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ORIGINAL ARTICLE

Associations of Serum Cystatin C with Depressive Symptoms, Suicidal Ideation and Cognitive Dysfunctions in Major Depressive Disorder

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ABSTRACT

Background: The common illness known as Major depressive disorder (MDD) is defined by significantly increased rates of illness and disease, impairment, and suicidal thoughts. Numerous investigations have demonstrated the significant impact cystatin C plays in cognitive impairment and major depressive disorder (MDD).

Aim: Toassess the relation between serum cystatin c concentration and depressive symptoms, suicidal ideation and cognitive dysfunctions in patients with MDD.

Methods: this case–control study was carried out on 69 patients with major depressive disorder diagnosed according to DSM-V criteria that attended outpatient clinic of the Psychiatry department El-Azazy psychiatric hospital & Psychiatry department at Zagazig university hospitals and 69 healthy controls. Cystatin C level was measured.

Results: Cystatin C level was significantly higher in major depression patients compared to controls. There was a significant positive correlation between cystatin C with age, Hamilton depression rating scale, BECK scale and MOCA scale. Cases in rural areas showed significant elevation in cystatin C level compared to cases in urban areas (p=0.025). There was a significant relation between degree of depression, suicidal ideation, cognitive dysfunction and cystatin C as it was significantly higher in these cases. Cystatin C was a significant predictor of major depressive disorder (AUC=0.851, P value<0.001). The suggested cut-off value (>1 mg/L) showed 66.7% sensitivity, 92.8% specificity, 90.3% PPV and 73.6% NPV

Conclusion: Serum Cys C levels are associated with depressive symptoms, cognitive dysfunction and suicidal ideation in MDD patients.

Keywords: Major Depressive Disorder, Cystatin C, Cognitive Dysfunction.

One of the most serious mental illnesses is major depressive disorder, or MDD and common mental diseases globally. As per the World Health Organization [WHO], Worldwide, major depressive disorder, or MDD, is the leading cause of disability. More than 350 million individuals worldwide currently suffer from depression, with a global prevalence rate of more than 4%. According to WHO estimates, this disease By 2030, it is projected that it will become the top-ranked cause of disease burden globally, following its position as the third biggest cause in 2008 **[1].**

The current DSM-5 diagnostic criteria include nine symptoms that define MDD. The following symptoms can be identified: 1. Depression of mood; 2. Anhedonia; 3. Loss of interest or pleasure; 4. Sleep disturbances characterized by either hypersomnia (extreme sleepiness) or insomnia (difficulty falling or staying asleep); 5. Abnormal physical activity during sleep, such as psychomotor agitation (restlessness) or retardation (slowed movements); 6. Persistent fatigue or a lack of energy; 7.widespread emotions of guilt or unworthiness; 8] Poor focus or indecision [Focus]; 9] Suicidal ideas, plans, or death-related thoughts [Suicidal ideas and activities] **[2].**

In order to receive a diagnosis of Major Depressive Disorder (MDD), a person needs to exhibit five of the aforementioned symptoms, with a sad mood or anhedonia impairing social or occupational functioning being one of them. To diagnose MDD, a history of manic or hypomanic episodes must be ruled out. There's a chance that kids and teenagers with MDD will exhibit irritability **[1].**

Suicide is a major public health concern on a global scale. In 2019, suicide ranked as the second most common cause of death for teenagers and young adults (10–24 years old). About 4 to 10.6% of MDD patients may eventually take their own lives, causing immense suffering for themselves and their families, in addition to imposing a substantial economic strain on society **[3].**

Compact protein cyclostatin C functions as an inhibitor of cysteine proteases [13.4 kDa] that is produced consistently in all cells with a nucleus. It is transcribed by the CST3 gene and released into the bloodstream, cerebrospinal fluid, and extracellular space. Cystatin C undergoes unimpeded filtration by the glomerulus, followed by reabsorption and complete breakdown without any secretion or further reabsorption into the bloodstream **[4].**

Several investigations have confirmed an association between the existence of serum Cys C and neurodegenerative conditions like Parkinson's and Alzheimer's. This suggests that increased amounts of Cys C in the bloodstream may accelerate the progression of these diseases. Furthermore, consistent with earlier findings, patients with elevated levels of Cys C demonstrate an increased susceptibility to depression **[5].**

The aim of this study was to assess the relationship between levels of cystatin c in the blood and symptoms of depression, suicidal thoughts, and cognitive deficits in persons diagnosed with Major Depressive Disorder (MDD).

METHODS

The research was carried out in the outpatient clinic of the Psychiatry department using a case-control design El-Azazy psychiatric hospital, ministry of health, Abo-Hammad city El-Sharqia governorate, Egypt in cooperation with Psychiatry department at Zagazig university hospitals.

Patients were selected by simple the method used for selecting samples is random sampling, and the participants were enrolled in a consecutive manner. Prior to the study, all participants Underwent a comprehensive assessment to see if they satisfied the specific criteria for inclusion and exclusion.

Male and female patients between the ages of 18 and 60, who have significant depressive disorder diagnosed according to DSM-V criteria and all socioeconomic classes Participated in the study.

Patients with history of psychiatric disorders other than major depressive disorder, evidence of substance abuse within the past

month, Prior administration of immunosuppressive medications, ongoing inflammatory conditions, and acute infections, any malignancy or history of treatment with chemotherapy or radiotherapy, chronic medical conditions e.g. diabetes mellitus, hyptension, chronic renal, liver and cardiac diseases…etc, any Examples of connective tissue illnesses include systemic lupus and rheumatoid arthritis, polyarteritisnodosa …., etc, mental subnormality and neurodegenerative disorders e.g early alzheimer and dementia were excluded from the study.

Socio-demographic and clinical data collection form:

The questionnaire consists of inquiries pertaining to the participants' sociodemographic characteristics, such as age, gender, place of residence, level of education, and marital status, and economic position, history of abuse, any present or past psychiatric history, smoking status, any previous hospitalization in a mental hospital, family history of a psychiatric disease, … etc.A sample of 92 Patients with The psychiatric records indicate that experienced clinical psychiatrists have diagnosed the individual with major depressive disorder in recent years using the The Arabic translation of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) was translated by ElMissery[6].

The following scales were applied:

The Hamilton Depression Rating Scale (HDRS) (7):

The Hamilton Rating Scale for Depression (HAMD-17) has been employed for numerous years to evaluate the intensity of depression. We used Arabic version translated by Lotfy Fateem. Clinician-rated scale, administrated in 20–30 minutes. The HDRS, commonly referred to as the Ham-D, is the predominant scale used by clinicians to assess depression. The initial version comprises 17 items (HDRS17) that relate to symptoms of depression encountered throughout the previous week. The HDRS was first designed for individuals admitted to hospitals, with the focus on melancholy and physical manifestations of depression. The scoring method differs depending on the version. The HDRS17 considers a score between 0 and 7 to be considered normal or in clinical remission. However, a minimum score of 20, indicating extreme severity or above, is often required for participation in a clinical investigation.

The Montreal Cognitive Assessment (MoCA):

An easy-to-use diagnostic tool for determining mild cognitive impairment is the Montreal Cognitive Assessment (MoCA). Various cognitive areas, including attention, concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and direction are measured by the assessment. While the MoCA can be administered by anybody who comprehends and adheres to the instructions, only a cognitive health professional with specialized knowledge can interpret the results. The duration required to perform The duration of the MoCA exam is around 10 minutes. The highest attainable score is 30 points, and a score of 26 or more is considered to be within the normal range. The initial normative data for the MoCA were derived from a sample of 90 Canadian individuals who served as controls. The average age of these individuals was 72.84 years, and their average level of education was 13.33 years. Based on the findings, a recommended threshold for normalcy was established to be greater than Scoring 26 out

of 30 points. The provided value exhibited a sensitivity of 90% and a specificity of 100% for MCI. We utilize Nasreddine translated the Arabic version of MoCA (**8**) and validated by Saleh et al.,**[9].**

Beck Scale for Suicidal Ideation (BSS):

The Beck Scale for Suicidal Ideation (BSS) is a 19-item tool used to measure the present severity of particular thoughts, actions, and intentions related to suicide. The administration of this scale requires roughly 10 to 15 minutes and must be conducted by persons with specialist training, the 19 items are "Desire to exist, Desire to cease existing, Purpose of existence, Active endeavor, Passive endeavor, Duration of thoughts, Frequency of ideation, Attitude toward ideation, Command over behavior, Factors that discourage attempts and factors that motivate attempts. The precision of planning, Availability/opportunity Capability, Expectancy, and Actual preparedness. Written expression of intent to commit suicide, Last actions, Deception" . Each item is comprised of three options that are assessed based on the level of suicidality intensity. All 19 questions are evaluated using a three-The point scale ranges from 0 to 2, with 0 indicating no ideation and 2 indicating strong ideation. The scale is employed to assess the magnitude of the issue, with 0 indicating no problem, 1 indicating a mild problem, and 2 indicating a serious problem. The total score can vary from 0 to 32. There are no exact scores that can be used to determine the severity of a condition or provide guidance for patient treatment. Higher scores indicate a higher risk of suicide, and every positive reaction should be thoroughly investigated **[10].**

A detailed review has been conducted on the validity and reliability of the BSSI in the English language. The Cronbach's alpha coefficient consistently above 0.85 in nearly all situations, indicating a high level of internal consistency. Moreover, the BSSI scores exhibited noteworthy associations with indicators of sadness, hopelessness, anxiety, past suicide attempts, and the probability of future suicide attempts. Beck et al. introduced the self-reporting version of the measure in 1988. The translation and verification of the Arabic version used in this study was done.

Blood sampling and analysis:

Five milliliters of venous blood were drawn from the elbow between 7:00 and 9:00 in the morning on the day before the assessment, and participants were instructed not to eat after 8:00 p.m. on the day before the assessment. Serum samples were collected by spinning at 3500 rpm for 10 minutes and stored at -80°C until analysis. The quantification of serum cystatin C levels was performed chronologically. resolved immunofluorescence analyzer (Tongzhou District Beijing, China ; Serial Number: NO.00320043~JUN). The Cys C reagent was acquired from the Chinese business DGT. Particle enhanced fluorescence immunochromatographiac An assay was employed to detect serum Cys C. In addition, the serum was also analyzed for levels of urea, creatinine (Cr), uric acid (UA), estimated glomerular filtration rate (eGFR), and high-sensitivity C-reactive protein (hs-CRP).Study of language and examination

Administrative design:

The Institutional Review Board (IRB) and the Zagazig University Department of Psychiatry gave their approval. An informed consent form outlining the study's objectives was sent to each student taking part in the research.

Statistical Analysis*:*

Version 20.0 of the IBM SPSS software program (IBM Corp., 2017) was used to feed

data into the computer and analyze them. IBM Corp., Armonk, NY, published IBM SPSS Statistics for Windows, Version 25.0. Quantitative data were represented using numerical values and numerical proportions. The distribution's normality was verified by the Shapiro-Wilk test. A variety of statistical measures, including the minimum and maximum values, mean, standard deviation, median, and interquartile range (IQR), were used to assess the quantitative data. A significance threshold of 5% was used to assess the results' significance. The Chi-square test, Student t-test, Mann Whitney test, Monte Carlo correction, Analysis of variance (ANOVA or F test), Kruskal-Wallis test, and Correlation analysis (using Spearman method), linear regression, and the ROC Curve (receiver operating characteristic).

RESULTS

In the MDD patients group (n=69), the cystatin C level ranged from 0.70 to 3.6 mg/L, with a median of 1.9 mg/L, a 95% of CI of the median of 1.80- 2.10 mg/L, and 25th Percentile –75th Percentile of 1.0- 2.4 mg/L. **In the control group (n=69),** the cystatin C level ranged from 0.70 to 1.0 mg/L, with a median of 0.80 mg/L, a 95% of CI of the median of 0.8- 0.9 mg/L, and 25th Percentile – 75th Percentile of 0.7- 0.9 mg/L. Cystatin C showed significant increase in major depression patients (MDD) compared to controls (p< 0.001) **(Table 1).**

Among patients with Major Depressive Disorder (MDD), a strong positive association was observed between cystatin C levels and age (r= 0.589, p<0.001), as well as with the Hamilton Depression Rating Scale (r= 0.899, p<0.001). Whereas, there was significant negative correlation between cystatin C with MOCA" scale (r= -0.818, p<0.001). In MDD patients without suicidal ideation (n=37), the cystatin C level ranged from 0.70 to 2.30 mg/L, with a median of 1.0 mg/L, a 95% of CI of the median of 1.0- 1.9 mg/L, and 25th Percentile –75th Percentile of 0.8- 1.8 mg/L. In MDD patients with suicidal ideation (n=32), the cystatin C level ranged from 1.9 to 3.6 mg/L, with a median of 2.55 mg/L, a 95% of CI of the median of 2.10- 3.20 mg/L, and 25th Percentile –75th Percentile of 2.1- 3.4 mg/L. Cystatin C showed significant increase in individuals diagnosed with Major Depressive Disorder (MDD) who experience thoughts of suicide, as compared to individuals with MDD who do not have such thoughts (p< 0.001) **(Table 2).**

In MDD patients without cognitive dysfunction (n=13), the cystatin C level ranged from 0.70 to 1.20 mg/L, with a median of 0.9 mg/L, a 95% of CI of the median of 0.80- 1.10 mg/L, and 25th Percentile –75th Percentile of 0.7- 1.0 mg/L. In MDD patients with cognitive dysfunction (n=56), the cystatin C level ranged from 0.7 to 2.75 mg/L, with a median of 2.10 mg/L, a 95% of CI of the median of 2.0- 2.60 mg/L, and 25th Percentile –75th Percentile of 0.70- 3.60 mg/L. Cystatin C showed significant There is a higher prevalence of cognitive dysfunction in people with Major Depressive Disorder (MDD) compared to those without cognitive dysfunction (p< 0.001) **(Table 3).**

Employee cases showed significant elevation in cystatin C level compared to not working cases (p=0.013) **(Table 4).**

In MDD patients, Cystatin C levels and age showed a high positive correlation (r= 0.589, p<0.001), as did the Hamilton depression assessment scale (r= 0.899, p<0.001). On the other hand, there was a noteworthy inverse relationship between cystatin C and the MOCA" scale (r=-0.818, p<0.001). **(Table 5).**

Cystatin C was a significant predictor of major depressive disorder (AUC=0.851, P value<0.001). The suggested cut-off value (>1 mg/L) showed 66.7% sensitivity, 92.8% specificity, 90.3% PPV and 73.6% NPV **(Figure 1).**

Table (1): Cystatin C level in major depression patients (MDD) and controls.

		MDD patients (N= 69)	Controls (N= 69)	Test value	P-value
Cystatin C (mg/L)	Mean± SD	1.89± 0.93	0.83± 0.11	Z_{MWU}= 7.202	<0.001**
	Median (IQR)	1.9 (1.0 – 2.4)	0.80 (0.70 – 0.90)		
	Range	0.70 – 3.6	0.70 – 1.00		

*p≤0.05 is significant, **p≤0.01 is high significant, SD: standard deviation, IQR: Interquartile range,

- Z_{MWU} :Mann Whitney U test

Table (2): Relation between Cystatin C level and suicidal ideation in major depression patients (MDD).

		No suicidal ideation (N= 37)	Suicidal ideation (N= 32)	Test value	P-value
Cystatin C (mg/L)	Mean± SD	1.21± 0.52	2.67± 0.62	Z_{MWU}= 6.576	<0.001**
	Median (IQR)	1.0 (0.8 – 1.8)	2.55 (2.10 – 3.40)		
	Range	0.70 – 2.30	1.90 – 3.60		

*p≤0.05 is significant, **p≤0.01 is high significant, SD: standard deviation, IQR: Interquartile range,

- Z_{MWU} :Mann Whitney U test

Table (3): Relation between Cystatin C level and cognitive dysfunction in major depression patients (MDD).

		No cognitive dysfunction (N= 13)	Cognitive dysfunction (N= 56)	Test value	P-value
Cystatin C (mg/L)	Mean± SD	0.88± 0.16	2.12± 0.87	Z_{MWU}= 4.447	<0.001**
	Median (IQR)	0.9 (0.7 – 1.0)	2.10 (1.8 – 2.75)		
	Range	0.70 – 1.20	0.7 – 3.60		

*p≤0.05 is significant, **p≤0.01 is high significant, SD: standard deviation, IQR: Interquartile range,

- Z_{MWU} :Mann Whitney U test

Table (4): Relation between cystatin C and demographic data.

		Cystatin C (mg/L)								Test value	P-value
		N	Mean	± SD	Median	IQR		Range			
Gender	Male	34	1.9	0.9	2	1.2	2.1	1	2.3	Z_{MWU}=0.421	0.674
	Female	35	1.9	1.0	1.9	1.2	2.3	0.9	2.5		
Highly education	No	30	2.0	0.9	1.9	1.8	2.3	1.1	2.9	Z_{MWU}=0.862	0.346
	Yes	39	1.9	0.9	1.9	1.0	2.1	0.8	2.4		
Residence	Rural	12	2.4	0.6	2.2	1.9	3.3	2.0	3.0	Z_{MWU}=0.959	0.338
	Urban	57	1.8	0.9	1.9	1.2	2.1	0.9	2.3		
Occupation	Not working	20	1.5	0.9	1.0	0.9	2.0	0.8	2.1	Z_{MWU}=2.480	0.013*
	Employee	49	2.0	0.9	2.0	1.9	2.2	1.1	2.6		
Marital status	Single	15	1.7	0.7	2.0	1.0	2.3	0.9	2.3	KW= 0.976	0.614
	Married	36	1.8	0.9	1.9	1.8	2.1	1.0	2.2		
	Divorced	18	2.1	1.1	2.1	1.0	3.2	1.0	3.3		

p≤0.05 is significant, p≤0.01 is high significant, SD: standard deviation, IQR: Interquartile range

Table (5): Correlations between Cystatin C with different parameters

	Cystatin C (mg/L)	
	$SP._r$	p- value
Age	0.589	<0.001
Hamilton depression rating scale	0.899	<0.001
Montreal Cognitive Assessment "MOCA" scale	-0.818	<0.001

*p≤0.05 is significant, **p≤0.01 is high significant, r: Spearman correlation

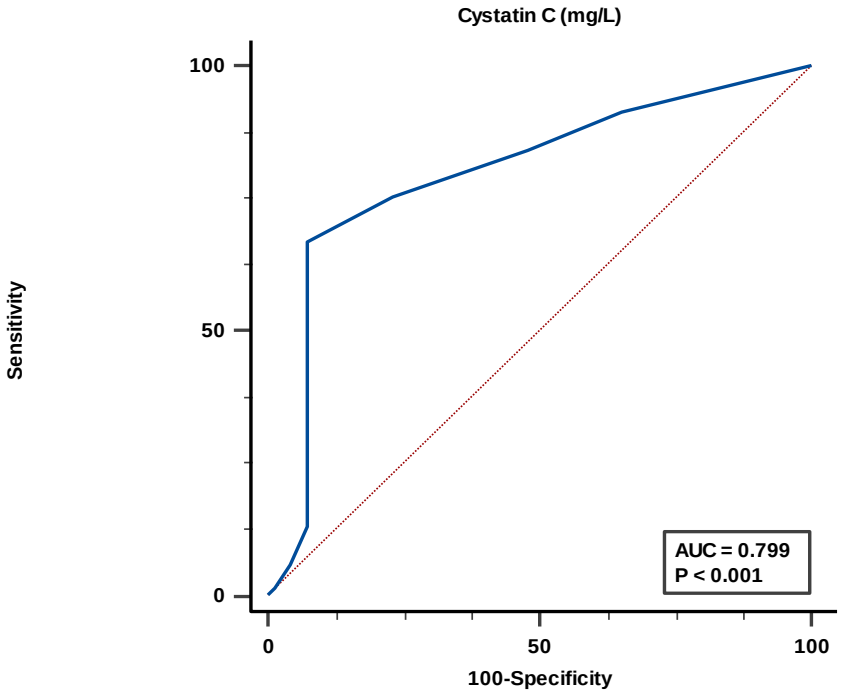

Figure (1): ROC curve of cystatin C in diagnosis of major depressive disorder.

DISCUSSION

Regarding our study, Cystatin C level The prevalence of serious depression was markedly greater in patients compared to controls. There was a notable favorable correlation between cystatin C with age, Hamilton depression rating scale, BECK scale and MOCA scale. Cases in rural areas showed significant elevation in cystatin C level compared to cases in urban areas [p=0.025]. Divorced cases showed significant elevation in cystatin C level compared to single and married cases.

Additionally, our findings demonstrated a strong correlation between the intensity of depression and the occurrence of suicidal ideation , cognitive dysfunction and cystatin C as it was significantly higher in these cases. Cystatin C was a significant predictor of major depressive disorder [AUC=0.851, P value<0.001]. The suggested cut-off value [>1 mg/L] showed 66.7% sensitivity, 92.8% specificity, 90.3% PPV and 73.6% NPV

Sun et al. discovered a positive association between the Hamilton depression rating scale and serum Cys C level in a retrospective study of MDD patients. This correlation held true even after adjusting for any confounding variables. These effects were unaffected by age, gender distribution, smoking, alcohol use, stressful life experiences, Family history of depression, High-sensitivity C-reactive protein (hs-CRP), estimated glomerular filtration rate (eGFR), and other parameters are measured. urea, creatinine (Cr), and uric acid (UA). Upon evaluating all of the specified parameters, it was seen that the outcomes for serum Cys C levels and suicidal thoughts were comparable ***[3].***

As per our agreement, Minev et al. investigated a possible relationship About the relationship between depression and cystatin C levels. Their findings demonstrated a noteworthy correlation between the degree of depression, suicidal thoughts, cognitive dysfunction, and cystatin C, with the latter being significantly elevated in these instances ***[11].***

In a similar vein, Wu et al.'s study, which included 1440 Chinese older adults [over 60], discovered a negative correlation A positive link exists between elevated levels of Cys C in the bloodstream and an augmented susceptibility to depression ***[5].***

Li et al. conducted a prospective cohort study on 11,847 Chinese individuals aged 45 and above, which revealed a correlation between elevated levels of Cys C and a higher chance of developing Depression. Utilizing a refined Poisson regression model, the researchers assessed the likelihood of depression and determined that, even after accounting for several covariates, there remained a strong correlation exists between serum Cys C levels and depression risk ***[12].***

Sun et al. findings support the previously mentioned observations by showing a substantial correlation between the intensity of depressive symptoms and blood levels of Cys C, which are associated with depression. This connection remains significant even after accounting for many possibly confounding variables ***[3].***

Moreover, cystatin C may be a key Gao et al. identified the role in the pathophysiology of depression. Cystatin C influences the susceptibility to depression through many mechanisms since it carries out its biological duties in numerous areas of biological activity and neuron physiology. First, serum Cys C influences neutrophil migration and is linked to inflammation ***[13].***

According to Zavori et al., this triggers the generation of pro-inflammatory cytokines like TNF and IFN-γ, which can disrupt the serotonin pathway in the brain, cause symptoms by stimulating the hypothalamic-pituitary-adrenal axis of depression by way of the inflammatory route ***[14].***

Second, apoptosis is another way that Cys C may affect the likelihood of developing depression. Depression may result from this, either directly or indirectly. By raising the amount by inhibiting the activity of the caspase-9 protein reduces the amount of B-cell leukemia 2 [Bcl-2] by turning on the pathway dependent on Jun-terminal kinase [JNK], Cys C induces neuronal death, which could be a notable contributing factor to depression ***[15].***

The final potential explanation is the connection between cystatin C and oxidative stress, which is a significant factor Experiencing depression. Previous research has shown that oxidative stress can increase the levels of Cys C in the cardiovascular and neurological systems. Although the exact mechanism is yet unknown, reactive oxygen species such as hydrogen peroxide, superoxide anion, hydroxyl radical, and others can contribute to the increase in Cys C level caused by oxidative stress ***[16].***

The aforementioned mechanisms could account for the abnormally high amount Measurement of Levels of cystatin C in patients with Major Depressive Disorder (MDD). The study revealed that individuals experiencing suicidal thoughts exhibited higher levels of blood Cys C in comparison to those without such thoughts. This indicates a notable correlation between serum Cys C levels and thoughts of suicide in people with major depressive disorder (MDD). Previous studies have shed important light on the relationship between depression and serum Cys C. Nonetheless, it is unknown how Cys C and suicidal thoughts in depressed individuals are related and has not been investigated ***[4].***

In addition, Sun et al. also Research has discovered Elevated concentrations of Cys C in the bloodstream are linked to a heightened susceptibility to suicidal ideation. This implies that Cys C may play a role in the formation of suicidal thoughts in individuals suffering from depression. Nevertheless, the precise mechanism behind this association remains unknown fully understood ***[3].***

A plausible explanation could be because variations in Cys C levels are linked to elevated neural inflammation, which could heighten suicidal thoughts in depressed individuals. Furthermore, Brundin et al. found that some inflammatory markers, such TNF-α and IL-6, influence the serotonergic system, which in turn affects the risk of suicide in depressed patients ***[17].***

Another possible explanation is that Cys C is crucial for triggering neuronal apoptosis, Polyamine-induced Apoptosis causes a decrease in the size of neurodegenerative grey matter, which is linked to a higher likelihood of suicide ***[18].***

both studies [***Brundin et al.***] suggests elevated neural inflammation, and [***Gauthier et al***.] suggests shrinkage of neurodegenerative grey matter volume and its relation with cystatin c level but didn't give us exact data about sensitivity or specificity.

Cys C may also affect suicidal thoughts in MDD patients by destroying white matter, which is a third method. Suicide may be connected to white matter damage the condition is a result of genetic mutations in the CST3 gene, which is responsible for the production of the protein cystatin C. These

mutations also raise cathepsin activity ***[19].***

CONCLUSIONS

Our study's findings point to a relationship between major depressive disorder (MDD) patients' serum Cys C levels and signs of depression, cognitive deterioration, and suicidal thoughts. These findings suggest that the dysfunction of Cys C is involved in both the severity of depression and the underlying physiological mechanism of Major Depressive Disorder (MDD). Hence, regulating the concentrations of serum Cys C holds the potential to precisely forecast the severity of depression and maybe aid in mitigating the chance of suicide in those with major depressive disorder (MDD) diagnosis. It is possible for serum Cys C to serve as a biomarker for suicidal thoughts and depression. There is Cystatin C (Cys C) available to have a connection with mild cognitive impairment (MCI), indicating that it may be a useful marker for predicting the probability of cognitive deterioration in patients with major depressive disorder.

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REFERENCES

1. **Bains N, Abdijadid S.** Major depressive disorder. In: StatPearls. StatPearls Publishing; 2022.
2. **Malgaroli M, Calderon A, Bonanno G.** Networks of major depressive disorder: A systematic review. Clin Psychol Rev. 2021;85:102000.
3. **Sun T, Chen Q, Li Y.** Associations of serum cystatin C with depressive symptoms and suicidal ideation in major depressive disorder. BMC Psychiatry. 2021;21(1):1-8.
4. **Huang Y, Huang W, Wei J, Yin Z, Liu H.** Increased Serum Cystatin C Levels Were Associated with Depressive Symptoms in Patients with Type 2 Diabetes. Diabetes Metab Syndr Obes. 2021;14:857-863.
5. **Wu L, Yan Z, Jiang H, Xing H, Li H, Qiu C.** Serum cystatin C, impaired kidney function, and geriatric depressive symptoms among older people living in a rural area: a population-based study. BMC Geriatr. 2018;18(1):265.
6. **First MB, Spitzer RL, Gibbon M, Williams JBW.** Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV). American Psychiatric Press; 1996.
7. **Hamilton M. A** rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23(1):56-62.
8. **Nasreddine Z, Phillips N, Bedirian V,Charbonneau, S., Whitehead, V., Collin, I., et al.** The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005;53(4):695-699.
9. **Saleh AA, Alkholy RS, Khalaf OO,Sabry, N. A., Amer, H., El-Jaafary, S., et al.** Validation of Montreal Cognitive Assessment-Basic in a sample of elderly Egyptians with neurocognitive disorders. Aging Ment Health. 2019;23(5):551-557.
10. **Beck AT, Kovacs M, Weissman A.** Assessment of suicidal intention: the scale for suicide ideation. J Consult Clin Psychol. 1979;47(2):343-352.
11. **Minev E, Unruh M, Shlipak MG,Simsonick, E., Yaffe, K., Leak, T. S., et al.** Association of cystatin C and depression in healthy elders: the health, aging and body composition study. Nephron Clin Pract. 2010;116(3):c241-c246.
12. **Li H, Wang A, Qi G,Guo, J., Li, X., Wang, W., et al.** Cystatin C and risk of new-onset depressive symptoms among individuals with a normal creatinine-based estimated glomerular filtration rate: A prospective cohort study. Psychiatry Res. 2019;273:75-81.
13. **Gao X, Tian Y, Liu ZL,Li, D., Liu, J. J., Yu, G. X., et al**. Tick salivary protein Cystatin: structure, anti-inflammation and molecular mechanism. Ticks Tick Borne Dis. 2024;15(2):102289.
14. **Zavori L, Molnar T, Varnai R,Kanizsai, A., Nagy, L., Vadkerti, B., et al.** Cystatin-c May

Indicate Subclinical Renal Involvement, While Orosomucoid Is Associated with Fatigue in Patients with Long-COVID Syndrome. J Pers Med. 2023;13(2):371.

15. **Niculescu H, Levey DF, Ayalew M,Palmer, L., Gavrin, L. M., Jain, N., et al.** Discovery and validation of blood biomarkers for suicidality. Mol Psychiatry. 2013;18(12):1249-1264.
16. **Manjrekar PA, Durgarao Y.** Evaluation of Cystatin C and Intercellular adhesion molecule-1 as markers of preclinical coronary artery disease in normoalbuminuric early type 2 diabetes individuals. Pak Heart J. 2024;57(1):98-102.
17. **Brundin L, Bryleva EY, Thirtamara Rajamani K.** Role of inflammation in suicide: from mechanisms to treatment. Neuropsy-chopharmacology. 2017; 42(1):271-283.
18. **Gauthier S, Kaur G, Mi W, Tizon B, Levy E.** Protective mechanisms by cystatin C in neurodegenerative diseases. Front Biosci (Schol Ed). 2011;3:541-554.
19. **Mitaki S, Nagai A, Sheikh AM, Terashima, M., Isomura, M., Nabika, T., et al.** Contribution of cystatin C gene polymorphisms to cerebral white matter lesions. Cerebrovasc Dis. 2011;32(5):489-496.

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