

# Spectrum of Hematological Diseases in West Bengal, India: Experience from a Tertiary Care Center

Ankit Jitani, Prakas Kumar Mandal\*, Prantar Chakrabarti, Shuvra Neel Baul, Rajib De, Tuphan Kanti Dolai

## ABSTRACT

**Background:** The epidemiology of hematological diseases in India is largely unknown due to paucity of data. Our centre caters to a major chunk of hematological patients in Eastern India and is one of the largest centers in terms of patient attendance. **Objective:** The objective of this study was to analyze the OPD data to decipher the hematological disease spectrum in Eastern India. **Methods:** Hospital data of hematology OPD from July 2015 to June, 2018 was retrieved from the hospital information management system. The number of new and follow-up (old) patients attending the OPD were analyzed to know the disease pattern in terms of various benign and malignant hematological disease was assessed. **Results:** The total number of OPD consultations for the three years was 78809, of which 21851 (27.7%) were new cases and 56958(72.3%) were follow-up (old) visits. Disease characterization could be done for 15517 (71.01%) patients; out of these, 73.3% (11377/15517) were benign and 26.7% (4140/15517) were malignant hematological diseases. Common reasons for consultation in hematology OPD were anemia 9170 cases (59.1%), leukemia 2544 (16.4%), bleeding disorder 1908 (12.3%), lymphoma 946 (6.1%) and myeloma 450(2.9%). Among the benign diseases, most common diagnosis was nutritional deficiency anemia 4403 (38.7%) followed by hemoglobinopathy 3868 (34%), immune thrombocytopenia 944 (8.3%), aplastic anemia 694 (6.1%), hemophilia 637 (5.6%), eosinophilia 148 (1.3%) and thrombosis 80 (0.7%). Among the malignant cases, common causes were leukemia 2351 (56.8%), lymphoma 940 (22.7%) and myeloma 451 (10.9%). **Conclusion:** Anemia remains the most common reason for OPD consultation even in a tertiary care hematology centre. The major burden of malignant hematological disease is leukemia.

**Key words:** Tertiary Care Center, Hematology Disease, Spectrum.

## INTRODUCTION

India is a country with a population of 1.21 billion as per the 15<sup>th</sup> National Census Survey in 2011.<sup>1</sup> Considering the population load and diversity, prevalence of hematological diseases in India should be alarming. However, the distribution of these diseases in our country is largely unknown. The reason for this may be multifactorial. Firstly, there are not many dedicated set-ups providing hematology services to the population. Secondly, the field of hematology has evolved tremendously over recent years; advanced laboratory and molecular diagnostic techniques has become imperative in making precise diagnosis, the facility for which are either not available or not accessible to our population especially those coming from distant rural areas. Thirdly, the health services are offered by multiple stakeholders. Public sector is overwhelmed with huge patients load and not many centers are able to maintain adequate data and private sector, which comes at a cost and are available to only a particular segment of the society.<sup>1</sup>

The center at which this study was conducted is a state government set-up providing dedicated hematology services to the people of West Bengal as well

as the neighboring states in Eastern India. It is one of the largest centers in terms of patient attendance in this region. Due to the availability of a good laboratory diagnostic facility, most of the patients are offered a concrete diagnosis with precise disease characterization, which makes the analyses of the disease spectrum possible. There is dearth of data pertaining to the distribution of the hematological disease in this region and the morbidity as well as mortality associated with the malignant as well as the benign hematological disease, especially disease with a genetic basis, is immense. Hence, the hospital data of a tertiary level hematology facility was analyzed to gauge into the spectrum of patients visiting health care facility for consultation pertaining to hematological issues. The aim was to analyze the pattern and distribution of hematological disease in Eastern India in general and the state of West Bengal in particular.

## MATERIAL AND METHODS

This was a descriptive study undertaken in the department of Hematology, Nilratan Sircar Medical College and Hospital. This hospital is located in the

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central part of the metropolitan city of Kolkata next to a major railway station and caters to the healthcare needs of not only the state of West Bengal but the neighbouring state and country. OPD services are provided for five days in a week, which includes a dedicated hemoglobinopathy clinic, hemato-oncology clinic and bleeding disorder clinic and on a given day, he number of patient visiting the OPD varies from 150 to 250 cases. The study was undertaken for a period of three years from July 2015 to June, 2018. Out-patient data from the hospital information system was retrieved and the number of new and follow-up patient attending our OPD for the period was retrospectively analyzed. All patients visiting the OPD for consultation during the study period for any reason was included. A patient visiting the OPD on multiple occasion was considered a single case during data analysis. For representation of distribution of disease, the cases for which concrete diagnosis could be confirmed by necessary investigations were included and cases that could not be characterized in any disease entity, either due to failure of the patient to follow-up or due to refusal to undergo a diagnostic procedure were excluded from the study. The institutional ethical committee clearance was obtained prior to data collection.

The patients were divided into new patients coming for first consultation and follow-up patients and expressed in terms of percentage. The number of new patients for whom disease characterization could be done was calculated. Among all these patients who were characterized, the disease distribution of benign and malignant condition was done in terms of percentage. Among the benign diseases, distribution of anemia of different types, hemoglobinopathy, bleeding disorder including platelet and coagulation disorder and other rare condition like thrombosis and eosinophilia were analyzed. Among the malignant conditions, we analyzed the data in terms of leukemia, lymphoma, myeloma and other rare conditions. Results were expressed in terms of absolute number or percentage.

## RESULTS

The data represented all age group of patients, including pediatric, adolescents, adult and geriatric age group. The total number of OPD visits in 3 years was 78809, out of which 21851 (27.7%) were new cases and 56958 (72.3%) were follow-ups. Among the new cases, disease characterization could be done for 71.01% (15517/21851) patients. Out of these cases, 73.3% (11377/15517) were benign and 26.7% (4140/15517) were malignant hematological diseases. Common reasons for consultation in hematology OPD, as shown in Table 1, were anemia 9170 (59.1%), leukemia 2351 (16.4%), bleeding disorder 1908 (12.3%), lymphoma 940 (6.1%) and myeloma 451 (2.9%).

Among the benign diseases, the most common diagnosis was nutritional anemia 4403 (38.7%) of which iron deficiency were 3698 (32.5%) and rest 705 (6.2%) were combined nutritional deficiency anemia hemoglobinopathy 3868 (34%) was the next common cause of anemia. Among them, 2412 (62.38%) were homozygous or compound heterozygous and 1456 (37.62%) were heterozygous. The distribution of hemoglobinopathy is shown in Table 2. The most common major phenotype was HbE $\beta$ -thalassemia which comprised 1318 (34.08%) of all hemoglobinopathies followed by  $\beta$ -thalassemia major at 722 (18.67%). HbEE homozygous were the next common with 305 (7.88%) and rest 68 (1.76%) were others consisting of HbSS and other compound heterozygous. Among the traits, 723 (18.69%) were  $\beta$ -thalassemia trait and 604 (15.62%) were HbE trait. HbS trait and HbD trait comprised 87 (2.24%) and 11 (0.27%) respectively and rest 19 (0.49%) were others including  $\delta\beta$ -thalassemia trait and HPFH heterozygous. Other hemolytic anemia comprised 318 (2.8%) cases, among which the most common diagnosis was autoimmune hemolytic anemia 171 (1.5%) and rest of the 147 (1.3%) cases included membranopathies, enzymopathies and other rare causes of hemolytic anemia.

**Table 1: The overall disease pattern of patients visiting hematology out-patient clinic.**

Disease type	Number of cases (n = 15517)	Percentage distribution
Anemia	9169	59.09%
Leukemia	2548	16.42%
Bleeding disorder	1889	12.17%
Lymphoma	941	6.06%
Myeloma	450	2.9%
Eosinophilia	109	0.7%
Splenomegaly (unclassifiable hematologically)	97	0.62%
Thrombotic disorder	79	0.5%
Others	225	1.45%

**Table 2: Distribution of hemoglobinopathy cases (n= 3,868).**

Type of hemoglobinopathy	Overall distribution	Sub-category distribution
Homozygous and compound heterozygous		62.38%
HbE $\beta$	34.08%	54.64%
$\beta$ -thalassemia major	18.67%	29.92%
HbE disease	7.88%	12.62%
Others	1.76%	2.81%
Heterozygous		37.62%
$\beta$ -thalassemia trait	18.69%	49.69%
HbE trait	15.62%	41.52%
HbS trait	2.24%	5.97%
HbD trait	0.27%	1.50%
Others	0.49%	1.30%

Aplastic anemia was the next common cause of anemia with 693 (6.1%) cases and it was the most common cause of pancytopenia requiring OPD consultation. Among the bleeding disorder, the most common entity was immune thrombocytopenia 944 (8.3%), followed by hemophilia 637 (5.6%) and other rare bleeding disorders 227 (2%). Among hemophilia, 87.3% were hemophilia A and 12.7% were hemophilia B. The other rare entities comprised cases of eosinophilia 148 (1.3%) and deep vein thrombosis in 80 (0.7%).

Among the malignant diseases, leukemia far exceeded the other malignancies comprising 2351 (56.81%) of the total 4140 cases. Acute leukemia comprised 1312 (31.7%) of all hematological malignancies and 55.78% among all leukemia. Among the acute leukemias, ALL was more common with 780 (59.5%) compared to AML (excluding APML) which comprised 457 (34.83%), while APML comprised 58 (4.4%) of all leukemia. Other rare variant like mixed phenotypic leukemia were 17 (1.2%). CML and CLL comprised 902 (21.8%) and 137 (3.3%) of all malignant cases and 38.48% and 5.74% of the leukemia cases respectively (Table 3). MPN were 194 (4.7%) of all hematological malignancies. Lymphoma was the 2<sup>nd</sup> most common malignant disorder with 940 (22.7%) cases among which non-Hodgkins lymphoma cases were 490 (52.2%) and Hodgkins

**Table 3: Distribution of different types of leukemias among all hematological malignancies (n=2,351).**

Leukemia types	Overall distribution among all malignant cases	Distribution of cases among all leukemias
<b>Acute Leukemia</b>	<b>31.67%</b>	<b>55.78%</b>
AML (excluding APML)	11.03%	19.45%
APML	1.40%	2.47%
ALL	18.86%	33.19%
Others	0.38%	0.67%
<b>Chronic leukemia</b>	<b>25.1%</b>	<b>44.22%</b>
CML	21.8%	38.48%
CLL	3.3%	5.74%

lymphoma were 450 (47.8%). Rest of the malignant cases were multiple myeloma 451 (10.9%), MDS and MDS/MPN 161 (3.9%).

## DISCUSSION

The HMIS data of the Hematology department for three years from June 2015 to July 2018 was collected and analyzed with the aim to understand the distribution of hematological diseases in the population visiting the OPD of haematology department of a tertiary hospital. Disease characterization could be done for 71% of the patient visiting for consultation. Rest of the 29% cases included patients for whom a precise hematological diagnosis could not be made that included patients who either did not follow-up after the first/second visit and hence diagnosis could not be confirmed, or patients who refused a diagnostic procedure/investigation, or cases that were referred to the hematology OPD from other speciality and superspeciality departments for procedural fitness or for complete blood count and or coagulation profiles or advice for other hematological tests which are done in our departmental laboratory.

The most common reason for consultation in the hematology OPD was anemia at 59.1% with nutritional anemia being the most common cause. According to WHO, there are two billion people with anemia in the world, with half of the anemia due to iron deficiency.<sup>2</sup> In South East Asia, 66% children, 60% women and 36% men are anemic.<sup>3</sup> In India, the NHFS-4 data showed that the prevalence of anemia among children of 6 to 59 months age was 58.5% and among adult (15 to 49 years) male and female were 22.7% and 53% respectively, while in West Bengal, the prevalence among children, adult male and female were 54.2%, 30.3% and 62.4% respectively.<sup>4</sup> In another study from North India, the prevalence of anemia was 69.6% with 31% cases being iron deficiency anemia.<sup>5</sup> In the present study, 32.5% of the patients were iron deficiency anemia while 6.2% were due to combined nutritional deficiency. Malnutrition is a major cause of nutritional anemia in our country. A study done in the school going children in West Bengal showed that 40% of the adolescent were malnourished and 40% showed the presence of clinical pallor.<sup>6</sup> Strategies like fortified food and nutrition supplements may help to control this public health problem. This data however do not represents the community and hence it is not reflective of the disease prevalence, but does emphasize that anemia is the most common reason for OPD consultation even in a tertiary care center and community level screen and preventive strategy needs to be strengthened to reduce the disease burden. In a large population based survey of hemoglobinopathy in West Bengal, it was shown that hemoglobinopathy is present in 12.17% cases and  $\beta$ -thalassemia trait was the commonest found in 4.60% patients followed by HbE trait (3.02%),  $\beta$  thalassemia major/intermedia (1.66%) and E $\beta$  thalassemia (1.16 %) cases.<sup>7</sup> A community based study of 50,487 cases showed that the distribution of heterozygous thalassemia was 10.26%, with  $\beta$ -trait and HbE trait being the common entities with 6.61% and

2.78% cases; and homozygous and compound heterozygous cases were 1.36%, with  $\beta$ -thalassemia major and HbE $\beta$  with 0.73% and 0.42% cases being the most common.<sup>8</sup> Another study from Eastern India, tried to look into the prevalence of hemoglobinopathies in the rural population of West Bengal and found that  $\beta$ -thalassemia trait was the most prevalent and was found in 10.38% cases, followed by HbE trait in 4.30%, sickle cell trait in 1.12% and Hb D trait 0.37%.<sup>9</sup> Hemoglobinopathy was the second most common reason of OPD consultation with 34% cases. There are multiple reasons for such high patient load of hemoglobinopathy patients visiting the OPD, mostly comprising of transfusion dependent thalassemia. Firstly, our center is a Nodal Center for the State Thalassemia Control Program and run a dedicated OPD once a week for thalassemia, where patient turn-out ranges from 220-250 per OPD. Second, it being a referral center for thalassemia management, the major patient load comprises of transfusion dependent thalassemia including E $\beta$  thalassemia and  $\beta$ -thalassemia major. Third, the distribution of homozygous state far exceeds heterozygous conditions as this is a hospital based data where mostly symptomatic patient comes for consultation and the heterozygous thalassemia are mainly cases that are referred from other specialty/super speciality departments and from different districts and sub-divisional hospitals for evaluation of anemia. This pattern is unlike the community based study data where the asymptomatic heterozygous thalassemia far exceeds the homozygous patients.<sup>8-9</sup> The distribution of nutritional anemia and thalassemia in our data is almost equal. The reason for this nearly similar distribution may be that the nutritional deficiency anemia are treated by other government and private hospitals in the region and also by other departments of our institute, but there are only a few centers managing hemoglobinopathy in this part of the country. Most of the suspected hemoglobinopathy attend OPD for diagnosis, which increases the percentage of this condition explaining the nearly similar distribution of thalassemia and nutritional anemia. The data aptly reflects thalassemia as a major disease burden in this part of India, emphasizing on the need to strengthen the screening program as well as prenatal diagnosis, to reduce the burden of transfusion dependent thalassemia.

With regard to inherent bleeding disorder, Manisha M *et al.*<sup>10</sup> evaluated the spectrum in Western India. In their cohort, 95.3% of the patients had coagulation disorder, of which Hemophilia A comprised 70.5% of the cases, followed by Hemophilia B (14%) and vWD (10.8%). Rest of the bleeding disorders was inherent platelet disorder. In our cohort, the most common cause of bleeding disorder was immune thrombocytopenia with 52% cases, followed by hemophilia with 32% cases, of which Hemophilia A comprised 87.3% cases and Hemophilia B included 12.7% cases. Rest of the bleeding disorder were other rare bleeding and coagulation defects like vWD, functional platelet defects and other rare coagulation factor deficiency and acquired defects of coagulation. We provide on-demand therapy to hemophilia patients and prophylaxis is limited to children, mainly due to limited resources. This prophylaxis program is supported by the World federation of hemophilia and hemophilia federation of India. The present data could have profound implication in terms of increasing the scope of prophylaxis to adults as well, increasing awareness among health care providers in terms of hemophilia management and increasing the number of centers providing hemophilia care, which will reduce the morbidity in the patients in long run. Shirley MH *et al.*<sup>11</sup> in a UK based study looked into the distribution of hematological malignancies in various ethnic groups including Indian. In their data leukemia comprised 31.4% and lymphoma 68.6% in patients overall and among the Indian populations, leukemia comprised 24.8% cases and lymphoma 75.2% cases. In a hospital based data from the neighboring country of Bangladesh, the distribution of AML was 28.3%, ALL was 14.1%, lymphoma was 20.8%, CML was 18.2%, multiple myeloma was 10.5% and CLL was 3.7%.<sup>12</sup> The present data shows a similar distribution of myeloma and lymphoma but a higher load of acute leukemia. This is probably because of increased number of cases referred from the neighboring areas for diagnosis and manage-

ment due to the availability of the facilities at our center. Also, there are a number of oncology centers which manage lymphoma and myelomas, but the acute leukemias are mostly referred to institutes specializing in the management of these disease and there are a handful of such institutes in this part of India, thus increasing the load of acute leukemia. Another interesting difference was the distribution of acute leukemia which was markedly different, with ALL being predominant in the present data, unlike AML in theirs. APML is regarded as one of the most curable form of acute leukemia. In the present study, APML comprised 11.26% of all AML cases. This is similar to the reported incidence of 10-15% of APML among all the AML cases.<sup>13</sup> The only way to look into the prevalence of these hematological malignancies is hospital based data from the specialized centers managing these disease. There is not much data available from eastern India which reflects the incidence and prevalence of the malignant hematological disease. The present data shows that the incidence of hematological malignancy in this region is staggering. Strengthening the resource, both infrastructure and human and increased numbers of specialized centers catering to these patients are required to manage them and provide quality services to the population. The importance of knowing the distribution serves multiple purposes. Firstly, by knowing the pattern, proper health care planning and budget allocation for better patient management is possible. Due to evolution in diagnostic tool and management with targeted therapies, hematology services have become expensive and not widely accessible and available. By knowing the disease pattern, planning in terms of diagnostic and treatment facilities required for managing the patient may be done. Secondly, nutritional anemia is the most prevalent cause of anemia in our data, targeted community screening for these deficiency may help in reduction of the disease burden, reducing the morbidity in the population, especially in the pediatric, geriatric, pregnant and nursing mothers. Thirdly, for genetic conditions like thalassemia and hemophilia community screening to detect carriers may be undertaken. Sate thalassemia control program under the aegis of government of West Bengal is trying to do the same in the field of thalassemia.

The limitation of the study is that this is a hospital based data and it cannot be used to extrapolate the incidence of the disease in the community. Benign diseases may be screened at the community level and rightly so, being done for diseases like nutritional deficiency and hemoglobinopathy. But community level screen is not possible for malignant disease and hospital based data remains the only way to look into the disease incidence and prevalence, explaining the importance of hospital based data in planning the infrastructure required for the management of the patients

## CONCLUSION

Hematological disease is highly prevalent in the community and data regarding distribution of the same is sparse in our country. The number of centers providing hematological services is also limited. Advanced diagnostic tool required for correct diagnosis and management makes the precise diagnosis difficult in centers that lack adequate facility. Benign hematological disease comprise a major disease burden and community level awareness is required to decrease this load. Hospital based data is probably the only way to gauge into the prevalence of malignant hematological disease and the present data show that high prevalence of the same in this region. These diseases are associated with high morbidity and mortality and to control them early diagnosis and management is imperative for which more number of centers providing quality care as well as increase in the health care expenditure to manage these diseases are required. We hope this will turn into reality in future with proper planning and public-private partnership.

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## CONFLICT OF INTEREST

The authors declare no conflict of interesting.

## ABBREVIATIONS

**OPD:** Out-patient department; **HMIS:** Hospital management information system; **ALL:** Acute lymphoblastic; **AML:** Acute myeloid leukemia; **APML:** Acute promyelocytic leukemia; **CML:** Chronic myeloid leukemia; **CLL:** Chronic lymphocytic leukemia; **MPN:** Myeloproliferative neoplasms; **MDS:** Myelodysplastic syndrome; **MDS/MPN:** Myelodysplastic syndrome/Myeloproliferative neoplasm; **NFHS-4:** National Family Health Survey 4; **vWD:** von Willebrand disease.

## SUMMARY

This study presents the spectrum of hematological disease in a tertiary care center. Anemia remains the most common reason for consultation in the OPD, most of which are secondary to nutritional deficiency and thalassemia. The proportion of malignant hematological disease is staggering and number of centers required to treat the patients are lacking. This data reflects urgent need of expansion of infrastructure to deal with these diseases.

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