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Review Article

Association of psychological and physical health with quality of life in patients with haemophilia: a brief review

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ABSTRACT

Hemophilia is an inherited bleeding disorder that is caused by an x-linked deficiency of clotting factors VIII in hemophilia A and IX in hemophilia B. Hemophilia A is more common than hemophilia B accounting for approximately 80-85% of all cases. Patients with hemophilia face several challenges due to bleeding episodes such as chronic arthropathy, functional disabilities, and many other health issues. Consequently, patients with hemophilia experience psychological comorbidities such as depression, anxiety, and social isolation. This emphasizes the importance of addressing both physical and mental health aspects in the overall care of these patients. To determine the association between psychological and physical health with quality of life in patients with hemophilia. This narrative review is conducted on databases from PubMed, Google Scholar, and ResearchGate. This review included 11 studies on the association between psychological and physical health with quality of life in patients with hemophilia. In conclusion, many studies show us different parameters between psychological health and physical health with quality of life in hemophilic patients but there is no research showing us the association between psychological and physical health with quality of life in hemophilic patients.

Keywords: Hemophilia, Depression, Anxiety, Quality of life, Functional ability

INTRODUCTION

Hemophilia is an X-linked genetic disorder that hinders the body's ability to form blood clots. There are two main types of hemophilia, Hemophilia A and Hemophilia B.[1] Hemophilia A is caused by a deficiency of clotting factor VIII, and hemophilia B is caused by a deficiency of clotting factor IX. Hemophilia A is more common than hemophilia B. Hemophilia A approximately accounts for 80-85% of all cases and hemophilia B accounts for approximately 15-20% of all cases. Hemophilia usually affects only males who inherit an affected maternal X chromosome. Females with hemophilia are rare; in such cases, both X chromosomes are affected or one is affected and the other is inactive. A female with one affected X chromosome is called a carrier of hemophilia.[2] The severity of bleeding tendencies, categorized as mild, moderate, or severe based on factor concentration, plays a crucial role in predicting bleeding risks, guiding management strategies, and predicting outcomes.[3] Hemophilia leads to prolonged bleeding after injuries, increased bruising, and higher risk of internal bleeding in joints or the brain. Bleeding into joints can cause lasting damage, while bleeding in the brain may result in headaches, seizures, or altered consciousness.[1] Patients with hemophilia must deal with the consequences of bleeding episodes, chronic arthropathy, functional disability dependence on blood transfusions, and an increased risk of virus transmission through blood products, which may result in psychological

comorbidities such as depression, anxiety and social isolation. The prevalence of depression and anxiety has been found to increase in patients with hemophilia.[4] The World Federation of hemophilia recognizes depression and anxiety as challenging comorbidities that can affect people with hemophilia.[5] People with hemophilia show lower levels of self-esteem as compared to those without the condition.[6] Depression is known to be associated with functional impairment, diminished quality of life, and poor adherence to medical treatments. Increased symptoms of depression correlate with an increase in health-related distress, as well as an increase in risky behaviors, such as drug and alcohol abuse. Thus, patients with hemophilia may be at increased risk for: symptoms of depression, depression contributing to poor outcomes, depression contributing to risky behavior, such as drug and alcohol abuse and depression contributing to lack of compliance with treatment protocols. Depressive symptoms in individuals with hemophilia provide an opportunity for intervention through counseling, behavioral modification, or pharmacologic therapies. Promoting social interaction, community engagement, education, and self-reliance is crucial for the well-being of patients with hemophilia.[7] Despite significant advancements in hemophilia treatment, mental health disorders (MHD) like depression, anxiety, and attention deficit hyperactivity disorder (ADHD) remain prevalent among individuals with hemophilia. This emphasizes the importance of addressing both physical and mental health aspects in the overall care of these patients.[5]

Replacement therapy, using either clotting factor VIII for hemophilia A or clotting factor IX for hemophilia B, or cryoprecipitate or fresh frozen plasma, is used to treat hemorrhagic episodes in people with hemophilia.[1] Adjunctive management for hemophilia is clotting factor precipitate with PRICE principle-protection, rest, ice, compression and elevation protocol for joint and muscle bleed and another approach is POLICE -protection, optimum loading, ice, compression and elevation. Ice is used to treat acute and chronic pain.[2]

METHODS

Studies are searched from the following search engines PubMed, Google scholar, and ResearchGate to review the literature. Studies include depression, anxiety, functional outcomes, and health-related quality of life. Keywords used to search studies are HRQoL, functional independence, psychological comorbidities, physical health and hemophilia.

Table 1: Other studies.

Authors	Objectives	Design	Characteristics of participants sample size	Material and Methods	Outcomes Measures	Results
Poonnoose et al[8]	To assess the functional independence in patients with hemophilia	Experimental study	63 patients with hemophilia	FISH was assessed in 63 hemophilic patients to measure the patient's independence in performing activities of daily living (grooming and eating, bathing and dressing), transfers (chair and floor), and mobility (walking, step climbing and running)	FISH assessed 8 activities and the score ranged from 1-4 for each activity on the basis of his ability to perform the activity.	FISH was found to be a reliable and valid tool with good internal consistency and responsiveness to therapy, for the assessment of functional independence in persons with hemophilia.
Walsh et al[9]	To compare HRQoL among adult males affected with mild hemophilia A due to same mutation to that of unaffected age	Cross-sectional study	80 patients included i.e.47 affected males and 33 controls	SF-36 (general health,body pain,vitality, social functioning, Mental health) to measure HRQoL and HAQ to measure physical function.	Scores for each of the SF-36 domains were lower in affected male. HAQ did not show much difference between both groups.	The affected males had a higher level of comorbidity, prior bleeding and existing damage than controls.
Von Mackensen et al[10]	To investigate HRQoL of elderly	Cross-Sectional study	elderly>65 years PwH	For generic and geriartic-generic EQ-5D, WHOQOL-BREF	HRQoL was worse in patients at WHOQOL-BREF.	Haem-A-QoL proved to be a reliable and valid

Continued.

Authors	Objectives	Design	Characteristics of participants sample size	Material and Methods	Outcomes Measures	Results
	hemophilia patients in comparison with their age-matched controls and to validate Haem-A-QoL questionnaire.			questionnaires were used and for hemophilia-specific Haem-A-QoL. questionnaire is used. 39 patients were investigated,33 with hemophilia A and 6 with hemophilia B and compared to 43 controls.	Highest impairments was found by Haem-A-QoL(physical activity,leisure,physical health).	tool for HRQoL assessment in hemophilic patients.
Rambod et al[11]	To evaluate the impact of psychological aspects and pain on HRQoL in adult patients with hemophilia.	Cross-sectional and correlational study	103 patients with hemophilia	Data collected using hemophilia specific qol(Haem-A-QoL)consisting physical health,feeling,family planning,future,workand school,and others),Depression Anxiety Sress Scale(DASS)consisting 21 items.	Haem-A-QoL questionnaire had good reliability and highest impairments were found in feeling,sports and leisure,physical health. Most PwH experienced normal levels of stress but have a moderate to severe form of depression and anxiety in the DASS	There is a significant association between HRQoL and depression, anxiety,stress and severity of pain.
Naous et al[12]	To assess the impact of hemophilia on HRQoL and social status of adult PwH	Cross-Sectional study	60 severe and moderate PwH. 112 healthy controls.	HRQoL was assessed using SF-36 questionnaire consisting 36 items including 8 dimensions (physical activity,physical pain,vitality,life,relationship,mental health and others).	PwH had worse scores in all SF-36 domains except for energy/fatigue. Affected joints and frequency of monthly bleed are inversely correlated with SF-36 domains.	As compared with controls, the majority of PwH has difficulties in social integration, has severe physical limitations and psychological impairments.
Trindade et al[13]	To evaluate the QoL of patients with hemophilia using the WHOQOL-bref and the Haem-A-QoL instruments.	Cross - Sectional Study	17 patients aged 18 year or older with hemophilia registered at hemocenter.	Data collected using a specific questionnaire Haem-A-QoLcomprised of 46 items on physical health,feelings,sports and leisure,future,family planning,relationship/sexuality and a generic questionnaire WHOQOL-bref comprising 26 questionnaires on general QOL,physical,psychological,social relations.	WHOQOL-bref questionnaire had highest score in the domain of social relation and Haem-A-QoL had highest score in family plannning	Hemophilia had high negative impact on physical,sports and leisure in sample subjects. Haem-A-QoL is more specific to evaluate QoL.
Tat et al[14]	The effects of MT in lower limb joints on functional independence score in hemophilia	Pilot study	Total 17 patients Control group=9 Manual therapy group=8	ROM,strength,pain measured by goniometer,joint health measured by FISH	ROM,strength,activity pain,HJHS and FISH improved in MTG	MT have greater effects on all functional variables.
Jimenez-Cebrian et al[15]	The impact of depression in adult patient with hemophilia and to	cross-sectional	100 participants. Hemophilic subjects=50 Healthy subjects=50	Subjects divided into 2 groups, hemophilic and non-hemophilic group. the scores of BDI intrument were compared between both groups.	Hemophilic subjects showed worse BDI results as compared to non-hemophilic subjects.	Patients with hemophilia are at increased risk of depressiveness.

Continued.

Authors	Objectives	Design	Characteristics of participants sample size	Material and Methods	Outcomes Measures	Results
	compare it with healthy matched paired control.					
Curtis et al[16]	To compare the impact of hemophilia on comorbidities Joint problems,HR QoL and health care utilization.	Observational study	PwH of two age groups:40-49 years and>50 years.	HUGSVI study recruited PwH AorB age>40 years.sample included 69 males.Data collected on joint pain,HRQoL,depression,anxiety,comorbidities.	Individuals >50 years had mild and moderate hemophilia than 40-49 years.>50 year old had more joint pain,limited ROM than younger group.	Older group experienced lower QoL,more comorbidities both of aging and hemophilic arthropathy and lower rates of health care utilization.
Fornari et al[17]	The influence of illness on psychosocial aspects of adult person with hemophilia and caregivers of person with hemophilia.	Observational study	120 PwH and 79 CPwH	Participants were recruited through online invitations with internet access. EQ-5D-5L and EQ-5D-Y with VAS is used to measure overall health status.	Mobility, pain and mental health domains of EQ-5D were mostly impaired in both patients and caregivers reducing qol.`	Hemophilia affects many aspects of an individual life and psychosocial factors have a central role in quality of life and interpersonal relation- ships of people with haemophilia and their caregivers.
Jhandai et al[18]	To determine walking ability by measuring the 50-m walk test time in severe hemophilic patients, as compared to the normal population.	Cross-Sectional Study	60 subjects (males) comprising 30 hemophilics and 30 in a control group.	Only patients with severe hemophilia and knee arthropathy were included aged 18-30 years. 50 m walking test was measured in seconds. 50 m walk test consisted both groups non-stop walking 2.5 times between 2 cones 10 m apart	It showed a normative value of 36.6sec in control and 67.2sec in hemophilic group.	50 m walking test of PwH is useful for planning treatment.

DISCUSSION

The physical health challenges faced by patients with hemophilia are profound and multifaceted. Frequent bleeding episodes, particularly into joints and muscles, lead to chronic pain, arthropathy, and mobility issues. These complications can severely restrict daily activities and diminish physical functioning, which in turn deteriorates QoL. Studies have shown that the severity and frequency of bleeds directly correlate with reduced physical QoL scores. Prophylactic treatment regimens have been effective in reducing the frequency of bleeding episodes but the burden of intravenous infusions can itself be a source of stress and inconvenience, affecting both physical and psychological health.

Psychological well-being in hemophilia patients is equally crucial and deeply intertwined with physical health. Chronic pain and physical limitations can lead to significant emotional distress, including anxiety, depression, and feelings of helplessness. Evidence suggests a high prevalence of psychological disorders among hemophilia patients. The relationship between physical and psychological health in hemophilia is bidirectional. Poor physical health can lead to psychological distress, and conversely, psychological issues can exacerbate physical symptoms. For example, anxiety and depression can negatively affect treatment adherence, leading to more frequent bleeding episodes and worsening physical health. A study by Walsh showed there are high level of comorbidities other than bleeding and existing damage in patients with hemophilia. Another study by Masoume Rambod showed that there is a significant association between HRQoL and depression, anxiety and stress. The quality of life in patients with hemophilia is significantly influenced by the interplay between physical and psychological health.

CONCLUSION

Despite significant advancements in hemophilia treatment, mental health disorders (MHD) like depression, anxiety, and attention deficit hyperactivity disorder (ADHD) remain prevalent among individuals with hemophilia. This emphasizes the importance of addressing both physical and mental health aspects in the overall care of these patients. In all above-mentioned studies, no definitive conclusion was seen with the association between psychological and physical health with quality of life in hemophilic patients due to multiple limitations in all the studies like insufficient sample size, less enrollment of people who suffer from hemophilia, and inability to follow-up. Many studies show us different parameters between psychological health and physical health with quality of life in hemophilic patients but there is no research showing us the association between psychological and physical health with quality of life in hemophilic patients. Hence to fill this gap of knowledge, we propose a study to determine the association between psychological and physical health in terms of depression, anxiety, functional impairments with quality of life in patients with hemophilia.

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