International Journal of Contemporary Pediatrics
Shah VB et al. Int J Contemp Pediatr. 2019 May;6(3):1168-1174
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20192006

Original Research Article

The study of disease pattern of various clinical classes of hemophilia in South Gujarat area, India

Vijay B. Shah, Neeraj Bansal, Kirti Mehta*

Department of Pediatrics, Govt. Medical College, Surat, Gujarat, India

Received: 20 January 2019
Accepted: 07 March 2019

***Correspondence:**
Dr. Kirti Mehta,
E-mail: drkirtimehtagamit@gmail.com

ABSTRACT

Background: Haemophilia is one of the most severe bleeding disorders. Seventy-five per cent of the global haemophiliacs live in developing countries, where probably only one in five cases is diagnosed, and there is little or no care available. Haemophilia as a disease and its management has a large impact on the community, including social integration and economics. Inability to be an active part of society and high cost of the medical care make this disease an important problem for all haemophilic patients.
Methods: A cross-sectional study, conducted over a period of one and half year. Institutional Ethics Committee permission was taken before starting the study. Information was gathered through personal interview of the patient's guardian with the help of predesigned questionnaires. Special emphasis was given to past history of bleeding. For each specific symptom/ specific site a detailed history and relevant details was taken and number of episodes of each symptom or number of episodes of involvement of a specific site was written.
Results: Out of 75 patients of haemophilia; 8 (10.7%) were Mild haemophilic, 17 (22.7%) were moderate haemophilic; and 50 (66.7%) were severe haemophilic. Most common site for spontaneous bleeding was muscle where 121 (25%) episodes of bleeding were reported, followed by knee joint 97 (20%), and ankle 79 (16.3%). The commonest site for traumatic bleeding was muscle where 201 (24.7%) episodes of bleeding were reported, followed by knee joint 175 (21.5%), ankle 143 (17.6%) and elbow joint 83 (10.2%). Site with highest duration of bleeding was intracranial for 6 days.
Conclusions: Frequency of traumatic dental and nasal bleeds was significantly higher in mild class as compared to moderate and severe classes. In severe category Knee, ankle, elbow and muscle were the commonest site where traumatic bleeding. There was no significant difference in bleeding frequencies at various sites in moderate and severe cases, whether spontaneous or traumatic bleed.

Keywords: Haemophilia, Spontaneous bleeding, Traumatic bleeding

INTRODUCTION

Haemophilia is a group of X-linked bleeding disorders due to deficiency of clotting factors VIII (Haemophilia A) and IX (Haemophilia B). The clinical manifestations of haemophilia A and haemophilia B are indistinguishable, and occur in mild, moderate, and severe forms. They are the only blood clotting disorders inherited in a sex-linked pattern. The severe forms of haemophilia are characterized mainly by frequent haemarthroses leading to chronic crippling haemarthropathy when not treated very early or prophylactically. Highly purified concentrates, prepared from human plasma and manufactured by recombinant technology, are available for treatment and are considered to be safe and effective. The main complication of treatment is the development of antibody inhibitors against either factor VIII or factor IX, which are more

common in patients with haemophilia A than in patients with haemophilia B.[1,2]

Haemophilia is the most severe bleeding disorder, after von Willebrand's disease which is the most common congenital bleeding disorder overall. In 2009, the World Federation of Haemophilia (WFH) has identified 153,251 people with haemophilia throughout the world.[3] This estimation included a survey of 91% of world population. The WFH estimates that the majority of people with haemophilia in the world do not receive adequate care.

Seventy-five per cent of the global haemophiliacs lives in developing countries, where probably only one in five cases is diagnosed, and there is little or no care available.[4] Haemophilia as a disease and its management has a large impact on the community, including social integration and economics. Inability to be an active part of society and high cost of the medical care make this disease an important problem for all haemophilic patients.

In developed countries, early treatment of bleeding episodes and home therapy quickly evolved as the primary management option. Presence of specialized interdisciplinary centres, training and education of patients are the main advantages of the comprehensive treatment concept in developed countries. This is not the case in most developing countries like India where the government does not have the resources to buy the necessary quantities of coagulation factors in the face of more urgent health priorities and hardly any patients can afford to pay for their own treatment even for on-demand home therapy. Other problems are insufficient supply with clotting factor concentrates, lack of access to these concentrates and absence of specialized care centers.[5]

There has been no previous study found on the symptomatology and disease pattern in Surat City. This study was conducted to determine the existing pattern of morbidity and associated severity of the disease, to study the variety of symptoms the patients in each clinical class can present with. Also, to help stakeholders involved in hemophilia care, such as providers, decision- and policy-makers identify and address the needs of people with hemophilia.

METHODS

It was a cross-sectional study, conducted over a period of one and half year in a tertiary care teaching hospital that caters urban, peri urban and rural population of South Gujarat.

Sample size and sampling method

Over the period of one and half year total 84 cases of hemophilia less than 12 year of age were visited the hospital. Among them only 75 cases could be included in the study according to inclusion and exclusion criteria.

Inclusion criteria

- Already diagnosed cases of hemophilia
- Aged less than 12 years
- Gave the voluntary informed written consent (from parents or guardian).

Exclusion criteria

- Person not fulfilling the inclusion criteria.

Data collection

For all eligible case a predesigned questionnaire was used to record patients' data. Initially personnel interview was conducted to record socio-demographic and personnel information. The cases selected were subjected to thorough interrogation with special references to clinical profile. Special emphasis was given to past history of bleeding. For each specific symptom/ specific site a detailed history and relevant details was taken and number of episodes of each symptom or number of episodes of involvement of a specific site was written (in the box provided for the same).

An approval was sought from the institutional ethical committee before the start of the study. As this study involve pediatric age group and special vulnerable group all care was taken to protect ethical rights of the patients. For the eligible children parents/guardian were informed in detail about the study and it's process. They were also explained about probable benefits and potential risk associated with the study in vernacular language. Then after, a written consent was taken in vernacular language. In case the parent or guardian was illiterate the consent form was filled up in present of literate witness. The statistical analysis was done using excel sheets. A high degree of confidentiality was maintained at all level from recruitment to data collection to analysis.

RESULTS

Total 75 cases with hemophilia could be included in final analysis. The severity of the disease of patients was graded based on the factor levels. Out of 75 patients of haemophilia; 8 (10.7%) were Mild haemophilic, 17 (22.7%) were moderate haemophilic; and 50 (66.7%) were severe haemophilic. Gender wise distribution shows, 71 (94.7%) were male and 4 (5.3%) were female. 46 out of 71 males were classified under severe case while all female classified under severe hemophilia. Two females had positive family history of hemophilia while two did not. Mean age at the time of presentation was 4.98 years while interview shows that mean age at the time of onset of symptoms were 15.92 months. Severity wise age of onset revealed that in severe cases age of onset is early (4.65 months) followed by moderate cases (9.5 months) and mild cases (17.2 months). It was found that out of 75, 70 (93.3%) cases were having haemophilia A while remaining 5 (6.7%) patients were suffering from

haemophilia type B. Out of total 70 cases of haemophilia A, 8 were in mild, 17 were in moderate and 45 were in severe category. All haemophilia B cases were clinically severe cases. Educational qualification of the patients revealed that out of 75, 57 (76%) were going to school while 8 (10.7%) were not yet old enough to go to school. Remaining 10 (13.3%) child were not going to school, 6 dropped out from school and 4 never went to school. Among the 75 cases of haemophilia, 64 cases were tested for certain other diseases. It was found that out of 64 none of the child was HbsAg positive while one child was HCV positive and one child was HIV positive. Inhibitors were found positive in 3 (4.7%) cases, all three suffering from haemophilia A.

Table 1: Socio-demographic distribution of hemophilia cases.

Parameter	Mild	Moderate	Severe	Frequency
Gender (%)				
Male	08 (100%)	17 (100%)	46 (92%)	71 (94.7%)
Female	00 (0%)	00 (0%)	04 (8%)	04 (5.3%)
Total	8 (100%)	17 (100%)	50 (100%)	75 (100%)
Age [mean (SD)]				
Age (in completed years) [mean (SD)]	4.9 (2.82)	5.6 (1.95)	4.77 (2.23)	4.98 (2.34)
Age of onset (in completed months) [mean (SD)]	17.2 (10.87)	9.5 (8.28)	4.65 (3.18)	15.92 (7.48)
Haemophilia types (%)				
A	8 (100%)	17 (100%)	45 (90%)	70 (93.3%)
B	0 (0%)	0 (0%)	5 (10%)	5 (6.7%)
Total	8 (100%)	17 (100%)	50 (100%)	75 (100%)
Schooling status				
Going to school	6 (75%)	13 (76.5%)	38 (76%)	57 (76%)
Never went to school	0 (0%)	1 (5.9%)	3 (6%)	4 (5.3%)
Dropped out	0 (0%)	1 (5.9%)	5 (10%)	6 (8%)
Not yet going to school	2 (25%)	2 (11.8%)	4 (8%)	8 (10.7%)
Total	8 (100%)	7 (100%)	50 (100%)	75 (100%)
Associated disease				
HbsAg	0	0	0	0
HCV	0	0	1	1
HIV	0	0	1	1
Inhibitors	0	1	2	3
Permanent deformity (%)				
Present	0 (0%)	1 (5.9%)	12 (24%)	13 (17.3%)
Absent	8 (100%)	16 (94.1%)	38 (76%)	62 (82.7%)
Total	8 (100%)	17 (100%)	50 (100%)	75 (100%)
Family history of hemophilia (%)				
Positive	1 (12.5%)	6 (35.3%)	22 (44%)	29 (38.7%)
Negative	7 (87.5%)	11 (64.7%)	28 (56%)	46 (61.3%)
Total	8 (100%)	17 (100%)	50 (100%)	75 (100%)

Only one cases had HCV positive and that is in severe clinical class. Similarly, only one case was HIV positive and that is in severe clinical class. Inhibitors were present in one case in moderate category and 2 cases in severe category. Permanent deformity was found in 13 cases out of 75 cases. So, the permanent deformity rate was 17.3%, out of which 1 case was in moderate category which contribute to 5.9% in moderate category while 12 cases were in severe category which contribute to 24.0% in severe category. Out of 75 cases of haemophilia Family History of haemophilia (diagnosed) was present in 29 (38.7%) cases. out of which 1 case was in mild category which contribute to 12.5% in mild category;6 cases were in moderate category which contribute to 35.3% in moderate category; and 22 cases were in severe category which contribute to 44.0% in severe category (Table 1).

Most common site for spontaneous bleeding was muscle where 121 (25%) episodes of bleeding were reported, followed by knee joint 97(20%), and ankle 79 (16.3%). Least common sites were intracranial (0%), nasal 21 (4.3%), shoulder 22 (4.5%) and wrist joint (6.8%). In mild category nasal was the commonest site where spontaneous bleeding was present in 60% cases. In

moderate category muscle, knee and ankle were the commonest site where spontaneous bleeding was present in 25%, 17.8% and 16.7% cases respectively. In severe category muscle and knee were the commonest site where spontaneous bleeding was present in 25% and 20.8% cases respectively. Comparison of traumatic dental, nasal and muscle bleeding in mild, moderate and severe cases shows the bleeding was significantly more ($p<0.05$) in mild case (Table 2).

Table 2: Spontaneous bleeding episodes.

Sites	Episodes (%)				Mean (SD)
	Mild	Moderate	Severe	Total	
Intracranial	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0
Knee	0 (0%)	17 (17.8%)	80 (20.8%)	97 (20%)	1.3 (1.84)
Ankle	0 (0%)	16 (16.7%)	63 (16.4%)	79 (16.3%)	1.21 (1.46)
Elbow	0 (0%)	11 (11.4%)	47 (12.2%)	58 (12%)	0.51 (1.25)
Wrist	0 (0%)	7 (7.3%)	26 (6.8%)	33 (6.8%)	0.41 (1.72)
Shoulder	0 (0%)	5 (5.2%)	17 (4.4%)	22 (4.5%)	1.20 (0.55)
Dental	3 (60%)	11 (11.4%)	40 (10.4%)	54 (11.1%)	0.55 (1.46)
Nasal	1 (20%)	5 (5.2%)	15 (3.9%)	21 (4.3%)	1.51(1.44)
Muscle	1 (20%)	24 (25%)	96 (25%)	121 (25%)	0.42 (1.76)
Total	5 (100%)	96 (100%)	384 (100%)	485 (100%)	

Table 3: Traumatic bleeding episodes.

Sites	Episodes (%)				Mean (SD)
	Mild	Moderate	Severe	Total	
Intracranial	0 (0%)	1 (0.5%)	2 (0.3%)	3 (0.4%)	0.33 (0.27)
Knee	0 (0%)	37 (20%)	138 (22.4%)	175 (21.5%)	3.33 (3.17)
Ankle	0 (0%)	31 (17%)	112 (18.2%)	143 (17.6%)	2.8 (3.47)
Elbow	0 (0%)	22 (11.9%)	61 (9.9%)	83 (10.2%)	1.34 (1.87)
Wrist	0 (0%)	11 (5.9%)	39 (6.3%)	50 (6.2%)	0.62 (1.67)
Shoulder	0 (0%)	8 (4.3%)	28 (4.5%)	36 (4.4%)	3.25 (1.23)
Dental	4 (36.4%)	17 (9.1%)	60 (9.7%)	81 (10%)	1.33 (4.59)
Nasal	5 (45.4%)	10 (5.4%)	24 (3.9%)	39 (4.8%)	3 (2.44)
Muscle	2 (18.2%)	48 (25.6%)	151 (24.55%)	201 (24.7%)	1.4 (2.97)
Total	11 (100%)	185 (100%)	615 (100%)	811 (100%)	

Also, the commonest site for traumatic bleeding was muscle where 201 (24.7%) episodes of bleeding were reported, followed by knee joint 175 (21.5%), ankle 143 (17.6%) and elbow joint 83 (10.2%). Least common sites were intracranial (0.4%), shoulder 36 (4.4%) and nasal 39 (4.8%) and wrist joint 50 (6.2%). In mild category Nasal and dental were the commonest site where traumatic bleeding was present in 45.4% and 36.4% cases respectively. In moderate category muscle, knee and ankle were the commonest site where traumatic bleeding was present in 25.6%, 20% and 17% cases respectively.

In severe category knee, ankle, elbow and muscle were the commonest site where traumatic bleeding was present in 86%, 68%, 66% and 66% cases respectively. Comparison of traumatic dental and nasal bleeding in mild, moderate and severe cases shows the bleeding was significantly more ($p <0.05$) in mild case (Table 3).

Site with highest duration was intracranial for 6 days, followed by knee joint and ankle joint bleeding. Nasal bleeding had shortest time of bleeding i.e. 1.18 days followed by dental related bleeding (1.55 days). In mild category shoulder bleeding last for 2.3 days while nasal and dental bleeding last for 1.25 days and 1.33 days respectively. In moderate category, long lasting bleeding where at knee joint, ankle joint and in muscles where it last for more than three days average. Nasal and dental bleeding stops comparatively early with an average duration of 1.46 days and 1.22 days respectively. In severe category, intracranial bleeding last for 6 days, knee joint bleeding last for 4.16 days while ankle bleeding last for 3.65 days (Table 4).

DISCUSSION

ICMR Task Force (1990) [101] estimates that 1330 children are born every year and 500000 patients of

haemophilia A are there of whom less than 5% have access to medical facilities.[6] The incidence of hereditary hemorrhagic disorders may vary according to the country and ethnic origin though Hemophilia is a disease that does not show any ethnic preferences. Hemophilia A remains the most common bleeding disorder in the Indian population, [108] followed by platelet function defects in India.[7]

In the present study, out of total 75 cases of haemophilia included in the study, 71 (94.7%) were male while remaining 4 (5.3%) were female. Thus, proportion of males was very high as expected. All the four females suffered from severe Hemophilia and two of the four females had a positive family history for Haemophilia A. Another study from Erciyes University, Turkey shows that of the Haemophiliacs, fourteen out of 18 patients were male, and four were female [104].[8] The study conducted by Mishra et al [105], regarding the prevalence of Hemophilia in Uttar Pradesh had 3 female with hemophilia 'B'.[9] National Hemophilia registry identifies nearly 802 females in India diagnosed as Hemophilia.

Mean age at the time of diagnosis was 15.92 (SD=7.5) months. Average age of onset of disease increased with decreasing severity. Clinical class wise age of onset revealed that in severe cases age of onset is early (4.65 months) followed by moderate cases (9.5 months) and mild cases (17.2 months). In the study conducted by Patiroglu T et al, the mean age of the pediatric patients was 42.1 months with higher number of patients with Mild Hemophilia forming the cohort.[8] In the study conducted by Kar A et al, on disability in hemophilia cases, patients age ranged from 5 to 55 years, mean age of 19.2 years.[10] However, the study conducted A. Kar had no age bound unlike present study which includes only patients with less than 12 years of age.

Also, in the Kar A et al, study Disability was significantly associated with age ($P < 0.001$), as 38.1% (n = 16), 67.6% (n = 46) and 79% patients (n = 30) in the 5-12 years, 13-24 and in the 25+ age group were severely disabled. In the present study, out of 75 cases of haemophilia permanent deformity was found in 13 cases. So, the permanent deformity rate was 17.3%. Remaining 62 (82.5%) cases were without any deformities. In the present study, out of 13 (17.3) cases with deformity 1 case was in moderate category which contribute to 5.9% in moderate category while 12 cases were in severe category which contribute to 24.0% in severe category. Studies are being carried out to evaluate the disability and permanent deformities related to the disease in the city.

In the present study, 70 (93.3%) cases were having haemophilia A while remaining 5 (6.7%) patients were suffering from haemophilia type B. Thus, this data reaffirms the fact that Haemophilia A is more common as compared to haemophilia B patients. Among total 70 cases of haemophilia A, 8 were in mild, 17 were in moderate and 45 were in severe category. All haemophilia B cases were clinically severe cases. Thus, in mild and moderate clinical category all cases are haemophilia A cases. The distribution may be attributable to the lack of diagnosis of the patients with Mild and Moderate Hemophilia in the region as compared to those with Severe Hemophilia A [107].[11] In the study conducted by Mishra et al, of 185 cases, 106 cases (57.3%) were mild, 59 cases (31.9%) were severe, and only 20 cases (10.8%) were moderately suffering from factor VIII deficiency. However, compared to hemophilia 'A', of the 55 cases of hemophilia 'B', 30 cases (54.5%) were mild, 18 cases (32.7%) were severe and only 7 cases (12.7%) were moderately suffering from factor IX deficiency. In mild hemophilia, the VIII/IX factor concentration exceeds 5 percent, and spontaneous bleeding is unusual. The factor level in individual patients does not vary much during life, but since the concept of mild hemophilia includes patients having factor levels of 6-40 percent, the tendency and risk of bleeding from different interventions varies widely.

In the present study, in mild category 6 (75%) were going to school while remaining 2 (25%) were yet not of school going age. In moderate category 13 (76.5%) were going to school while one cases never went to school, one was dropped out from school and 2 were younger for school. In severe cases category 38 (76%) were going to school while 3 (6%) cases never went to school, 5 (105) was dropped out from school and 4 (8%) were younger for school. This means out of the 67 eligible for going to school, 57 (85%) were going to school. In the study conducted by Kar A et al, [106] on disability in hemophilia cases, 59.2% cases were educated while 40.8% cases were not educated.[10] Among those who are educated 34.5% were educated upto primary level, 36.8% cases were educated upto secondary level and 28.7% were educated upto graduate level. No reliable data are available to compare the education of Hemophiliacs in pediatric population.

Total 64 cases were tested for associated disease. It was found that out of 64, one child was HCV positive and one child was HIV positive, while none of the children was HbsAg positive. Both of the children belonged to severe class of Hemophilia. Inhibitors were found positive in 3 (4.7%) cases. Inhibitors were present in one case in moderate category and 2 cases in severe category. Ghosh et al, [50] worked out the prevalence of inhibitors in India and found 7.3% of patients of hemophilia 'A' and 2.4% of hemophilia 'B' to have developed inhibitor.[12] The emergence and transmission of HIV, HBV and HCV through clotting factor products resulted in high mortality of people with hemophilia in the 1980s and early 1990s [118].[13] However, many studies conducted all over the world indicate that HIV, HBV, and HCV transmission through factor concentrate has been almost completely eliminated [119].[14] This is a result of the implementation of several risk-mitigating steps, which include careful selection of donors and screening of plasma, effective virucidal steps in the manufacturing process, and

advances in sensitive diagnostic technologies for detection of various pathogens [120].[15]

Hemophilia generally affects males on the maternal side. However, both F8 and F9 genes are prone for new mutations, and as many as 1/3 of all cases are the result of spontaneous mutation where there is no prior family history. In the present study out of 75 cases family history was present in 29 (38.7%) cases out of which 1 case was in mild category which contribute to 12.5% in mild category; 6 cases were in moderate category which contribute to 35.3% in moderate category; and 22 cases were in severe category which contribute to 44.0% in severe category. In comparison to the expected 66%, presence of positive family history in only 38.7% cases reflects was the vast under diagnosis and low awareness of the condition in the region. Genetic counseling is the main tool for the prevention and control of genetic disorders, targeted at families with an affected birth or with a family history of the disorder. Although genetic services are available through the private health sector, a public health programme is needed to ensure that prevention and control of genetic disorders can be implemented on a nation-wide basis.

The most common spontaneous and traumatic bleeding site was muscle while site with highest duration was intracranial for 6 days, followed by knee joint and ankle joint bleeding. Nasal bleeding had shortest time of bleeding i.e. 1.18 days followed by dental related bleeding (1.55 days).

Traumatic dental bleed was present in 36.4% of mild cases while it was there in 9.1% moderate cases and in 9.7% severe cases with p value less than 0.05, both while comparing mild with moderate and mild with severe classes indicating that dental bleeding was significantly more in mild cases. Traumatic nasal bleed was present in 45.4 % of mild cases while it was there in 5.4% moderate cases and in 3.9% severe cases with p value less than 0.05, both while comparing mild with moderate and mild with severe classes indicating that nasal bleeding was significantly more in mild cases. Traumatic muscle bleed were present in 18.2% of mild cases while it was there in 25.6% moderate cases and in 24.55% of severe cases with p value more than 0.05, both while comparing mild with moderate and mild with severe classes indicating that muscle bleeding did not differ in mild, moderate and severe cases. Application of chi-square test revealed that there was no significant different in bleeding frequencies at various sites with traumatic bleeding in moderate and severe cases.

Spontaneous dental bleed was present in 60% of mild cases while it was there in 11.4% moderate cases and in 10.9% severe cases with p value less than 0.05, both while comparing mild with moderate and mild with severe classes indicating that dental bleeding was significantly more in mild cases. Spontaneous nasal bleed was present in 20% of mild cases while it was there in 5.2% of moderate cases and in 3.9% of severe cases with p value less than 0.05 both while comparing mild with moderate and mild with severe classes indicating that nasal bleeding was significantly more in mild cases. Spontaneous muscle bleed was present in 20% of mild cases while it was there in 25% of both moderate cases with p value less than 0.05 both while comparing mild with moderate and mild with severe classes indicating that muscle bleeding was significantly more in mild cases. Application of chi-square test revealed that there was no significant different in bleeding frequencies at various sites with spontaneous bleeding in moderate and severe cases.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Klinge J, Ananyeva NM, Hauser CA, Saenko EL. Hemophilia A-from basic science to clinical practice. InSeminars in thrombosis and haemostasis. 2002;28(3):309-22.
2. Bolton-Maggs, PH, Pasi KJ. Haemophilias A and B. Lancet, 2003;361(9371):1801-9.
3. World Federation of Haemophilia, Report on the Annual Global Survey. 2009:14. Available at: http://www1.wfh.org/publications/files/pdf-1428.pdf.
4. World Federation of Haemophilia, Global Incidence and Prevalence Rates Approved by the President's Strategic Council. 2003.
5. Evatt BL. The natural evolution of haemophilia care: developing and sustaining comprehensive care globally. Haemophilia. 2006 Jul;12:13-21.
6. ICMR Task Force. Collaborative Study on Hemophilia., New Delhi, Indian Council of Medical Research, 1990.
7. Gupta M, Maitreyee B, Choudhry VP, Saxena R. Spectrum of Inherited Bleeding Disorders in Indians. Clin App Thrombosis/Hemostasis. 2005;11:325-30.
8. Patiroglu T, Ozdemir MA, Unal E, Torun YA, Coskun A, Menku A, Mutlu FT, Karakukcu M. Intracranial hemorrhage in children with congenital factor deficiencies. Child's Nervous System. 2011 Nov 1;27(11):1963.
9. Mishra KL, Kumar A, Gupta A. An experience of single centre at CSM Medical University, Lucknow, for the prevalence of hemophilia in Uttar Pradesh. Indian J Hematol Blood Transf. 2008;24(2):49-53.
10. Kar A, Mirkazemi R, Singh P, Potnis-Lele M, Lohade S, Lalwani A, et al. Disability in Indian patients with haemophilia. Haemophilia. 2007;13(4):398-404.
11. Trasi S, Shetty S, Ghosh K, Mohanty D. Prevalenceand spectrum of von Willebrand disease from western India. Med Res 2005;121(5):653-8.

12. Ghosh K, Joshi SH, Shetty S, Pawar A, Chipkar S, Pujari V, et al. Transfusion transmitted diseases in haemophilics from western India. Indian J Med Res. 2000;112:61-4.
13. Lee C, Sabin C, Phillips A, Elford J, Pasi J. Morbidity and mortality from transfusion-transmitted disease in haemophilia. Lancet. 1995;345(8960):1309.
14. Mauser-Bunschoten EP, Posthouwer D, Fischer K, Van Den Berg HM. Safety and efficacy of a plasma-derived monoclonal purified factor VIII concentrate during 10 years of follow-up. Haemophilia. 2007;13(6):697-700.
15. Ludlam CA, Mannucci PM, Powderly WG, European Interdisciplinary Working Group. Addressing current challenges in haemophilia care: consensus recommendations of a European Interdisciplinary Working Group. Haemophilia. 2005;11(5):433-7.

Cite this article as: Shah VB, Bansal N, Mehta K. The study of disease pattern of various clinical classes of hemophilia in South Gujarat area, India. Int J Contemp Pediatr 2019;6:1168-74.