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Assessment of Quality Of Life and Functional Disability among Hemophilia A Patients

Rucha M[1], Gaurav D[1], Neha K[2], Hrishikesh G[1*]

[1]*Department of Pharmacy, Government collage of Pharmacy, Amravati, Maharashtra, India*

[2]*Day care Unit, District General Hospital, Amravati, Maharashtra, India*

***Corresponding author e-mail:** hri_gupta@rediffmail.com

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ABSTRACT

Hemophilia is characterized by spontaneous and post-traumatic bleeding and its complications in joints and muscles leads to severe pain, severe joint damage, disability, and a dramatic impairment of quality of life (QOL).
The purpose of the study is to access the QOL and to determine the functional disability affecting the individuals with hemophilia A.

102 patients of hemophilia A of age > 5 years and on clotting factor concentrate treatment (on- demand protocol) were included in the study. QOL was assessed with SF-36 questionnaire which includes 36 questions measuring physical and mental health with respect to eight health domains. Functional evaluation was done by World Federation of Hemophilia (WFH) approved Gilbert scoring system. Pearson Correlation explored the association between age of diagnosis, functional disability and QOL.
In our study, QOL of hemophilia A patients was seems to be satisfactory and negative correlation was found between the quality of life and functional disability in hemophilic patients.

Key words: Hemophilia, quality of life, functional disability, SF-36, Gilbert scale

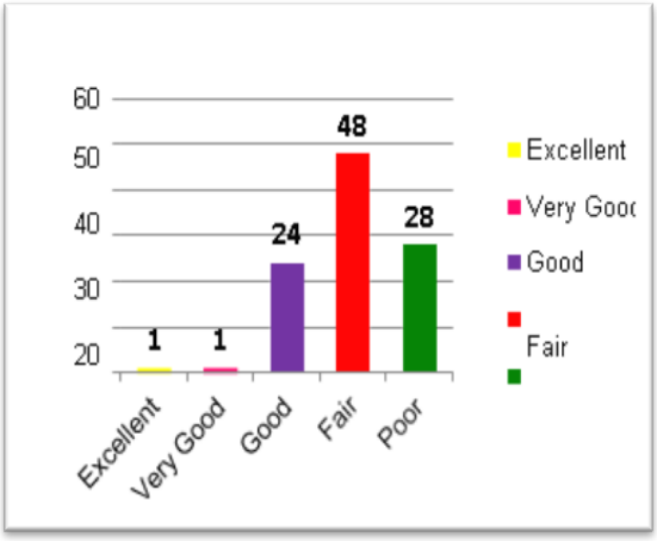
INTRODUCTION

Hemophilia is an X-linked, recessive bleeding disorder caused by deficiency of clotting factor VIII (FVIII) in hemophilia A and factor IX (FIX) in hemophilia B, which may be inherited or acquired from mutations of the respective clotting factor genes. Hemophilia A is found to be more common than hemophilia B, exhibiting 80-85% of the total hemophilia population. Hemophilia usually affects males on the maternal side. However, both F8 and F9 genes are liable to new mutations, and as many as 75% of all cases are the result of spontaneous mutation where there is no significant family history [1].

Hemophilia has an estimated incidence of approximately one in 10,000 births. As per the World Federation of Hemophilia's annual global survey in 2015, it was indicated that the number of people with hemophilia in the world were approximately 4, 00,000 and in India they were approximately 17,346. Out of which 14,508 were of hemophilia A and 2,127 of hemophilia B and 711 of unknown type Figure 1 and Table 1 [2].

Table 1: General Health

In general, would you say your health is		Compared to one year ago, how would you rate your health in general now?	
Excellent	1	Much better now than one year ago	12
Very Good	1	Somewhat better now than one year ago	49
Good	24	About the same	27
Fair	48	Somewhat worse now than one year ago	9
Poor	28	Much worse than one year ago	5



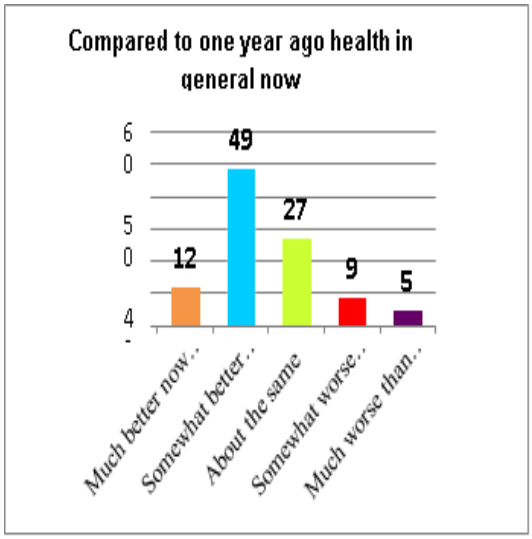


Figure 1A and 1B: general health

Patient with hemophilia may present with spontaneous bleeding specifically into the joint cavities or uncontrollable bleeding even after minimal injury. The hemorrhagic episodes of hemophilia are treated with replacement therapy, with clotting factor VIII for hemophilia A and clotting factor IX for hemophilia B, or with cryoprecipitate or fresh frozen plasma. If inappropriately managed, complications from joint bleeds, including impairment and deterioration in joint function, deformity, and loss of function, most commonly in knees, elbows and ankles can occur Figure 2 and

Table 2 [3]. Patients with hemophilia A or B often have poorer health-related quality of life than the general population.

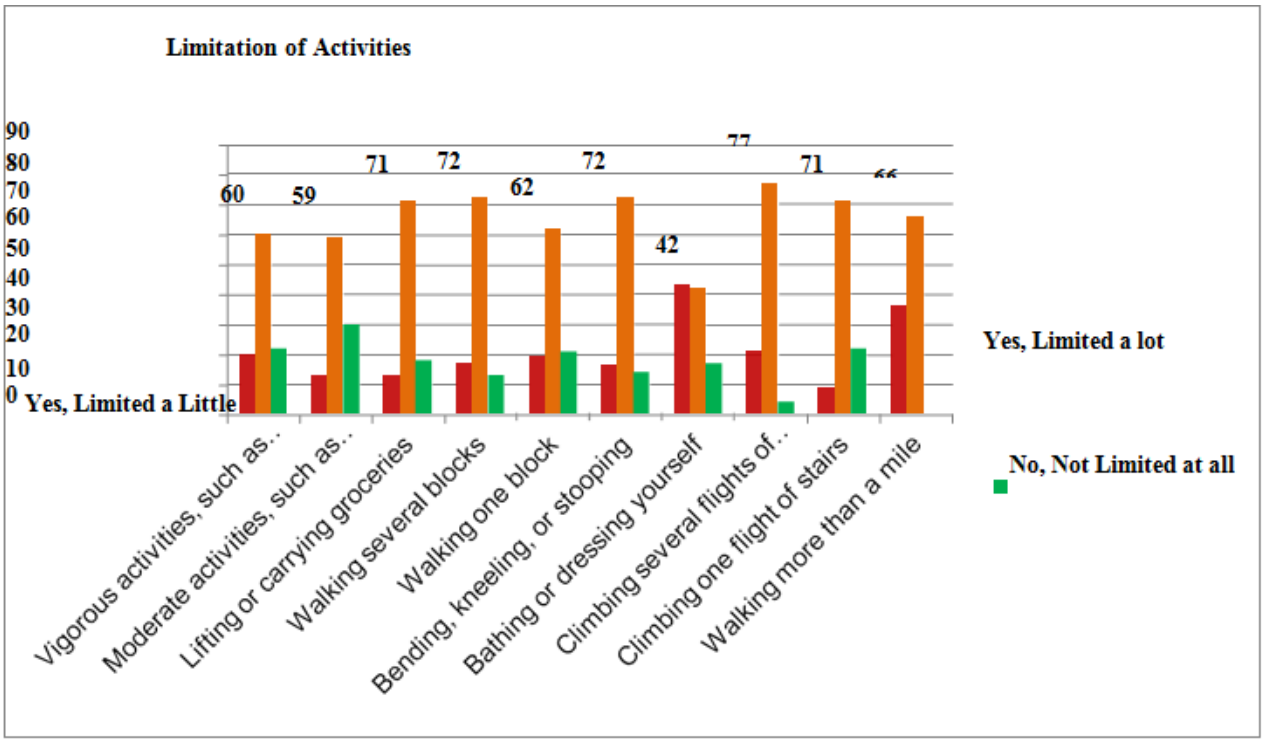


Figure 2: Limitation of activities

Table 2: Limitation of activities

Activity	Yes, limited a lot	Yes, limited a little	No, not limited at all
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.	20	60	22
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	13	59	30
Lifting or carrying groceries	13	71	18
Walking several blocks	17	72	13
Walking one block	19	62	21
Bending, kneeling, or stooping	16	72	14
Bathing or dressing yourself	43	42	17
Climbing several flights of stairs	21	77	4
Climbing one flight of stairs	9	71	22

Patients with severe hemophilia often have limitations in performing their job or more likely to be unemployed due to problems such as pain or frequent absence from work imposing significant economic burden on society Figure 3 and Table 3 [4].

Table 3: Physical Health Problems

	Yes	No
Cut down the amount of time you spent on work or other activities	68	34
Accomplished less than you would like	65	35
Were limited in the kind of work or other activities	78	24
Had difficulty performing the work or other activities (for example, it took extra effort)	71	31

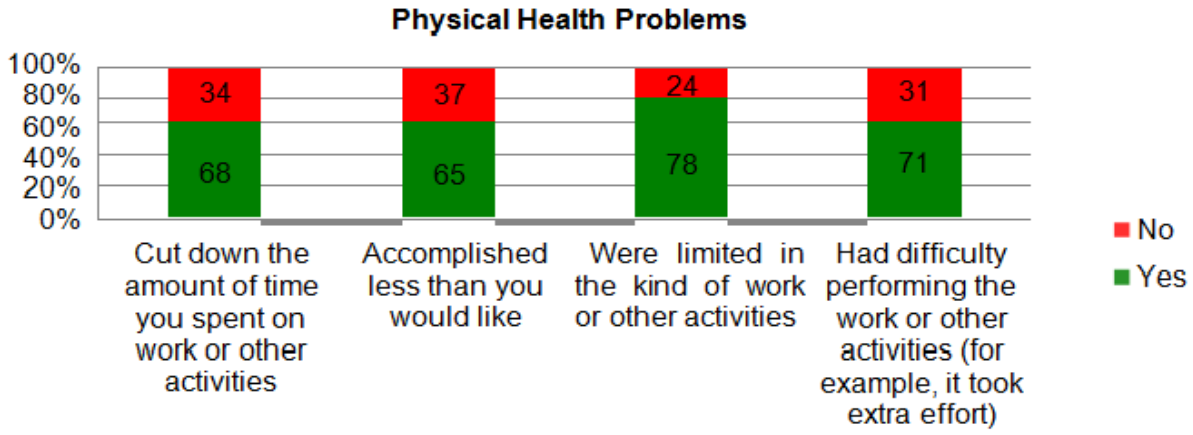


Figure 3: Physical health problems

Health and economic burden of hemophilia in the Indian scenario

Clotting factor concentrate is an orphan drug and its high cost places the drug out of reach of the majority of Indian patients. The lack of sufficient treatment product for pain relief, for life threatening hemorrhagic episodes and for the prevention of disability results in orthopedic morbidity, premature mortality and extensive OOP (Out Of Pocket) expenditure. The social costs in hemophilia occur as a result of lack of access to treatment and subsequent impact on schooling, employment, morbidity and mortality, Parents are financially affected due to the OOP expenditure, and experiences significant guilt and distress at being unable to offer appropriate treatment to the child [5].

Most of the costs in hemophilia are direct costs, which include investigations, anti- hemophilic medication, haematologist and orthopaedic visits, hospitalizations, medical and surgical procedures. Indirect costs are those affiliated with reduced productivity and increased absenteeism, disability and death. The intangible costs include the influence of the disease on QOL, as well as the emotional and psychological effects of the disease: the pain and suffering resulting from hemophilia are also important to consider [6].

In spite of, the healthcare of these patients defrays a huge amount of economic and human resources, hence it is necessary to frame them in the context of the level of quality of life provided. Moreover, there are a very few data about hemophilia in India. Many patients in India end up with severe disability due to late recognition, unavailability of factor or inappropriate treatment. This study is designed to measure QOL and functional disability among hemophilia patients Figure 4 and Table 4.

Table No. 4: Emotional Health Problems

	Yes	No
Cut down the amount of time you spent on work or other activities	49	53
Accomplished less than you would like	30	72
Didn't do work or other activities as carefully as usual	30	72

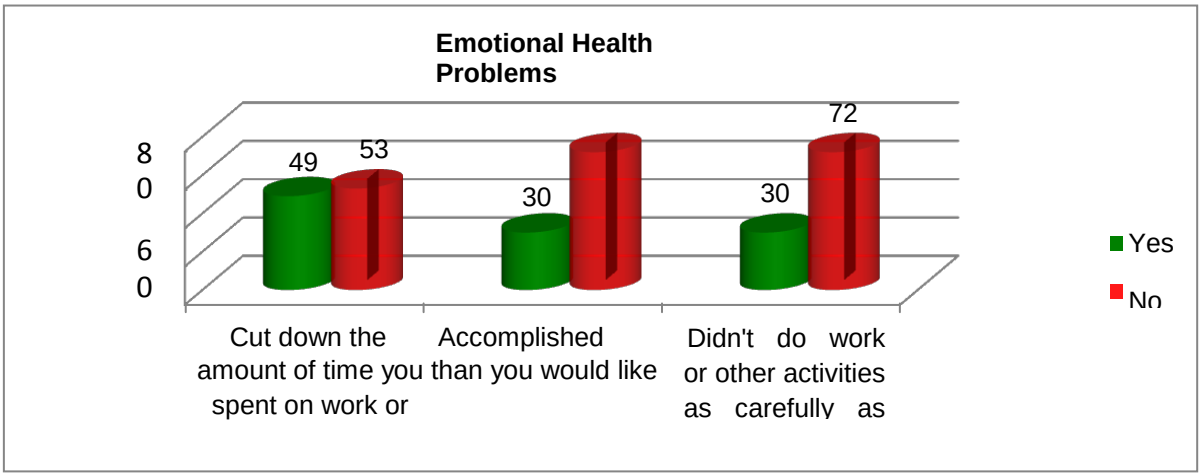


Figure 4: Emotional health problems

METHODOLOGY

Research design and setting

This was an observational study conducted for the 6 months in the Day Care Unit of District General Hospital Amravati during 2016-2017. The consent was taken from each participant or participant's parent/guardian before enrolling in the study. The objective of the study was explained to the participants and/or parent/guardian and confidentiality of identity was assured.

Study subjects

Inclusion criteria

All the males who are the diagnosed cases of hemophilia A of age > 5 years and on hemophilia treatment in an on-demand protocol were included in the study whether they attended the Day Care Unit (DCU) or were admitted to pediatric ward.

Exclusion criteria

Unwilling patient, Patients having factor deficiency other than factor VIII, Patients with hemophilia B, Von Willebrand disease and other bleeding disorders, Patients with inhibitors.

Quality of life assessment

QOL was assessed with SF-36 (Medical Outcomes Study Questionnaire Short Form 36 Health Survey).The SF-36 is a standardized questionnaire derived from a larger set of questions used in the US Medical Outcomes Study in the mid-1980s (Ware and Sherbourne 1992). These are generic, multi-dimensional measures of self-reported health status.

The SF-36 questionnaire consists of 36 questions measuring physical and mental health status in relation to eight health domains: Physical functioning, Role limitations due to physical health, Bodily pain, General health perceptions, Vitality (energy/fatigue), Social functioning, Role limitations due to

emotional health, General mental health (psychological distress/wellbeing) Responses to each of the SF-36 question are scored and summed on a 0-100 scale for all of the eight health concepts Table 5. Higher scores indicate better self-perceived health [7].

Table 5: Social Activities

	All of the time	A good Bit of the Time	Most of the time	A little bit of the time	Some of the time	None of the Time
During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?	4	18	23	40	17	0

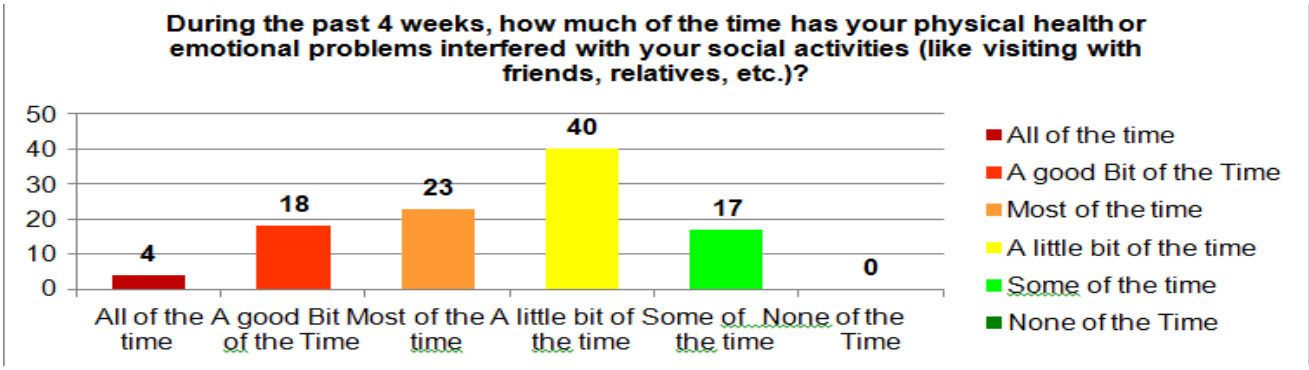


Figure 5: Social activities

Functional and physical examination tool

Functional evaluation was done by World Federation of Hemophilia approved Gilbert scoring system. The tool measures joint health and deterioration of the joints most commonly affected by bleeding in hemophilia – knees, ankles, and elbows Figure 6 and Table 6.

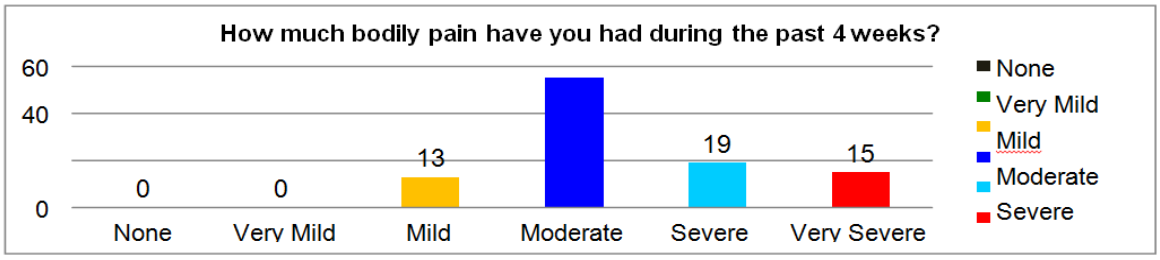


Figure 6: Pain

Table 6: Pain

	None	Very Mild	Mild	Moderate	Severe	Very Severe
How much bodily pain have you had during the past 4 weeks?	0	0	13	55	19	15

Gilbert score was used for evaluation of functional disability, which includes–

1. Pain (No pain/ mild / moderate / severe pain)
2. Bleeding (No bleeds/ Minor/ Majorbleeds)

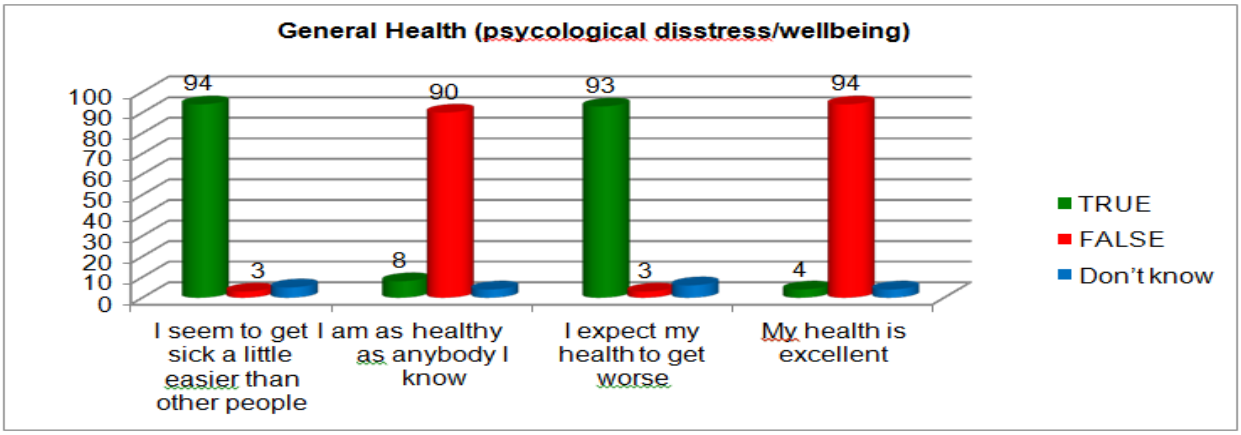


Figure 7: General Health (psychological distress/wellbeing)

3. Physical examination: swelling, muscle atrophy, axial deformity at knee and ankle, crepitus on motion, range of motion, flexion contracture, instability Figure 7 and Table 7.

Table 7: General Health (psychological distress/wellbeing)

I seem to get sick a little easier than other people		I am as healthy as anybody I know	I expect my health to get worse	My health is excellent
TRUE	94	8	93	4
FALSE	3	90	3	93
Don't know	5	4	6	4

Equipment/space required: Plinth/bed, Goniometer, Tape measure. Total score is 18. The score is considered 0 being normal joint and 18 being most affected. For a joint, increase in the score means increase in the functional disability.

RESULTS

One hundred and two patients with Hemophilia A were enrolled for the study. None of the patient was with inhibitors and no one on prophylaxis. All the patients were on-episodic transfusion basis (on demand treatment) and were treated with appropriate doses of factor VIII calculated as per standard method.

Participants ages ranged from 6 years to 57 years (mean: 20.2 years). Mean age at diagnosis was 6.5 years. Questionnaires were filled by patients themselves and they were allowed to ask questions about questionnaire items if they had problem in understanding. Young patients (6-8 years) were interviewed in a quiet room in front of their parents.

Quality of life

The mean overall score was 81.44 for the entire sample which indicates good quality of life. The greatest impairment in total subjects was in physical heath, pain perception and general mental health. The dimensions with the lowest impairment were emotional health and social activities Figure 8 and Table 8.

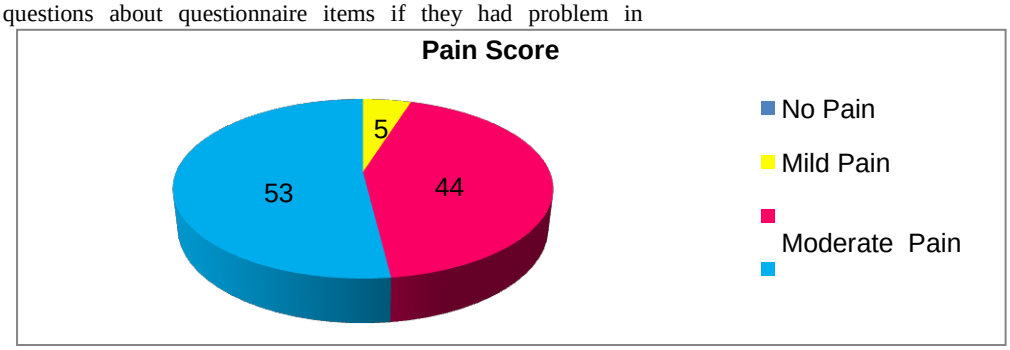


Figure 8: Pain score

Table No. 8: Functional and physical examination: Gilbert Score

Pain Score	Severity of Pain	No. of Patients
0	No Pain	0
1	Mild Pain	5
2	Moderate Pain	44
3	Severe Pain	53

Correlation between SF 36 score and gilbert score

Functional disability and the quality of life was correlated using Pearson correlation to find out the correlation. The r value was found to be - 0.21 (95% CI: -0.3964 to -0.02545). One tailed P value 0.01 and two tailed 0.02 was obtained. The results of analysis clearly indicate negative correlation between functional disability and quality of life.

In the present study, it was found that, as the age of diagnosis increases; the quality of life decreases with r = - 0.28 (95% CI: -0.4555 to -0.09739) and P (two-tailed) = 0.0035. Also, increase in the age of diagnosis is associated with increase in functional disability with r = 0.38 (95% CI: 0.2021 to 0.5362) and P (two tailed) <0.0001.

DISCUSSION

Studies into the quality of life of hemophilic patients as a function of hemophilia treatment and integral health care are still rare. Also functional disability in hemophilia is also a very less discussed issue.

Our study determined the QOL of children and adults with hemophilia A with SF 36 questionnaire. It was found that adolescents and adults were more impaired in total SF 36 scores compared to children aged 6-12 years. These results were consistent with the study of Witkop et al. They revealed that psychosocial factors also have an important impact on patient's quality of life [8].The result of our study revealed that mean overall score on the SF 36 was 81.44.

Comparison of the QOL between the present study and of Kavia A. et al. and Mishra et al. indicated that the QOL of patients with hemophilia in our study was satisfactory [12,13]. However, Gringeri and the Haemo - QOL group, Van der Net J et al. and Broderick et al. found that QOL in hemophilia patients in developed countries (Western Europe and Austrelia) has improved greatly because of the widespread access of patients to home treatment and prophylaxis and participation in sports [9-11].

In our study we correlated the quality of life with functional disability and we found a strong negative correlation between the functional disability and quality of life as when the functional disability increases there is decrease in quality of life [12,14]. Also, in a Spanish study, Aznar et al. reported the QOL of 70 patients related to orthopedic status, and found QOL to be negatively affected by severe orthopedic impairment via hemophilia [15]. The limitation of the present study was we have not used the disease - specific questionnaire to assess the QOL among hemophilia patients.

CONCLUSION

The QOL of hemophilic patients was seems to be satisfactory. It is considered that the availability of clotting factor concentrates and specialized services by the healthcare professionals for the management of the haemophilic patients are responsible for the improved quality of life.

We found that the mean Gilbert score increases as the age increases i.e. the functional disability increases with the age Figure 9 and Table 9.

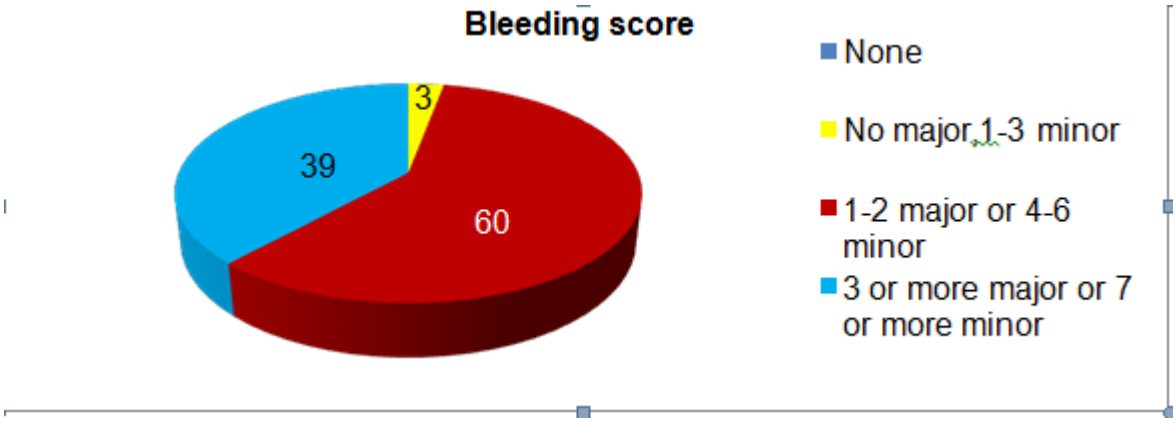


Figure 9: Bleeding score

Table 9: Bleeding Score

Bleeding score	Severity of Bleed	No. of Patients
0	None	0
1	No major,1-3 minor	3
2	1-2 major or 4-6 minor	60
3	3 or more major or 7 or more minor	39

We also found that there was negative correlation between the quality of life and functional disability among hemophilic patients, i.e. as the functional disability increases in the haemophiliacs, the QOL decreases Figure 10 and Table 10.

Table 10: Total Gilbert Score

Score range	Total score
between 0-6	4
between 7-12	60
between 13-18	38

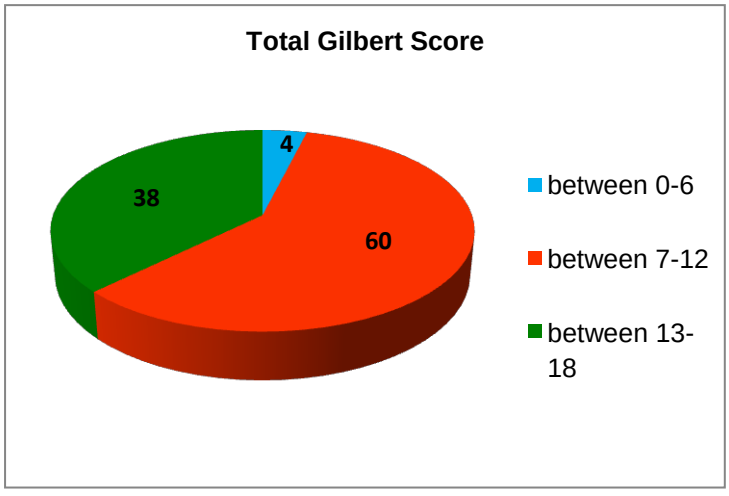


Figure 10: Total Gilbert Score

In hemophilia with increased availability of clotting factor concentrates for treatment, it is necessary to forget the old habit of keeping hemophilia patients away from physical activities to prevent traumatic joint injuries. The hemophilia patients should be engaged in sports, for the physical benefits and as a mechanism for social inclusion also. Moreover prophylaxis appears crucial in improving the health and economic consequences of hemophilia, ensuring a better quality of life for

hemophiliacs and hence a lower disease burden.

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