Genetic Diagnostic Approach. View project Prevalence of Beta thalassemia trait and Hb E trait in Bangladeshi school children and health burden of thalassemia in our population [Internet]. 2005 [cited 2020 Nov 16]. Available from: https://www.researchgate.net/-publication/200176529

5. Uddin MM, Akteruzzaman S, Rahman T, Hasan AKMM, Shekhar HU. Pattern of β -Thalassemia and Other Haemoglobinopathies: A Cross-Sectional Study in Bangladesh . ISRN Hematol [Internet]. 2012 [cited 2020 Nov 16];2012:1–6. Available from: https://pubmed.ncbi.nlm.nih.gov/22778980/

6. T.H.J. Huisman JHPJ. The hemoglobinopathies: techniques of identification. Marcel Dekker, New York [Internet]. 1977 [cited 2020 Dec 11]; Available from: https://scholar.google.com/scholar_lookup?title=The Hemoglobinopathies%2C Techniques of Identification%2C Vol. 6&publication_-year=1977&author=Huisman%2CT. H. J.&author=Jonxis%2CJ. H. P.

7. Merrill RD, Ahmed Shamim A, Ali MBBS H, Labrique AB, Schulze K, Christian DrPH P, et al. High prevalence of anemia with lack of iron deficiency among women in rural Bangladesh: a role for thalassemia and iron in groundwater. Vol. 21, Asia Pac J Clin Nutr. 2012.

8. Noor FA, Sultana N, Bhuyan GS, Islam MT, Hossain M, Sarker SK, et al. Nationwide carrier detection and molecular characterization of β-thalassemia and hemoglobin e variants in Bangladeshi population. Orphanet J Rare Dis [Internet]. 2020 Jan 15 [cited 2020 Nov 16];15(1). Available from: /pmc/articles/PMC6961315/?report=abstract

9. Konar K, Karmakar A, Mondal BC. Clinico-hematological Pattern of Thalassemias and Hemoglobinopathies in Children Presenting with Microcytic Anemia: An Outdoor-based Study at Burdwan, West Bengal. Int J Curr Res Rev. 2018;10.

10. Karim MF, Hasan M, Shekhar HU. Hematological and biochemical status of Beta-thalassemia major patients in Bangladesh: A comparative analysis. Vol. 5, International Journal of Hematology-Oncology and Stem Cell Research. 2016.

11. Tahura S. Thalassemia and other Hemoglobinopathies in Bangladeshi Children.