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Original Article

Physical Medicine and Rehabilitation Section

Impact of Functional Disability on Quality of Life in Patients with Haemophilia: An Observational Study

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ABSTRACT

Introduction: Haemophilia is a disease characterised by multiple episodes of spontaneous as well as traumatic bleeding leading to joint pains, joint damage. As a result, there may be disability ultimately leading to a compromised Health Related Quality of Life (HRQoL). This impairment is related to the severity of the clotting factor defect, bleeding frequency and orthopaedic problems.

Aim: To find out the correlation of quality of life with functional disability in patients with haemophilia A and B.

Materials and Methods: This observational study was conducted from April 2012 to November 2013 on 88 patients with haemophilia A and B, aged between 11 to 50 years. The Physical Component Summary (PCS) and Mental Component Summary (MCS) score was calculated using the short form health survey (SF-36) questionnaire, which is used to assess HRQoL. Gilbert score was used for assessing functional disability. The patients were analysed at initial presentation and then at six months follow-up. All scores were calculated at both times, and comparison was done according to different age groups as well severity of haemophilia. Correlation between SF-36 and Gilbert score was evaluated using various statistical methods.

Results: All 88 patients were males with the mean age of 21±9.9 years, with 90.91% being type A haemophilia and 9.09% being type B haemophilia. Clinical presentation of haemophilia patients included bleeding into joints and muscles, gum bleed and epistaxis. Mean scores for PCS and MCS at the initial evaluation were 26.34 and 28.53 and after six months the scores were 29.79 and 29.87, respectively. The overall mean Gilbert score for different age group at initial evaluation and six months were 4.46 and 3.20, respectively. Gilbert score increased with age as well increasing severity of haemophilia. In comparison, PCS and MCS scores decreased with age as well as with increasing severity. Using linear regression and correlation, a negative correlation between functional disability and HRQoL was found.

Conclusion: Negative correlation between functional disability and quality of life suggested that when there is increase in functional disability there is a decrease in quality of life. Also, as severity of haemophilia increases the functional disability and quality of life decreases. Therefore, an early intervention in haemophilia patients is important to reduce functional disability. The quality of life can be improved by limiting the functional disability. These findings should aid in improving healthcare delivery to the patients of haemophilia.

Keywords: Gilbert score, Mental component summary, Physical component summary

INTRODUCTION

Haemophilia is an X-linked inherited recessive bleeding illness marked by clotting factor VIII (classic haemophilia, or haemophilia A) or IX deficiency (haemophilia B). Haemophilia A affects one in every 5000 male births, and haemophilia B affects one in every 30,000 male births [1].

Haemophilia has an estimated incidence of approximately one in 10,000 births. As per the World Federation of Haemophilia's (WFH) annual global survey in 2019, number of patients with haemophilia in India is approximately 23,666. Out of which 19,690 were of haemophilia A and 3,150 of haemophilia B and 826 of unknown type [2]. The severity of the condition is determined by the level of clotting factor. People with severe haemophilia have a clotting factor activity of 1%, moderately affected patients have a clotting factor activity of 1-5%, and mild patients have a clotting factor activity of 6-40% [3].

Lower clotting factor levels, especially in severe individuals, cause spontaneous haemorrhages in muscles and joints, but they can also impact other organs. Repetitive haemorrhages in joints, in particular, can lead to debilitating haemophilic arthropathy [4]. One explanation for this is that the vast majority of patients (about 80%) [5] lives in developing countries where financial constraints exist.

Joint bleeding, persistent pain, and other clinical consequences can have great impact on haemophilia patient's quality of life during the course of the disease [6]. Variables that have been linked to a lower HRQoL in haemophilia patients include- the severity of the clotting defect, bleeding frequency as well as orthopaedic issues. Therefore, HRQoL has become a very important factor in follow-up of patients with haemophilia. The short form health survey (SF-36) is a very commonly used tool to calculate HRQoL [7]. The WFH has used Gilbert score [8], a technique used to determine joint health and functional impairment in haemophilia patients.

Several studies have addressed quality of life issues in haemophilia population using different quality of life questionnaires. Some have used haemophilia-specific quality of life index [9,10] while others have evaluated using SF-36 [11]. However, very few have focused on the importance of functional disability in haemophilia patients [11], so the present study was conducted to measure and correlate functional disability and quality of life to know better about the situation through which haemophilia patients were undergoing.

MATERIALS AND METHODS

This observational study was conducted in the Department of Physical Medicine and Rehabilitation (PMR) at Sawai Mansingh Medical College and Hospital in Jaipur, Rajasthan, India, from April 2012 to November 2013. Permission from the Institute Ethics Committee and Research Review Board was obtained (Letter No. 11834 dated 18/04/2012).

Inclusion criteria: Patients of haemophilia A and B aged 11 to 50-year-old, including both the Inpatient and Outpatient Department, irrespective of whether having severe, moderate or mild haemophilia [3].

Exclusion criteria: Unwilling patients, patients with other bleeding disorders like Von Willebrand disease, other than haemophilia A and B, were excluded from the study.

All patients with haemophilic arthropathy who were seen or admitted to the Department of PMR were clinically assessed, screened, and informed about the study's kind and purpose. The participants who gave their informed consent were recruited in the study. Total 88 patients formed the sample size. The patient demographic data was filled out, and the functional evaluation was done using WFH approved Gilbert scoring system and World Health Organisation (WHO) SF-36 scale [7,12] was used to assess health related QoL.

Outcome Variables

SF-36 Scale

The SF-36 scale [7,12] was used to measure quality of life at admission and at six months from admission. SF-36 questionnaire determines HRQoL on eight dimensions: physical functioning, social functioning, physical and mental role limitations, mental health, energy/vitality, pain and general health perception. Results for each dimension were scored and transformed on to a scale from 0 (worst health) to 100 (best score). Results from SF-36 were reported as a Physical Component Scale (PCS) and Mental Component Scale (MCS).

Gilbert Score

The Gilbert score [8] was used to assess functional disability which includes physical examination, swelling, muscle atrophy, axial deformity at knee and ankle, crepitus on motion, range of motion, flexion contracture and instability. Total score is 12. Zero (0) being normal joint and 12 being most affected. An (s) was added after the number if chronic synovitis was clinically diagnosed. For any joint, increase in the score meant increase in the functional disability.

STATISTICAL ANALYSIS

All haemophilia patients were analysed at initial presentation and at six months follow-up. Gilbert score was calculated in different age groups using mean. Correlation between Gilbert score and SF-36 score was done by using linear regression and correlation both at the time of admission and at six months follow-up. Data was expressed as median with interquartile range, mean, and standard deviation or percentage as appropriate. Student t-test for unpaired data was applied, when testing differences between groups. Associations between Gilbert Score and SF-36 scales were evaluated with Pearson or Spearman correlations. Two-tailed p-values <0.05 were considered to indicate statistical significance. All analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) software, version 20.0.

RESULTS

The study included a total of 88 participants with haemophilia A (n=80) and haemophilia B (n=8). All the patients were males. Majority of the patients had severe haemophilia [Table/Fig-1]. The mean age of the study population was 21±9.9 years. As seen in [Table/Fig-2], maximum cases of Haemophilia A were in between age group of 21-30 years while Haemophilia B was maximum in 11-20 years.

Variable	N, (%)
Haemophilia A	80 (90.91%)
Haemophilia B	8 (9.09%)
Severity	
Mild	5 (5.68%)
Moderate	30 (34.09%)
Severe	53 (60.23%)

[Table/Fig-1]: Distribution of haemophilia (n=88).

Age group (in years)	Haemophilia A	Haemophilia B	Total
11-20	24	3	27
21-30	29	2	31
31-40	18	1	19
41-50	9	2	11
Total	80	8	88

[Table/Fig-2]: Distribution of Haemophilia A and B cases in different age groups.

In the study population, it was found that the mean Gilbert score increased with the increase in age group, suggestive that functional disability increases with age due to repeated joint involvement [Table/Fig-3]. The PCS score was highest in 11-20 years age group both at initial evaluation and at six-month follow-up; while MCS score was highest in 31-40 years age group at initial evaluation and in 11-20 age group at six-month follow-up. As per [Table/Fig-3], there was significant difference between Gilbert score at initial evaluation and at six months follow-up in 31-40 years age group. Similar significant difference was noted in PCS score in 21-30 years age group.

On analysis of data at initial presentation and at six months between functional disability and physical component a strong negative correlation was found. Similarly, analysis of data between functional disability and mental component at initial presentation and 6 months showed negative correlation [Table/Fig-4]. Gilbert score increased as the severity of haemophilia increased; in comparison the overall PCS and MCS score decreased with increasing severity, although none of this was statistically significant [Table/Fig-5].

Age groups (in years)	Gilbert score			SF-36					
				Physical component score			Mental component score		
	initial evaluation	6 months follow-up	p-value	Initial evaluation	6-month follow-up	p-value	Initial evaluation	6-month follow-up	p-value
11-20	3.77	2.97	0.41	30.96	32.41	0.16	29.00	31.70	0.19
21-30	4.50	3.18	0.09	22.60	29.59	0.05	25.86	25.27	0.31
31-40	4.67	3.63	0.04	25.26	29.10	0.11	29.52	27.90	0.15
41-50	4.75	3.75	0.20	20.55	26.75	0.08	19.24	23.85	0.07
Overall	4.46	3.20	0.10	26.34	29.79	0.07	28.53	29.87	0.18

[Table/Fig-3]: Gilbert score and SF-36 PCS and MCS in different age groups.

Correlation between	r-value		p one tailed value		p two tailed value		df	
	Initial	At 6 months	Initial	At 6 months	Initial	At 6 months	Initial	At 6 months
Functional disability and Physical component	-0.910	-0.906	0.042	0.048	0.09	0.09	2	2
Functional disability and Mental component	-0.521	-0.662	0.239	0.169	0.478	0.338	2	2

[Table/Fig-4]: Correlation findings between functional disability and Physical Component Score (PCS) and Mental Component Score (MCS).

Severity of haemophilia (n)	Gilbert score			SF-36					
				Physical component score			Mental component score		
	Initial evaluation	6 months follow-up	p-value	Initial evaluation	6 month follow-up	p-value	Initial evaluation	6 month follow-up	p-value
Mild (5)	1.24	1.55	0.13	31.40	30.12	0.15	30.25	28.97	0.12
Moderate (30)	3.67	4.31	0.07	29.88	29.67	0.42	28.17	27.36	0.22
Severe (53)	4.02	4.19	0.17	24.14	22.46	0.08	25.04	22.89	0.06

[Table/Fig-5]: Gilbert score and SF-36 PCS and MCS values in relation to severity of haemophilia.

DISCUSSION

Haemophilia patients suffer from haemorrhagic episodes leading impairment and deterioration of joint function leading to an overall poor quality of life. The HRQoL is considered to be one of the most relevant health outcome measure in medicine. Studies into the quality of life of haemophilic patients are still rare and it is a recent focus of research. Evaluation of functional disability in haemophilia is also a very less described topic. Correlation of QoL and functional disability in these patients can allow us to know how much the QoL is affected which can guide about the measures to be taken to improve QoL and reduce functional disability.

In the study all the patients were males which are in contrast to WFH data of 2019, wherein the incidence of haemophilia A and B in females was found to be 4% and 6%, respectively [2]. The WFH data of 2020 [13] reports this incidence in females to be 3% and 5%, respectively. The ratio of haemophilia A and haemophilia B patients was 10:1 in the study population. As per WFH data of 2020, ratio in Indian population is about 6.1:1 (18928:3104) [13]. In the study by Mishra S et al., the ratio was about 7.5:1 [10]. Majority of the patients had severe haemophilia (>60%), similar to other studies on Indian population [10,14].

The WFH physical examination score also known as Gilbert score measures joint health and function [2,8]. It is primarily designed for adults and children with established arthropathy for calculating functional disability. It helps to evaluate for need for orthopaedic intervention and to see the outcomes following physical therapy interventions. In the study, it was found that mean Gilbert score increased from 1.4 in mild haemophilia patients to 3.9 in severe haemophilics. It was found that with increasing severity of haemophilia there was an increase in the functional disability. In haemophilia, although bleeding may occur in any area of the body, the hallmark is haemarthrosis [15]. Repeated haemarthroses lead to the development of target joints, which are more prone to continuous bleeding and the development of chronic arthropathy [16]. Similar conclusion has been reported in many other studies conducted worldwide [16-18].

The functional disability in different age group increases with increasing age, which signifies that as the number of episodes of haemophilic arthropathy increase there is an increase in functional disability in the elderly age group. It was observed that Gilbert score increased in all age groups at six month follow-up indicating worsening of functional disability. Joint bleeding leads to adverse changes in both the synovial tissue and the articular cartilage causing severe limitation of daily normal activities [16]. Repeated episodes of joint bleed leading to development and worsening of chronic haemophilic arthropathy and an increase in Gilbert Score [16]. Hayam M et al., in a study on 30 haemophilic patients reported a significant positive correlation was found between the Gilbert score and the age of the patients, as found in the present study also [18].

There are many questionnaires available for evaluation of the HRQoL. Some studies have used haemophilia specific QoL questionnaires like Hemophilia-Specific Quality of Life Index (Haemo-QoL) [9,10] while others have used SF-36 which is one of the most widely used generic HRQol instrument which has been validated in many diseases in many studies conducted in India and other countries [12]. In this study, the QoL analysis using PCS score and MCS score showed that the quality of life of haemophilia patients decreased over six month follow-up from the time of initial evaluation. Another important analysis done between PCS, MCS and Gilbert score found a strong negative correlation between the two i.e., when functional disability increases there was decrease in QoL. This was in concordance with the study done by Sinha R et al., although the study population included children as well [12]. In another study done on adult patients in Italy, by Scalone L et al., {Cost Of Care Inhibitors Study (COCIS study)}, was the first study which showed that HRQoL in haemophilia patients on inhibitors is impaired by their orthopaedic status, while other aspects do not seem to influence patients' global wellbeing [19]. Both these studies used the SF-36 questionnaire for patient evaluation.

Limitation(s)

An important limitation of the present study is not using haemophilia-specific questionnaire to assess the HRQoL like Haemo-QoL, as done in many other studies [9,10]. Also, it would be better if such a study is carried out with a greater number of participants as well including female patients.

CONCLUSION(S)

The findings of the study suggested that there was negative correlation between functional disability and quality of life both at initial evaluation and at six months follow-up, the increase in functional disability leads to poor QoL. So by focusing on reducing the functional disability we can improve the QoL of haemophilia patient. Early intervention in haemophilia patients to reduce functional disability can prove to very important step in improving the quality of life of haemophilia patients. To reduce the functional disability, focus on early treatment of bleeding in joints, by early availability of clotting factors and by providing good rehabilitative care to the patient so that the restriction of joint range of motion can be limited.

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