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Prevalence of Depression in Hemophilia Patients: A Cross-Sectional Study

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ABSTRACT

Background: Chronic and debilitating diseases induce several psychiatric consequences. The current research determines the prevalence of depression in hemophilia patients.

Methods: This is a cross-sectional study of 80 hemophilia patients referred to Mohammad Kermanshahi Hospital in Iran in 2020. The subjects were selected using the sampling method. The data collection tool includes a demographic information checklist, clinical and medical records, and Beck Depression Inventory-Second Edition (BDI-II). Data analysis was performed using frequency, percentage, and Chi-square tests.

Results: The results demonstrated that the prevalence of depression in hemophilia patients was 57.5%. Furthermore, the prevalence of depression was not associated with age, education, occupation, marital status, type of hemophilia, disease severity, age of onset (i.e., disease diagnosis age), orthopedic complications, and monthly bleeding episodes (P-Values > 0.05). However, among the patients who consumed narcotics, only 25.8% were not depressed; on the other hand, 53.1% of those who did not consume narcotics were. A clear statistically significant correlation between narcotics use and the prevalence of depression was presented (P-Value < 0.01).

Conclusions: The present study reveals a significant prevalence of depression among hemophilia patients, with a notable correlation observed between depression rates and the use of narcotics drugs.

Keywords: Prevalence; depression; mental disorders; hemophilia, narcotics.

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Introduction

Depression and chronic illness have a reciprocal effect, as is increasingly apparent. Studies have revealed that depression can promote or exacerbate the symptoms of chronic illness in people who live with chronic illness (Baghaei Naeini et al., 2023; Barlow, Stapley, & Ellard, 2007; Barlow, Stapley, et al., 2007; Ford, 2008; Zarebavani et al., 2023).

Hemophilia is an inherited X-linked bleeding disorder whose most common types are associated with a deficiency of coagulation factor VIII (hemophilia A) or factor IX (hemophilia B) (Golpayegani et al., 2021; Srivastava et al., 2013). Patients with hemophilia often face multiple complications, perceived risks, and functional limitations. To promote the mental and physical health of adults with hemophilia, it is crucial to examine the prevalence and risk factors associated with depression (Barlow, Stapley, et al., 2007). The World Federation of Hemophilia (WFH) estimates that about 400,000 people worldwide suffer from the disease (Chen et al., 2014). According to the Iranian Hemophilia Society (IHS), almost 12,000 people suffer from coagulation disorders, of which 6.500 have hemophilia (*www.hemophilia.org.ir*.). Almost all hemophiliacs suffer from joint injuries that result from intra-articular bleeding (hemarthrosis). The presence of joint damage caused by frequent intra-articular bleeding leads to impaired daily function, as well as the presence of chronic pain and decreased mobility in these patients (Aledort et al., 1994; Lannoy & Hermans, 2010; Liesner et al., 1996; Nilsson et al., 1992).

Furthermore, some other concerns of hemophilia patients include treatment and relevant expenses, joint deformity that leads to changes in the physical shape of the body, arthritis, blood product safety complications, especially coagulation factors, and the risk of transmission of viral infections through coagulation factors (Dekoven et al., 2013; Malek et al., 2024; Mashayekhi et al., 2023). Each of the concerns, by itself or in combination, affects different aspects of a person's life and quality of life and can predispose a hemophiliac to mental disorders such as depression and anxiety (Von Mackensen, 2007). In some cases, depression, anxiety, and other psychological disorders are neglected in hemophilia patients. According to some research, while more than half of hemophilia patients are afflicted with moderate to severe symptoms of depression or anxiety, the symptoms are overlooked in experiments and practical and theoretical research on this susceptible group of patients (Witkop et al., 2019). Depression is associated with functional impairment, decreased quality of life, and poor adherence to medical treatment. Increased depressive symptoms are associated with increased health-related anxiety and increased risk of behaviors such as narcotic or illegal drugs and alcohol abuse (Ford, 2008; Kravitz & Ford, 2008; Martin et al., 2006; Unützer et al., 2002). Evidence suggests that screening and taking care of people with depression can improve health and adherence to treatment in hemophilia patients (Iannone et al., 2012). Therefore, due to the high prevalence of psychological complications in hemophilia patients and their prominent influence on performance, quality of life, and treatment adherence, the present study was conducted to investigate the reason for the prevalence of depression among hemophiliacs.

Methods

The present study is cross-sectional research on 80 patients with hemophilia who were referred to the Daily Clinic for Rare Disease Patients in Mohammad Kermanshahi Hospital (Kermanshah University of Medical Sciences, Iran) in 2020 to receive coagulation factor and regular clinical examinations. Likewise, their hemophilia was diagnosed and had an active profile. They were selected by sampling method.

Inclusion criteria included all men and women affected by hemophilia A or B, a minimum age of 14 years, and having a profile in the hemophilia treatment center. Exclusion criteria included dissatisfaction with participation in the study, incomplete questionnaire, and affliction with

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mental disorders (except for mood disorders) that a psychiatrist diagnosed.

To execute the project, some preliminary steps were required to be taken by the researcher. After obtaining the relevant permits and making the necessary arrangements in the specified time interval, the researcher visited the research population, explained the research objectives, and obtained their consent. Then, eligible hemophilia patients were included in the study according to the inclusion and exclusion criteria. The CONSORT 2010 flowchart is in (Figure 1).

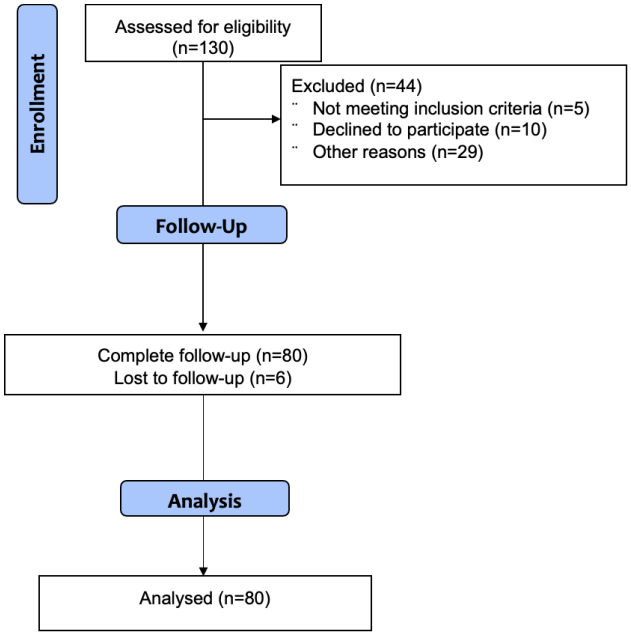

Figure 1. CONSORT 2010 flow diagram of the cross-sectional study. It depicts the number of participants that were recruited, followed, and lost to follow- up.

Demographic information such as age, occupation, education, and marital status, as well as medical and clinical records including the type of hemophilia, disease severity, age of diagnosis, orthopedic complications and monthly bleeding episode, and use of narcotics (such as oxycodone, tramadol, and illegal drugs), were included in a pre-designed checklist through interview and checking the patient profiles. Furthermore, the Beck Depression Inventory was used to assess depression. The collected data were entered into SPSS18 software by a statistics expert and statistically analyzed with relevant analytical techniques.

Beck Depression Inventory-Second Edition (BDI-II)

The Beck Depression Inventory (BDI), initially developed by Beck in 1978 and later revised by Beck, Steer, and Brown in 1996, assesses the severity of depression through 21 items covering various depressive symptoms. Each item is scored on a scale of 0 to 3, resulting in a total score ranging from 0 to 63. In this study, internal consistency reliability for the BDI was found to be high, with Cronbach's alpha coefficients ranging from 0.73 to 0.92 and a mean of 0.86. Specifically, alpha coefficients were 0.86 for the patient group and 0.81 for the non-patient group (Beck et al., 1996). In the Persian version of this questionnaire, which was administered to 354 subjects, Cronbach's alpha coefficient was reported to be 0.91 (Dabson, 2007).

Descriptive statistical methods were used in the form of frequency and percentage to determine age distribution, occupation, education, marital status, depression levels, type of hemophilia, severity of

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the disease, age of diagnosis, orthopedic complications, monthly bleeding frequency, and use of narcotics or illegal drugs.

According to the Beck questionnaire, individuals scoring between 0 and 10 are considered within the normal range. Scores ranging from 11 to 16 indicate mild mood disorder, while those between 17 and 20 suggest borderline clinical depression. Moderate depression is indicated by scores falling within the range of 21 to 30, while scores between 31 and 40 point to severe depression. Finally, scores ranging from 41 to 63 indicate extreme depression.

Data analysis and statistics

The Chi-square (X^2) test was used to assess the association between demographic, medical, and clinical variables with depression and its levels in hemophilia patients. Furthermore, all analyses were performed using SPSS-18 statistical software. The significance level was considered to be 0.05.

Results

The prevalence of depression in patients was 57.5% (46 patients), and 34 patients (42.5%) did not have depression; 15 (18.75%) were afflicted with a mild mood disorder, 4 (5%) with borderline clinical depression, 13 with moderate depression, 5 with severe depression, and 9 with extreme depression. In terms of age, 19 patients (23.75%) were under 20, 22 (27.5%) were 21 to 32 years, 25 (31.25%) were 33 to 44 years, and 14 (17.5%) were over 45 years. Most patients had a diploma/less than high school diploma (71.25%), unemployed (63.75%), and married (55%) in terms of education, employment, and marital status, respectively. The results demonstrated that there were no significant correlations between age (P-Values = 0.77), level of education (P-Values = 0.23), occupation (P-Values = 0.22), and marital status (P-Values = 0.82) with depression levels (Figure 2).

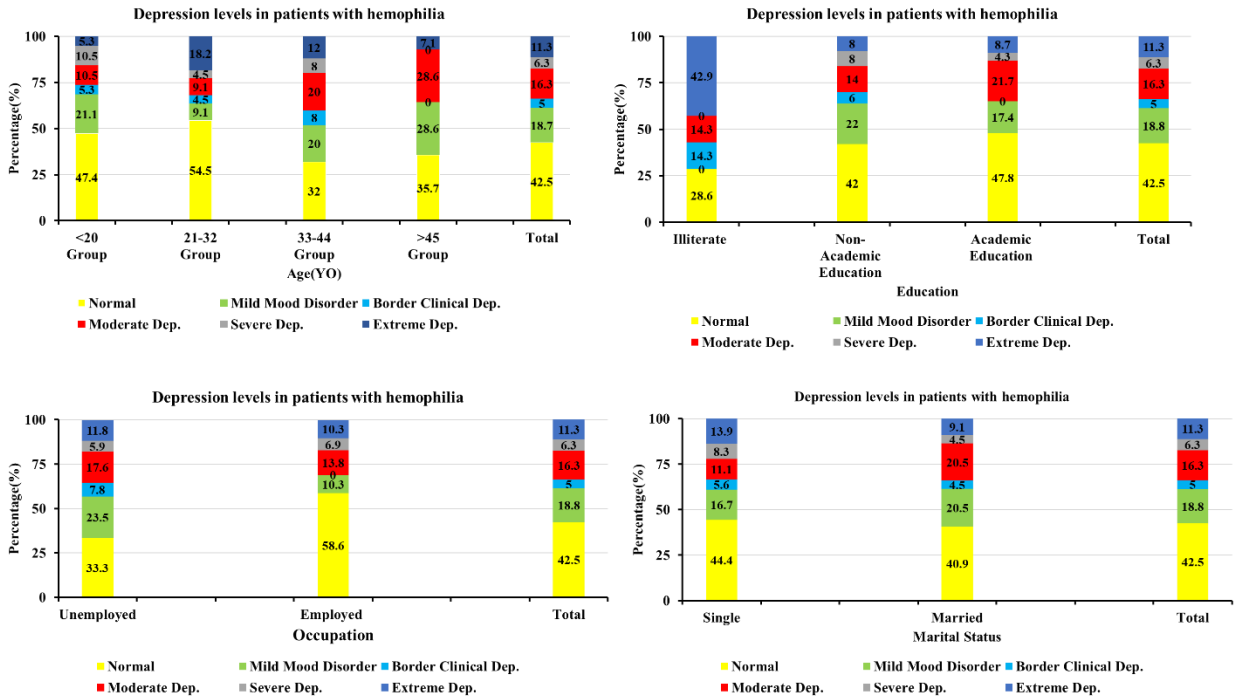

Figure 2. Depression levels in patients with hemophilia based on demographic information

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The following information depicts that the highest statistics of normal people were observed among employed and single individuals aged 21-32 with academic education. According to the Beck questionnaire, a person whose score is 0-10 is normal, 11-16 mild mood disorder, 17-20 borderline clinical depression, 21-30 moderate depression, 31-40 severe depression, and 41-63 extreme depression.

According to the results of the current research on marital status in patients with depression, 14 patients (38.9%) were single, and 17 (38.6%) were married. Regarding marital status in the patients with non-depressive hemophilia, 22 patients (61.1) were single, and 27 (61.4%) were married (Figure 3).

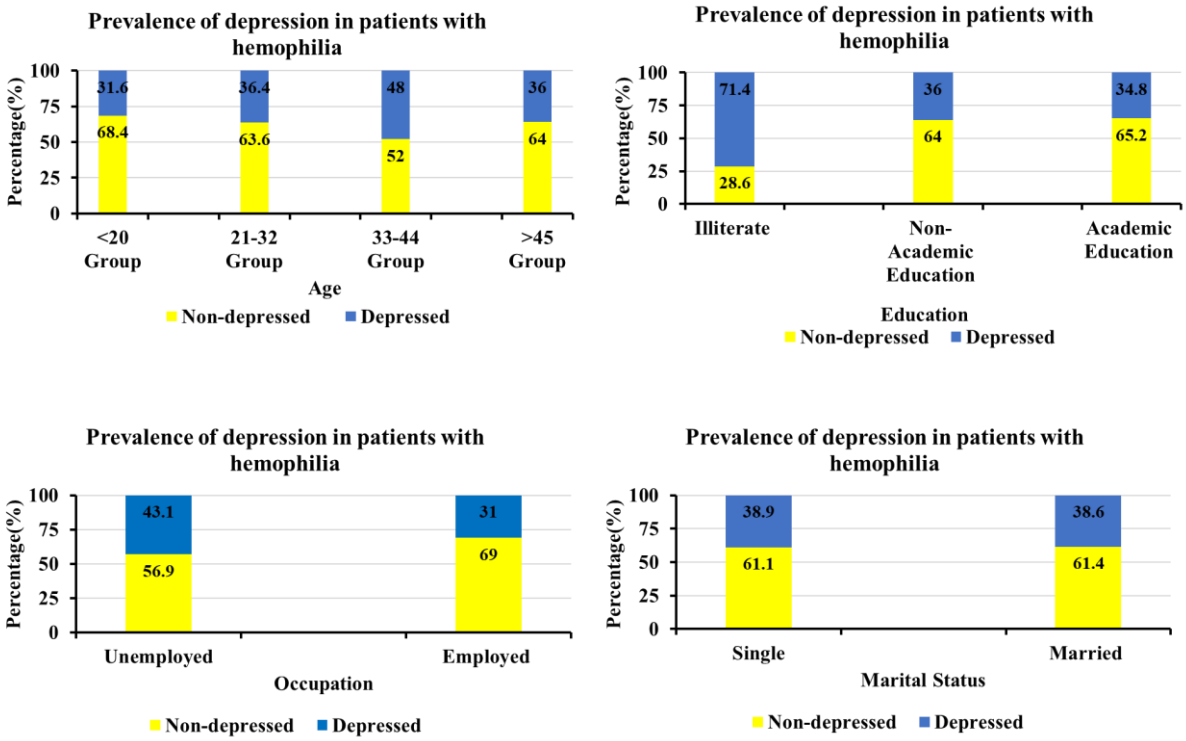

Figure 3. Prevalence of depression in patients with hemophilia based on demographic information.

The findings further delineated the hemophilia subtype and the presence of depression among patients. Specifically, among the cohort, 66 individuals were diagnosed with hemophilia type A, while 14 were identified with type B. Notably, 57% of those with hemophilia A and 57.14% of individuals with type B were observed to experience mental health disorders (Table 1).

Table 1. Prevalence of depression levels based on disease severity and complications (BOC = By orthopedic complication, WOC = Without orthopedic complication).

Variable	Levels	Depression Levels						χ2	P-Value
		Normal	Mild Mood Disorder	Borderline Clinical Dep.	Moderate Dep.	Severe Dep.	Extreme Dep.		
Type of Hemophilia	A	28 (42.4%)	14(21.2%)	3 (4.5%)	8 (12.1%)	4 (6.1%)	9 (13.6%)	7.26	0.2
	B	6 (42.9%)	1 (7.1%)	1 (7.1%)	5 (35%)	1 (7.1%)	0 (0%)		
	Total	34 (42.5%)	15 (18.75%)	4 (5%)	13 (16.25%)	5 (6.25%)	9 (11.25%)		
Severity of Disease	5-50% (Mild)	7 (43.8%)	3 (18.8%)	0 (0%)	5 (31.3%)	1 (6.3%)	0 (0%)	12.32	0.26
	1-5%	7 (46.7%)	3 (20%)	0 (0%)	0 (0%)	1 (6.7%)	4 (26.7%)		

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Table 1. Prevalence of depression levels based on disease severity and complications (BOC = By orthopedic complication, WOC = Without orthopedic complication).

Variable	Levels	Depression Levels						χ2	P-Value
		Normal	Mild Mood Disorder	Borderline Clinical Dep.	Moderate Dep.	Severe Dep.	Extreme Dep.		
Disease Diagnosis Age	(Moderate) < 1% (Severe)	20(40.8%)	9 (18.4%)	4 (8.2%)	8 (16.3%)	3 (6.1%)	5 (10.2%)	10.08	0.81
	Total	34 (42.5%)	15 (18.8%)	4 (5%)	13 (16.3%)	5 (6.3%)	9 (11.3%)		
	< 20	12 (38.7%)	7 (22.6%)	1 (3.2%)	6 (19.4%)	3 (9.7%)	2 (6.5%)		
	20-30	12 (44.4%)	4 (14.8%)	1 (3.7%)	3 (11.1%)	2 (7.4%)	5 (18.5%)		
	31-41	6 (42.9%)	2 (14.3%)	2 (14.3%)	2 (14.3%)	0 (0%)	2 (14.3%)		
	> 42	4 (50%)	2 (25%)	0 (0%)	2 (25%)	0 (0%)	0 (0%)		
	Total	34 (42.5%)	15 (18.8%)	4 (5%)	13 (16.3%)	5 (6.3%)	9 (11.3%)		
Orthopedic Complications	BOC	21 (37.5%)	12 (21.4%)	3 (5.4%)	9 (16.1%)	3 (5.4%)	8 (14.3%)	3.63	0.60
	WOC	13 (54.2%)	3 (12.5%)	1 (4.2%)	4 (16.7%)	2 (8.3%)	1 (4.2%)		
	Total	34 (42.5%)	15 (18.75%)	4 (5%)	13 (١٦.٢٥%)	5 (6.25%)	9 (11.25%)		
Use of Narcotic Drugs	Use Narcotics	8 (25.8%)	5 (16.1%)	1 (3.2%)	6 (19.4%)	3 (9.7%)	8 (25.8%)	14.60	0.01
	Don't use Narcotics	26 (53.1%)	10 (20.4%)	3 (6.1%)	7 (14.3%)	2 (4.1%)	1 (2%)		
	Total	34 (42.5%)	15 (18.8%)	4 (5%)	13 (16.3%)	5 (6.3%)	9 (11.3%)		
Monthly Bleeding Episodes	0	11 (64.7%)	2 (11.8%)	0 (0%)	2 (11.8%)	1 (5.9%)	1 (5.9%)	12.03	0.67
	1-2	6 (31.6%)	3 (15.8%)	2 (10.5%)	6 (31.6%)	1 (5.3%)	1 (5.3%)		
	3-5	7 (35%)	5 (25%)	1 (5%)	2 (10%)	2 (10%)	3 (15%)		
	> 5	10 (41.7%)	5 (20.8%)	1 (4.2%)	3 (12.5%)	1 (4.2%)	4 (16.7%)		
	Total	34 (42.5%)	15 (18.8%)	4 (5%)	13 (16.3%)	5 (6.3%)	9 (11.3%)		

In terms of orthopedic complications, 37.5% of hemophilia patients with orthopedic complications and 54.2% without orthopedic complications were reported to be normal. While, in depressed patients, 8 patients lacked orthopedic complications, and 23 patients had orthopedic complications, and in patients with non-depressive hemophilia, 16 patients lacked orthopedic complications and 33 had orthopedic complications.

The results obtained on the use of narcotics just 25.8% of patients who use narcotics did not have depression; on the other hand, 53.1 % of patients who did not use narcotics were not depressed. In addition, in patients with depression show that 13 patients did not use drugs and 18 patients used drugs. Of the patients with non-depressive hemophilia, 36 did not use drugs and 13 had taken the drug.

As can be deduced from Table 1, most patients without mental disorders 46.7% seen in patients without monthly bleeding episodes. Besides, the monthly bleeding episodes among patients with depression varied: 4 patients reported no bleeding, 10 experienced bleeding 1-2 times per month, 8 had episodes 3-5 times monthly, and 9 encountered bleeding more than 5 times a month. In contrast, among patients with non-depressive hemophilia, 13 had no bleeding, 9 experienced bleeding 1-2 times per month, 12 had episodes 3-5 times monthly, and 15 faced bleeding more than 5 times monthly (Table 2).

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Table 2. Prevalence of depression based on disease severity and complications (BOC = By orthopedic complication, WOC = Without orthopedic complication).

Variable	Levels	Depression		$\chi 2$	P-Value
		Non-Depressed	Depressed		
Type of Hemophilia	A	(42) 63.6%	(24) 36.4%	0.90	0.34
	B	(7) 50%	(7) 50%		
Severity of Disease	5-50% (Mild)	(10) 62.5%	(6) 37.5%	0.28	0.86
	1-5% (Moderate)	(10) 66.7%	(5) 33.3%		
	< 1% (Severe)	(29) 59.2%	(20) 40.8%		
Disease Diagnosis Age	< 20	(19) 61.3%	(12) 38.7%	0.78	0.85
	20-32	(16) 59.3%	(11) 40.7%		
	31-41	(8) 57.1%	(6) 42.9%		
	> 42	(6) 75%	(2) 25%		
Orthopedic Complications	BOC	(16) 66.7%	(8) 33.3%	0.42	0.51
	WOC	(33) 58.9%	(23) 41.1%		
Use of Narcotic Drugs	Use Narcotic	(36) 73.5%	(13) 26.5%	7.95	0.005
	Don't use Narcotic	(13) 41.9%	(18) 58.1%		
Monthly Bleeding Episodes	0	(13) 76.5%	(4) 23.5%	3.23	0.35
	1-2	(9) 47.4%	(10) 52.6%		
	3-5	(12) 60%	(8) 40%		
	> 5	(15) 62.5%	(9) 37.5%		

The results showed that there were no significant correlations between the levels of depression and its prevalence with type of hemophilia, disease severity, age of diagnosis, orthopedic complications, and monthly bleeding episodes. However, there is a significant correlation between the prevalence of depression and the use of narcotic drugs (P = 0.01).

Discussion

The current research that was performed to determine the prevalence of depression in hemophilia patients, who were referred to the Daily Clinic for Rare Disease Patients in Mohammad Kermanshahi Hospital, was 57.5%, and almost 33.9% reported moderate to severe depressive symptoms. However, prior research has revealed that 33% of hemophilia patients experience depression, as determined by Beck questionnaires, which is consistent with the 33% of chronically ill adults who also experience depression (Canclini et al., 2003; Hartl et al., 2008). In line with the results from this research, Iannone et al.'s (M Iannone et al., 2012) research results demonstrated that depressive criteria were observed in 37% of hemophilia patients, of which 53% of these depressed patients showed moderate to severe depressive symptoms, and 76% revealed functional disorders due to depression symptoms. Additionally, the lack of social support and unemployment was significantly associated with these high scores.

The research conducted by Lannone (M. Iannone et al., 2012) indicated that 53% of hemophilia patients lacked depression. Of the depressed patients, 38.1% revealed mild depression, 7.9% moderate, and 3.2% severe. Fakhari et al. (Fakhari & Dolatkhah, 2014) reported a 60% prevalence of depression in hemophilia patients. Consequently, patients with chronic illness and adult patients appear to be at a higher risk of suffering from depression, especially compared to the lower rates of depression reported in the primary care setting (16%) (Katon et al., 2010; Zarebavani et al., 2023). Moreover, it can be alleged that the occurrence of mental disorders following the development of chronic physical or infectious diseases is common (Moradi et al., 2023; Navidian et al., 2006). The study in 2000

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reported that patients with hemophilia were at risk for joint bleeding (especially knee, ankle, and elbow joints), soft tissue hematomas, bruises, intraperitoneal bleeding, intracranial hemorrhage, and postoperative hemorrhage (Kasper, 2000). Also, in 2007, Manco-Johnson reported that the complications of recurrent hemarthrosis and soft tissue hematomas can lead to acute arthropathy, joint shrinkage, and development of pseudotumors, which can end in chronic pain, disability, and poor health-related quality of life (Manco-Johnson et al., 2007). Furthermore, in this study, patients suffered from joint bleeding and orthopedic complications such as acute arthropathy, and joint shrinkage.

On the other hand, Ghanizadeh & Jahromi (Ghanizadeh & Baligh-Jahromi, 2009) in their research reported that the major depression rate is 6% and one-third of children and adolescents suffer from irritability. The results are not in line with those of the present study, and in explaining this finding; we can refer to the age range of the participants and depression assessment tools. The results revealed that there were no significant correlations between age, education, employment, marriage, type and severity of hemophilia, hemophilia diagnosis time, orthopedic complications, and monthly bleeding episodes with depression. These findings are partly consistent with those obtained by Hashemi, Broujeni, and Kokab in 2011 on the prevalence of major depression and anxiety in patients with hemophilia and thalassemia, showing that there were no significant correlations between gender and age with depression in hemophiliacs (Hashemi et al., 2012). Furthermore, the results revealed that there was a significant correlation between narcotic drug use and depression, and 74.2 % of patients who used narcotics showed depression symptoms. The results of a study by Iannone et al. revealed that the prevalence of depression in hemophilia patients taking narcotics is 50% (M Iannone et al., 2012). Some research has shown that people who used opioid drugs for 90 to 180 days had a 25 percent increased risk of developing depression. People who used opioid drugs for 180 days or more were 53 percent more likely to be depressed than others (Semenkovich et al., 2014). It is vital for hemophilia patients to be aware of the signs and symptoms of depression and to seek help with combination therapy to help them improve their quality of life.

As there were some limitations in the present research (e.g., the sample merely included patients with hemophilia in Kermanshah), care should be taken in generalizing the findings to patients in other geographical areas. Further, the lack of complete control of disturbing variables such as personality, physical and psychological variables, and social, economic, and cultural variables relevant to patients should also be taken into account.

Conclusion

The present research findings indicate that there is a high prevalence of depression among hemophilia patients, and there is a correlation between the prevalence of depression and the use of narcotics or illegal drugs. Therefore, treating psychological complications in conjunction with medical therapy is recommended for hemophilia patients.

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Conflict of interest

The authors declare no potential conflicts of interest related to this study. The data that support the findings of this study are available from the corresponding author on request. The authors received no financial support for the research, authorship, and/or publication of this article. All authors gave their consent for submission of this manuscript to this journal.

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Ethical consideration

This study was approved by the Ethics Committee of Kermanshah University of Medical Sciences. The informed consent was taken from

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parents and first relatives.

Code of ethics

KUMS.REC.1394.412

Authors' contributions

MR. G, P. F, was involved with methodology; A. L, did data collection; MR. FG, P. F, did the writing; F. K, MR. T, was involved with the original draft; N. S, A. F, did data analysis; M. F, MR. G, did the supervision; P. F, N. S, Formal Analysis, Writing – Review and Editing. All the authors read and approved the final manuscript and were responsible for any questions related to the article.

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