

Suicide, Impulsivity and its Relationship to Platelet Serotonin Levels

Abhishek Kumar¹, Srinivas Gupta², MSVK Raju³, Anuj Sharma⁴, Ashok Prasad⁵

ABSTRACT

Introduction: A broad range of mental disorders are found to be associated with suicidal behavior. The study on platelet serotonin levels, and its relationship to suicide might yield information relevant to primary prevention of completed suicide. Thus this study was carried out to assess and estimate suicidal intentions and impulsivity, and to find its association with platelet serotonin levels.

Material and Methods: A total 31 suicide attempters, who visited a general hospital setup, were included in the study. All subjects were assessed for their socio-demographic profile. All subjects underwent standard psychiatry interview and appropriate psychiatric diagnosis was obtained. Subjects were assessed by Enzyme Immunometric Assay, Beck's Scale for Suicidal Ideation, Structured Interview for impulsivity, Balance Tilting Factor Assessment Procedure.

Results: 31 subjects (Mean Age 30.6 yrs) consisted of 10 males (Mean Age 32.9) and 21 females (Mean Age 29.5) with no significant difference was found in age as well as educational status in among male and female subjects. The differences in the diagnostic categories were statistically significant. Platelet Serotonin levels were found negatively correlated ($r=-0.37$) with impulsivity scores, which was statistically significant. Impulsivity was negatively correlated to platelet Serotonin among males. However in female subjects showed no significant correlation between impulsivity and platelet Serotonin levels.

Conclusions: The present study revealed low platelet Serotonin levels in attempted suicide subjects. Low Serotonin levels were found to be inversely related to impulsivity only in males.

Keywords: Suicide, Impulsivity, Platelet serotonin levels.

The ratio between attempted suicides and suicides was found to be as high as 10:1.⁶ However, in India the ratio was found to be 4:1.⁷ Some authorities quoted that life time prevalence of suicidal thoughts as high as 50%.⁸

Asberg⁹ reported reduced concentration of 5-Hydroxy Indole Acetic Acid (5-HIAA) in the CSF of attempted suicides, brain Serotonergic system has become the focus of attention as far as biological factors are concerned. This area has not been explored by investigators. Saldanha¹⁰ have estimated plasma serotonin levels of patients with attempted suicide. They found no statistically significant correlation between suicidal attempts and plasma serotonin levels (Saldanha personal communication). In another study Raju et al assessed 44% of attempted suicides had sub sensitive post synaptic 5HT1A receptors in the brain. They also attempted to correlate personality factors as measured by 16 personality factor and Rorschach ink blot test and they found that overt extraversion correlated to sub sensitive post synaptic 5HT1A receptors. It is difficult to infer primary dysfunction at the level of 5HT1A receptors as they have reciprocal relationship with post synaptic 5HT2A receptors. It's pertinent to note that receptors are dynamic structures and get up regulated or down regulated as per the availability of Serotonin.¹¹ Moreover, measuring the function of Serotonin receptor in real time needs sophisticated technology like Positron Emission Tomography. The platelets in the blood are found to be similar to central nervous system neurons. The importance of intra neuronal serotonin levels can be realized from the fact that impaired Tryptophan Hydroxylase, a rate limiting enzyme in Serotonin synthesis has been described as a marker for suicide.¹² However, it appears that actual level of serotonin in platelets has not been measured so far. A broad range of mental disorders are found to be associated with suicidal behavior.^{4,5,7} It's undeniable that a suicidal attempt is the outcome of escalating mental anguish which may not be discernible to the naked eye or to an open ear. The present investigator noted that persons committing self destructive acts are brought to the casualty department of hospital at the rate of about 3-4 per month. In view of the gravity of the condition as such and also the implication for potential successful suicides later on, it was considered that a study on platelet serotonin levels, and its relationship to suicide, personality factors and impulsivity might yield information

INTRODUCTION

Human self destructive behavior runs counter to the fundamental drive to survive.¹ Suicide is defined as a human act of self inflicted self intentioned cessation. It is described as a multidimensional malady, where a person laboring under inimitable life stressors take himself into a cascade of noxious thoughts ultimately leading to a perception that the termination of one's life is the only solution for a seemingly intolerable life situation. In vulnerable individuals this perceptual constriction gets translated into effective action.²

The numbers of suicides have steadily increased over the years outpacing the growth of population in proportion. The rate of completed suicide stood at 11.4 per 1 lac population in the year 2010, whereas it was hovering around 10.8 per lac in the year 2008.³ In recent times a distinction is sought to be made between suicides and attempted suicides. Self destructive behavior and non fatal suicide attempts have been conceptualized as "Para Suicide".⁴ Further, a distinction is also made between self destructive behavior (deliberate self harm) where the intent is to inflict hurt to self and attempted suicide where the intent is to die but somehow turned unsuccessful.⁵ Some posited that the intent to die is not as strong as that of a completed suicide.

¹Assistant Professor, Central Institute of Psychiatry, ⁴Former SR, ⁵Professor and Head, Department of Psychiatry, RIMS, Ranchi, ²Graded Specialist, Department of Psychiatry, 166 Military Hospital, Jammu. ³Ex-Professor, Department of Psychiatry, People's college of Medical Sciences and Research Centre, Bhopal, MP, India

Corresponding author: Dr. Abhishek Kumar, Assistant Professor Central Institute of Psychiatry, Ranchi, India-834009

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relevant to primary prevention of completed suicide. Thus aim of this study was to assess and estimate suicidal intentions and impulsivity, and to find its association with platelet serotonin levels.

MATERIALS AND METHODS

The study was conducted at a tertiary hospital in department of psychiatry. All persons, above 18 years of age, who were brought to the casualty department with history of self-destructive behavior, were included in the study. The investigator introduced himself as a doctor who was doing research on human self-destructive behavior and solicited cooperation from the prospective candidates as well as the caretakers who were attending the persons to participate in the study. The investigator assured the patient, as well as the caregivers with full confidentiality. Informed consent was obtained from all. The study was approved by institution's ethical committee. All 31 subjects were subjected to standard psychiatry interview and appropriate psychiatric diagnosis was obtained if any constellation of symptoms satisfied the criteria of ICD-10, diagnostic criteria for research.

Tools

Socio-demographic Data Sheet: The socio demographic data sheet included age, marital status, religion, education and occupation.

Beck's Scale for Suicidal Ideation (BSSI): It is a 21 item self-reported scale prepared by Aaron Beck and A. Steer.¹³ The scale has a five item part-1 serving the purpose of screening interview. It mothers various aspects in relation to suicide which includes intent, thoughts, plans, motivation etc. Maximum score is 42. No norms are available.

Structured Interview for Impulsivity: This 25 item structured interview was taken out of diagnostic interview for borderlines (DIB) by Zanarini et al.¹⁴ This instrument has been translated and back translated into Marathi at Maharashtra Institute of

Mental Health by Chitalkar and Phadke.¹⁵ Upto 2 marks can be given for each positive answer, maximum score is 50.

Platelet Serotonin Estimation: It was carried out by Enzyme Immunometric Assay. The kit for the study was obtained from M/s Enzo Life Sciences, PA, USA.

All blood samples were collected under full aseptic conditions and samples were labeled by alpha numeric code to maintain confidentiality. After collection of blood it was centrifuged at 16000 x g for 15 minutes. White buffy coat was collected. The platelets were washed twice using physiological saline and centrifuged at 2000 x g for 10 minutes and again washed. Platelet pellet was re-suspended using distilled water. Suspension thus obtained was frozen, thawed shortly before carrying final assay. The samples were stored at -20 C before final estimation at the facilities provided at the Interactive Research School for Health Affairs (IRSHA), an autonomous research institute of the parent university.

STATISTICAL ANALYSIS

The collected data of all patients was statistically analyzed. X² test was used to test significance of categorical data. Fisher's test was used where X² test could not be used. In case of continuous data Student's t test was used. Pearson's product moment correlation was used for correlations. However as the data were not balanced and platykurtic data were transformed into log 10 as per Holmes et al 2006. Only percentages were used at places for drawing comparisons.

RESULTS

A total of 31 subjects completed this study. The data regarding mean age among male and female subjects, their occupation, education and marital status is shown in table 1. Methods of suicidal attempts and diagnostic categories are showed in table 2.

The BSSI, Impulsivity and platelet serotonin levels among male and female subjects are shown in table 3.

| | | Male | Female | t / X ² | Df | P value |
|--------------------|--------------------|--------|-----------|----------------------|------|----------|
| Mean age in years | | 32.9 | 29.52 | 0.64 | 0.29 | >0.05 |
| Occupation | Student | 2(20%) | 6(28.5%) | | | P=0.0098 |
| | Employed | 7(70%) | 3(14.3%) | | | |
| | Unemployed | 1(10%) | 12(57.1%) | | | |
| Years of education | Illiterate | 2(20%) | 4(19%) | | | P=0.097 |
| | Less than 10 years | 6(60%) | 10(47.6%) | | | |
| | More than 10 years | 2(20%) | 7(33.3%) | | | |
| Marital status | Married | 5(50%) | 14(66.6%) | X ² =0.62 | 1 | p>0.05 |
| | Unmarried | 5(50%) | 7(33.3%) | | | |

Table-1: Age and sex of the sample and socio occupational distribution

| | | Male | Female | Fisher's exact test |
|----------------------------|----------------------|-----------|-----------|---------------------|
| Method of suicidal attempt | Medicine overdose | 6(28.5%) | 1(20%) | P=0.0128 |
| | Pesticide | 13(61.9%) | 6(60%) | |
| | Wrist slashing | 0 | 2(20%) | |
| | Hanging | 2(9.5%) | 1(20%) | |
| Diagnoses | Depression | 5(50%) | 11(52.4%) | P=0.0037 |
| | Adjustment disorder | 1(10%) | 4(19%) | |
| | Personality disorder | 3(30%) | 1(4.7%) | |
| | No diagnosis | 1(10%) | 5(23.8%) | |

Table-2: Clinical variables methods of suicidal attempts and diagnosis.

Depressed patients were significantly more suicidal (mean BSI score 19.8) in comparison to that of other categories (mean BSI score 15). Impulsivity scores in suicidal patients with personality disorders (mean 13) was significantly higher than depressed patients (mean 3.44) while there was no significant difference between depressive patients and patients with no diagnosis as shown in table 4.

Mean Platelet Serotonin levels in different mental illness shown in table 5. Mean Serotonin level of persons with miscellaneous diagnoses was found to be significantly low in comparison with that of those with no diagnoses (table 5).

DISCUSSION

The risk of suicide in persons with psychiatric diagnoses is known to be considerably high where Non biological methods of predicting suicide have turned out to be of not much utility.⁴ Therefore identifying biological factors underlying self-destructive behaviour have become very important area of investigation in recent time. After the landmark study of Asberg⁹ showing reduced 5HIAA in the suicidal patients, the serotonin system has been the target of some very intense investigatory efforts in suicidology. Platelets and central Serotonergic neurons share many structural and functional similarities^{16,17} and offer a good opportunity to study central 5HT neurons from the periphery. In a recent review of suicide in India, Lakshmi Vijayakumar mentioned of the limited number of studies on the biology of suicide in our country.¹⁸ This is an exploratory study on an observational design to explore platelet serotonin levels in attempted suicidal subjects.

Maharashtra is one of the leading suicide states of India. Among the completed suicides in our country a male: female ratio of 65:35 has been reported.³ As far as attempted suicides

are concerned a reverse trend has been reported by various workers.¹⁹⁻²¹

A male to female ratio of 1:1.5 has been reported in the 16 centre European study.¹⁹ In India Srivastava and Kulshreshtha reported male under 35 were at risk.²¹ While Lal and Sethi reported housewives below 30 years of age were at risk.²⁰ No official figures for suicide attempts are available. There is no epidemiological data on attempted suicides. In the present study females outnumbered males by 2:1 which perhaps reflect the present trend.

26% of the present study samples were students and 42% were unemployed (which included housewives). These figures are quiet in contrast with those of completed suicide where 26.1% were unemployed and only 5.5% were students.³ among the males 70% had some job whereas only 14.1% of females held a job. 57% females were housewives and in all 71% of the females were not employed whereas in completed suicides 18.6% were housewives.³ The preponderance of unemployed in women (71%) and employed in men (70%) is striking and found to be statistically significant. 19% of the sample were illiterate, 52% had up to 10 years of education and the remaining 29% had college education. The figures are comparable to those of completed suicides.³

61% of the samples were married and 39% unmarried which appears to be the same as of completed suicide. Though more females are married (66% vs 50%) than males, the difference was not significant statistically. Lal and Sethi²⁰ commented on the preponderance of housewives in their samples. Divorces and separated formed 4% of completed suicide.³ There are no divorces and separated in the present study sample.

61% of the sample used insecticides, 22.6% took overdose of medicines making in all, 83.6% of the sample resort to this

| | Male | Female | t | DF | P value |
|----------------------------------|------|--------|------|----|---------|
| Beck scale for suicidal ideation | 17.6 | 18.4 | 0.01 | 29 | >0.05 |
| Impulsivity | 7.60 | 4.39 | 0.40 | 29 | >0.05 |
| Platelet serotonin (ng/ml) | 57.3 | 56.05 | 0.11 | 29 | >0.05 |

Table-3: Gender difference in bssi, impulsivity and platelet serotonin level.

| | | Mean | t | df | P value |
|---|--------------------------------|-------|-------|----|----------|
| BSSI depression vs other category | Depression, N=16 | 19.83 | 2.57 | 29 | <0.025* |
| | Other diagnostic category n=15 | 15.6 | | | |
| Impulsivity in depression vs personality disorder | Depression, N=16 | 3.44 | 17.09 | 29 | <0.001** |
| | Personality Disorders, N=4 | 13 | | | |

*Statistically significant at p value <0.05; ** Statistically significant at p value <0.001

Table-4: BSSI and impulsivity across diagnostic categories

| | | Mean | t | df | P value |
|-------------------------------------|---------------------------|-------|------|----|----------|
| Depression Vs Personality Disorders | Depression N=16 | 53.94 | 0.03 | 18 | p>0.05 |
| | Personality Disorders N=4 | 52.25 | | | |
| Depression vs no diagnosis | Depression N=16 | 53.94 | 1.35 | 20 | p>0.05 |
| | No Diagnosis N=6 | 74.17 | | | |
| Depression vs misc diagnosis | Depression, N=16 | 53.94 | 1.13 | 19 | p>0.05 |
| | misc diagnosis N=5 | 36.4 | | | |
| Misc. vs no diagnoses | misc diagnosis N=5 | 36.4 | 2.97 | 9 | p<0.025* |
| | No Diagnosis N=6 | 74.17 | | | |

*Statistically significant at p value <0.05

Table-5: Platelet serotonin levels comparison across diagnoses.

method. Only 33—34% of completed suicide used this method.³ while 31-32% completed suicide resort to hanging, only 10% of the study sample used this method. None of them used lethal methods like jumping under train, from buildings or drowning. 29% of the females used drug overdose while only 10% males used this method. 20% of males slashed wrists. None of the females used this method. These differences between genders were found to be significant.

It is reported that 90 to 94% of people who completed suicide had mental illness^{22,23} and mood disorders were reported in 45-77% of suicides²⁴, though the figures for suicidal attempts are not known. But Adjustment Disorders and Personality disorders reported to be more likely in suicidal attempts while mood disorder, psychosis and substance use predominate in completed suicides.⁴ In the present study 51% had depression which corresponds to Barraclough et al²⁴ and Bagadia et al.²⁵ In 19% of cases no diagnoses could be made. In both sexes the absence of psychosis and substance use is quite striking. 71% of females had depression or adjustment disorder with depressed mood, while 50% of the males had depression 25% of the females had no diagnosable disorder. 30% of the males had personality disorder and 5% of males had no diagnosable disorder. In this way attempted suicide seems to be similar to mood disorders in some ways and differ in other respects. The differences between male and female found to be significant ($P=0.0037$).

The maximum score for BSI is 38. The mean score for the total sample was 18 which placed the study sample at mild-moderate risk for suicide. There was no gender difference in the scores. The originators¹³ recommend every positive response to be taken seriously. This perhaps gives a clear indication that every proposed attempt is a potential suicide. 10% had no wish to die and 49% expressed moderate/strong wish to live (these are the answers for item 2 of BSI). Only 50% had a moderate to strong wish to live. Clearly not all suicides are manipulative efforts to establish contact with significant others. It appears “to be or not to be” is a painful dilemma that these people confront and are obliged to contend with.

Two putative factors are assumed to be underlying suicide. A common genetic factor predisposing for mental illness in general and an independent risk factor for suicide of which the biological factor may be related to the serotonergic system while the psychological factors were found to be impulsivity and aggression.¹

The concept of impulsivity covers a wide range of “actions that are poorly conceived, prematurely expressed, unduly risky or inappropriate to the situation and that often result in undesirable outcomes. Impulsivity may be made up of several independent factors and there is little unanimity what these factors are.²⁶ The Barrat Impulsiveness scale (BIS) developed by Barrat et al²⁷ has gone through several revisions. There is no consensus on the best way to measure impulsivity.²⁶ To circumvent the problem of translating and standardizing the BIS 11, which is currently in use, the worker utilized the 25 items on impulsivity from the Diagnostic Interview for Borderlines¹⁴ which was translated into Marathi by Phadke et al.¹⁵ The 25 items appear to give adequate coverage to tap various aspects of impulsivity. Norms for the scale, obviously are not available. The possible maximum marks are 50. The mean score for the study population was 5.45 and that of males and females were 7.6 and 4.39 respectively.

But the difference in the means was not significant.

The mean Platelet Serotonin level was 51.3 ng/ml in current study which in males was 57.3 ng/ml and in females it was 56.05 ng/ml. Only one study quoted platelet Serotonin levels in normal individuals. Devasis Ghosh¹⁷ correlated little finger length and platelet serotonin levels in 48 healthy subjects. He postulated that little finger length was related to neuroticism which is known to be associated with depression and anxiety. In his study Serotonin levels in the males were 160.57 (non-neuroticism) and 86.38 (neuroticism). While in females they were 182.76 (non-neuroticism) and 126.16 (neuroticism). Perhaps it can be understood from the fact that his sample consisted of healthy individuals. The platelet Serotonin levels of the present study are lower than those reported by Ghosh.¹⁷ Which brings out of the fact that all attempted suicides have low platelet Serotonin levels. Walderhaug et al²⁸ reported reduced Serotonin levels (by tryptophan depletion) caused increased impulsivity in healthy individuals and impulsivity is associated with suicidality.¹ In the present study no difference in platelet Serotonin levels between males and females was found.

The depressed patients were more suicidal than other patients ($P<0.025$). The BSI score for the depressed group was just above the half way mark of 19. Mood disorders are known to be associated with suicidality.^{25,29-31} Suicide rates in bipolar disorder can be as high as 20% and 10% of schizophrenia patients are known to commit suicide.^{4,32} 25% of suicides were found to have alcoholism.³³ Significantly no cases of schizophrenia, bipolar disorder nor alcoholism were found in the study sample. Obviously para suicide though share some similarities in certain areas do differ in areas like psychiatric diagnoses when compared with completed suicides.

Contrary findings have been reported about the relationship between impulsivity and platelet serotonin levels.³⁴⁻⁴⁰ Platelet serotonin levels were found to be low in suicidal patients and corresponds to other studies.^{34-36,38} However Askenazy³⁷ found elevated 5HT levels in platelets of suicidal attempt patients.

Given the low levels of platelet Serotonin in the study sample and the reported association of impulsivity and suicidality an attempt was made to correlate the impulsivity scores with platelet Serotonin levels.¹ A significant negative correlation was obtained. Experimental and human studies have shown association of serotonin with impulsivity and aggression.⁴¹⁻⁴ On further analysis to see if impulsivity associated with gender it was observed that a significant negative association between platelet serotonin and impulsivity was present in males ($P<0.05$) and not in females. This divergent finding is not due to high serotonin content in females as found by Le-Quan-Bui et al⁴⁵ because platelet serotonin levels in females were actually marginally higher in females in this study (table-3). It appears that low impulsivity scores (mean 4.39) in females in comparison to males (mean 7.60) have contributed to this gender specific correlation of impulsivity with platelet serotonin. The researchers are not aware of any study showing similar finding. The most important biological factor appears to be low Serotonin function. Limitation of this present study includes hospital based, small sample size and observational design.

CONCLUSION

The present study revealed low platelet Serotonin levels in

attempted suicide subjects. Low Serotonin levels were found to be inversely related to impulsivity only in males.

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