Original Article

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Screening of Biochemical Abnormalities in Suicide Attempters Irrespective of Psychiatric Diagnosis: A Cross-sectional Study

Biochemistry Section

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ABSTRACT

Introduction: Empirical studies have documented the impact of membrane cholesterol on serotonergic function which might influence the suicidality in various psychiatric disorders. Most studies in last two decades demonstrated low cholesterol as potential predictor of suicidality in depression but trends of metabolic disorders and current status of hypercholesterolemia and biochemical abnormalities in suicidal spectrum population is scarce.

Aim: To comprehensively evaluate the blood levels of cholesterol and other biochemical abnormalities (serum electrolytes, proteins, blood pH etc.,) irrespective of any psychiatric disorders in suicide attempters.

Materials and Methods: A cross-sectional study was conducted on a total of 202 patients who visited our emergency hospital services with a suicidal attempt from 1st January 2019 till 31st December 2019 for a duration of 12 months. Blood evaluation and analysis were done on the same day of hospitalisation for complete blood counts, serum electrolytes, proteins and cholesterol levels. Clinical and standardised psychological evaluations for psychiatric diagnosis were performed. The results were analysed and compared using descriptive and inferential statistics based on SPSS software 21.0.

Results: Out of 202 total suicide attempters, 120 (59.4%) were males and 82 (40.6%) were females with 111 (54.9%) falling in the age range of 20-29; while 175 (86.6%) of patients had their first ever suicide or deliberate harm. A total of 169 (83.7%) of patients had normal complete blood counts but 106 (52.5%) showed acidic pH (<7.3) while only 5 (2.5%) of the patients had alkalosis. Serum potassium was abnormal in 43 (21.3%) patients. Further serum chloride was deranged in 13 (6.4%) while serum albumin was deranged in 17 (8.4%). About 27 (13.4%) found to have increased serum cholesterol and none of them had low cholesterol.

Conclusion: Excessive and dampened reactivity of biomolecular parameters including hypercholesterolemia may modulate the neurobiological stress system associated with increased suicidality. This may be one of the predictors irrespective of the underlying psychiatric disorders.

Keywords: Biomolecular abnormalities, Cholesterol levels, Depression, Suicidality

INTRODUCTION

Several biological abnormalities varying from dysregulated corticotropin-releasing hormone and cortisol levels to dyslipidemia have been observed in suicidal behaviour; it is still not clear which of these abnormalities may be a cause or a consequence of suicide or are mainly associated with suicidal behaviour [1,2]. Traditionally cholesterol has been linked as a risk factor for metabolic, cardiovascular and cerebrovascular diseases for more than a century. Recently neuroscience has found fascinating evidence about the implications of cholesterol in organisation and functions of many neuroreceptors, neuronal membrane and/or synapse (s). Empirical study have documented the impact of membrane cholesterol on serotonergic function through its influence on the function of membrane-bound serotonergic structures by altering membrane fluidity as well as reduction in serotonin transporter activity after cholesterol depletion [3]. Cholesterol depletion induced by mevastatin, one of the potent inhibitors of HMG-CoA reductase, has been associated with an impaired functioning of 5-Hydroxy Tryptamine 1A (5-HT1A) and 5-HT7 receptors [4] and gamma-amino butyric acid transmission [5] and indeed there are a bunch of studies illustrating the link between levels of cholesterol and suicide attempt in depressive disorders.

Most of these studies [6,7] support the notion that low levels of cholesterol are modestly associated with depressive disorder and suicidality; while very few studies contradict this notion [8]. Suicide is globally recognised as critical public health issue accounting for nearly 800,000 deaths every year and World Health Organisation (WHO) has exemplified in its comprehensive mental health action plan that every nation should have national suicide preventive strategy so that by the end of 2020 global suicide mortality would be reduced by 10% [9]. However, prevalence of obesity, eating disorders, hypercholesterolemia and cardiovascular morbidity is rapidly on the rise in many developed as well as developing countries like India but the suicidal rate has barely altered over the last decade [10]. The drivers of suicidal processes have the complex web of factors from individual's intent, dynamics of family and from socio-religious values to core biological processes interplay and somehow affecting cross-validated neuronal network pathways for suicide.

Short-term suicide risk prediction is clinically helpful for targeted interventions but less is known about those underlying predictors even after extensive research. Many researchers have been interested in identifying biological markers that could predict suicidal behaviour and to our surprise few of the micro-RNA like miR-185 [11] have emerged as an invaluable tool for both understanding the prognosis and pinpoint the targets for therapeutic applications. However, in developing nations like India analysis of such expensive techniques is distinctly far from reach and practically implausible. Therefore, the present study is planned to comprehensively evaluate the blood levels of cholesterol and biochemical abnormalities irrespective of any psychiatric disorders who try to commit suicide in prospective course of hospital visits in south India.

MATERIALS AND METHODS

The cross-sectional study design was conducted in collaboration with the Emergency Medicine, Clinical Psychiatry, Hospital Administration and Department of Biochemistry at a four-decade old tertiary care teaching hospital affiliated to medical school in South India. The authors began recruiting the cases of Deliberate Self-Harm (DSH) for comprehensive clinical and laboratory evaluations of various blood and biochemical parameters as soon as they were admitted in emergency or critical care unit.

The study was approved (254/Ethics Committee/KIMS/NKP/2019) by the institutional ethical committee of KIMS Medical College before beginning the data collection. The authors began the recruitment and analysis from 1st January 2019 till 31st December 2019 for a duration of 12 months. This helped in improving the modest sample size of 202 patients to achieve minimum sample error of no more than 5% (95% confidence). DSM-IV-TR based psychiatric diagnosis were only recruited and assessed [12].

Inclusion and Exclusion criteria: The authors included either gender, above age of 18 years and of all socio-economic status using Modified Kuppuswamy Scale [13] were evaluated for biochemical abnormalities to all those who had been attempting suicide but failed and could give their consent for the study irrespective of their medical or psychiatric diagnosis. The refusal of the consent for evaluation was respected and there was strict confidentiality maintained on data sheet.

Study Procedure

Blood evaluation and analysis were done on the same day of hospitalisation for complete blood counts, serum electrolytes, proteins and cholesterol. To measure the blood cholesterol level, 5 mL of blood sample was collected after at least 8 hours of fasting from the subjects and analysis was done on BS-390 automated Chemistry analyser using cholesterol oxidase peroxidase method [14]. The authors used the following standardised Instruments for evaluation: Schedules for Clinical Assessments in Neuropsychiatry (SCAN) [15]; Structured Clinical Interview for DSM disorders Clinical Version-1 (SCID CV-1); Deliberate Self Harm Inventory [16]; International Personality Disorder Examination; Beck's Suicide Intent Scale [17]; Socio-demographic and clinical profile sheet.

STATISTICAL ANALYSIS

Data obtained were analysed using SPSS 21.0 version of software. The appropriate descriptive (frequency, percentage, mean) as well as inferential (for degree of association, Pearson's correlation and multivariate regression analysis for identifying the covariance of suicidality with serum cholesterol and other biochemical abnormalities like serum proteins, blood pH and electrolyte disturbances) statistical tests like Chi-square test for qualitative variables were applied. For all tests of probability, p-value less than 0.05 was considered significant.

RESULTS

A total of 202 patients were evaluated in the present study, among them 120 (59.4%) were males while remaining 82 (40.6%) were females with 111 (54.9%) falling in the age range of 20-29 years. Further it observed as the age progressed the frequency of suicidal attempts reduced, however there was very minimal difference of 25 (12.4%) vs 22 (10.9%) prevalence between 40-49 years and more than 50 years respectively [Table/Fig-1]. This suggests two changing trends, one is suicidal attempts are getting common in employed as well as unemployed and Indian families are getting differentiated into nuclear families not only in urban and metro cities but in rural India as well. As far as the clinical scenario of mode of deliberate harm is concerned as seen in [Table/Fig-2], poisoning 178 (88.1%) was preferred mode followed by hanging 14 (6.9%) irrespective of genders. Out of the 202 patients in the study, 175 patients came in with first ever suicide attempt or deliberate harm attempters. It was observed that 22 (10.9%) had second attempt over a period of 6 months and 5 (2.5%) individuals had multiple suicidal attempts. When the variety of the intent of most of the patients was analysed 83 (41.1%) had moderate intent followed by severe intent in about 64 (31.7%) of patients.

Socio-demographic parameter	Categories	Frequency N=202	Percentage %
Age (Years)	20-29	111	54.9
	30-39	44	21.8
	40-49	25	12.4
	50-60	22	10.9
Gender	Male	120	59.4
	Female	82	40.6
Education	Literate	168	83.2
	Illiterate	34	16.8
Occupation	Unemployed/Student	78	38.6
	Employee	78	38.6
	Skilled laborer	21	10.4
	Professionals	2	1.0
	House-maker	23	11.4
Type of family	Nuclear	176	87.1
	Joint	26	12.9
Domicile	Rural	144	71.3
	Semi-Urban	52	25.7
	Urban	6	3.0
Socio-economic status (*Modified Kuppuswamy Scale)	Middle	22	10.9
	Lower middle	104	51.5
	Lower	76	37.6
Marital status	Married	137	67.8
	Unmarried	65	32.2

[Table/Fig-1]: Socio-demographic profile of patients in study.

Variables	Suicide attempt characteristics	Frequency (N)	Percentage (%)
Mode	Hanging	14	6.9
	Poisoning	178	88.1
	Other modes	10	5.0
Frequency	First attempt	175	86.6
	Second attempt	22	10.9
	Multiple attempts	5	2.5
Severity (Beck's Suicidal Inventory)	Mild (15-19)	55	27.2
	Moderate (20-28)	83	41.1
	Severe (>29)	64	31.7
Emergency treatment	Given	194	96.0
	Not given (Wait and Watch)	8	4.0

[Table/Fig-2]: Suicide attempt profile using Beck's suicidal inventory. N=202

The dispersion of psychiatric diagnosis in suicide attempters were mainly depressive disorder, substance use disorder, dual diagnostics, bipolar disorder, Borderline Personality Disorder (BPD) formed major chunk of population as shown in [Table/Fig-3]. But interestingly 13 (6.4%) patients were also having debilitating medical diseases like cancer(s) while 4 (2.0%) patients had intense anxiety (panic) attacks. Suicidal attempts were relatively more common in schizophrenia 7 (3.5%) than delusional disorders 4 (2.0%). Almost 169 (83.7%) of patients had normal complete blood counts but 106 (52.5%) showed acidic pH (<7.3) while only 5 (2.5%) of patients had alkalosis. Serum sodium levels were abnormal only in 16 (7.9%) of patients, while serum potassium was abnormal in 43 (21.3%) of patients. Further serum chloride was deranged in 13 (6.4%) while serum [Table/Fig-4] albumin was deranged in 17 (8.4%). About

13.4% (27 out of 202 patients) were found to have increased serum cholesterol while rest had surprisingly normal levels of cholesterol and almost similar number of patients had abnormal liver function test. The authors observed a strong and significant (p=<0.01) positive association with serum potassium, serum cholesterol and serum pH levels, while others were insignificant [Table/Fig-5]. In furthering inferential statistical analysis as reflected in [Table/Fig-6], the multinomial regression method generalises logistic regression to multiclass problems, for example with more than two possible discrete outcomes which occurs with suicidal patients. We know that age and gender have been found to be important predictors of suicidality and the authors chose additional three more factors which can influence the likelihood ratio of suicidal behaviour in patients of DSH like frequency of deliberate harms, severity of intent, level of education apart from the serum cholesterol levels. The likelihood covariance was highest and clearly significant with increased serum cholesterol (Chi-square value: 26.084; df: 10; p*=0.004), closely followed by suicidal intent just before the attempt (Chi-square value: 17.490; df: 10; p=0.064) and effect of age (Chi-square value: 40.588; df: 10; p=0.094).

Diagnosis	Frequency (n)	Percentage (%)
Substance use disorder	32	15.8
Schizophrenia	7	3.5
Delusional disorder	4	2.0
Bipolar disorder	25	12.4
Depressive disorder	36	17.8
Panic disorder	4	2.0
Impulse control disorder	16	7.9
Borderline personality disorder	25	12.4
Other personality disorders	10	4.9
Dual diagnosis	30	14.9
Medical debilitating diseases	13	6.4
Total	202	100.0

[Table/Fig-3]: Psychiatric diagnosis in suicidal patients.

Biochemical parameters	Categories	Frequency (n)	Percentage (%)
CBC	Normal	169	83.7
	Abnormal	33	16.3
Serum pH	Acidosis	106	52.5
	Normal	91	45.0
	Alkalosis	5	2.5
Serum sodium	Normal	186	92.1
	Abnormal	16	7.9
Serum potassium	Normal	159	78.7
	Abnormal	43	21.3
Serum chloride	Normal	189	93.6
	Abnormal	13	6.4
Serum albumin	Normal	185	91.6
	Abnormal	17	8.4
Serum cholesterol	Normal	175	86.6
	Increased	27	13.4
LFT	Normal	175	86.6
	Abnormal	27	13.4

[Table/Fig-4]: Biochemical parameters.

Variable	Statistical parameter	Suicidal intent scale scores	Frequency of suicide attempt
Complete blood counts	Pearson correlation	0.163	0.060
	Sig. (2-tailed)	0.020*	0.394
pH	Pearson correlation	0.313	-0.032
	Sig. (2-tailed)	0.001**	0.646
Serum sodium	Pearson correlation	0.061	0.161
	Sig. (2-tailed)	0.392	0.022*
Serum potassium	Pearson correlation	0.215	0.107
	Sig. (2-tailed)	0.002**	0.129
Serum chloride	Pearson correlation	0.103	-0.049
	Sig. (2-tailed)	0.146	0.490
Serum albumin	Pearson correlation	0.017	0.116
	Sig. (2-tailed)	0.814	0.100
Serum cholesterol	Pearson correlation	0.114	0.698
	Sig. (2-tailed)	0.007*	0.027
Liver function test	Pearson correlation	0.114	0.698
	Sig. (2-tailed)	0.007*	0.027

[Table/Fig-5]: Correlation analysis of various biochemical factors with suicidal intentions.
*p<0.05, **p<0.005

Effect	Model fitting criteria	Likelihood ratio tests		
	-2 Log likelihood of reduced model	Chi-square	df	p-value
Intercept	480.351a	0.000	0	.
Frequency of deliberate self-harm	495.005	14.654	10	0.145
Severity of intent	497.840	17.490	10	0.064
Serum cholesterol	506.435	26.084	10	0.004
Age	520.938	40.588	10	0.094
gender	492.316	11.966	10	0.287
education	491.578	11.227	10	0.340

[Table/Fig-6]: Multinomial regression analysis.

DISCUSSION

Since there are no other studies in suicidal patients for abnormal biochemical parameters like pH, serum electrolyte, serum proteins and most of the focus had remained on levels of cholesterol, the present discussion has been related to debate on cholesterol levels in suicidal neurobiology. Excessive and dampened reactivity of the neurobiological stress system have been associated with increased vulnerability for psychiatric disorders [18]. The present study demonstrated that in contrast to the conventional understanding of low serum cholesterol diathesis a newer trend of analysis was indeed required which this study bridges. The study evaluates all possible routine biochemical blood parameters with more emphasis on serum cholesterol levels of all suicidal patients visiting emergency services.

A meta-analysis by Wu S et al., in 2016 of as many as 65 epidemiological studies using predominantly Cochrane database from 1980 to 2014 using random effect model with a total sample of 510,392 participants clearly found that suicidal patients had significantly lower total cholesterol (WAD:- 24.75, 95% CI- 27.71 to -21.78) [19]. Further they reported that lower serum total cholesterol levels were associated with 123% higher risk of suicide attempt (95% of CI: 24% to 302%). However, the major limitation of their meta-analysis was potential heterogeneity, narrow range of cholesterol depletion and there was not a single Indian study included to compare. Further, obesity prevalence has increased significantly every decade. Therefore, in the present study authors have attempted to re-examine the real effect of cholesterol on suicidality from rural tertiary care health services from south India. We have evaluated all prospective suicidal attempters visiting our tertiary health care set up in emergency medicine services for identifying if serum cholesterol affects suicidal behaviour, not only as risk factor for depressive mood state but irrespective of any psychiatric diagnosis which makes the present study clearly different from many others [20-22]. However, the present study has the conforming comparisons for blood cholesterol levels with few other studies [23-26].

Interestingly, there are studies which demonstrated that lower serum cholesterol levels are also linked with major depressive disorder (OR 4.229 CI 95% 2.555-7.000, p<0.001) and suicide attempt (OR 5.540 CI 95% 2.825-10.866, p<0.001) in their study by Segoviano-Mendoza M et al., [27]. Similarly, a study by Morgan RE et al., published in lancet that plasma cholesterol and depressive symptoms in older men found that depression was three times more common in the group with low plasma cholesterol (<4.14 mmol/L) than in those with higher concentrations (5/31 (16%) vs 22/363 (6%); p=0.033) [28]. In support of hypocholesterolemia and impulsive suicidality in BPD, a study by Atmaca M et al., in 16 BPD found that mean cholesterol and leptin levels of the patient group were significantly (p<0.05) lower than those of the controls [29]. In another study, [30] in 60 psychotic patients of which only 13 patients attempted suicide, just marginal and insignificant (p-value=0.91) change of mean serum cholesterol level was reported in their results, though they highlighted it as significant positive predictor.

Another interesting study from Poland evaluated 148 schizophrenic suicidal patient and assessed serum cholesterol along with LDL, HDL and triglycerides and reflected that in depressed patients, low cholesterol can be state- dependent risk factor for suicidal behaviour [31]. Even para-suicidal schizophrenics have also reported with lower cholesterol levels [32,33]. On the contrary, Huang T et al., 2000 in Taiwanese population of schizophrenics found no difference in serum cholesterol levels irrespective of suicidal attempt [34]. On contrary, a study from Korea found correlation between low cholesterol and suicidality holding true only for depression but not for schizophrenia [35]. And on neutral/equivocal levels another group of investigators compared serum lipid levels of 282 schizophrenics, 72 bipolar disorders and 242 major depressive disorders and concluded that biological levels of serum lipids do not predict suicide risk [36]. Finally, like the present study findings, an earlier study from India by John S et al., did not support the use of biological indicators such as serum total cholesterol HDL LDL or TAG either to predict any functional psychiatric outcome including suicidality [37].

Compared to most previous studies [6,20,22,23,27], why the present study suicidal patients have not shown lower serum cholesterol levels? One of the reasons could be that epidemiologically violent suicide attempts were found more commonly with low cholesterol levels thus in the present study most of the suicidal attempters were perhaps not having violent suicidality compared to western countries. Another reason could be huge intergroup variation based on psychopathologies and metabolic status in suicide attempters. As seen in [Table/Fig-6] of the present study, the multinomial regression reflects serum levels of cholesterol as one of the significant biochemical abnormality in suicidal patients. The support for this also comes from a recently published case control study from Italy in 2019 [38]. Over recent years, in usual clinical practice, most psychiatric patients are following sedentary lifestyles and they have less control over eating; many of them avoid physical exercise and modest number of them have weight gain, metabolic or cardiac problems.

Limitation(s)

The present study has certain limitations which needs to be considered as main issue of approach in identifying the biochemical abnormalities including serum cholesterol should never been just a mere cross-sectional or hospital-based study as method of evaluation. The practical inability to assess the fluctuation of blood cholesterol with the fluctuation of mood, impulsivity, sleep deprivation status, type of diet one had or missed just before the suicide attempt which might impair its direct causal association as noted in current findings always remains difficult domains to be controlled.

CONCLUSION(S)

This is an encouraging study supporting notion that though dyslipidemia influences suicidal behaviour than other biochemical abnormalities, there is still the lack of convincing power of cholesterol as a putative biomarker for suicidal behaviour and more research is required in this vast field to determine the neurochemistry of suicidal behaviour. This can only be made possible by building for national healthcare database from India to have one homogeneous voice rather than discrete formulation of changing hypothesis. Its indeed a nature's puzzle which keeps us pondering for perfect molecular diagnostic answer as there are many psychological conditions and the on-going medications for treatment of medical disorders which might influence one's eating and exercise habits, and subsequently cholesterol levels. There is also a possibility that cholesterol might be a bystander of the association between suicide and some of these factors as we conclude that no single biological marker may be sufficiently accurate for complex suicidal behaviour prediction.

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