DEPRESSION IN PATIENTS WITH THALASSEMIA MAJOR
Prevalence and contributing factors

Done by:
Shams Mohammed Ibrahim

Supervised by:
Dr. Zahraa Najah

Abstract:

Background : Thalassemia major is a chronic disease requiring lifetime treatment. A recent study showed that 11-62% of thalassemia patients developed depression, which is associated with high morbidity and mortality. Understanding the extent of the problem related to depression and its contributing factors is important for early management.

Objective : To determine the prevalence and contributing factors for depression in children with thalassemia major.

Methods: A cross-sectional study aged 15 to <30 years recruited two groups: Group I included 100 patients diagnosed with βTM on regular blood transfusions. Group II included 100 healthy control people with no underlying chronic illness.
A detailed history was taken, and clinical examination was performed; also, laboratory investigations including full blood picture and serum ferritin were done.
Subjects completed The Beck Depression Inventory (BDI) questionnaire. Depression was defined as a total score > 9 .
Data were analysed using SPSS for Windows ver. 22.0.

Results: The prevalence of depression among thalassemia adolescents was 35.7% compared with 23.5% of comparison group. Mild depression was the most frequently reported category among both groups while moderate, sever and very severe ones were significantly higher among thalassemia patients.

Conclusions: The high prevalence of depression highlights the urgent need for the establishment of interventions for the prevention, early detection, and treatment of depression among patients with βTM.

Introduction:

Definition:
Thalassemia is the most common form of inherited anemia worldwide. Beta-thalassemia (BT) is a thalassemia type characterized by anomalies in the synthesis of the beta chains of hemoglobin, which results in various phenotypes ranging from clinically asymptomatic to severe anemia. The world Health Organization (WHO) in 2019 reported that around 50,000 infants were born with BT every year. [1]

Clinical manifestations:
According to their clinical and laboratory results, beta-thalassemia is classified into three categories. A heterozygous form with moderate anemia that is typically asymptomatic is known as beta-thalassemia minor, commonly referred to as carrier or trait. Beta-thalassemia major and intermedia are two more severe forms of anemia caused by homozygosity or compound heterozygosity for beta-thalassemia mutations. Clinically, transfusion dependency separates the two of them. Transfusions are not necessary for intermedia; however, they are for beta-thalassemia major. [2]

Thalassemia is still very common, especially in the thalassemic belt area.
In order to improve their chances of survival, patients with thalassemia major require ongoing, recurring iron-chelating medication and blood transfusions, which means frequent hospital stays and check-ups.Patients may develop psychosocial issues associated with the illness or its treatments. According to one study, 80% of thalassemia major patients are susceptible to psychological illnesses like depression and anxiety.

Diagnosis:

The diagnosis of β-thalassemia is established in a proband older than age 12 months by identification of microcytic hypochromic anemia, absence of iron deficiency, Anisopoikilocytosis with nucleated red blood cells on peripheral blood smear and decreased or complete absence of hemoglobin A (HbA) and increased hemoglobin A_2 (HbA_2) and often hemoglobin F (HbF) on hemoglobin analysis. Identification of biallelic pathogenic variants in HBB on molecular genetic testing can establish the diagnosis in individuals younger than age 12 months who have a positive or suggestive newborn screening result and/or unexplained microcytic hypochromic anemia with Anisopoikilocytosis and nucleated red blood cells on peripheral blood smear. [3]

Psychological import of thalassemia patients:
Chronic thalassemia is a disease that has a significant psychological impact on patients. Some of these psychological effects include frequent hospitalizations, fear of blood-transmitted infections, daily iron chelator use, iron overload complications, missing work and school to attend blood transfusion sessions, financial strain, loss of friends and family due to the disease, abnormal hormone levels, and disfiguring abnormalities from bone marrow expansion. [4]

Depression is a long-term mental illness that affects behavior, emotions, cognitive abilities, and physical health. This is a dangerous disease that can make it difficult to enjoy life and reduce one's ability to perform daily tasks, even when performing basic responsibilities. Chronic stress, thalassemia, and its treatment and sequelae can all be direct causes of depression in patients with the disease.[5]

Patients with thalassemia require a multidisciplinary strategy that includes psychiatric treatments and psychological support in order to ensure that they receive the appropriate, complete care that they deserve, but unfortunately, this is not always used

The conducted study aims to identify the prevalence of depression in patients with thalassemia major and its contributing factors. using the Beck Depression Inventory (BDI) which is aself-report questionnaire used to measure the severity of depression and compare the results to healthy children, and to correlate the results with different clinical variables.
Identifying such factors can help with prevention, administering early management, preventing complications of depression, and increasing patient quality of life.

Methodology:

From 9-1-2023 to 2-1-2024, a cross-sectional study was carried out at the haematology centre of Baqubah Teaching Hospital.
One hundred patients, with no preference for one sex, were enrolled, ranging in age from fifteen to thirty years.
A further one hundred control cases with the same range and no preference for one sex were gathered.
The Diyala University College of Medicine Council gave their approval to the study. Every patient enrolled in the research study gave verbal informed permission.
Within the hospital, in an isolated space, each participant filled out a recruitment survey. All of the participants who agreed and fulfilled the inclusion criteria were interviewed in person to collect data. A minimum of 10 to 15 minutes were spent on each interview.

The 21 questions on a Likert scale that make up the Beck Depression Inventory (BDI) are self-reported.
Scores of 1 through 9 denote little to no depression,
10 to 15 mild depression,
16 to 23 moderate depression,
24 to 36 severe depression,
and 37 and higher indicate very severe depression.

The validity of the BDI has been applied in multiple cultural settings several researchers worldwide
Using IBM SPSS software version 21.0, the data were examined using analytical statistics (generalized linear regression model) and descriptive statistics (mean, standard deviation, frequency, and percentage). At $P < 0.05$, the traditional significance level, the results were considered significant. Because all thalassemia patients experienced at least minimal to mild depression and no one was free from depression symptoms, the minimal to mild depression variable was taken into consideration as a referral factor in this study when the regression was analyzed.

Results:

Our results of this research showed significant valuation of the (Age, Sex, HB level, Serum ferritin and the chelating therapy). While showed a non-significant valuation of the (Age of diagnoses, Age of blood transfusion and the number of blood transfusion).
In comparison to control group frequency and percentage of depression was 71(71%) higher in individuals who had thalassemia than in normal individuals 47(47.8%)

Table (1): age distribution of study and control cases .

Age Group	Depression scores of study cases						Total	Total of depression
		0-9 No depression	10-15 Mild depression	16-23 Moderate depression	24-36 SeverDepression	>37 Very Severedepression		
10-19 years	frequency	13	14	9	9	7	52	39
	Percentage	13.0%	14.0%	9.0%	9.0%	7.0%	52.0 %	39%
20-30 years	frequency	16	9	12	6	5	48	32
	Percentage	16.0%	9.0%	12.0%	6.0%	5.0%	48.0 %	32%
Depression scores of control cases								
10-19 years	Frequency	19	9	5	3	0	36	17
	Percentage	19.2%	9.1%	5.1%	3.0%	0.0%	36.4 %	17%
20-30 years	Frequency	33	11	13	6	0	63	30
	Percentage	33.3%	11.1%	13.1%	6.1%	0.0%	63.6 %	30%

Table 1 indicate that no. and % of depression is higher in teenage group patients of thalassemia)39%) than in patients age 20-30yrs (32%), while the incidence of depression in control group was (17%) in teenagers than (30%) in patients age 20-30yrs. These results were statistically not significant. P-value (0.305)

Table (2): sex distribution of study and control cases

Sex		Depression scores in study patient					Total	Total of depression
		0-9 No depression	10-15 Mild depression	16-23 Moderate depression	24-36 SeverDepression	>37 Very Severe depression		
Male	frequency	11	10	7	8	4	40	29
	Percentage	11.0%	10.0%	7.0%	8.0%	4.0%	40.0%	29%
Female	frequency	18	13	14	7	8	60	42
	Percentage	18.0%	13.0%	14.0%	7.0%	8.0%	60.0%	42%
Depression scores of control cases								
Male	frequency	23	11	7	5	0	46	23
	Percentage	23.2%	11-1%	7.1%	5.1%	0.0%	46.5%	23%
Female	frequency	29	9	11	4	0	53	24
	Percentage	29.3%	9.1%	11.1%	4.0%	0.0%	53.5%	24%

Table 2 indicate that No. and % of depression is higher in female group patients of thalassemia (42%) than in male patients (29%) , while the incidence of depression in control group was (23%) in male than (24%) in female. These results were statistically significant. P-value (0.021)

Table(3): hemoglobin level in study and control cases

The Hb "g/dl"		Depression scores of study cases					Total	Total of depression
		0-9 No depression	10-15 Mild depression	16-23 Moderate depression	24-36 SeverDepression	>37 Very Severe depression		
<9 g/dl	frequency	28	22	19	14	12	95	67
	Percentage	28.0%	22.0%	19.0%	15.0%	12.0%	95.0%	67%
>9 g/dl	frequency	1	1	2	1	0	5	4
	Percentage	1.0%	1.0%	2.0%	1.0%	0.0%	5.0%	4%
Depression scores of control cases								
<9 g/dl	frequency	0	0	0	0	0	0	0
	Percentage	0.0%	0.0%	0.0%	0.0%	0.0%	0.0 %	0.0%
>9 g/dl	frequency	52	20	18	9	0	99	47
	Percentage	52.5%	20.2%	18.2%	9.1%	0.0%	100%	47.5%

Table 3 indicate that No. and % of depression is higher in thalassemic group with hb <9 (67%) than in patients with hb >9 (4%) , while all depressed cases in control group was with hb >9 (47%). These results was statistically significant. P-value (0.001)

Table (4) : Serum Ferritin ng/dL * Depression

Serum Ferritin Ng/dL		Depression scores of study cases					Total	Total of depression
		0-9 No depression	10-15 Mild depression	16-23 Moderate depression	24-36 Severe Depression	>37 Very Severe depression		
<1000 Ng/dL	Frequency	4	5	5	2	3	19	15
	Percentage	4.0%	5.0%	5.0%	2.0%	3.0%	19.0%	15%
>1000 Ng/dL	Frequency	25	18	16	13	9	81	56
	Percentage	25.0%	18.0%	16.0%	13.0%	9.0%	81.0%	56%
Depression scores of control cases								
<1000 Ng/dL	Frequency	52	20	18	9	0	99	47
	Percentage	52.5%	20.2%	18.2%	9.1%	0.0%	100%	47.5%
>1000 Ng/dL	Frequency	0	0	0	0	0	0	0
	Percentage	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Table 4 indicate that No. and % of depression is higher in thalassemic group with s.ferritin >1000 (56%) than in patients with s.ferritin <1000 (15%) , while all depressed cases in control group was with s.ferritin <1000 (47%). These results statistically significant. P-value (0.033)

Table(5): no. of blood transfusions * Depression

Number of Blood transfusions per year		Depression scores pf study cases					Total	Total of depression
		0-9 No depression	10-15 Mild depression	16-23 Moderate depression	24-36 Severe Depression	>37 Very Severe depression		
<6-15	Frequency	8	8	9	3	4	32	24
	Percentage	8.0%	8.0%	9.0%	3.0%	4.0%	32.0%	24%
15-24	Frequency	19	14	10	12	7	62	43
	Percentage	19.0%	14.0%	10.0%	12.0%	7.0%	62.0%	43%
>24	Frequency	2	1	2	0	1	6	4
	Percentage	2.0%	1.0%	2.0%	0.0%	1.0%	6.0%	4%
Depression scores of control cases								
<6-15	Frequency	None	None	None	None	None	None	None
	Percentage							
15-24	Frequency	None	None	None	None	None	None	None
	Percentage							
>24	Frequency	None	None	None	None	None	None	None
	Percentage							

Table 5 No. and % of depression is higher in Thalassemic group of patients with no. Of blood transfusion per year between (15-25 years) (43%) than patients with no. of years <15 (24%) and >24 (4%) , while there is no incidence in control group. These results are statistically not significant. P-value (0.774)

Table(6): Chelating agent therapy * Depression

Chelating agents		Depression scores of study cases					Total	Total of depression
		0-9 No depression	10-15 Mild depression	16-23 Moderate depression	24-36 Severe Depression	>37 Very Severe depression		
Deferasirox	**Frequency**	14	12	11	9	5	51	37
	Percentage	14.0%	12.0%	11.0%	9.0%	5.0%	51.0%	37%
Deferoxamine	**Frequency**	15	9	9	5	5	43	28
	Percentage	15.0%	9.0%	9.0%	5.0%	5.0%	43.0%	28%
Depression scores of control cases								
Deferasirox	**Frequency**	None	None	None	None	None	None	None
	Percentage							
Deferoxamine	**Frequency**	None	None	None	None	None	None	None
	Percentage							

Table 6 No. and % of depression is higher in Thalassemic group of patients used Deferasirox (37%) than in patients used Deferoxamine (28%) , while there is no incidence in control group. These results are statistically significant. P-value (0.006)

Table(7): comparison of depression between study group and control group.

Depression * Thalassemia Cross tabulation					
			Thalassemia		Total
			Yes	No	
Depression	0-9 "No Depression"	Count	29	52	81
		% of Total	14.6%	26.1%	40.7%
	10-15 "Mild Depression"	Count	23	19	42
		% of Total	11.6%	9.5%	21.1%
	16-23 "Moderate Depression"	Count	21	18	39
		% of Total	10.6%	9.0%	19.6%
	24-36 "Severe Depression"	Count	15	10	25
		% of Total	7.5%	5.0%	12.6%
	>37 "Very Severe Depression"	Count	12	0	12
		% of Total	6.0%	0.0%	6.0%
Total		Count	100	99	199
		% of Total	50.3%	49.7%	100.0%
Total of depression		Count	71	47	
		% of Total	71%	47.8%	

By comparison of control group frequency and percentage of depression and in individuals who had thalassemia the results were higher in thalassemic patients (71%) than in normal individuals (47.8%) These results statistically significant with p. value “0.000469 “as shown in table 7

Discussion:

The purpose of this study was to determine the incidence of depressive symptoms and risk variables among beta thalassemia major patients in the Diyala Governorate.
According to the Beck Depression Scale, most of the samples in the current study (71%) exhibited moderate to very severe depression. Numerous things could have an impact on this result. the incapacity to fully engage in educational programs, the impossibility of getting married in some circumstances, and other personal issues not included in the data.
In earlier research.

According to the Beck Depression Scale most of the samples (78.5%) had moderate to severe depression, according to Adnan L. Sarhan et al. (2022). [5]
Moreover, Faza N. Wardhani et al. (2021) discovered that the majority of Bandung City's BTM patients were depressed (52%) [6]

This result is consistent with another study conducted in 2019 by Liqaa H. Yousif et al., which discovered that 67% of adolescents with thalassemia in Erbil, Iraq, had depression.[7]
The adolescent patient group did not exhibit a statistically significant increase in depression, although it was revealed that female adolescents had depression at much greater rates than male adolescents.
According to a different study by Adnan L. Sarhan et al. (2022), men are 6.0 times more likely than women to report having serious depression symptoms.[5]
Higher depression ratings were linked to female gender, according to a different study by Patel et al. (2019), which supports our findings. [8]
Another study by Akbar Sh. Et al. (2014), found no significant relationship between age or gender and the BDI results.[9]

Adnan L. Sarhan et al.'s (2022) study, which also identified a substantial association between depressed symptoms and the requirement for thalassemia drugs, concurs with the study's findings that oral chelation (Deferasirox) was significantly connected with depression.[5]

Additionally, this study demonstrated a significant connection between depression and ferritin and haemoglobin levels.
A 2010 study by Am J Hematol et al. revealed no evidence of a significant correlation between serum ferritin levels and depressive or anxious symptoms.[10]
In another study, Alexander M. et al. (2020) found that patients, having serum ferritin levels over 2,000 ng/mL, had higher mean DAS scores than other patients.[11]

The factors that did not significantly predict depression in thalassemia patients, such as age at diagnosis, duration of blood transfusion, number of blood transfusions, and length of time, are also noteworthy.
There are a number of limitations with this study that could open up possibilities for future studies. The study's data came from the thalassemia patients' self-reports. It's unclear how well

they grasped the work or felt pressured to answer the interviewers' questions because many had no college education.
The only psychological measure employed in our study was the Beck Depression Inventory (BDI); no additional psychological measures used.

Conclusion:

Adolescent thalassemia patients were shown to have a higher prevalence of depression than typical teens. Depression is more common in the female gender. Adolescents with thalassemia may benefit from preventive programs which screen for depression in order to minimize the effects of this chronic illness and better prepare them for healthy, productive lives.

Recombination:

These findings bring to light the need for screening, monitoring, and offering treatment interventions for individuals with thalassemia throughout the lifetime. Additionally, programs addressing obstacles and access to education, employment and psychological support for individuals affected by thalassemia may mitigate and alleviate the consequent depression over time.