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A COMPARATIVE STUDY OF INFLAMMATORY MARKER HIGHLY SENSITIVE C-REACTIVE PROTEIN BETWEEN DEPRESSION PATIENTS WITH SUICIDAL ATTEMPT AND DEPRESSION PATIENTS WITH SUICIDAL IDEATION

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ABSTRACT

Background: Suicidal ideation and attempt in context of depression is very common. Many studies have demonstrated an association between suicidal behaviour and inflammatory markers primarily CRP. We explore a clinical inflammatory marker (CRP) in psychiatric patients hospitalized in an acute adult inpatient facility following suicidal attempt and ideation.

Aims: To compare hsCRP levels between depression patients with suicidal attempt and 25 depression patients with suicidal ideation.

Methodology: Comparison of 25 depression patients with suicidal attempt and 25 depression patients with suicidal ideation was done, diagnosis as per ICD10. Hamilton Depression Rating Scale (HDRS-17), Beck Scale for Suicidal Ideation (BSSI), Suicide behaviour Questionnaire- Revised (SBQ-R), were applied for assessment of depression and suicidality. Highly sensitive CRP was measured using autoanalyzer.

Results: hsCRP levels were significantly high in depression patients with suicidal attempt (6.11 mg/dl) than depression with suicidal ideation (2.14 mg/dl). Duration of illness, HAM-D, BSSI & SBQ-R scores correlated positively with hsCRP levels.

Conclusion: Depression with suicidal attempt patients demonstrated a statistically higher hs-CRP levels than depression with suicidal ideation. Patients of depression with suicidal attempt have a strong positive correlation between hs-CRP levels and HAM-D, BSSI & SBQ-R scores.

KEY WORDS : suicide; depression; C-Reactive Protein; inflammatory marker

Introduction-

Suicidal behavior is a leading cause of death and disability worldwide. Fortunately, recent developments in suicide theory and research promise to meaningfully advance knowledge and prevention.[1] For the goal of improved detection and treatment of suicidal individuals to be achieved, we need to develop a detailed understanding of the origin, mechanisms and outcomes of inflammation in suicidal behaviour.[2]

C-reactive protein (CRP) is an acute-phase inflammatory protein synthesized by hepatic Kupffer cells signalling other body cells for destruction by the complement system.[3] Inflammation has been linked with a potential vital role in suicidality, among which hs-CRP play an important role. Suicidal ideation and attempt in context of depression is very common. Many studies have demonstrated an association between suicidal behaviour and inflammatory markers primarily CRP.[4-10]

However, the caveats of most studies was that they evaluated the CRP in patients demonstrating suicidal behaviour but not in settings of depression, leading to a bias and variations due to controls having different pathophysiology making it difficult to differentiate the altered inflammatory states that could be attributed to suicidality in depression or other causes. Most of the studies have not differentiated between suicidal attempt and ideation since both can influence CRP levels acutely and chronically. Our study is a pioneer research in comparing hsCRP levels in depression patients with suicidal attempt and with suicidal ideation.

In the present study, we explore a clinical inflammatory marker (CRP) in psychiatric patients hospitalized in an acute adult inpatient facility following suicidal attempt and ideation. We hypothesized that patients hospitalized in a "real world" adult inpatient population following a recent suicidal attempt will display higher CRP values than those with suicidal ideation.

Methodology-

The present study was conducted at Department of Psychiatry, M.G.M Medical College, Indore. This is a cross-sectional comparative study conducted between January 2018 to December 2018. After

obtaining the Institutional Review Board (scientific and ethical) approval, 50 consecutive subjects (25 each in depression with suicidal attempt and depression with suicidal ideation group) who attended in-patient treatment from the Psychiatry Department of a Tertiary Care Medical College were taken.

Inclusion criteria

Patients aged 18–65 years, both genders, who satisfied the ICD diagnostic criteria for research-10 (ICD DCR-10)11 criteria for Depression (F32) or RDD (F33), without psychotic symptoms were included. As per Diagnostic and Statistical Manual of Mental Disorders (DSM-V) active suicidal attempt is a self-initiated sequence of behaviours by an individual who at the time of initiation, expected the set of actions would lead to his or her own death. The specifiers include current- not more than 12 months since last attempt and in early remission- 12-24 months since last attempt. While the suicidal ideation group has never attempted suicide but have ideas of suicide. Only those patients who were drug naïve or treatment free for more than 3 months before the onset of current episode and subjects/informants who gave written informed consent were taken.

Exclusion criteria

Any other psychiatric comorbidity (schizoaffective, bipolar affective disorder, organic mood disorder). Current use of anti-psychotics, anti-depressant, mood stabilizers, or drug free < 3 months. Patients with history of mental retardation, seizure disorder, permanent neurological deficits, cognitive impairment and affective illness secondary to general medical condition or psychoactive substance use (except tobacco) were excluded. We also excluded patients with poor physical health and those with informants who cannot provide adequate information.

Subjects were taken from Dept of psychiatry, MGM Medical College- MY Hospital and Mental Hospital Indore fulfilling the inclusion criteria. After complete description of the study to the subjects, written informed consent was obtained from all participants. A detailed physical examination was done to rule out major medical or neurological illness. Socio-demographic data was collected. After that clinical assessment of patient group was done using Hamilton

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Depression Rating Scale (HAM-D), 12 Beck Scale for Suicidal Ideation (BSSI), 13 Suicide Behaviour Questionnaire (SBQ-R). 14 Blood samples of all groups were drawn after explaining the procedure and were collected in a clot activator (red top) tube at MY Hospital Indore Dept. of biochemistry. Post which serum was processed from the sample via centrifuge machine and the serum was analysed for hs-CRP with Automated analyser using Immunoturbidimetry method. Results were analysed using SPSS 23.

Flowchart explaining the recruitment, sampling, assessment process.



Results-

Table 1- Sociodemographic variables of the patients

	Depression with suicidal attempt (N=25)	Depression without suicidal ideation (N=25)
Age(mean) in years	28.64 years	35.52 years
Males	14 (56%)	12 (48%)
Females	11 (44%)	13 (52%)
Marital status in %:		
Married	56%	68%
Unmarried	32%	16%
Divorced	4%	4%
Widowed	4%	4%
Remarried	4%	8%
Religion in %:		
Hindu	80%	62%
Muslim	20%	38%
Education in %:		
Illiterate	16%	20%
Primary (5th)	28%	36%
Middle(8th)	20%	20%
High School	16%	8%
Inter	8%	8%
Diploma/Graduate/Post graduate Professional	12%	8%
Socioeconomic		
Low	76%	72%
Middle	22%	24%
High	2%	4%
Occupation		
Employed	34%	46%
Unemployed	66%	54%
Family type		
Nuclear	64%	44%
Extended/ Joint.	36%	56%
Locality		
Urban	64%	68%
Rural	36%	32%
Family history		
Positive	19 (76%)	21 (84%)
Negative	6 (24%)	4 (16%)

Positive	19 (76%)	21 (84%)
Negative	6 (24%)	4 (16%)

In comparison to the depression with suicidal ideation the depression with suicidal attempt group had younger age of onset (28.64 years), more male (56%), unmarried (32%), Hindu faith (80%), literates, low socioeconomic (76%), unemployed (66%), nuclear family (64%) subjects. About a quarter (24%) of patients had family history of suicidal attempt in the attempt group which is higher than ideation group (16%).

Table 2. Description of duration of illness (months) in study participants in depression patients with suicidal attempt and depression with suicidal ideation

	N	Minimum	Maximum	Mean	Std. Deviation
Suicidal attempt patients	25	3	12	6.32	2.322
Suicidal ideation patients	25	2	11	4.84	2.511

Depression patients attempting suicide had a mean duration of illness as 6.32 ± 2.32 months while depression with suicidal ideation group had a mean duration of 4.84 ± 2.51 months. The minimum duration for attempt group was 3 months while that for ideation group was 2 months, while maximum duration for attempt and ideation group was 12 and 11 months respectively, this duration is when the patient presented to the O.P.D and could have been more.

Table 3. Description of age of onset of depression (years) in study participants in depression patients with suicidal attempt and depression with suicidal ideation

	N	Minimum	Maximum	Mean	Std. Deviation
Suicidal attempt patients	25	18	54	28.24	9.333
Suicidal ideation patients	25	18	65	37.04	12.733

Suicidal attempt group had mean age of onset at 28.24 ± 9.33 years while ideation group had onset at 37.04 ± 12.733 years. The minimum age of onset for both the case and control group was 18 years while maximum for attempt group was 54 years while that of ideation group was 65 years.

Table 4. Clinical characteristics of depression patients with suicidal attempt and depression with suicidal ideation (continuous variables)

Variables	Suicidal attempt patients Mean \pm SD N=25	Suicidal ideation patients Mean \pm SD N=25	t value	p value
HAM-D SCORES	23.92 ± 6.35	16.80 ± 5.87	4.11	.001
BECK'S SSI SCORES	22.92 ± 7.44	16.48 ± 4.08	3.79	0.001
SBQ-R SCORES	12.20 ± 3.22	8.60 ± 2.21	4.59	0.001

HAM-D scores showed a higher mean 23.92 ± 6.35 in the suicidal attempt group while the ideation group mean was 16.80 ± 5.87 , the t test demonstrated statistical significance. Beck's scale for suicidal ideation showed a higher mean of 22.92 ± 7.44 in the suicidal attempt group in comparison to 16.48 ± 4.08 as mean for ideation group, the t test demonstrated statistical significance. The Suicide behaviour questionnaire revealed mean scores of 12.20 ± 3.22 and 8.60 ± 2.21 for attempt and ideation group respectively with a statistical significance of t test for higher mean SBQ score for

attempt group.

Table 5. Comparison of hs-CRP between depression patients with suicidal attempt and suicidal ideation

hs-CRP (mg/L)	Suicidal attempt patients (N=25)	Suicidal ideation Patients (N=25)
Mean	6.11	2.14
N	25	25
Std. Deviation	6.09	2.10
Std. Error of Mean	1.21	0.43
Minimum	.27	.12
Maximum	26.80	6.76
Range	26.53	6.64
t value	3.07	
p value	0.005*	

*statistically significant

Table 5 shows comparison of hs-CRP levels between depression patient with suicidal attempt and ideation. The attempt group had a mean hs-CRP value of 6.11 ± 6.09 mg/L which is considered as high value as per our criteria for cut off (≥ 3 mg/L), while ideation group had a mean of 2.14 ± 2.10 mg/L. Suicidal attempt patient group has shown higher hs-CRP levels than ideation patient group of depression which was statistically significant.

Table 6. Severity of depression in depression patients with suicidal attempt and suicidal ideation

Depression severity	Suicidal Attempt N=25	Suicidal Ideation N=25
Mild	0 (0%)	5 (20%)
Moderate	6 (24%)	10 (40%)
Severe	19 (76%)	10 (40%)

Table 6 displays depression severity as per ICD-10 criteria. Severe depression was 76% in suicidal attempt patients and 40% in suicidal ideation patients. About 24% patients were in the moderate depression category belonging to the attempt group while 40% ideation subjects had moderate depression. 20% patients had mild depression with suicidal ideation while there were no patients in the suicidal attempt group who had mild depression.

Table 7. comparison of hs-CRP with severity of depression between depression patients with suicidal attempt and ideation

	hs-CRP (mg/L) Suicidal attempt patients (N=25)	hs-CRP (mg/L) Suicidal ideation patients (N=25)	t value	p value
Mild depression	-	.81 \pm .66	-	-
Moderate depression	3.16 ± 1.91	2.04 ± 2.01	0.94	0.37
Severe depression	7.04 ± 6.68	3.53 ± 2.33	2.06	0.05

Table 7 show comparison of hs-CRP within depression with suicidal behaviour group. The attempt group had the highest mean hs-CRP value 7.04 ± 6.68 mg/L while ideation group had 3.53 ± 2.33 mg/L hs-CRP in severe depression. In moderate depression, the attempt group had a greater mean in comparison to ideation group. T test revealed no statistical difference in means of hs-CRP as per severity of depression in the intragroup comparison.

Table 8. Chi square test for hs-CRP samples (low & high) between depression with suicidal attempt and suicidal ideation

	hs-CRP result		Total
	hs-CRP high (value >3 mg/L)	hs-CRP low (value ≤ 3 mg/L)	

Suicidal Attempt	Count	16	9	25
Expected count		11.0	14.0	25.0
Suicidal Ideation	Count	6	19	25
Expected count		11.0	14.0	25.0
Total	Count	22	28	50
Expected count		22.0	28.0	50.0
Pearson chi-square		8.11		
p value		0.004		
Cramer's V		0.403		

Pearson chi-square value = 8.11, p=0.004

Table 8 describes the high and low hs-CRP counts which is defined by a cut off of 3mg/L as per literature and methodology in depression patients with suicidal attempt and depression patients with suicidal ideation. The chi square test was statistically significant implying that depression patients with suicidal attempt have more hs-CRP samples in high group than depression patients with suicidal ideation.

Cramer's v = .403, moderate effect size

Table 9. Correlation of hs-CRP with HAM-D scores in patients of depression with suicidal attempt and depression with suicidal ideation

hs-CRP	HAM-D suicidal attempt		HAM-D suicidal ideation	
	r	p	r	p
	.519**	.008	.735**	.001

**. Correlation is significant at the 0.01 level

Table 9 displays Pearson correlation between hsCRP and HAM-D scores. There is a statistically significant strong positive correlation between HAM-D scores and hs-CRP levels in suicidal attempt group, while the suicidal ideation group also had a strong positive correlation between HAM-D scores and hs-CRP.

Table 10. Correlation of hs-CRP with SBQ-R scores in patients of depression with suicidal attempt and depression with suicidal ideation

hs-CRP	SBQ-R suicidal attempt		SBQ-R suicidal ideation	
	r	p	r	p
	.483*	.015	.311	.130

*. Correlation is significant at the 0.05 level

Table 10 displays Pearson correlation between hsCRP and SBQ-R scores. There is a statistically significant medium positive correlation between SBQ-R scores and hs-CRP levels in suicidal attempt group, while the suicidal ideation group also had a medium positive correlation between SBQ-R scores and hs-CRP.

Table 11. Correlation of hs-CRP with BSSI scores in patients of depression with suicidal attempt and depression with suicidal ideation

hs-CRP	BSSI suicidal attempt		BSSI suicidal ideation	
	r	p	r	p
	.512**	.009	.456*	.022

**. Correlation is significant at the 0.01 level *. Correlation is significant at the 0.05 level

Table 11 displays Pearson correlation between hsCRP and BSSI scores. There is a statistically significant strong positive correlation between BSSI scores and hs-CRP levels in suicidal attempt group, while the suicidal ideation group had a medium positive correlation between BSSI scores and hs-CRP.

Discussion-

The sociodemographic parameters (Table 1) revealed the mean age of depression with suicidal attempt was 33.08 ± 11.9 years while that of depression with suicidal ideation group was 34.20 ± 10.3 years, this implies that suicidality appears earlier in presence of depression.^{15, 16} The number of female patients were higher in the depression without suicidal behaviour group (58%) than depression with suicidal behaviour group. Our results suggest that males have higher suicidal behaviour than females. The married subjects were higher in depression with suicidal behaviour group (68%) than depression without suicidal behaviour (64%) groups. Our results suggest that being married might have protective effect on suicidal behaviour due to better social and interpersonal support.^{17, 18} The depression with suicidal behaviour group had higher preponderance of (76%) Hindu subjects which is in agreement of the local geographical distribution of the religion.¹⁶ Most participants in both depression with suicidal behaviour (32%) and depression without suicidal behaviour (32%) group were literate till primary education, depression without suicidal behaviour group had more percentage of illiterates (22%), Previous studies found that poorly educated subjects were more vulnerable to suicidal attempts.¹⁹ Low socio-economic income groups were found to be the majority in both depression with suicidal behaviour (74%) and depression without suicidal behaviour groups (76%). In terms of sociodemographic variables studies have shown that depression is more common in subjects from poor economic background.^{20, 21} The distribution of depression with suicidal behaviour group (66%) and depression without suicidal behaviour (62%) sample were urban dwelling in majority, while about one third sample in both groups belonged to rural background.²² The depression with suicidal behaviour group had higher composition of nuclear family (66%) than depression without suicidal behaviour group (54%).²²

Patients attempting suicide had a mean duration of illness as 6.32 ± 2.32 months, suicidal ideation group had a mean duration of 4.84 ± 2.51 months (Table 2). These findings are similar to the mean duration of depression in most literature.²³ Therefore, we suggest the depression with suicidal behaviour patients presented to the health-care settings later as compared to depression without suicidal behaviour patients whereas the suicidal ideation subgroup presented earlier in comparison to the suicidal attempt subgroup. Since majority of suicidal attempt patients were in the severe depression category the above finding can be attributed to severe psychomotor retardation in severe depression and poor interpersonal interaction in suicide attempters.

All the samples of our study were identified with major depression as per inclusion criteria and the mean age of all 50 subjects was 32.6 ± 11.9 years, similar mean age have been found in multiple previous studies.^{10, 22, 24} The mean age of onset in the suicidal attempt subgroup was 28.24 ± 9.33 years while in the ideation subgroup was 37.04 ± 12.70 years (Table 3), suggesting that suicidal attempt patients develop depression at an earlier age in comparison to suicidal ideation counterparts. Hence, young impressionable age is another risk factor for suicidal attempt. Our results are in concordance with previous the studies where in one 73% of the patients with suicidal behaviour were <30 years of age,²⁵ and in another study age at <25 years was reported as being a significant risk factor for suicidal attempt.¹⁹

The mean HAM-D scores in suicidal attempt subgroup (Table 4) were higher 23.92 ± 6.35 than the suicidal ideation subgroup was 16.80 ± 5.80 , suggesting attempt can be an indicator for severe depression since suicidal attempt patients were in the very severe category of depression as per HAM-D scale,¹² and that suicidal ideation alone does not warrant the diagnosis of severe depression. As per literature severe depression was found to be associated with suicidal attempt one study found severe depression as one of the factors significantly associated with suicide, (OR=2.20, 95%

CI=1.05–4.60).²⁶ In another study it was seen that finding of severe depression was associated with a sensitivity of 87.3% and specificity of 63% for suicide attempt.^{27, 28}

The suicidal attempt group had a mean BECK'S SSI Score of 22.92 ± 7.44 in comparison to 16.48 ± 4.08 as mean for ideation group (Table 4), the student's t-test demonstrated statistical significance. As the BECK'S SSI relates positively with the suicidal behaviour the suicidal attempt group had a higher mean score. SBQ-R scores more than 8 are suggestive of suicidal behaviour which is seen in our sample population.¹³

The SBQ-R mean scores of 12.20 ± 3.22 and 8.60 ± 2.21 for attempt and ideation group (Table 4) respectively with a statistical significance of t test for higher mean SBQ-R score in the attempt group.¹⁴

Comparison of hs-CRP levels between subgroups of depression patient with suicidal attempt and ideation (Table 5) the attempt group had a higher mean hs-CRP (6.11 ± 6.09 mg/L) value than ideation group (2.14 ± 2.10 mg/L). Suicidal attempt patient group has shown statistically significant high mean hs-CRP than ideation patient group of depression. To the best of our knowledge no study had replicated the above results comparing suicidal attempt with suicidal ideation in context of hs-CRP. However, in a previous study conducted in 2015 no significant difference in CRP levels between high vs low suicidal ideation was reported.⁴

Comparison of depression patients with suicidal attempt and ideation revealed severe depression was 76% in suicidal attempt patients and 40% in suicidal ideation patients (Table 6) which is in agreement with most guidelines which states suicidal attempt is an indicator of severe depression. However, moderate and severe depression made up for 80% of patients in having suicidal ideation.

On evaluating hs-CRP mean as per severity of depression (Table 7) we found a statistically significant difference in means of hs-CRP cases amongst mild, moderate and severe depression. The depression with suicidal attempt group had the highest mean hs-CRP value 7.04 ± 6.68 mg/L while ideation group had 3.53 ± 2.33 mg/L hs-CRP in severe depression. In moderate depression, the attempt group had a greater mean in comparison to ideation group. T test revealed no statistical difference in means of hs-CRP as per severity of depression in the intragroup comparison.

Chi square test was applied in the suicidal attempt and ideation patients (Table 8) the high and low hs-CRP counts which is defined by a cut off of 3mg/L as per literature and methodology in depression patients with suicidal attempt and depression patients with suicidal ideation. The chi square test was statistically significant implying that depression patients with suicidal attempt have more hs-CRP samples in high group than depression patients with suicidal ideation. The Cramer's v score was .403 which is suggestive of a moderate effect size.

There is a statistically significant strong positive correlation ($r=0.51$) between HAM-D scores and hs-CRP levels in suicidal attempt group, while the suicidal ideation group also had a strong positive correlation ($r=0.73$) between HAM-D scores and hs-CRP (Table 9). In previous literature it was found that HAM-D scores to be correlated positively with hs-CRP.²⁹ In another study it was found that individuals with higher depression scores have higher levels of hs-CRP.³⁰

There is a statistically significant medium positive correlation ($r=0.48$) between SBQ-R scores and hs-CRP levels in suicidal attempt group, while the suicidal ideation group also had a medium positive correlation ($r=0.31$) between SBQ-R scores and hs-CRP (Table 10).

There is a statistically significant strong positive correlation ($r=0.51$)

between BSSI scores and hs-CRP levels in suicidal attempt group, while the suicidal ideation group had a medium positive correlation ($r=0.45$) between HAM-D scores and hs-CRP (Table 11).

There are a few limitations to our study design like there is a lack of longitudinal follow-up which could be utilized to compare hs-CRP scores before and after intervention. Inflammatory marker hs-CRP could be confounded by other inflammatory conditions despite strict inclusion criteria. Sample size and study duration can attribute to factors limiting the study.

Conclusion-

Depression patients with suicidal attempt have more hs-CRP high ($\geq 3\text{mg/L}$) samples than depression patients with suicidal ideation. There is a strong positive correlation between HAM-D scores and hs-CRP levels in suicidal attempt group, while the suicidal ideation group also had a strong positive correlation. Moderate positive correlation was found between SBQ-R scores and hs-CRP levels in suicidal attempt and ideation group. Strong positive correlation exists between BSSI scores and hs-CRP levels in suicidal attempt group, while the suicidal ideation group have a moderate positive correlation between HAM-D scores and hs-CRP suicidal attempt contributed to the higher hs-CRP levels in depression patients. Thus hs-CRP an inflammatory marker can serve as a potential marker of suicidal behaviour in depression patients and such at risk patients may be identified prior to suicidal attempt by high hs-CRP levels.

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Conflicts of interest

There are no conflicts of interest.

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