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A STUDY OF CLINICAL PROFILE OF HAEMOPHILIA PATIENTS AND ASSESSMENT OF THEIR QUALITY OF LIFE.

Paediatrics

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ABSTRACT

Background: Haemophilia is an inherited disorder of bleeding that occurs due to coagulation factors deficiencies. Haemophilia A is a X-linked recessive disorder owing to deficiency of coagulation factor VIII. Haemophilia B (Christmas Disease) occurs due to the deficiency of coagulation factor IX and is also a X-linked recessive disorder. On the basis of residual factor activity level expressed as a % of normal or in IU/ml, haemophilia can be classified into mild, moderate and severe. "Health related quality of life (HR-QoL)" is a current area of research in haemophiliacs for assessing their quality of life in multiple dimensions. The "HAEMO-QoL (haemophilia-related quality of life) is the first specific HR-QoL for haemophilia patients" and which can be used with ease even on follow-up. **Aim and objectives:** This was a study of clinical profile of haemophilia patients including the role of physiotherapy and RICE therapy, role of factor replacement therapy, incidence of inhibitor formation and assessment of their quality of life using Haemo-QoL questionnaire. **Material and methods:** This study was conducted at ICHH (integrated centre for hemoglobinopathies and hemophilia), department of pediatrics, PMCH, Patna. The study duration was of 18 months from January 2021 to July 2022. This was a hospital based cross-sectional study done on 115 pediatrics patients with Hemophilia attending the department. **Results:** In this study, 103 cases (89.6%) had haemophilia A and 12 (10.4%) had haemophilia B. 55 cases (47.83%) had severe, 42 cases (36.52%) had moderate and 18 cases (15.65%) had mild hemophilia. The most common clinical manifestation was joint bleed in 70 cases (60.87%) followed by muscular bleed, then gum bleed, genitourinary bleed, CNS bleed and gastrointestinal bleed. There was very significant correlation between factor replacement frequency and severity of hemophilia (p-value <0.000). The HAEMO-QoL scores were higher for all the parameters for group III patients (age- 13 to 16 years) and also, they were higher for those with severe hemophilia. **Conclusion:** Haemophilia is an inherited disease which has a high prevalence in our country. India has second highest prevalence of haemophilia in the world. Early diagnosis and management of these patients, regular check-up for factor levels, inhibitor levels and viral markers is required for these patients. For assuring quality of life of these patients require more monitoring, complete immunization, regular follow-ups and physiotherapy for those with haemophilic arthropathy and we need to create a safe and supportive environment for them.

KEYWORDS

Haemophilia, Quality of life (QoL), inhibitors.

INTRODUCTION:

Haemophilia is an inherited disorder of bleeding that occurs due to coagulation factors deficiencies[1]. Haemophilia A is a X-linked recessive disorder owing to deficiency of coagulation factor VIII[2]. Haemophilia B (Christmas Disease) occurs due to the deficiency of coagulation factor IX and is also a X-linked recessive disorder[2]. Haemophilia C is due to insufficiency of factor XI with an autosomal dominant inheritance[3]. This is quite rare with only mild to moderate bleeding manifestations[3].

Haemophilia A is the most common disorder amongst these and more likely to cause severe bleeding manifestations. Haemophilia A affects around 1 in 5,000 whereas, haemophilia B affects 1 in 30,000 live male babies. On the basis of residual factor activity level expressed as a % of normal or in IU/ml, haemophilia can be classified into mild, moderate and severe. The extent of bleeding symptoms directly correlates with the factor level in the blood**.**

Mild haemophilia is having factor activity level of >5 to <40% of normal (≥0.05 and <0.40 IU/ml)[4]. Moderate haemophilia – It is defined as factor activity level ≥1% of normal and ≤5% of normal (≥0.01 and ≤0.05 IU/ml)[5]. Severe haemophilia – It is defined as <1% of factor activity (<0.01 IU/ml).

Bleeding from impaired haemostasis, sequelae from bleeding, or complication of coagulation factor infusion includes the clinical manifestations of haemophilia patients. Severe haemophiliacs have more tendency of spontaneous, life-threatening haemorrhage and an earlier age at initial bleeding episode which can begin as soon as from the time of birth as prolonged bleeding from umbilical stump or as multiple bruises from normal delivery. Common sites of bleeding in neonates include CNS bleeds, cephalohematomas and from the sites of medical interventions including those of circumcision, heel pricks, venepunctures. Once children begin walking symptoms like bruises and musculoskeletal bleedings become more apparent. In those, of age group above 5 years, joints and muscles become common sites of bleeding[4].

Use of prophylactic methods and use of factor replacement therapy has led to overall decline in frequency of bleeding in India. In spite of this, majority of patients remain underdiagnosed or not registered in our country. Frequent absenteeism from school due to physical activity limitation which is a result of extreme pain and discomfort associated with haemorrhagic episodes is common in these patients[4]. "Health related quality of life (HR-QoL)" is a current area of research in haemophiliacs for assessing their quality of life in multiple dimensions.

The "HAEMO-QoL (haemophilia-related quality of life) is the first specific HR-QoL for haemophilia patients" and which can be used with ease even on follow-up[5]. HAEMO-QoL is the first haemophilia specific HRQoL questionnaire and is obtainable for 3 age group versions as self-reports in children. Version I is for those with age 4 to 7 years (21 items), in the form of an interview. Version II is for children aged 8 to 12 years (64 items) and version III is for adolescents aged 13-16 years (77 items). It also has three proxy versions for parents reports respectively[6]. For children a questionnaire in 8-12 dimensions have been created according to age groups, including lesser items for younger children. For version I items used are "physical health, feeling, view, family, friends, others, sports and school". Another work/school has also been added in few studies. For version II and III there are additional items like "perceived support, dealing with hemophilia, future and relationship" are used. The higher scores indicate high impairment of QoL[7]. The scores are given on a scale of 0 to 100 for each item where, 0 is taken as the best score and 100 as the worst score with poor QoL[8].

AIMS AND OBJECTIVES:

This was a study of clinical profile of haemophilia patients and assessment of their quality of life. The objectives were to describe clinical profile of haemophilia patients in paediatrics age group at PMCH, Patna, Bihar, to describe the role of physiotherapy and RICE (rest, ice, compression and elevation) for better quality of life of haemophilia patients. This study also aimed to determine the role of factor replacement therapy in haemophilia patients, to determine the

incidence of formation of inhibitors in treated patients of haemophilia and to assess the quality of life of haemophilia patients through the HAEMO-QoL questionnaire.

MATERIALS AND METHODS:

This study was conducted at ICHH (integrated centre for hemoglobinopathies and hemophilia), department of pediatrics, PMCH, Patna. The study duration was of 18 months from January 2021 to July 2022. This was a hospital based cross-sectional study done on 115 pediatrics patients with Hemophilia attending the department. The informed consent from parents was taken and the approval of the ethical committee was obtained from the respective department and the college for conducting this study.

Inclusion Criteria:

All paediatric patients with haemophilia A or B whose guardians consented were included in the study. The known patients with haemophilia attending pediatrics emergency with musculoskeletal bleeding, joint bleeding, trauma etc for factor replacement therapy and those with platelet count >1,50,000/mm3 were included in the study.

Exclusion Criteria:

The patients who did not belong to pediatrics age group and patients with deficiency of factors other than FVIII and FIX have been excluded. Patients having bleeding due to platelet deficiency, patients with joint swelling due to juvenile rheumatoid arthritis (JRA), metabolic diseases affecting bone and similar diseases which can mimic arthritis (i.e., joint swelling not due to hemarthrosis as in hemophilia) patients, with bleeding due to chronic liver disease and patients with competing risks like symptomatic HIV, active TB were excluded from this study.

Study Details:

This study was done on 115 hemophilia patients. A thorough clinical profile including manifestations while attending the hospital, history of previous admissions, treatment received, age at onset of the disease, family history of any bleeding diseases was taken. A history of blood transfusions and immunization was also taken. The patients were also accounted to scrupulous clinical evaluation, relevant investigations and radiological imaging. HAEMO-QoL questionnaire were utilized for assessing quality of life of these cases.

Blood investigations included:

- Coagulation profile: PT, aPTT.
- Viral markers: HBsAg, HCV, HIV 1&2
- CBC (complete blood count)
- Factor assay

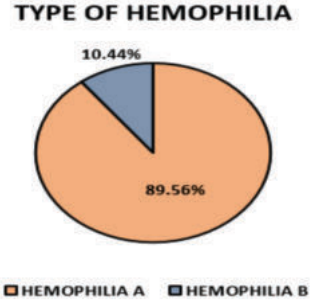
Also, Calculation of FISH score (functional independence score in haemophilia) was done and QoL of the patients was assessed using HAEMO-QoL Questionnaire. Radiological imaging, most commonly X-rays of the involved joint was taken for classification of the arthropathy radiologically. The data was analysed using SPSS software for mean, standard deviation, Anova test and chi-square test.

RESULTS:

Data in this study were analysed using arithmetic mean, standard deviation and correlation coefficient. 115 patients of haemophilia were studied and the results have been charted below.

Table 1: Type Of Hemophilia

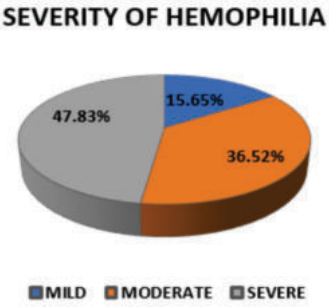
TYPE	NO. OF PATIENTS	PERCENTAGE (%)
HAEMOPHILIA A	103	89.56%
HAEMOPHILIA B	12	10.44%



Among this study population, 89.56% were cases of haemophilia A and 10.44% were haemophilia B cases.

Table 2: Showing Severity Of Hemophilia

SEVERITY	NO. OF PATIENTS	PERCENTAGE (%)
MILD	18	15.65%
MODERATE	42	36.52%
SEVERE	55	47.83%



In this study, 55 (47.83%) cases had severe haemophilia, 42 (36.52%) cases had moderate haemophilia and 18 (15.65%) cases had mild haemophilia.

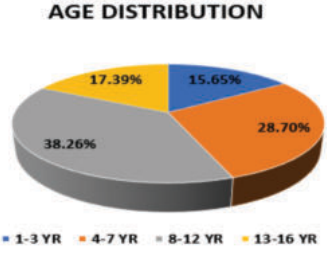
Table 3: Distribution Of Cases According To Religion

RELIGION	NO. OF PATIENTS	PERCENTAGE
HINDU	101	87.83%
MUSLIM	14	12.17%

Among this study 101 (87.83%) patients belonged to Hindu religion and 14 (12.17%) patients were Muslim. No patients from other religions presented to our center during my study period.

Table 4: Age Distribution

AGE (YEARS)	NO. OF PATIENTS	PERCENTAGE (%)
1-3	18	15.65%
4-7	33	28.7%
8-12	44	38.26%
13-16	20	17.39%



Among this study 18 (15.65%) patients were of age 1-3 years, 33 (28.7%) patients were of age 4-7 years, 44 (38.26%) patients were of age 8-12 years and 20 (17.39%) patients were of age 13-16 years. Those above 16 years have not been included in this study.

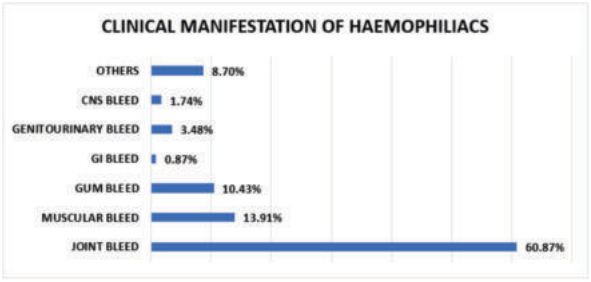
Table 5: Showing Gender Distribution

GENDER	NO. OF PATIENTS	PERCENTAGE (%)
MALE	115	100%
FEMALE	0	0%

In this study all the 115 (100%) patients were male.

Table 6: Showing Clinical Manifestation

CLINICAL MANIFESTATION	NO. OF PATIENTS	PERCENTAGE
JOINT BLEED	70	60.87%
MUSCULAR BLEED	16	13.91%
GUM BLEED	12	10.43%
GI BLEED	1	0.87%
GENITOURINARY BLEED	4	3.48%
CNS BLEED	2	1.74%
OTHERS	10	8.70%



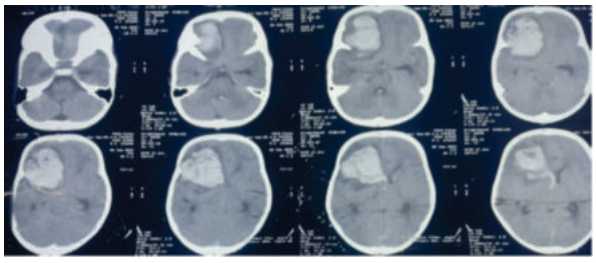
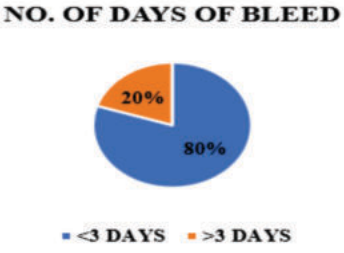


Image Showing Intracranial Bleeding In A Hemophilia Patient

In this study 70 (60.87%) patients came with joint bleed, 16 (13.91%) patients had muscular bleed, 12 (10.43%) had gum bleed, 1 (0.87%) patient came with gastrointestinal (GI) bleed, 4 (3.48%) patients had genitourinary (GU) bleed, 2 (1.74%) patients had CNS bleed. Others, 10 (8.7%) patients had bleeding in the form of epistaxis, following falling of deciduous teeth and bleeding from sites other than those mentioned above.

Table 7: Showing Average Duration Of Bleeding In The Haemophilia Patients.

NO. OF DAYS OF BLEED	NO. OF PATIENTS	PERCENTAGE
≤3 DAYS	92	80%
>3 DAYS	23	20%



Among this study, 92 (80%) patients had ≤3 days of bleeding during an episode and 23 (20%) had bleeding for >3 days.

Table 8: Showing Frequency Of Factor Replacement In An Year.

FREQUENCY	NO. OF PATIENTS	PERCENTAGE (%)
≤15 TIMES	44	38.26%
>15 TIMES	71	61.74%

In this study 44 (38.26%) patients had factor replacement for ≤15 times in an year and 71 (61.74%) patients had factor replacement >15 times in an year.

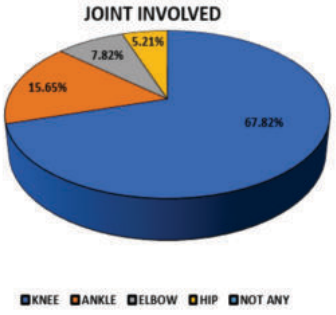
Table 9: Correlation Between Factor Replacement And Severity Of Hemophilia.

FACTOR REPLACEMENT- FREQUENCY		
SEVERITY	AVERAGE	STANDARD DEVIATION
MILD	9.11	2.78
MODERATE	15	3.67
SEVERE	17.54	3.74
p-value-< 0.000		
HIGHLY SIGNIFICANT		
ANOVA		

As depicted in the above table, the correlation between frequency of factor replacement and hemophilia was found to be highly significant, i.e., p-value was <0.000. for mild hemophilia mean factor replacement in a year was 9.11±2.78, for moderate it was 15±3.67 and for severe hemophilia, it was 17.54±3.74.

Table 10: Showing Most Common Joint Involved.

JOINT INVOLVED	NO. OF PATIENTS	PERCENTAGE
KNEE	78	67.82%
ANKLE	18	15.65%
ELBOW	9	7.82%
HIP	6	5.21%
NOT ANY	4	3.5%



As shown in the above table, images and pie chart: among 115 patients in my study 78 (67.82%) patients had involvement of knee joint, 18 (15.65%) patients had involvement of ankle joint, 9 (7.82%) patients had elbow joint, 6 (5.21%) patients had involvement of hip joint and 4 (3.5%) patients had involvement of no any joint.

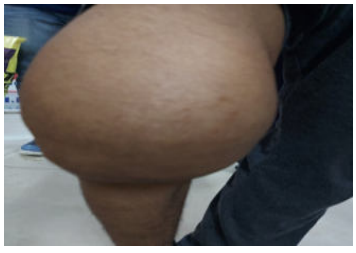
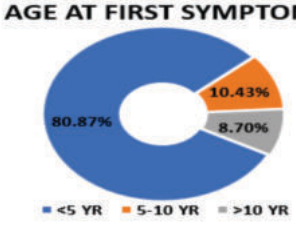


Image Showing Target Joint Formation (knee Joint)

Image Showing Target Joint Formation (elbow Joints)

Table 11: Showing Age At First Symptoms

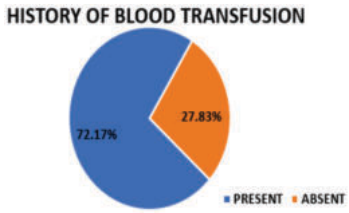
AGE (YEARS)	NO. OF PATIENTS	PERCENTAGE (%)
<5 YEARS	93	80.87%
5-10 YEARS	12	10.43%
>10 YEARS	10	8.7%



In my study, 93 (80.87%) patients had presentation at less than 5 years of age. 12 (10.43%) patients had presentation at 5 to 10 years of age. Only 10 (8.7%) out of 115 patients presented after 10 years of age.

Table 12: Showing History Of Prior Transfusion Of Blood

HISTORY OF PRIOR BLOOD TRANSFUSION	NO. OF PATIENTS	PERCENTAGE (%)
PRESENT	83	72.17%
ABSENT	32	27.83%



Out of 115 patients in this study, 83 (72.17%) patients had history of prior blood transfusion as FFP or PRBC transfusion or both. And 32 (27.83%) patients had no history of blood transfusion.

Table 13: Showing Vaccination Status Against Hepatitis B

HEPATITIS B VACCINATION	NO. OF PATIENTS	PERCENTAGE (%)
RECEIVED	54	46.95%
NOT RECEIVED	61	53.05%

In this study, 56 (48.7%) patients out 115 had been fully vaccinated for Hepatitis B. And the other 59 (51.3%) patients were not vaccinated.

Table 14: Showing Positive Viral Markers (hcv/hiv/hbsag) Or Transfusion Related Infections

POSITIVE	NO. OF PATIENTS	PERCENTAGE (%)
NO	109	94.8%
YES	6, out of which: HIV- 2 HCV- 1 HBsAg- 3	5.2%, out of which: HIV- 1.73% HCV- 0.87% HBsAg- 2.60%

In our study, from 115 cases, 109 (94.80%) were negative for viral markers. 2 (1.73%) patients were positive for HIV, 1 (0.87%) patient was positive for HCV. And 3 (2.60%) patients were positive for HBsAg.

Table 15: Showing Family History

FAMILY HISTORY	NO. OF PATIENTS	PERCENTAGE (%)
PRESENT	46	40%
ABSENT	69	60%

Among 115 patients in this study, only 46 (40%) patients had positive family history. Other 69 (60%) patients had no family history.

Table 16: Showing Pt And Aptt Parameters

PARAMETERS	AVERAGE	STANDARD DEVIATION
PT	13.81	1.60
aPTT	58.71	8.91

aPTT analysis showed increased values in all 115 (100%) patients. The extended aPTT denotes intrinsic and common coagulation pathway defect. In this study, aPTT was 58.71±8.91 seconds. PT values were in normal range.

Table 17: History Of Minor Trauma Needing Factor Replacement Therapy (present/absent).

H/O TRAUMA (in a year)	NO. OF PATIENTS	PERCENTAGE (%)
PRESENT	23	20%
ABSENT	92	80%

Only 23 (20%) of patients out of total 115 patients required factor replacement following trivial trauma. While, 92 (80%) patients did not require factor after trivial trauma.

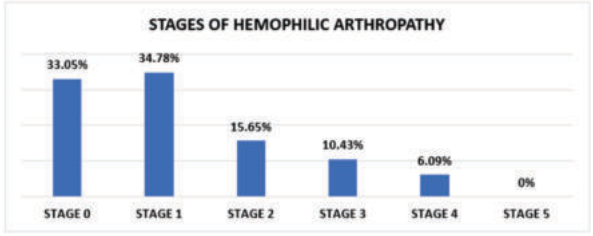
Table 18: Showing Presence Of Target Joint

TARGET JOINT	NO. OF PATIENTS	PERCENTAGE (%)
PRESENT	85	74%
ABSENT	30	26%

Among this study, 85 (74%) out of 115 patients had presence of target joints in which they had recurrent bleeding. Other 30 (26%) patients had no target joint formation.

Table 19: Stages Of Haemophilic Arthropathy On Radiography

STAGES OF HAEMOPHILIC ARTHROPATHY A/C TO ARNOLD HILGARTNER CLASSIFICATION	NO. OF PATIENTS	PERCENTAGE (%)
STAGE 0	38	33.05%
STAGE 1	40	34.78%
STAGE 2	18	15.65%
STAGE 3	12	10.43%
STAGE 4	7	6.09%
STAGE 5	0	0%



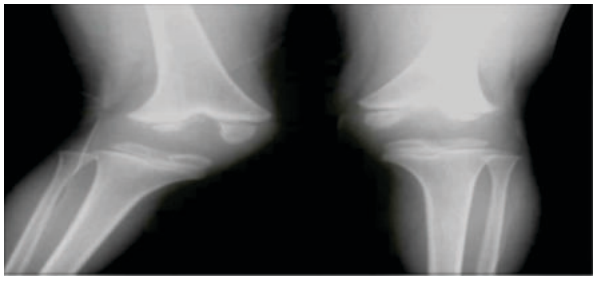


Image Showing X-ray Of B/l Knee Joints Showing Haemophilic Arthropathy

As shown in above table and column 33.05% (38/115) patients had stage 0, 34.78% (40/115) had stage 1, 15.65% (18/115) had stage 2, 10.43% (12/115) had stage 3, 6.09% (7/115) had stage 4 and none had stage 5 hemophilic arthropathy on x-ray of the involved joint classified according to Arnold-Hilgartner classification.

Table 20: Showing Presence Of Inhibitors

INHIBITORS	NO. OF PATIENTS	PERCENTAGE (%)
PRESENT	10	8.7%
ABSENT	105	91.3%

In this study, 10 (8.7%) out of 115 patients had presence of inhibitors and all of them had severe hemophilia with factor level <1%. Other 105 (91.3%) patients had no inhibitor and responded well to factor replacement therapy.

Table 21: Functional Independence Score In Hemophilia (fish) Scoring.

FISH SCORE	NO. OF PATIENTS	PERCENTAGE (%)
<15	26	22.6%
>15	89	77.4%

FISH (Functional Independence Score for patients with Hemophilia) has been developed as a measure of disability in patients with hemophilia. It can be used to evaluate change in functional independence over time, or after a therapeutic intervention. The FISH is meant to complement other scores that measure body structure and function such as the clinical joint evaluation score, and the radiological score. The scores that are achieved in each task are summed and giving a total from 8 to 32 points with 32 indicating highest level of functional independence score.

Calculation of FISH score for 115 patients of this study showed a mean of 23.71±6.03. 26 (22.6%) patients had score of <15 and 89 (77.4%) patients had a score of >15.

Table 22: Severity And Stages Of Joint Radiography

SEVERITY			
STAGING OF JOINT RADIOGRAPHY	MILD	MODERATE	SEVERE
0	17	10	11
1	1	21	18
2	0	7	11
3	0	4	8
4	0	0	7
5	0	0	0

p-value- 0.000
HIGHLY SIGNIFICANT
CHI-SQUARE TEST

As shown in above table, the correlation between stages of joint radiography and severity of hemophilia came to be highly significant i.e., p-value was <0.000 by performing a chi square test.

Table 23: Joint Radiography Stages And Target Joint (yes/no)

STAGES	YES	NO
0	19	19
1	35	5
2	13	5
3	11	1
4	7	0
5	0	0
p-value: 0.000		
HIGHLY SIGNIFICANT		
CHI-SQUARE TEST		

According to above table the co-relation between stages of haemophilic arthropathy and development of the target joint was highly significant and the *p-value* was <0.000 which was calculated using chi square test.

Table 24: Showing Relief With Physiotherapy And Rice

RELIEF	NO. OF PATIENTS	PERCENTAGE (%)
YES	100	87%
NO	15	13%

In this study 100 (87%) out of 115 patients had relief with physiotherapy and RICE therapy i.e., they had decreased frequency of factor replacement and relief from swelling and pain. While, 15 (13%) patients had no relief.

Table 25: Mean±sd Of Haemo-qol Scores According To Different Age Groups.

PARAMETERS	GROUP I (4-7YR)	GROUP II (8-12YR)	GROUP III (13-16YR)
PHYSICAL HEALTH	47.6±15.4	55.75±10.23	61.65±10.99
FEELINGS	47.3±16.83	57.47±11.9	63.9±12.03
VIEW	45.09±16.5	57.3±11.07	65.85±11.8
FAMILY	36.09±14.35	45.04±11.17	51.85±11.89
PERCIEVED SUPPORT	-	55.2±12.4	62.95±13.63
OTHERS	41.03±15.79	56.09±12.71	63.15±13.24
SPORTS	44.66±16.92	58.72±11.6	66.15±11.23
DEALING	-	57.38±11.9	64.8±12.84
TREATMENT	41.66±17.51	55.79±13.10	61.25±12.55
FUTURE	-	-	64.7±12.24
RELATIONSHIP	-	-	62.1±14.3
WORK/SCHOOL	42±16.63	55.2±10.95	61.9±13.66
FRIENDS	32.63±13.7	42.68±9.11	51.15±12.75

The above table shows the HAEMO-QoL Scores for all 115 patients in our study. As described earlier, the patients are divided into 3 groups and they all have sets of questionnaires including various parameters. The score is provided on a scale of 0 to 100. The score is considered to be, lower the better. For group I (4-7 years old) parameters like perceived support, dealing with hemophilia, future and relationships are not taken into account. Similarly, for group II (8-12 years old) parameters like future and relationships are not taken into account. As we can clearly observe from the above table that group III patients have highest mean scores for all the parameters taken into account when compared to group II and group I.

Also, group II patients have higher scores from group I patients. This shows that the QoL of group III patients were more severely affected than the other two groups. The QoL score for sports in group III and group II was highest, which were 66.15±11.23 and 58.72±11.6 respectively. For group I QoL score for physical health was highest which was 47.6±15.4. The higher score denotes more impairment in that particular area.

Table 26: Mean±sd Of Haemo-qol Scores According To The Severity Of Haemophilia.

PARAMETERS	MILD	MODERATE	SEVERE
PHYSICAL HEALTH	41.18±10.05	50.06±13.10	57.84±13
FEELING	40.89±11.65	50.28±15.56	59.51±15.5
VIEW	41.11±13.16	50.69±16.12	58.88±14.43
FAMILY	33.7±9.02	40.44±12.61	46.13±14.2
PERCIEVED SUPPORT	41.83±7.68	56.46±13.64	61.47±12.64
OTHERS	39.81±12.89	48.77±16.29	55.98±16.14
SPORTS	42.33±14.66	50.94±15.90	59.14±14.97
DEALING	46.5±10.33	57.71±12.93	62.93±12.65
TREATMENT	38.81±12.6	48.25±15.87	55.94±16.14
FUTURE	44±0	55.5±9.35	73.27±5.69
RELATIONSHIP	32±0	51.62±8.92	72.45±6.07
WORK/SCHOOL	39.44±12.54	48.66±16.34	55.70±15.18
FRIENDS	32.51±10.58	38.74±13.55	43.38±13.65

The above table for HAEMO-QoL scores has been arranged according to severity of haemophilia for each parameter. The highest score for mild and moderate haemophilia patients was for parameter 'dealing with haemophilia' and they were 46.5±10.33 and 57.71±12.93 respectively. For severe haemophiliacs the highest score was for 'future' parameter which was 73.27±5.69.

DISCUSSION:

This was a study conducted at Integrated Center for Hemo globinopathies and Haemophilia of pediatrics department at PMCH, Patna. This study was conducted on 115 patients for a period from January 2021 to July 2022.

In this study, 103 cases (89.6%) were of haemophilia A and 12 cases (10.4%) were of Haemophilia B. There were 18 cases (15.65%) of mild haemophilia, 42 cases (36.52%) of moderate haemophilia and 55 cases (47.83%) of severe haemophilia. There were 101 cases (87.83%) who were Hindu and 14 cases (12.17%) who were Muslim by religion. 18 cases (15.65%) were of age group <3 years, 33 cases (28.7%) belonged to 4-7 years, 44 cases (38.26%) were of age group 8-12 years and 20 cases (17.39%) were of age group 13-16 years. These age groups were formed for the ease of assessment of QoL using HAEMO-QoL questionnaire. 100% cases in our study were male.

In the study, by Rajendra Kumar Nigam et al[9] 89% cases were of haemophilia A and 11% cases were of haemophilia B. 4% cases were below 5 years and 49% were of 6-15 years of age. Study by Gustavo Cambraia Trindade et al[10], 82.4% were haemophilia A cases and 17.6% were of haemophilia B cases. They had 11.8% cases of mild, 23.5% cases of moderate and 64.7% cases of severe haemophilia. In another study conducted by Bidyut Kumar Khuntdar et al[11] haemophilia A cases were 81.25% and 18.75% were haemophilia B cases. Out of these, 20.31% cases were of moderate hemophilia and rest 79.69% cases were of severe hemophilia and all the cases were male. The study by Saurabh Mishra et al[7] had 88.3% haemophilia A cases and 11.7% haemophilia B cases. Out of these, 26.9% cases were mild, 3.8% were moderate and rest 69.2% were of severe hemophilia.

In our study, the most common presentation was joint bleed (60.87%) which involved knee joint (67.82%) most commonly followed by ankle joint (15.65%). The frequency of factor replacement was less than 15 times in a year in 38.26% cases and more than 15 times in a year in 61.74% cases. The duration of bleeding was less than 3 days in 80% and more than 3 days in 20% cases. The age of presentation for 80.87% cases was <5years.

In a similar study, by Jasbir Singh et al[12] the commonest involvement was of knee joint (31.8%) and then ankle joint (27.27%). In a study, by Sandeep Kumar et al[13] most common presenting clinical feature was prolonged bleeding. In a study, by Madhu Singh et al[14] most common presentation was hemarthroses (91.39%) out of which most commonly affected joint was knee joint (64.7%). In a study, by Saurabh Mishra et al[7] hemarthroses were present in 77.9% cases out of which most commonly affected joint was knee joint (57.1%). These findings were similar to that of our study.

In our study, 72.17% cases had history of prior blood transfusion in form of FFP, PRBC or cryoprecipitate. The history of immunization was present in 47% cases and incomplete or not done or not available in 53% cases. 48.7% cases had received hepatitis B vaccination and 51.30% cases did not. There were 6 cases (5.2%) who had positive

viral markers, out of which 2 (1.73%) were HIV positive, 3 (2.6%) had HBsAg and 1 (0.87%) was positive for HCV. Only 46 cases (40%) had positive family history of hemophilia and 69 cases (60%) had no family history and were sporadic cases.

In a study conducted by Sandeep Kumar et al[13] on haemophiliacs, 74.68% cases had history of prior blood transfusions in the form of FFP, PRBC and cryoprecipitate. 36.70% patients had history of BT ≥3 times and 37.97% patients had history of transfusion for <3 times. 64.13% cases in their study had family history for hemophilia and 5.43% cases had history of consanguineous marriage of their parents and out of these 5.43% only 3.26% cases had positive family history. In a study by Saurabh Mishra et al[7] 58.4% patients had positive family history for hemophilia and they had 6.5% patients who were hepatitis B positive, 9.1% patients who were HCV positive and none who were HIV positive.

In a study by Bidyut Kumar Khuntdar et al[11] 64.06% patients had positive family history and rest 35.94% patients had no history in the family. In a study by Rajendra Kumar Nigam et al[9] 57% had positive family history for hemophilia. In a study by Sajini Varghese et al[15] 60% had positive family history and 40% did not.

In our study, PT values were 13.81±1.59 (mean±SD). The aPTT values were 58.71±8.91 (mean±SD). In the study by Sandeep Kumar et al[13] mean PT was found to be 14.06±1.06 and mean aPTT was 80.33±19.20. In a study by Rajendra Kumar Nigam et al[9] 57% patients have raised aPTT which was more than 80 seconds and aPTT was found to be raised in all the patients.

In our study, history of trivial trauma leading to bleeding was present in 23 cases (20%) and it was absent in 92 cases (80%). The co-relation between factor replacement frequency and the hemophilia severity came to be very significant i.e., *p-value* was <0.000. this was established by performing ANOVA test. The mean±SD factor replacement frequency was 9.11±2.78 in mild hemophilia, 15±3.67 in moderate hemophilia and 17.54±3.74 times in severe hemophilia patients. In most (74%) of our cases target joint was formed and knee joint was involved most commonly, in which recurrent bleeding used to occur. In 38 cases (33.05%) there was no joint arthropathy. But, the rest 77 cases (66.95%) had already developed joint arthropathy.

In the study by Sandeep Kumar et al[13] 18.75% had developed joint arthropathy. In a study by Sajini Varghese et[15] al 25% patients had developed hemophilic joint arthropathy.

In our study, the correlation between stages of joint radiography and formation of target joint was found to be very significant (*p-value* <0.000) by chi-square test. The co-relation between severity of hemophilia and the stages of joint radiography was also found to be highly significant (*p-value* <0.000) using chi-square test. There were 10 cases (8.7%) in our study who developed inhibitors and all of them were cases of severe hemophilia A. The FISH Score was <15 for 26 cases (22.6%) and >15 for 89 cases (77.4%). The average FISH score was 23.71±6.03 for all participants.

In a similar article by Sandeep Kumar et al[13] 3.39% cases had formed inhibitors. In a study by Madhu Singh et al[14] 1.07% cases of haemophilia A had formed inhibitors while, none with haemophilia B formed inhibitors. In a study by Sangita Darshan Shah et al[16] 20.57% cases having haemophilia A and 6.06% patients having haemophilia B formed inhibitor and also, 84.61% patients with hemarthrosis had development of inhibitors. In a study by Sajini Varghese et al[15] 5% patients had developed inhibitors. In a study by Alberto Tlacuilo-Parra et al[17] mean FISH score was found to be 25.8±3.6. In a study by Osama Ahmed Ibrahiem et al[18] on hemophilia patients average FISH score was found to be 21.11±4.5.

In our study, 100 cases (87%) had relief with physiotherapy and RICE therapy and 15 cases (13%) did not have any relief with this therapy. The HAEMO-QoL in our study varied for different age groups and the score was higher for group III cases (age-13 to 16 years) than those of group I and II. Also, the score for various parameters from the questionnaire were higher for severe haemophiliacs than those with mild and moderate hemophilia. These have been discussed in details in the result section.

In an article by Saurabh Mishra et al[7] average QoL score for children was 39.6±15.0. In a study by Gustavo Cambraia Trindade et al[10] the mean QoL score for physical health was 61.13±13.29 and for relationship, it was 76.47±21.69.

CONCLUSION:

Haemophilia is an inherited disease which has a high prevalence in our country. India has second highest prevalence of haemophilia in the world. This the commonest cause of hereditary bleeding disorder and affects males most commonly. But females can also get affected. The disease manifests in the early years of life usually following trauma in the form of bruises or prolonged bleeding from minor cuts or spontaneous mucosal bleedings. Eventually, it leads to bleeding in the joints which is recurrent and spontaneous and finally if the patients do not receive prophylactic factor replacement therapy, leads to development of haemophilic joint arthropathy.

Major bleeds can occur following trauma like CNS bleeds, those in tight compartments and severe blood loss which can also cause death of these patients if not addressed promptly. If a patient develops inhibitor against factor therapy, it can lead to dire situations. So, these patients have to be counselled about the disease manifestations, complications and development of inhibitors.

Patients should receive prophylactic factor replacement therapy rather than, on demand factor replacement therapy for maintenance of a normal quality of life. Those around the patients like their parents, siblings, teachers, relatives and friends should also understand the disease and support them as much as needed. The psychological health of the patient means a lot for maintenance of a normal, healthy lifestyle and growth, especially for children. They have to be informed and educated about the physiotherapy so as to avoid formation of joint arthropathy and about the RICE therapy which can decrease the need for factor replacement therapy. They should receive regular counselling on these matters.

Early diagnosis and management of these patients, regular check-up for factor levels, inhibitor levels and viral markers is required for these patients. Antenatal check-up facilities for carrier detection and for patient detection should be available at a few centres in a state. In a developing country like ours with financial constraints and restricted availability of resources we need to make the disease manageable from the very basic level. Our government is doing their best by providing the factors at no cost at our center which is dedicated to these patients. For assuring quality of life of these patients require more monitoring, complete immunization, regular follow-ups and physiotherapy for those with haemophilic arthropathy and we need to create a safe and supportive environment for them.

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