Correlation between Melancholic Depression and Markers of Coagulopathy in Hemodialysis Patients

Original Article

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ABSTRACT

Background: Approximately 280 million individuals have depression worldwide. Melancholic depression has shown an increase after the COVID-19 pandemic, which is known to induce a pro-coagulant condition.

Aim of the Work: We intend to examine the potential association between melancholic depression and coagulopathy in hemodialysis patients. Hemodialysis have high risk for depression.

Methods: This research used a cross-sectional design and included a sample of forty-one patients aged between 18 and 69 years who were undergoing regular haemodialysis (HD) for a duration exceeding six months. The patient had an interview that included the Sydney Melancholia Scale. After obtaining written informed permission from all patients, CBC, D-dimer, Fibrinogen, Protein C, Protein S, and Factor VII were collected for each patient.

Results: Elevated D-dimer levels were positively correlated with depression in patients with both melancholic and non-melancholic depression compared with patients without depression. Moreover, elevated D-dimer levels were positively correlated with the Sydney melancholia prototype index SMPI; that is, patients with melancholic depression have significantly higher D-dimer levels than patients with other types of depression and non-depressed patients. Patients with melancholic depression had a significantly lower mean total leukocytic count than those without depression did.

Conclusion: Depression is a disabling illness that may include several types of presentations. The percentage of depression in our sample about 68.29%. There's significant correlation that has been established in this research work between depression and the presence of coagulopathy markers. This could have a role in the future in prophylaxis and decreasing incidence of depression in high risk patients and also decreases thrombosis risk.

Key Words: Coagulopathy, depression, haemodialysis, melancholia prototype Index.

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INTRODUCTION

Depression is a common disease worldwide, 3.8 % of the population worldwide has depression, including 5% of adults (4% of men and 6% of women). Approximately 280 million individuals are affected[1]. According to recent studies, the prevalence of dialysis in Egypt in 2019 was reported to be 0.61 per 1000 people, with an incidence estimate of 0.19 per 1000 people[2].

Melancholic depression is a severe kind of depression that is marked by daily changes in mood, inability to feel pleasure from things that are typically enjoyable, excessive guilt, feelings of hopelessness, slowed physical movements, and weight loss.

The Sydney Melancholia Prototype Index (SMPI) is a specialized scale designed to enhance the accuracy of diagnosing melancholia. The measure consists of 24 items, with 12 items related to symptoms and disease associated with melancholic depression in the left column, and 12 items related to non-melancholic depression in the right column[3].

The Sydney Melancholia Prototype Index (SMPI) combines psychomotor symptoms and Examining clinical aspects such as past medical history and factors linked to the advancement of the disease in comparison to the CORE and other conventional scales used to measure melancholia. Psychomotor disturbance (PMD) signs are less common in younger patients and those who are not in the most severe stage of the episode. The scale was

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designed to be a comprehensive and practical inventory of depressive symptoms, covering cognition, psychomotor retardation, previous personality, and behavior[3].

Depression is up to three times more prevalent in dialysis patients than in the general population[4]. A meta-analysis was conducted on a sample of 83,381 adult patients with chronic kidney disease (CKD), out of which 33,125 were undergoing dialysis. The analysis found that 12,063 of these patients were diagnosed with clinical depression, with an average prevalence rate of 27.4%. The diagnosis was based on clinical data from Diagnostic and Statistical Manual of Mental Disorders criteria[5]. In a sample of 5256 hemodialysis patients from different facilities, in the unadjusted model the mortality risk was 42 % of patients diagnosed with depression using a medical questionnaire[6]. Depression occurring with chronic kidney disease might be more resistant to treatment[7].

The incidence of melancholic depression increased in patients in post covid era which was associated with increased incidence of coagulopathy so we are trying to find a correlation between coagulopathy and depression. Hemodialysis patients have high risk for depression, coagulopathy and covid-19.

There is a lack of research providing evidence for a connection between depression and coagulopathy in hemodialysis patients. As per the Diagnostic and Statistical Manual of Mental Disorders (DSM), depression is characterized by a lack of interest or enjoyment in life, notable changes in eating habits, disruptions in sleep patterns, alterations in physical movements, reduced energy levels or heightened fatigue, feelings of worthlessness, and difficulties in concentrating and making decisions. The scale used in our investigation was tailored specifically for melancholic sadness. In the latest research including 103 patients undergoing long-term hemodialysis, 35 individuals were found to have a current Major Depressive Episode (MDE). Out of these patients, 65.7% exhibited melancholic symptoms, while 25.7% had a history of recurring depressive illness, and 26% were diagnosed with anxiety disorders[8].

AIM OF THE WORK

To find a correlation between coagulopathy and melancholic depression in hemodialysis patients who have high risk for depression.

PATIENTS AND METHODS

This cross-sectional study was conducted on a sample of forty-one patients (18 female and 23 male) aged between 18 and 69 years, who were undergoing regular haemodialysis (HD) for a minimum of six months. This study aims to find a correlation between melancholic depression and detection of thrombotic etiology by coagulopathy markers in this sample of chronic illness.The patients were required to have sufficient proficiency in the Arabic language and were selected from those attending Nasr City National Health Insurance Hospital between February 2022 and August 2022.

ETHICAL CONSIDERATION

The study was conducted after approval from the research ethics committee (REC) for Human and Animal Research of the Faculty of Medicine, Helwan University (ID: 77-2021). Additionally, written permission forms were received from all participating patients. Also patients have the right to refuse collaboration and drop out from the study anytime without any negative consequences. All appropriate procedures to maintain the confidentiality of the study participants' data were done. All participants will understand all procedures of the study and were given enough time to ask all his questions and write the consent.

Patients who refused to complete the questionnaire or exhibited symptoms of psychosis or cognitive impairment were excluded. Additionally, patients under the age of 18, patients who had been on dialysis for less than 6 months, and those with idiopathic thrombocytopenic purpura, haemophilia, any coagulation disorder, or chronic liver disease were also excluded.

Each patient had a personal interview to verify their eligibility. During the interview, the interviewer collected demographic data such as age, gender, residence, phone number, and the start of dialysis.

Blood Sampling Procedure

Prior to the hemodialysis session, blood sampling was conducted. After a 15-minute period of rest in a seated position, the cubital vein was punctured. A total of 12 ml of blood was drawn into a 20-ml syringe.

From this, 3 ml was transferred into an EDTA tube (ethylenediamine tetra acetic acid), and 1.8 ml was transferred into four citrate tubes (each containing 1.8 ml of blood and 0.700 ml of citrate). The levels of haemoglobin, total leukocytes, and platelets were quantified using an automated counter called Sysmex. After centrifugation, the plasma from the four citrate tubes was divided into smaller portions. D-dimer levels were assessed using an automated quantitative assay (Siemenis Immulite 2000). A threshold of above 250 g/L was used as the criterion for a positive result. A coagulation test was conducted to determine fibrinogen levels using a coagulometric method, which is based on prothrombin time and measures clotting factor VII. Enzyme-linked immunosorbent assay (ELISA) was used to assess the amounts of protein S and C without any cost.

The lead investigator selected all pertinent items from the Sydney Melancholia Prototype Inventory (SMPI)-Clinician-rated version that he deemed as 'typical' in relation to patients' present or past depressive experiences. Patients and physicians were required to score all 24 SMPI questions. Additionally, they were asked to complete a five-point SMPI appendix, which allowed them to assess the extent to which the patient aligns with either the melancholic or non-melancholic prototype, using a scale of 1 to 5.

RESULTS

Table (1) showed blood cell counts were comparable between the groups. Patients with melancholic depression had a significantly lower mean WBCs compared to those without depression between the studied groups.

Table 1: Comparison of melancholic, non-melancholic, absence of depression with TLC, Hb levels and platelet count in the study group.

Blood cell counts		No depression	Melancholic depression	Non- Melancholic depression	Test statistic	*p-value*
WBCs	Mean ± SD	7.39 ± 1.76 b	5.07 ± 1.61 a	6.69 ± 1.43	F = 8.680	0.001*
	Low	0 (0.0%)	3 (14.3%)	0 (0.0%)	X^{2FFH}=2.027	0.273
	Normal	13 (100.0%)	18 (85.7%)	7 (100.0%)		
Hb	Mean ± SD	9.74 ± 1.88	10.69 ± 1.71	10.61 ± .90	F = 1.382	0.263
	Microcytic hypochromic	2 (15.4%)	4 (19.0%)	0 (0.0%)	X^{2FFH}=1.639	0.894
	Normocytic normochromic	6 (46.2%)	8 (38.1%)	4 (57.1%)		
	No anemia	5 (38.5%)	9 (42.9%)	3 (42.9%)		
Plt	Mean ± SD	177.85 ± 51.29	181.9TH and `± 33.69	161.43 ± 38.30	F = 0.669	0.518
	Low	1 (7.7%)	2 (9.5%)	2 (28.6%)	X^{2FFH}=2.092	0.363
	Normal	12 (92.3%)	19 (90.5%)	5 (71.4%)		

IQR: interquartile range (25^{th} – 75^{th} percentiles); SD: standard deviation; Max: maximum; Min: minimum; NA: not-applicable; X^{2FFH}: Fisher-Freeman-Halton exact test; F: one-way ANOVA test; Z: Kruskal-Wallis test; * significant at $p<0.05$. a: significant difference from no depression group; b: significant difference from melancholic group; c: significant difference from non-melancholic group.

Table (2) showed that the biomarkers for coagulability were comparable between the studied groups while D-dimer was significantly different between the studied groups (p=0.007). D-dimer was significantly elevated in depressed patients compared to non-depression patients and higher number of patients with melancholic depression showed elevated levels of d-dimer.

Table 2: Comparison between variable types of depression with coagulation profile of the study group.

Biomarkers for coagulability		No depression	Melancholic depression	Non-Melancholic depression	Test statistic	*p-value*
D-dimer	Mean ± SD	0.28 ± 0.08 b,c	0.43 ± 0.21 a	0.47 ± 0.17 a	F = 7.165	0.007*
	Normal	6 (46.2%)	6 (28.6%)	1 (14.3%)	X^{2FFH}=2.136	0.394
	Above normal	7 (53.8%)	15 (71.4%)	6 (85.7%)		
Fibrinogen	Median [IQR]	206.0 [161.0 - 305.0]	335.0 [213.0 - 365.0]	379.0 [197.0 - 420.0]	Z = 2.634	0.268
	Below normal	4 (30.8%)	4 (19.0%)	2 (28.6%)	X^{2FFH}=5.127	0.271
	Normal	7 (53.8%)	11 (52.4%)	1 (14.3%)		
	Above normal	2 (15.4%)	6 (28.6%)	4 (57.1%)		
FVII	Median [IQR]	70.0 [40.0- 102.0]	83.0 [70.0 - 92.0]	70.0 [68.0 - 83.0]	Z = 2.321	0.313
	Below normal	5 (38.5%)	3 (14.3%)	2 (28.6%)	X^{2FFH}=3.745	0.418
	Normal	7 (53.8%)	17 (81.0%)	5 (71.4%)		
	Above normal	1 (7.7%)	1 (4.8%)	0 (0.0%)		
protein C	Mean ± SD	101.38 ± 20.94	94.62 ± 27.01	95.43 ± 19.18	F = 0.332	0.719
	Below normal	0 (0.0%)	2 (9.5%)	0 (0.0%)	X^{2FFH}=1.348	0.667
	Normal	13 (100.0%)	19 (90.5%)	7 (100.0%)		
Protein S	Mean ± SD	119.23 ± 21.05	112.43 ± 23.22	110.07 ± 23.36	F = 0.504	0.608
	Normal	13 (100.0%)	21 (100.0%)	7 (100.0%)	NA	NA

IQR: interquartile range (25^{th} – 75^{th} percentiles); SD: standard deviation; Max: maximum; Min: minimum; NA: not-applicable; X^{2FFH}: Fisher-Freeman-Halton exact test; F: one-way ANOVA test; Z: Kruskal-Wallis test; * significant at p<0.05. a: significant difference from no depression group; b: significant difference from melancholic group; c: significant difference from non-melancholic group.

Table (3) shows that younger patients had significantly higher d-dimer levels than older patients ($P = 0.021$). Sex, dialysis duration, SMPI score, number of comorbidities, and the frequency of each type of comorbidity were comparable between groups ($p > 0.05$).

Table 3: Comparison between D-dimer levels and demographic and clinical characteristics in the study group.

		D-dimer Normal range ($n = 13$)	D-dimer Above normal ($n = 28$)	Test statistic	*p-value*
Age	Mean ± SD	50.5 ± 12.7	40.5 ± 12.2	T = 2.41	0.021*
	18 – 28	2 (15.4%)	6 (21.4%)	X^{2L}=4.531	0.036*
	29 – 38	0 (0.0%)	6 (21.4%)		
	39 – 48	2 (15.4%)	9 (32.1%)		
	49 – 58	5 (38.5%)	4 (14.3%)		
	>59	4 (30.8%)	3 (10.7%)		
Sex	Female	6 (33.3%)	12 (66.7%)	X^{2ChS}= 0.039	0.843
	Male	7 (30.4%)	16 (69.6%)		
Dialysis onset (years)	Median [IQR]	2.91 [1.91 - 4.50]	2.75[1.50 - 4.00]	Z = 0.056	0.967
SMPI score	No depression	6 (46.2%)	7 (53.8%)	X^{2FFH}= 2.339	0.746
	A	2 (28.6%)	5 (71.4%)		
	A>B	4 (28.6%)	10 (71.4%)		
	A=B	1 (16.7%)	5 (83.3%)		
	B>A	0 (0.0%)	1 (100.0%)		
Number of comorbidities	One	11 (31.4%)	24 (68.6%)	0.790	1.000
	Two	1 (50.0%)	1 (50.0%)		
	Three or more	1 (25.0%)	3 (75.0%)		
Comorbidities	Hypertension	8 (36.4%)	14 (63.6%)	X^{2ChS}= 0.475	0.491
	Lupus	2 (16.7%)	10 (83.3%)	FE	0.276
	Diabetes	1 (50.0%)	1 (50.0%)	FE	0.539
	IHD	3 (50.0%)	3 (50.0%)	FE	0.361
	Hypothyroid	0 (0.0%)	1 (100.0%)	FE	1.000
	heart failure	0 (0.0%)	1 (100.0%)	FE	1.000
	Gout	0 (0.0%)	1 (100.0%)	FE	1.000
	ischemic cardiomyopathy	1 (100.0%)	0 (0.0%)	FE	0.317
	tertiary hyperparathyroidism	0 (0.0%)	1 (100.0%)	FE	1.000
	secondary hyperparathyroidism	0 (0.0%)	1 (100.0%)	FE	1.000
	primary oxaluria	1 (100.0%)	0 (0.0%)	FE	0.317
	CIDP	0 (0.0%)	1 (100.0%)	FE	1.000
	renal stones	0 (0.0%)	1 (100.0%)	FE	1.000

IHD: ischemic heart disease; IQR: interquartile range (25^{th} – 75^{th} percentiles); SD: standard deviation; Max: maximum; Min: minimum; X^{2ChS}: Pearson's Chi-square test for independence of observations; X^{2FFH}= Fisher-Freeman-Halton exact test; X^{2L}: Chi-square test for trend (linear-linear-association); t: Independent samples T-test; Z: Mann-Whitney test; * significant at $p<0.05$.

Table (4) shows that the WBCs, hemoglobin level, and platelet count showed insignificant differences between the elevated and normal D-dimer levels ($p > 0.05$). However, the prevalence of microcytic hypochromic anemia was higher in patients with normal D-dimer levels, whereas normocytic normochromic anemia was more prevalent in patients with elevated D-dimer levels ($p = 0.012$).

Table 4: Comparison of D-dimer levels with TLC, Hg levels and platelet count in the study group.

		D-dimer Normal range	D-dimer Above normal	Test statistic	*p-value*
WBCs	Mean ± SD	5.93 ± 2.13	6.15 ± 1.85	T = 0.35	0.728
	Low	1 (7.7%)	2 (7.1%)	FE	1.000
	Normal	12 (92.3%)	26 (92.9%)		
Hb	Mean ± SD	10.22 ± 1.84	10.45 ± 1.64	T = 0.404	0.688
	Microcytic hypochromic	5 (38.5%)$+	1 (3.6%)$-	8.314	0.012*
	Normocytic normochromic	3 (23.1%)	15 (53.6%)		
	No anemia	5 (38.5%)	12 (42.9%)		
Plt	Mean ± SD	168.46 ± 53.17	181.18 ± 33.29	T = 0.937	0.355
	Low	3 (23.1%)	2 (7.1%)	FE	0.304
	Normal	10 (76.9%)	26 (92.9%)		

SD: standard deviation; Max: maximum; Min: minimum; t: independent samples T-test; significant at $p<0.05$.

Table (5) demonstrates that patients with normal fibrinogen levels had a significantly lower mean platelet count than those with low fibrinogen level ($p = 0.009$). There were insignificant differences in WBCs, and haemoglobin levels between the groups.

Table 5: Comparison of fibrinogen levels with TLC, Hg levels and platelet count in the study group.

		Fibrinogen Below normal range ($n = 10$)	Fibrinogen Normal range ($n = 19$)	Fibrinogen Above normal range ($n = 12$)	Test statistic	*p-value*
WBCs	Mean ± SD	6.97 ± 2.38	5.71 ± 1.66	5.93 ± 1.82	F = 1.505	0.235
	Low	1 (10.0%)	1 (5.3%)	1 (8.3%)	X^{2FFH}= 0.772	1.000
	Normal	9 (90.0%)	18 (94a .7%)	11 (91.7%)		
Hb	Mean ± SD	10.38 ± 1.36	9.89 ± 1.96	11.13 ± 1.22	F = 2.067	0.141
	Microcytic hypochromic	1 (10.0%)	4 (21.1%)	1 (8.3%)	X^{2FFH}= 2.564	0.702
	Normocytic normochromic	5 (50.0%)	9 (47.4%)	4 (33.3%)		
	No anemia	4 (40.0%)	6 (31.6%)	7 (58.3%)		
Plt	Mean ± SD	208.60 ± 30.02 b	161.95 ± 40.43 a	175.00 ± 34.91	F = 5.347	0.009*
	Low	0 (0.0%)	4 (21.1%)	1 (8.3%)	X^{2FFH}= 2.333	0.410
	Normal	10 (100.0%)	15 (78.9%)	11 (91.7%)		

SD: standard deviation; Max: maximum; Min: minimum; F: one-way ANOVA test; * significant at $p<0.05$, b: significant difference from fibrinogen above normal; a: significant difference from fibrinogen below normal.

In Table (6) patients with melancholic depression, SMPI score correlated positively with D-dimer levels and negatively correlated with protein S (60-150%). The WBCs had a significant negative correlation with FVII (70-120%). The PLT count showed negative correlation with Fibrinogen (180-350mg/dl).

Table 6: Correlation between each of the SMPI scores, TLC, haemoglobin level and platelet count and the measured coagulopathy markers.

		SMPI score	WBCs	Hb	plt
WBCs	Rs	-0.238		0.124	0.127
	p-value	0.135		0.440	0.429
Hb	Rs	0.188	0.124		0.013
	p-value	0.240	0.440		0.937
Plt	Rs	-0.111	0.127	0.013	
	p-value	0.488	0.429	0.937	
D-dimer up to 0.25	Rs	0.387	-0.223	0.106	0.002
	p-value	0.012*	0.161	0.511	0.988
Fibrinogen 180-350	Rs	0.262	-0.223	0.250	-0.377
	p-value	0.098	0.161	0.116	0.015*
FVII70-120	Rs	0.067	-0.380	0.231	-0.253
	p-value	0.675	0.014*	0.145	0.111
protein C 70-160	Rs	-0.132	0.199	-0.111	-0.003
	p-value	0.412	0.212	0.491	0.984
protein S60-150	Rs	-0.316	0.038	-0.277	0.069
	p-value	0.044*	0.815	0.080	0.667

rs: coefficient of Spearman's rank-order correlation; moderate: r =0.3-0.7; strong: r>0.7; * significant at $p<0.05$. negative rs indicates an inverse correlation (e.g., one measurement increases and the other decreases.

Table 7: Sydney Melancholia Prototype Inventory (SMPI)-Clinician-rated version.
Below are two descriptions of depression (A and B). Read each carefully and select any statement that characterises the patient's experience of depression (when feeling at their worst). You should select all appropriate and characteristic statements from the descriptions below

Description A	Description B
□ I have very low energy and find it extremely hard to get out of bed and get going. (A1) □ My depressed mood completely prevents me from getting any real pleasure in life, and normally pleasing or humorous things won't lift my mood – or, at best, only superficially. (A2) □ My mood and energy levels are worse in the mornings. (A3) □ I completely lose interest in things, including hobbies and activities that I would usually enjoy when not depressed. (A4) □ I find that I can't look forward to anything in life. (A5) □ In walking and talking, I'm distinctly physically slowed, at times almost feeling 'paralysed' or as if I'm walking through sand. (A6) □ My concentration is distinctly affected and slowed. (A7) □ I tend to lose weight when I'm depressed. (A8) □ The severity of my depressive episodes appears far worse than would be expected in the circumstances. (A9) □ I don't think that my early years were any more difficult- when compared to most people - in terms of having any major difficulties with parents or bullying. (A10) □ When I'm not depressed my relationships and school performances are generally good. (A11) □ My depressions can sometimes come 'out of the blue' without any particularly clear reason. (A12)	□ Even when my depression is severe, I can generally look forward to something really nice coming up. (B1) □ If my concentration is affected during a depressive episode, it is usually because I am worrying too much and have lots of thoughts going through my head distracting me. (B2) □ Even when my depression is severe, I can generally be cheered up when people are really supportive. (B3) □ My mood lifts (even if temporarily) and I can obtain some temporary relief when something nice happens. (B4) □ I find that I become distinctly more irritable and/or angry when I'm depressed. (B5) □ I often get food cravings and/or increased appetite when I'm depressed. (B6) □ I view myself as generally more inclined than most people to become emotional about things. (B7) □ Every time I get depressed, I can find some cause that explains the depression to me. (B8) □ Even when I'm not depressed, I tend to have some difficulties in dealing with my friends, family and other relationships. (B9) □ In childhood and early adolescence, I experienced more stressful events and major difficulties with my parents and others than most people experience. (B10) □ Even when I'm not depressed, I tend to worry more than most people, particularly when under stress. (B11) The severity of my depressions can be explained by what is happing in my life at the time. (B12)

RATING (please tick or circle one):
Now, rate the degree to which you believe one of the categories above best matches the patient's overall profile

1	2	3	4	5
Description A best matches the overall profile	Description A is somewhat closer to the overall profile than Description B	The overall profile has equal features of Descriptions A and B	Description B is somewhat closer to the overall profile than Description A	Description B best matches the Overall profile

Table 8: Demographic and clinical characterization of patients in the study group.

		All patients (*n* = 41)
Age (years)	Mean ± SD	43.7 ± 13.1
	Min – Max	22.0 - 64.0
Gender	Female	18 (43.9%)
	Male	23 (56.1%)
onset of dialysis (yr ago)	Median [IQR]	2.83 [1.58 - 4.00]
	Min – Max	0.66 - 17.25
Depression	Absent	13 (31.7%)
	Present	28 (68.3%)
SMPI score	A	7 (17.1%)
	A>B	14 (34.1%)
	A=B	6 (14.6%)
	B>A	1 (2.4%)
Number of comorbidities	One	35 (85.4%)
	Two	2 (4.9%)
	Three or more	4 (9.8%)
Comorbidities	Hypertension	22 (53.7%)
	Lupus	12 (29.3%)
	Diabetes	2 (4.9%)
	ischemic heart disease	6 (14.6%)
	hypothyroid	1 (2.4%)
	heart failure	1 (2.4%)
	gout	1 (2.4%)
	ischemic cardiomyopathy	1 (2.4%)
	tertiary hyperparathyroidism	1 (2.4%)
	secondary hyperparathyroidism	1 (2.4%)
	primary oxaluria	1 (2.4%)
	CID	1 (2.4%)
	Polyneuropathy	1 (2.4%)
	renal stones	1 (2.4%)

IQR: interquartile range (25^{th} – 75^{th} percentiles); SD: standard deviation; Max: maximum; Min: minimum
A = melancholic type of depression, A>B =depression with features melancholic morethan non-melancholic, A = B depression with features of both melancholic and non-melancholic types, B>A = depression with features of non-melancholic types

Statistical Analysis

The statistical analysis was conducted using SPSS v26 (IBM Corp., Armonk, NY, USA). Quantitative variables are represented using the mean and standard deviation (SD) in the independent samples T-test (for two groups) or the one-way analysis of variance (ANOVA) test (for more than two groups). If the results are significant, a post hoc test is conducted. When dealing with numerical data that does not adhere to the normal distribution, the data was summarized using the median and interquartile range. To compare the data, the Mann-Whitney test was used for two groups, while the Kruskal-Wallis test was used for more than two groups. If the results were significant, a post hoc test was conducted. Qualitative variables were examined using the Chi-square test or Fisher's exact test, as applicable, and provided as frequency and percentage (%). Spearman's rank-order correlation was used to assess the correlations between the numerical and ordinal variables, namely the SMPI score. When dealing with categorical data, variables are condensed into frequencies, which are expressed as counts and percentages. The chi-square test for independence of data, as developed by Pearson, is a statistical method used to determine whether there is a relationship between two categorical variables. Statistical significance was determined as a *P-value* less than 0.05, calculated for both tails of the distribution.

DISCUSSION

Haemodialysis patients have a much higher prevalence of depression than the general population[9]. Depression occurring in chronic kidney disease (CKD) patients may be more resistant to treatment[7]. Our research found that 17.1% of patients scored for melancholic depression (score A) using the SMPI score. Additionally, about 14.63% of patients scored for depression with both melancholic and non-melancholic traits (score A=B), if we talk about the percentage of depression in our sample about 68.29%.

Our study revealed a direct relationship between high levels of D-dimer and depression in haemodialysis patients. This finding supports the main hypothesis that there may be a connection between coagulopathy and depression in haemodialysis patients. Specifically, we observed a significant increase in D-dimer levels (0.43 ± 0.21, 0.47 ± 0.17 consecutively, *P*= 0.007) in depressed patients of both melancholic and non-melancholic types undergoing regular haemodialysis compared to non-depressed patients. There were no notable disparities in hemoglobin, platelet count, fibrinogen levels, factor VII activity, protein C concentration, and protein S concentration between the depressed and non-depressed groups.

Our study revealed a noteworthy statistical finding: patients diagnosed with depression exhibited significantly lower average levels of total lymphocyte count (TLC) compared to those without depression. This difference was observed across the three SMPI scores: A, A>B, and A=B. Additionally, patients with a high melancholic score had the lowest TLC levels when compared to other categories. Patients diagnosed with melancholic depression had a notably lower average total leukocytic count in comparison to those without melancholic (5.07 ± 1.61 vs. 7.39 ± 1.76, p =0.001). This finding was in contrast to that of ***Euteneuer et al., 2017***[4] that reported an increase in the neutrophil count along with increase in monocyte counts, and NLR in Major Depression[4].

Sørensen et al.,[10] also found leukocytosis, higher numbers of neutrophils, lower numbers of lymphocytes and subsequently an increased neutrophil/lymphocyte ratio in their meta-analysis of the composition of circulating immune cells in unipolar depression. This discrepancy may be attributed to the small number of patients included in our study[10].

We have also discovered a correlation between FVII and PC levels, indicating that a higher proportion of patients with elevated FVII have low PC levels. This finding further supports the presence of a coagulopathy, where there is an excess of clotting factor along with a deficiency of an anticoagulant protein, specifically low PC levels in this case. This supports our finding of increased risk of thrombosis and depression in a greater percentage of our sample.

In a study by Lu and Liao[11] in Taiwan, a study was conducted with 3564 patients with end-stage renal disease (ESRD). The incidence rate of deep vein thrombosis (DVT) was significantly greater in the ESRD group compared to the non-ESRD group (20.9 vs. 1.46 per 10^4 person-years). Patients with end-stage renal disease (ESRD) who had three or more comorbidities had a significantly higher likelihood of developing deep vein thrombosis (DVT) compared to those without comorbidities (adjusted hazard ratio [aHR] 1.45; 95% confidence interval [CI] 1.03–2.03; *P* = 0.03). Our research found that those with depression had markedly elevated levels of D-dimer compared to those without depression also the greater percentage have higher D-dimer levels. In our investigation, the only coagulation profile levels that showed an increase were the higher levels of D-dimer. In contrast, the levels of fibrinogen, FVII, protein C, and protein S were the same in both individuals with and without depression.

Similarly Lu and Liao,[11] 2018 showed that Cox regression models demonstrated a significant association between age, gender, and comorbidities with increased chances of deep vein thrombosis (DVT) in the end-stage renal disease (ESRD) group compared to the non-ESRD group. The inclusion of a large number of patients further supports the greater incidence of thrombosis in the ESRD group. Contrary to expectations, our analysis revealed a distinct correlation: younger patients had notably greater levels of D-dimer compared to older patients. This was particularly evident since the majority of patients with elevated D-dimer levels were under the age of 48[11] these opposite results in our study may be related to small number of patients in our study.

In an observational study Among 11,265 patients across 13 New York hospitals admitted between March 1 and April 27 2020, an elevation in D-dimer level was associated with a lower median haemoglobin level and higher serum ferritin level in patients with COVID-19[12].

A study by[13] found an association between elevated plasma fibrinogen levels and depression in 73 367 subjects[14]. compared 78 hemodialysis patients and 40 controls as regard levels of fibrinogen, D-dimer and Vwf and found significantly higher levels, 3.44 g/L vs. 2.55 g/L, $p<0.01$; 1.81 µgFEU /ml vs. 0.50 µg FEU /ml, $p<0.01$; 152.9 % vs. 85.6 %, $p<0.001$ respectively than controls. The results of the first study may differ from those of our study due to the small sample number of participants in our study, but still stronger than other studies due to large sample in the study.

In our investigation, we observed a significant link between the SMPI score and protein S levels, showing a negative relationship. However, we did not find any association between the SMPI score and protein C levels. Patients with melancholic sadness have reduced protein S levels. This aligns with the research conducted by Hoirisch-Clapauch and Nardi[15], which revealed a significant occurrence of psychotic symptoms in individuals with hereditary protein S deficiency. Their discoveries were marvelous as they were the first ones to document a significant occurrence of psychotic symptoms (50% compared to 6% in the general population) and psychotic illnesses (29% compared to 2% in the general population) among individuals with hereditary protein S deficiency. Further investigation is necessary to validate our results and elucidate the underlying reason[15].

This population based cohort study was conducted with information regarding psychiatric illnesses and medical comorbidities in 29,467 patients with concurrent depressive, bipolar, and schizophrenic disorders and 117,868 controls, and concluded that the overall incidence of DVT was significantly higher (3.214-fold) in the study cohort than in the reference cohort (11.59 vs. 4.79 per 10,000 person-years), with an aHR of 3.103 (95% CI: 2.671–3.701, $P < 0.001$) after adjusting the model to control for the effects of age, sex, comorbidities, and catastrophic illnesses other than mental illnesses[16].

The age-specific risk of DVT occurence in the study cohort, relative to the reference cohort, was significantly higher in patients aged < 55 years old (aHR: 4.002, 95% CI: 3.121–5.003, $P < 0.001$)[16]. This may be similar to increased D-dimer level in younger patients in the results of our study, which may require further research. Our study find a correlation between melancholic depression and coagulopathy in high-risk patients. Our study have a significant contribution to highlight thromboembolic risk as an etiology of melancholic depression which is often an associated illness in chronic ill patients and may contribute to prophylaxis or treatment of melancholic depression.

CONCLUSION

Depression is a disabling illness that may include several types of presentations. Our research found that 17.1% of patients scored for melancholic depression (score A) using the SMPI score. The percentage of depression in our sample about 68.29%. There's significant correlation that has been established in this research work between depression and the presence of coagulopathy markers. This correlation may have a role in treatment and prophylaxis against melancholic depression in hemodialysis patients and also in chronic ill patients and also decrease thrombosis risk. Further research could highlight more this correlation.

DECLARATION FORM

Khaled gamal el ghamery contributed to the design and implementation of the research, Khaled gamal el ghamery, Mohammed Atef alawam and Rania Mohamed Afifi contributed to the analysis of the results and to the writing of the manuscript. Prof Mamdouh Mahmoud Mahdy conceived the original and supervised the project.

CONFLICT OF INTEREST

The investigators declare no conflict of interest.

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العلاقة بين الاكتئاب الميلانكوليا ودلالات تجلط الدم لدى مرضى غسيل الكلوي

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الخلفية: ما يقرب من٢٨٠ مليون فرد يعانون من الاكتئاب في جميع أنحاء العالم. وقد أظهر الاكتئاب الميلانكوليا زيادة بعد جائحة كوفيد-١٩، ومن المعروف أنه يزيد من نسبة حدوث جلطات بالدم.

الهدف: قمنا بدراسة الارتباط المحتمل بين الاكتئاب الميلانكوليا واعتلال تجلط الدم لدى مرضى غسيل الكلى حيث أن مرضى غسيل الكلى معرضون أكثر للإصابة بالاكتئاب.

الطرق: استخدم هذا البحث تصميمًا مقطعيًا وشمل عينة من واحد وأربعين مريض غسيل كلوي تتراوح أعمارهم بين ١٨ و٦٩ عامًا. أجرى المريض مقابلة تضمنت استبيان سيدني للكآبة و بعد الحصول على إذن كتابي من جميع المرضى، تم سحب تعداد الدم الكامل، ودي ديمر، وفيبرينوجين، وبروتين سي، وبروتين إس، والعامل السابع لكل مريض.

النتائج: ارتبطت مستويات دي-دايمر المرتفعة بشكل إيجابي بالاكتئاب سواء المرضي الذين يعانون من الاكتئاب الميلانكوليا و الأنواع الأخري مقارنة بالمرضى الذين لا يعانون من الاكتئاب. علاوة على ذلك، ارتبطت مستويات دي-دايمر المرتفعة بمؤشر سيدني النموذجي للاكتئاب و كذلك المرضي الذين يعانون من الاكتئاب الميلانكوليا لديهم عدد كرات دم بيضاء أقل من المرضي الذين لا يعانون من الاكتئاب.

الاستنتاج: الاكتئاب مرض معوق قد يشمل عدة أنواع من الأعراض. هناك ارتباط تم إنشاؤه في هذا العمل البحثي بين انتشار الاكتئاب ووجود اعتلال تجلط الدم. يمكن أن يكون لهذا دور في المستقبل في الوقاية وتقليل حدوث الاكتئاب لدى المرضى المعرضين للإصابة بالاكتئاب وخطر الإصابة بالجلطات.