

## RESEARCH ARTICLE

# Neutrophil-to-lymphocyte ratio and C-reactive protein in non-fatal suicidal attempts: A cross-sectional pilot study in Bangladesh

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## Abstract

**Background:** Precise identification of risk factors for suicide has been found as fundamentally challenging for the stakeholders. In search of that, the determination of potential biological markers of suicide has been scrutinizing in recent days. However, replicative studies across the culture and time are warranted to utilize the biomarkers in decision-making while considering suicide prevention.

**Objectives:** We aimed to measure the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) in non-fatal suicidal attempts.

**Methods:** This cross-sectional study was conducted from August 2020 to May 2021. Data were collected from 26 hospitalized patients after an immediate non-fatal suicidal attempt. We collected blood samples and assessed the complete blood count, NLR, and CRP. Data were analyzed by Statistical Package for the Social Science version 24.0 and Microsoft Excel software. We performed the independent *Mann-Whitney U* test to determine the variations between the groups. A value  $<.05$  was considered as the level of significance.

**Results:** The mean age of the study population was 24.1 ( $\pm 7.3$ ), more than half of them ( $n = 19$ , 73.1%) were female. The mode of attempt was either hanging ( $n = 13$ , 50.0%) or poisoning ( $n = 13$ , 50.0%). The previous attempt was noted in 12 (46.2%) cases. The mean CRP level was 16.8 ( $\pm 30.2$ ) mg/L and the mean NLR level was 8.3 ( $\pm 6.8$ ) for the total sample. Both the CRP and NLR were significantly higher among those who attempted hanging ( $P = .019$  and  $.001$ ).

**Conclusions:** The current study revealed preliminary findings on CRP and NLR among non-fatal suicides in Bangladesh where both of the parameters were significantly higher in non-fatal hanging.

## KEYWORDS

cross-sectional analysis, C-reactive protein, neutrophil-to-lymphocyte ratio, non-fatal suicidal attempts, suicide in Bangladesh

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## 1 | INTRODUCTION

Suicidal behavior (SB) is a global preventable public health problem.<sup>1</sup> It takes away about 1 million lives and accounts for 1.4% of all deaths worldwide.<sup>1,2</sup> Along with this death burden, non-fatal attempts have been happening more than 20 times of fatal attempts.<sup>1</sup> The burden of these combined fatal and non-fatal attempts can be minimized by adopting appropriate prevention strategies.<sup>1</sup> However, suicide is the result of a complicated interplay of various vulnerable domains namely biological, psychological, social, and cultural risk factors.<sup>1,3</sup> Despite the identification of multiple risk factors, precise computation of risk factors for suicide has eluded researchers, and a comprehensive explanation of its neurobiology remains elusive.<sup>4</sup> Along with the identification of risk factors in other domains, recent attempts have been coming out to determine several biological markers of SB even though the findings are yet to be cemented as universal. Clinical and epidemiological observations have suggested a probable relationship between immunological response and suicidality.<sup>3,5</sup> As a result, identifying biomarkers could be a viable approach for precisely estimating risk and considering clinical interventions to prevent suicides.<sup>6</sup> A growing body of evidence suggests that neuroinflammation appears to have a key role in the pathobiology of SB.<sup>7</sup>

Along with few other inflammatory markers such as tumor necrosis factor-alpha, elevated interleukin-6 (IL-6), reduced IL-2, and C-reactive protein (CRP) have shown promise while ascertaining the precise relationship.<sup>3,8</sup> Nevertheless, further replicative studies across the cultures and time are warranted. Increased neutrophil-lymphocyte ratio (NLR) has also been projected as a marker of low-grade systemic inflammation in mental diseases, albeit, there is a lack of robust studies. A number of limited studies suggest that NLR is higher in suicide attempters with and without psychiatric morbidity than in the control group.<sup>9</sup> In comparison to the other inflammatory markers, NLR is an easier and cost-effective marker that could be assessed quickly across all resource settings. Against this background, in this current study, we aimed to assess the NLR and CRP in non-fatal suicidal attempts in Bangladesh, which would act as a baseline study in the country as well as could test the replicability of the biomarkers across the countries.

## 2 | METHODS

### 2.1 | Data collection

This cross-sectional study was conducted from August 2020 to May 2021. Data were collected from 26 hospitalized patients after an immediate non-fatal suicidal attempt. We collected blood samples to assess the complete blood count (CBC), NLR, and CRP. We included the patients admitted through the emergency department within 24 hours of an immediate non-fatal attempt and blood samples were collected immediately after the hospitalization.

### 2.2 | Instruments

The blood sample was analyzed by using an automated Hematology Analyzer, XT-2000 I, SYSMEX, Japan to find out the CBC. For CRP, it was analyzed by an automated biochemistry analyzer, cobas c311 (Roche-Hitachi, Japan). The reference value of Leukocytes was 4000 to 10 000/ $\mu$ L, neutrophil 40% to 80%, lymphocyte 20% to 40%, and CRP <6 mg/L.

### 2.3 | Data analysis

Data were analyzed by Statistical Package for the Social Science version 24.0 and Microsoft Excel (2010) software. Simple descriptive analysis was performed and expressed as frequency, percentages, mean, and SD. We performed the independent *Mann-WhitneyU* test to determine the variations between the groups. A value <.05 was considered the level of significance.

### 2.4 | Ethical aspects

Ethical approval was taken from the ethical review committee of Enam Medical College on August 8, 2020 (EMC/ERC/2020/08-1). The study purpose was described before collecting the samples. Informed written consent was obtained from the admitted patients without any influence.

## 3 | RESULTS

### 3.1 | Demographic variables

The mean age of the sample was 24.1 ( $\pm$ 7.3) years. More than half of the sample (n = 19, 73.1%) were female. Majority were married (n = 15, 57.7%), educated below matriculation grade (n = 16, 61.5%), student (n = 11, 42.3%), hailed from suburban areas (n = 21, 80.8%), were non-smokers (n = 20, 76.9%), came from nuclear families (n = 16, 61.5%), and had no associated co-morbidity (n = 25, 96.2%; Table 1). The mode of attempt was either hanging (n = 13, 50.0%) or poisoning (n = 13, 50.0%).

### 3.2 | Risk factors

A history of previous attempts was noted in 12 (46.2%) cases. The stated motive was to die in majority of cases (n = 15, 57.7%) and most attempts were timed after noon (n = 19, 73.1%). The distribution of risk factors were as follows: marital discord (n = 9, 34.6%), familial strife (n = 6, 23.1%), relationship issues (n = 5, 19.2%), demanding behavior (n = 3, 11.5%), break-up of affair (n = 1, 3.8%), sexual abuse (n = 1, 3.8%), and extramarital relationship issue (n = 1, 3.8%). Among the 26 admitted patients, 14 (53.4%) had a diagnosable psychiatric

**TABLE 1** Demography and blood counts of the cases

| Variable                     | Overdose [n (%)]     | Hanging [n (%)]      | Total [n (%)]        |
|------------------------------|----------------------|----------------------|----------------------|
| Age                          | 22.38 ± 6.19 (15-35) | 25.92 ± 8.16 (15-40) | 24.15 ± 7.32 (15-40) |
| Sex                          |                      |                      |                      |
| Male                         | 3 (42.85)            | 4 (57.15)            | 7 (100)              |
| Female                       | 10 (52.63)           | 9 (47.37)            | 19 (100)             |
| Education                    |                      |                      |                      |
| Below matriculation          | 6 (37.5)             | 10 (62.5)            | 16 (100)             |
| Matriculation                | 2 (66.67)            | 1 (33.33)            | 3 (100)              |
| Higher secondary certificate | 3 (60)               | 2 (40)               | 5 (100)              |
| Graduation and above         | 2 (100)              |                      | 2 (100)              |
| Marital status               |                      |                      |                      |
| Married                      | 6 (40)               | 9 (60)               | 15 (100)             |
| Unmarried                    | 6 (60)               | 4 (40)               | 10 (100)             |
| Widow                        | 1 (100)              |                      | 1 (100)              |
| Occupation                   |                      |                      |                      |
| Student                      | 8 (72.73)            | 3 (27.27)            | 11 (100)             |
| Housewife                    | 4 (44.44)            | 5 (55.56)            | 9 (100)              |
| Others                       | 1 (25)               | 3 (75)               | 4 (100)              |
| Unemployed                   |                      | 2 (100)              | 2 (100)              |
| Smoker                       | 2 (33.33)            | 4 (66.67)            | 6 (100)              |
| Substance abuse              |                      | 2 (100)              | 2 (100)              |
| Past attempt                 | 7 (58.33)            | 5 (41.67)            | 12 (100)             |

**TABLE 2** Blood counts of patients with non-fatal suicidal attempts (n = 26)

| Variable                           | Overdose               | Hanging                 | Total                   |
|------------------------------------|------------------------|-------------------------|-------------------------|
| Raised CRP                         | 5 (38.46)              | 8 (61.54)               | 12 (100)                |
| Leukocyte/ $\mu$ L (mean $\pm$ SD) | 10 442.3 $\pm$ 2749.97 | 15 816.15 $\pm$ 4891.51 | 13 129.23 $\pm$ 4891.51 |
| Leukocytosis                       | 6 (35.29)              | 11 (64.71)              | 17 (100)                |
| Neutrophilia                       | 3 (21.42)              | 11 (78.57)              | 14 (100)                |
| Lymphopenia                        | 5 (29.41)              | 12 (70.59)              | 17 (100)                |
| Total                              | 13 (50)                | 13 (50)                 | 26 (100)                |

Abbreviation: CRP, C-reactive protein.

disorder. The distribution of the psychiatric disorders revealed as adjustment disorder (n = 1, 3.8%), amphetamine use disorder (n = 3, 11.5%), anorexia nervosa (n = 1, 3.8%), borderline personality disorder (n = 6, 23%), conversion disorder (n = 2, 7.7%), and major depressive depression (n = 1, 3.8%).

### 3.3 | Markers

The mean CRP level was 16.8 ( $\pm$ 30.2) mg/L and the mean NLR level was 8.3 ( $\pm$ 6.8) for the total sample. The CRP was raised in 12 (46.1%) of patients, which was higher in hanging (Table 2). Leukocytosis was found in 17 (65.4%), neutrophilia was found in 14 (53.8%), and lymphopenia was found in 17 (65.4%) of patients

(Table 2). All these three parameters were comparatively higher in hanging mode (Table 2). The mean CRP was 5.92  $\pm$  7.3 mg/L in overdose and 27.57  $\pm$  39.9 mg/L in hanging (Table 3). The difference was statistically significant ( $U = 38.5$ ;  $P = .019$ ). The mean NLR was 4.32  $\pm$  3.6 in overdose and 12.21  $\pm$  7.1 in hanging (Table 3). The difference was statistically significant ( $U = 20$ ;  $P = .001$ ). No significant differences were observed in CRP levels ( $P = .440$ ) between those with a history of previous attempt(s) (n = 12, 16.6  $\pm$  39.8) versus those without (n = 14, 16.9  $\pm$  20.3). Similarly, the NLR did not differ ( $P = .662$ ) between those with (n = 12, 8.3  $\pm$  8.4) and without a prior attempt history (n = 12, 8.2  $\pm$  5.5). Between males and females, no significant differences were noted either in levels of CRP (9.5  $\pm$  11.2 vs 19.4  $\pm$  34.6;  $P = .563$ ) or NLR (8.7  $\pm$  8.4 vs 8.1  $\pm$  6.4;  $P = .817$ ).

| Marker                  | Overdose   | Hanging      | U    | P-value |
|-------------------------|------------|--------------|------|---------|
| CRP in mg/L (mean ± SD) | 5.92 ± 7.3 | 27.57 ± 39.9 | 38.5 | .019    |
| NLR                     | 4.32 ± 3.6 | 12.21 ± 7.1  | 20   | .001    |

**TABLE 3** Comparison of CRP and NLR between the two modes of attempt assessed by *t*-test

Abbreviations: CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio.

## 4 | DISCUSSION

### 4.1 | Key findings

Suicide is an extremely complex phenomenon where an individual takes his/her own life with the intention to die.<sup>1</sup> Researchers, academicians, and clinicians are still unable to pinpoint any specific risk factor or correctly identify an individual who is suicidal. Identification of potential biomarkers has been getting attention gradually as an increased number of studies are coming out. We aimed to assess NLR and CRP in non-fatal suicidal attempts in Bangladesh that have not been attempted previously in the country. The study revealed that both NLR and CRP were significantly higher in non-fatal hanging than the overdose patients. We did not find any association on the basis of psychiatric morbidities, past history of suicide, or gender; however, it is possible that our analysis may have been underpowered to detect some of these differences due to the small sample size. It has been revealed that NLR is a potential biomarker of suicidality in patients with major depressive illness and it was suggested that NLR might be used to predict suicide risk in patients with depression.<sup>10</sup> NLR was also shown to be higher among individuals who tried suicide in both depression and suicide groups, according to another study.<sup>11</sup> It has been proposed as a marker of low-grade systemic inflammation in mental disorders, and preliminary evidence reveals that NLR is higher in suicide attempters with and without psychiatric morbidity than in the control group.<sup>9</sup> One previous case series of four non-fatal hanging from Bangladesh revealed raised NLR that also supports the current study findings.<sup>12</sup>

Apart from the illnesses listed above, there is mounting evidence that readily available biomarkers of inflammation, such as the NLR, can be utilized to stratify patient risks and personalize treatment strategies across a wide range of medical problems. Increased NLR has been proposed as a marker of low-grade systemic inflammation in various diseases like diabetes mellitus,<sup>13</sup> irritable bowel disease,<sup>14</sup> thyroiditis,<sup>15</sup> ulcerative colitis,<sup>16</sup> hepatosteatosis,<sup>17</sup> and cancers.<sup>18</sup> The other clinical conditions where NLR is increased include major cardiac events,<sup>19</sup> ischemic stroke,<sup>20</sup> intracerebral hemorrhage,<sup>21</sup> tumors,<sup>22</sup> sepsis, and infectious pathologies.<sup>23</sup>

Raised CRP has also been reported in series of studies that support the finding of the current study.<sup>4,8</sup> Batty identified that those with high levels of inflammation, especially high levels of CRP, have a four-fold greater risk of suicide compared to people with low levels of inflammation.<sup>24</sup>

### 4.2 | Implications

Raised biomarkers in non-fatal attempts of hanging than the poisoning could have several implications. Tissue injury, more in non-fatal hanging, is supposed to be an important explanation attributing the raised

CRP and NLR.<sup>12</sup> Other two important reasons are psychological stress and systemic inflammations. It is impossible to explain the attribution based on the two factors from this study's results. However, one study identified that NLR was more raised in the violent suicide groups.<sup>25</sup> The results also replicated the possibilities of potential biomarkers in a different country setting. As a cheap and readily available investigation, NLR could be a universal biomarker across the resource settings to predict a suicidal attempt that could help the clinicians to take necessary initiatives to prevent suicides.

### 4.3 | Strengths and limitations

This is the first study assessing the biochemical changes among the non-fatal suicidal attempts in Bangladesh, which would act as a baseline reference in the country. To draw broad conclusions from our study, systemic inflammation could play a role in suicide attempts. However, the study has several limitations. The biochemical analyses were performed cross-sectionally while follow-up investigations could reveal different parameters that limit the changes of estimates with changes of time. The body mass index of the patients was not considered, which could be a potential source of bias as BMI affects the white blood cell counts. The study was conducted in a tertiary care hospital, which limits the representativeness of the samples. The sample size was relatively small that limit the generalization of the study results. Samples were chosen conveniently can also be a source of bias that could limit the generalization of the findings.

## 5 | CONCLUSIONS

The current pilot study revealed preliminary findings on CRP and NLR among non-fatal suicides in Bangladesh where both of the parameters were significantly higher in non-fatal hanging. However, prudential interpretation is warranted to generalize the study results. Further well-designed follow-up studies are needed to assess any cause and effect association. In addition, associations between the biological markers and SB with and without psychiatric disorders could be a potential area to investigate in the country.

### CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

### AUTHOR CONTRIBUTIONS

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## TRANSPARENCY STATEMENT

The lead author S M Yasir Arafat affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

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