ABSTRACT: BACKGROUND: Thalassaemia and other structural haemoglobinopathies are the major genetic disorders prevalent in certain parts of the world including India. This study presents the pattern of haemoglobinopathies amongst the referred patients of anaemia in an one year period. OBJECTIVES: To assess the clinical spectrum of Haemoglobinopathies in all patients above 12 yrs of age attending the Medicine Department. METHODS: A total of 100 patients were studied during a one-year period for anaemia investigation. Haematological indices, sickling test, haemoglobin electrophoresis with quantification of the bands and serum iron study was done in all cases. RESULTS: Out of 100 cases, 53(53%) were normal and 47(47%) cases had abnormal haemoglobin pattern. Of the 47 abnormal cases, 24(51%) were males and 23(49%) were females. Amongst the cases of hemoglobinopathies, there was a high incidence of HbE, (47%) of which 54% cases were HbE trait and 46% cases were of HbE disease. Apart from Hb E Variants, 21% cases of thalassemia minor , 15% cases of HbS were found of which 28% were HbS traits and 72% were HbS disease, 17% cases of HbE thalassemia was also found. CONCLUSION: It is suggested that haemoglobin electrophoresis should be carried out in all the high-risk groups with anaemia. There should be an initiative towards population screening, genetic counseling and prenatal diagnosis to counter the magnitude of problem.

KEYWORDS: Haemoglobinopathies, Anaemia, Thalassemia.

INTRODUCTION: Thalassemias and Haemoglobinopathies are the most common monogenic disorders of erythrocytes. India is the home of several Haemoglobin Variants causing much suffering to afflicted individuals and impose considerable financial, genetic, and psychosocial burden on family, society and nation at large.

The incidence of Haemoglobinopathies also differs in different parts of India. In Orissa HbS is very common, while in West Bengal Commonest Hemoglobinopathy is HbE Disease. Hb D punjab occurs with greatest prevalence in Sikhs (2%) in Punjab. ICMR study showed that that the HbE was mainly seen in Assam (23.9%) and Kolkata in West Bengal (3.92%).

The HbE gene has been detected across all the ethnic groups in Assam like the Ahom, Koch, Chutia, Muttock, Deori, Sonowal, and Mishing groups of North Eastern India. The highest incidence has been detected in the Bodo Kacharis an ethnic group speaking Tibeto Burma languages, although all have a common ancestry.

It is well established that that the incidence of HbE gene In the North Eastern India is the highest in the world. Different states of the North Eastern region show a variable incidence of HbE varying from 16.2% to 47.3%. A huge migrant tea garden population also shows a high incidence of Hb S.
Homozygous HbE, Heterozygous HbE, Sickle Cell Trait and β Thalassemia Trait are asymptomatic. However, the identification of these individuals is of crucial importance as they may be transmitters of abnormal gene giving rise to combination hemoglobinopathies and Thalassemias in their progeny which may be symptomatic and have high morbidity.\textsuperscript{13} They are generally not curable but can be prevented by population screening, genetic counseling and prenatal diagnosis.\textsuperscript{14} (R.S Balgir, 2000).

The present study was undertaken to create a profile of hemoglobinopathies referred to this hospital and comparing the results with other hospital based studies. As this is a Tertiary care Hospital which caters patients from all over the southern area of Assam, the study represents the pattern of hemoglobinopathies in this area.

MATERIALS AND METHODS:

**MATERIALS:** The present study, a hospital based study is conducted at the Silchar Medical College & Hospital. The samples were selected from the patients either attending the OPD of Medicine Department or admitted in the Medicine ward of Silchar Medical College & Hospital who are suspected of having haemoglobinopathy mostly on the basis of Peripheral blood film examination and complete blood count report and clinical examination of patients.

The catchment area of Silchar Medical College & Hospital consists of Silchar in Cachar District and the neighbouring Districts Hailakandi and Karimganj and also from the neighbouring States like Tripura, Mizoram and Manipur.

**Study Period:** The study is conducted from October 2013 to September 2014.

**Inclusion Criteria:**
1. Patient showing suggestive clinical features and various stigmata of hemoglobinopathies in complete blood count, Peripheral Blood Film and in other investigations.
2. Both male and female patient above 12 years of age and all religions are included.

**Exclusion Criteria:**
1. Patients less than 12 years of age.
2. Anaemia due to other causes.

**METHODS:**

**Collection of Blood:** Blood samples were collected either before any blood transfusion or after 1 month of blood transfusion to avoid any fallacious results. About 4-6 ml of blood was collected aseptically preferably from the antecubital vein with a sterilised syringe and about 2 ml were taken in a clotted vial for Iron assessment and 4ml of blood equally divided into 2 parts in K3 EDTA vial was sent for complete hemogram and hemoglobin electrophoresis. Peripheral blood smears were prepared from a fresh drop of blood.

**Haemoglobin Electrophoresis:** Haemoglobin electrophoresis was done in all cases by fully automated Sebia capillary electrophoresis machine. This machine can differentiate between 24 different haemoglobin variants.
Statistical Methods: Descriptive statistical analysis was carried out in the present study. Results on categorical measurements are presented in Number (%).

Statistical Software: The Statistical software SPSS 15.0 was used for the analysis of the data and Microsoft Office Word and Excel 2013 have been used to generate graphs, tables etc.

RESULTS:

A total of 100 cases were examined suspected to be having haemoglobinopathy on the basis of complete blood count and peripheral blood film examination and were taken up for capillary electrophoresis. A total of 47 cases were found to be having abnormal haemoglobins.

| Abnormal Haemoglobins   | Total No. of Cases | Percentage |
|-------------------------|--------------------|------------|
| HbE Trait               | 12                 | 26%        |
| HbE Disease             | 10                 | 21%        |
| HbE Thalessemia         | 8                  | 17%        |
| Thalassemia Minor       | 10                 | 21%        |
| Thalassemia Major       | 0                  | 0%         |
| HbS Trait               | 5                  | 11%        |
| HbS Disease             | 2                  | 4%         |

Table 1: Table Showing Percentage of different Haemoglobins
Table 2: Table Showing Age Distribution

| Age (In Years) | HbE Trait | HbE Disease | HbE Thalassemia | Thalassemia Minor | HbS Trait | HbS Disease | Total |
|---------------|-----------|-------------|-----------------|------------------|-----------|-------------|-------|
| 11 - 20       | 1         | 4           | 6               | 5                | 1         | 2           | 19    |
| 21 - 30       | 6         | 4           | 2               | 4                | 1         | 0           | 17    |
| 31 - 40       | 2         | 0           | 0               | 0                | 2         | 0           | 4     |
| 41 - 50       | 2         | 1           | 0               | 0                | 1         | 0           | 4     |
| 51 - 60       | 0         | 0           | 0               | 0                | 0         | 0           | 0     |
| 61 - 70       | 1         | 1           | 0               | 1                | 0         | 0           | 3     |

Table 3: Showing Gender Distribution of Hemoglobinopathies

| Haemoglobinopathies | Male | Female |
|---------------------|------|--------|
| Number | Percentage | Number | Percentage |
| HbE Trait | 6 | 50% | 6 | 50% |
| HbE Disease | 7 | 70% | 3 | 30% |
| HbE Thalassemia | 5 | 63% | 3 | 38% |
| Thalassemia Minor | 5 | 50% | 5 | 50% |
| HbS Trait | 1 | 20% | 4 | 80% |
| HbS Disease | 0 | 0% | 2 | 100% |
| Total | 24 | 51% | 23 | 49% |
PRESENTING SIGNS AND SYMPTOMS: Generalized weakness with easy fatiguability was the commonest presenting symptom being present in all 100% of Patients with haemoglobinopathies. Exertional Dyspnoea was the next most common complaint. It was present in 25% of pts with HbE Trait and 40% pts of HbE Disease, 20% pts of Thalassemia Minor, 50% pts of HbE Thalassemia and in 1 pt of HbS Disease. Palpitation was complained of by 30% pts of HbE Disease and 50% pts of HbE Thalassemia and in 1 pt of HbS Disease. Giddiness was found in 30% of pts with HbE Disease and 50% pts of HbE Thalassemia.

Pain abdomen was complained by 50% pts. with HbE Thalassemia and HbS Disease. Swelling of feet was complained of by 25% pts. of HbE Thalassemia and 1 pt. of HbS Disease. Yellowish Discolouration of Sclera was seen in 40% pts. of HbE Disease, 50% pts of HbE Thalassemia and in one pt. of HbS Disease.

Pallor was present in all the pts examined with Haemoglobinopathies. Icterus was the next most common sign found in the patients. It was present in 50% pts of HbE Thalassemia and 1 pt of HbS Disease, 25% pts with HbE Trait, 40% pts of HbE Disease and 30% pts of Thalassemia Minor. Pedal Oedema was present in 50% pts oh HbE Thalassemia. Splenomegaly was seen in 20% pts of HbE Disease, 100% pts of HbE Thalassemia and in 1 out of 2 pts of HbS Disease. Hepatomegaly was seen in 20% pts of HbE Disease, 20% pts of Thalassemia Minor and 50% pts of HbE Thalassemia and 1 pt of HbS Disease. Leg ulcers were not seen amongst any pt of Haemoglobinopathy. A total of 3 cases of cholelithiasis were found where 1 case of HbE Disease and 2 cases of HbE Thalassemia were found. 1 case of HbE Thalassemia was found to have hair on end appearance on Skull X-Ray.

DISCUSSION: In the present study out of 100 suspected cases of haemoglobinopathy 47(47%) had abnormal Hemoglobin. Amongst the 47 cases of hemoglobinopathies 22(47%) had HbE of which 12(26%) cases were HbE trait and 10(21%) cases were of HbE disease. Apart from Hb E Variants, 10(21%) cases were of thalassemia minor, 7(15%) cases of HbS were found of which 2 were HbS traits and 5 were HbS disease. The results of the present study is consistent with the study by M. Baruah et al. HbE thallassemia in 8(17%) cases of present study is consistent with study of B. M. Jha et al. The incidence of Sickle cell Trait in (11%) is high because there is an abundance of Tea Garden...
population in the catchment area of Silchar Medical College. The incidence of Thalessemia Minor was 21.27% and this is consistent with the study done by Machumi Saikia Pathak et al.\textsuperscript{17}

**PERCENTAGE OF HEMOGLOBINOPATHIES:**

| Authors            | Hb E Thal | Thal. Minor | HbS Trait | HbS Disease |
|--------------------|-----------|-------------|-----------|-------------|
| B. M Jha et al.\textsuperscript{16} 2011 | 14.28%     | -           | -         | -           |
| Mauchumi Pathak.\textsuperscript{17} et al, 2014 | -          | 18.12%      | -         | -           |
| M. Baruah et al.\textsuperscript{15} 2014 | 1.26%      | 3.48%       | 2.10%     | 2.26%       |
| Present Study, 2014 | 17%        | 21%         | 10.63%    | 4.25%       |

**AGE DISTRIBUTION:** In the present study HbE cases were found mostly in the age group of 21-30 yrs. This is consistent with the study done by B.M Jha et al.\textsuperscript{16}

**SEX DISTRIBUTION:** The total percentage of affected males was 51% and affected females were 49%. HbE Disease was predominantly seen in males (70%) while there was equal distribution of disease amongst the males and females in HbE Trait. A study done by B. M Jha et al.\textsuperscript{16} shows all most similar sex distribution. In the present study all cases of Sickle cell disease and 4 out of 5 cases of Sickle cell Trait were found only in female .In a study of Sickle cell disease done by BalK. Sharma,\textsuperscript{18}(2011) 56% females and 44% males were affected, showing slight female preponderance In the study by Kasturi Chiklikar,\textsuperscript{19}(2014) on Sickle cell trait, females (72.34%) outnumbered males (27.65%). Wintrobe,\textsuperscript{20} also states high incidence of Sickle cell trait in female.

**PRESENTING SIGN AND SYMPTOMS:**

**Symptoms:** Generalized Weakness (100%), Easy Fatigability (100%), Dyspnea on Exertion (50%) and Palpitations (50%) were the commonest presenting symptoms. High incidence of generalized weakness in patients with haemoglobinopathies was reported by Mauchumi Saikia Pathak.\textsuperscript{17} Other symptoms seen in her study were abdominal pain, Joint pain and fever of which abdominal pain was seen in 11.11% pts of Hb E Thalassemia.

**Signs:** Pallor was present in all the 47 cases of Hemoglobinopathies. (100%) Icterus was found in 25% of HbE trait, 40% case of HbE disease, 30% cases of thalassemia minor, 50 % cases of HbE thalassemia cases, 20% of cases in HbS trait and 50 % of HbS disease cases. Mehta et al.\textsuperscript{21} reported jaundice in patients with HbE Thalassaemia. Chernoff et al.\textsuperscript{22} found jaundice in HbE Disease.

Splenomegaly was found in 100% cases of HbE thalassemia which is consistent with observations of S. Agarwal et al.\textsuperscript{23} and Mauchumi Saikia Pathak.\textsuperscript{17} Splenomegalyt was also found in 2 cases of HbE disease and 1 case of Sickle cell disease. DeGruchy (1976) mentioned that splenomegaly may be a common feature in HbE disease.

In the present study, Hepatomegaly was found in 2 cases of Thalassemia Minor and HbE Disease, 1 case of Sickle cell Disease and in 50% cases of HbE Thalassemia (50%) and similar incidence was reported by Muchumi Saikia Pathak.\textsuperscript{17} In a study of HbE Thalassaemia, Mehta et al.\textsuperscript{21} (1980) found hepatomegaly in all the cases.
CONCLUSION: From the present study it is concluded that patient who has symptom like generalised weakness, easy fatigability, dyspnoea on exertion, palpitation with anaemia, splenomegaly, jaundice should be investigated for haemoglobinopathy. The spectrum of abnormal haemoglobin in the patient from the catchment area of Silchar Medical College is as HbE trait 26%, HbE disease 21%, Thalassemia 21%, HbE thalassemia 17%, HbS trait 11%, HbS Disease 4%.

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