



## Clinico Epidemiological Profile of Children- With Hemophilia in South Kerala

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### ABSTRACT

**Objective:** to document the clinic epidemiological profile of children with hemophilia in south Kerala.

**Methods:** observational prospective follow up study. 60 simultaneous children who attended SAT hemophilia clinic were included in the study. Data collected using predesigned questionnaire and clinical assessment. The variables include type of hemophilia, factor level, age of first bleed, type of first bleed, types of past bleeding, family history etc. inhibitor screening was done in each patient.

**Results:** 60 children were included in the study. Majority were found to be hemophilia A & out of them majority are severe. Most of them presented in the first half of infancy with skin and subcutaneous bleeding as the most common presentation. Only 30 % give positive family history. Only 4 of them were inhibitor positive.

**Keywords:** Hemophilia A and B, Inhibitors.

### Introduction

Genetic disorders even though are of low public priority in India, accounts for significant morbidity for patients and their family members. Though the government is supporting them via various schemes, the social and economic impact of the disorder are huge for the patient. One recent study suggest a significant burden of Thalassemia in India <sup>(1, 2)</sup>. For other genetic disorders like hemophilia cystic fibrosis etc. there are limited systematic epidemiological data. Due to its demographic characteristics, in absolute numbers, genetic disorders may affect significant numbers of individuals in India. India has the largest birth cohort globally, with 27 million new births in 2014 <sup>(3)</sup>. The country has the second largest global population of 1.21 billion <sup>(4)</sup> and a high birth rate of 21.8 <sup>(5)</sup>. As genetic disorders arise in the

population through spontaneous mutations and through affected births, in families with known risk of genetic disorder, in absolute numbers, the birth prevalence of genetic disorders is likely to be high in India.

Bleeding disorders reportedly affect 1 in 1000 men and women globally <sup>(6)</sup>. Most of them affect males as most of these disorders are x-linked recessive in nature. Hemophilia A and B <sup>(7,8,9)</sup> and von-willebrand disease make up most of these disorders. Hemophilia A and B are single gene disorders, occurring due to mutation in either coagulation factor VIII or coagulation factor IX gene. Their deficiency leads to bleeding tendency. They are divided into three groups depending on the factor level. Mild hemophilia means factor level of 5-40%, moderate means 1-5%, severe means <1 %. The frequency and the severity of

bleeding depends on whether they are mild, moderate or severe. Patients with severe hemophilia A Constitutes around 70% of the patients with bleeding disorders. Most common symptoms of hemophilia are Spontaneous bleeding, hematomas, hemarthrosis, hematuria, soft tissue bleeding including life threatening bleeds of the CNS, oral bleeds etc. Frequency depends on severity and genotype

Due to methodological challenges of studying rare disorders, it is difficult to approach genetic disorders from an epidemiological perspective and explore prevention. This review on hemophilia tries to determine the available information on the reported number of haemophilic children in south Kerala. SAT Hospital being a tertiary care centre caters to most of the bleeding disorders from south Kerala, and we are running a clinic exclusively for hemophilic children here.

## Methods

Observational prospective follow up study

## Study Setting

Hemophilia clinic, SAT hospital, Medical College, Trivandrum

## Sample Size

From the available records we presume there are 50-60 hemophilic children in south Kerala (as per haemophilic society records).we would like to collect the clinicoepidemiological details of these children.

**Table: 1** Severity of hemophilia

variable	Category	Severity			Total
		Mild	Moderate	Severe	
Type of Hemophilia	A	1	8	43	52
	B	1	4	3	8
TOTAL		2	12	46	60

29 children (48.3%) had their first bleed in infancy. Out of these 2 children presented in newborn period, one with umbilical stump bleeding and one with intracranial haemorrhage. Rest 27 children had their first bleeding in second half of infancy. 20 children (33.3%) presented

## Tools

Data collected using interview utilizing semi structured questionnaire and clinical Assessment

## Data Collection

Every child registered in haemophilia clinic was enrolled in the study, after getting informed consent. Using a predesigned schedule history was taken. Inhibitor screening was done in all children.

## Study Variables

- Number of patients
- Type of hemophilia with severity
- Number of patients with inhibitors
- Age of first bleed
- Type of first bleed
- Types of past bleed
- Level of factor in each patient

## Results

Total no of children included were 60. As haemophilia is an x-linked disorder all are males. There were 7 children below 3 years, 2 children between 3&6 years, 18 children between 6&9 years and 28 children above 9 years. Out of 60, 52 children were diagnosed to have Hemophilia A (86.7%) and 8 were Hemophilia B (13.3%). Among 52 children with Hemophilia A 43(82%) were of severe variety, 8 were moderate (15.4%) & 1 (3%) mild. Among 8 children with Hemophilia B, 3 (37.5) belong to severe variety, 4(50%) were moderate & 1 (12.5%) mild. (Table 1)

between age 1 and 3. 8 children (13.3%) had their first bleed between 3 and 6 years. 3 children (5.9%) presented for the 1<sup>st</sup> time after the age of 6 years. (Table 2). 22 (36.7%) children had skin and subcutaneous bleed as their initial presentation. 16 (26.7%) children presented initially with

Gum bleeding/Epistaxis.10 (16.7%) had muscle bleeds initially.8 children (13.3%) had joint bleeds initially.2 children (3.3%) had intracranial bleeds. One child presented with umbilical stump bleeding.

**Table 2.** Age distribution of 1<sup>st</sup> bleed

variable	Age	Frequency	Percentage
Age distribution of 1 <sup>st</sup> bleed	<1.0	29	48.3
	1.0 – 2.9	20	33.3
	3.0 – 5.9	8	13.3
	>6.0	3	5
	Total	60	100

28.3% of children give a positive Family History of Bleeding Disorder. 77.7% had no Family History. Regarding inhibitors in our study 4 out of 60 children are found to be inhibitor positive. All of them belong to Hemophilia A. Unfortunately one of them died during study period due to repeated intracranial haemorrhage.

### Discussion

In our study majority (86.7%) of children were found to be Hemophilia A and (13.3%) were Hemophilia B. This is similar to the study by Kulkarni et al <sup>(12)</sup> who found that majority (81%) of their hemophilia patients belongs to A type & rest were hemophilia B (19%). In the Maharashtra <sup>(10)</sup> study the ratio of hemophilia A: B is 4.2:1. In our study 76.7% of patients belong to severe variety where as 20 % are moderate & 2.3% mild. In the US cohort <sup>(13)</sup> 65 % belong to severe variety & 22.5 % belong to moderate. Regarding age of first presentation Charles et al states that age of first bleed vary from 1 week to 12 years. 8 of their cases presenting in infancy & 25 between 1 & 5 years. In our study 48 % of children presented in infancy 33% presented between 1 & 3 years'

Considering type of first bleed 36,7% of our children had skin / subcutaneous bleed as first presentation, 26.7 had gum bleeding & 13.3 % had joint bleed. 18,7% had initial muscle bleeds.

Charles et al states <sup>(11)</sup> that majority of their study group also had skin/subcutaneous bleed as initial presentation. 3 were detected due to bleeding

following circumcision, 2 following head trauma 1 having multiple hematoma.

28% of our children give positive family history were as 77 % had no family history. This is in sharp contrast to western studies which shows 66% having positive family history. This may be due to poor detection facilities and lack of screening.

One of the complications of replacement therapy is the development of allo -antibodies called inhibitors. These IgG molecules neutralize clotting factor concentrates so that clotting factors become ineffective. literature shows 25 to 33 % of hemophiliacs becoming inhibitor positive during their life time. We have 4 out of 60 who showed inhibitor positivity. Unfortunately one of them died due to intracranial hemorrhage. As age advances more & more children are likely to become inhibitor positive, as inhibitor could develop anytime during their life time.

### Conclusions

- Similar to worldwide distribution, Hemophilia A is more than hemophilia B in the study, 86.7 % and 13.3% respectively.
- In majority of hemophiliacs, first bleed occurs in second half of infancy.
- Most common mode of first presentation is skin and subcutaneous bleeds.
- Family history was positive in 28.3% only.
- 6.7% of hemophiliacs are inhibitor positive

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