Original Research Article

Aetiology and clinical significance of thrombocytopaenia in critically ill COVID-19 patients: A single centre study

Abstract

Introduction

SARS-CoV-2 infection can cause manifestations in multiple systems in the body.(1) Haematological system is one such system which can be affected by both SARS-CoV-2 infection and critical illness. There are some studies that have shown that thrombocytopaenia can be associated in patients with SARS-CoV-2 infection.(2) There is minimal data on its prevalence and outcome on critically ill patients. One study has shown that low platelet is associated with worsening of respiratory parameters and long term adverse outcome in critically ill.(3) Identifying the presence of thrombocytopaenia and its consequences is important to manage critically ill COVID-19 patients.

Aims

To identify the prevalence , consequences and of thrombocytopaenia and the presence of other causes of thrombocytopaenia in critically ill COVID-19 patients.

Study design

A retrospective clinical analysis

Study set up

This was done in COVID designated Intensive care unit and High dependency unit in Base Hospital-Teldeniya, Sri Lanka.

Methodology

All patients with positive SARS-CoV-2 testing who later develops pneumonia with oxygen dependency and requiring ICU or HDU care were included in the study. Data was collected from patient records for the duration from 1st of January 2021 to 30th of June 2021. Their demographic data, data related to platelet counts and other causes leading to thrombocytopaenia were collected. Thrombocytopaenia was categorised as mild (platelet count 100-150× 10^9/L), Moderate (50-100×10^9/L) and severe (less than 50×10^9/L)

Results

Total of 189 patients were admitted to either ICU or HDU requiring oxygen therapy due to COVID pneumonia during the study period. The mean age was 60.59 years with SD of 14.9. Age range was 16 to 94 years. 63 patients (33.33%) had thrombocytopenia with 8 (12.69%), 19 (30.15%) and 36 (57.14%) had severe, moderate and mild thrombocytopenia respectively. 28 (44.4%) of the patients had low platelets at the time of admission. 28.5% of the patients had another cause for thrombocytopenia. Out of the patents who had thrombocytopenia 20 (31.7%) patients died. This was equal to 48.7% of all critical care deaths. The proportion of death among patients with thrombocytopenia was found to be significant compared to that of patients with a normal platelet count. (p=0.045)

Conclusions

Thrombocytopenia may arise due to multiple aetiologies in critically ill patients. Our study shows that at least 1/3 of the critically ill patients with COVID-19 infection develop thrombocytopenia at some point of their course of illness. It is important to have an insight on the progression of the illness and the outcome in order to plan discharge and follow up for these patients.

Keywords : Thrombocytopenia, COVID-19, Critically ill patients, Platelets

Introduction

SARS-CoV-2 infection was declared a pandemic in March 2020 by the world health organisation. Since the beginning of the pandemic there are more than 263 million cases recorded worldwide.[1] Sri Lanka was also badly affected by the pandemic recording 565000 cases with nearly 14000 deaths by end of November 2021.[1] SARS-CoV 2 infection causes a spectrum of diseases with most individuals suffering only from asymptomatic or mild infection. About 10-20% of hospitalised patients requires Intensive care unit admission.[2] The mortality is high in patients who ends up in ICU. The most common cause of death in the ICU is the severe respiratory failure related to COVID-19 pneumonia. SARS-CoV- 2 infection also affects systems other than respiratory system. One such system is the haematological system and all cell lines may be affected due to that.[3]

Thrombocytopenia is found to be the commonest laboratory abnormality in non-COVID intensive care unit patients.[4] The incidence of thrombocytopenia in non-COVID critically ill patients is between 13% and 60%.[5,6,7] It has been associated with an increased risk of blood product transfusions, bleeding, length of stay, and mortality.[8,9] In non-COVID set up thrombocytopenia can be a result of decreased platelet production, increased destruction, increased aggregation, dilution, and sequestration.[10] The cause of thrombocytopenia in ICU may be difficult to determine and is often multifactorial.

Mild thrombocytopenia has been observed in approximately 5–10% of patients with symptomatic SARS-CoV-2 infection.[11] The incidence of thrombocytopenia in ICU patients are not known. But there are many case reports reporting thrombocytopenia in these patients. Various mechanisms have been suggested, including decreased platelet production and enhanced platelet destruction, as for other viral infections.

Several case reports have shown that SARS-CoV-2 can be associated with immune mediated thrombocytopenia often presenting as Immune thrombocytopenic purpura. Some of the cases were severe, requiring platelet transfusions. There are some cases of thrombocytopenia associated with thrombosis. Thrombosis has also been reported commonly in COVID-19 patients. There are many cases of diagnosed heparin induced thrombocytopenia with the presentation of thrombosis and thrombocytopenia.

Meta analysis done by Pranata etal has shown that thrombocytopenia in COVID 19 patients is associated with a poor prognosis. The same analysis has shown that it has a high specificity but low sensitivity in determining prognosis.[12]

When considering the above factors, thrombocytopenia is an important clinical finding in critically ill COVID -19 patients. No data related to thrombocytopenia and their outcome in ICU patients are

available in Sri Lankan population. Therefore this study was planned in order to identify the incidence and clinical outcome of critically ill COVID 19 patients in a single centre in Sri Lanka.

Methodology

A retrospective observational study was done in COVID designated Intensive care unit and High dependency unit in Base Hospital- Teldeniya, Sri Lanka. All patients with positive SARS-CoV-2 testing who later develops pneumonia with oxygen dependency and requiring ICU or HDU care were included in the study. Data was collected from patient records for the duration from 1st of January 2021 to 30th of June 2021 using data collection form. Patients less than 16 years of age, patients who were admitted to ICU, but later found to have false positive PCR results or patients who had doubtful PCT/RAT status , and pregnant patients were excluded from the study.

Their demographic data, clinical details, data related to platelet counts and other causes leading to thrombocytopaenia were collected.

Thrombocytopenia will be diagnosed using full blood count (FBC). FBC is done in all patients routinely on admission and then daily to every other day depending on the clinical condition during the ICU stay. Thrombocytopenia will be categorised as follows,

1- Mild – platelet count from 100-150000 /ml

2- Moderate – Platelet count from 50-100000/ml

3- Severe – Platelet count less than 50000/ml

Statistical analysis

Statistical analysis was performed using Minitab statistical software 17.1. Parametric numerical data were given as mean ± SD, and nonparametric numerical data were given as median, interquartile range, frequency, and percentage. The Student t-test was used to assess the statistical significance of the difference between two study group means.

Results

During the study period 189 patients were admitted to ICU or HDU requiring oxygen therapy due to COVID pneumonia. The mean age was 60.59 years with SD of 14.9. Age range was 16 to 94 years.

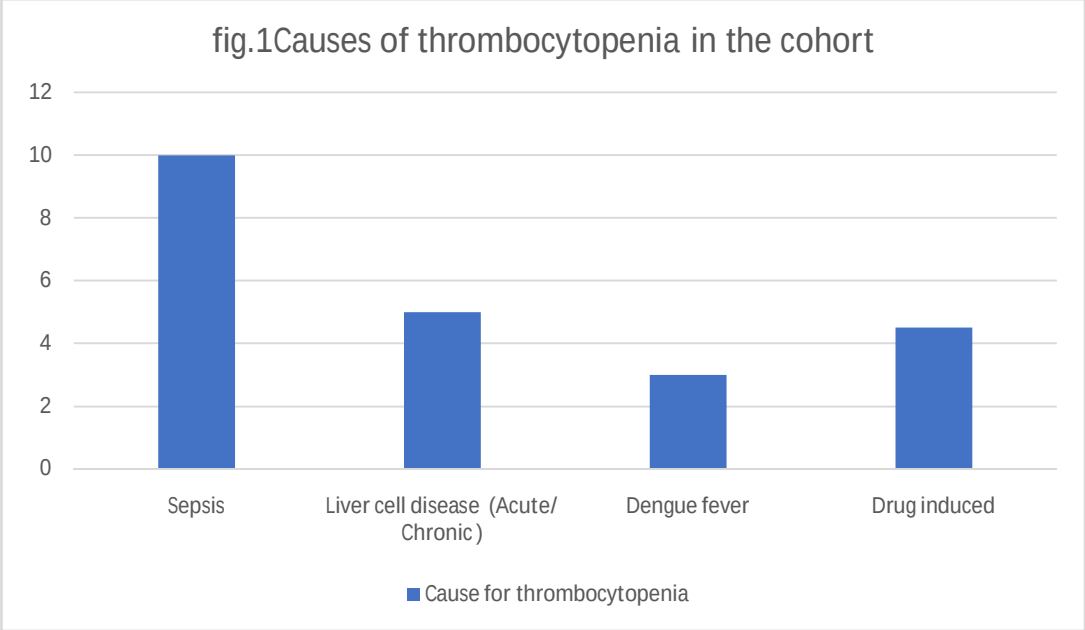
Out of 189 patients , 63 patients (33.33%) had thrombocytopenia at one point of critically ill period. Out of them 8 (12.69%), 19 (30.15%) and 36 (57.14%) had severe, moderate and mild thrombocytopenia respectively. 28 (44.4%) of the patients had low platelets at the time of admission.

Table 1 shows baseline characteristics of patients with thrombocytopenia.

Variables	Values
Total number with thrombocytopenia	63
Severity of Thrombocytopaenia	
Mild	36(57.14%)
Moderate	19 (30.15%)

Severe	8 (12.69%)
Age	62.14 (SD 13.12)
Gender Male Female	 35 (55.5%) 28 (44.44%)
Co-morbidities Diabetes mellitus Hypertension Cardiac disease Chronic renal disease Malignant conditions- Active or treated	 33 (63%) 25 (38.6%) 10 (15.8%) 4 (6.3%) 3 (4.7%)
Outcome Discharged alive Death	 46 (73.01%) 17 (26.98%)

20 (31.7%) of the patients had another cause for thrombocytopenia. Figure 1 shows other causes contributed to thrombocytopenia.

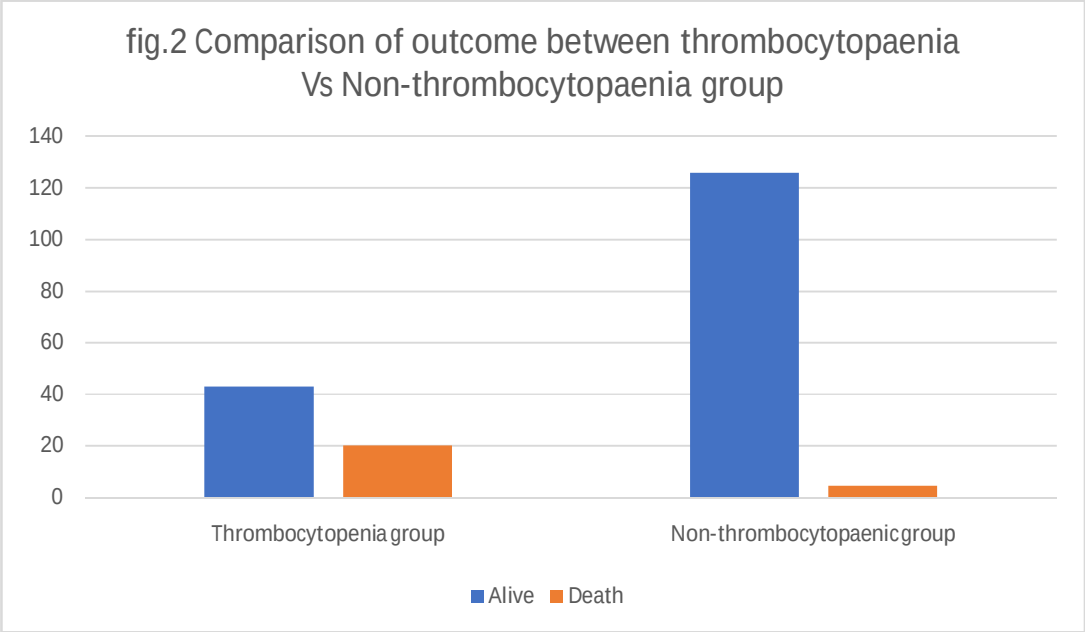


Out of the patients with severe thrombocytopaenia , 5 patients develops significant bleeding requiring platelet and blood transfusion. All patients required transfusions died during ICU stay.

Out of the patents who had thrombocytopenia 20 (31.7%) patients died. This was equal to 48.7% of all critical care deaths. Figure 2 shows comparison of deaths between patients with thrombocytopenia and non-thrombocytopenia. The proportion of death among patients with

thrombocytopenia was found to be significant compared to that of patients with a normal platelet count. (p=0.045)

Figure 2



Discussion

With the onset of COVID-19 pandemic the burden to ICU was increased dramatically. Being a multi system disorder, SARS-CoV-2 infection affect almost all the systems in the body. The effect on the haematological system is variable. Lymphopenia is considered as a cardinal laboratory finding, with a prognostic value. Neutrophil/lymphocyte ratio and peak platelet/lymphocyte ratio has also been used in prognostication in severe cases.[13]

Thrombocytopenia is found to be the commonest laboratory abnormality in non-COVID intensive care unit patients.[4] The incidence of thrombocytopenia in non-COVID critically ill patients is between 13% and 60%.[5,6,7] Platelet count abnormalities has been studied as a marker of prognostication. There are studies that shows thrombocytopenia is associated with the severity of the disease. [14] Other studies have highlighted that patients with significantly elevated platelets had longer duration of hospitalization stays.[15] The second hypothesis is consistent with the correlation between the platelet count and the SARS-COV-2-associated cytokine storm, as the IL-6 promotes the generation of megakaryocytes by stimulating the increase of TPO levels. [16]

In our study, we found that about 1/3 of patients who are critically ill with SARS-CoV-2 infection develops thrombocytopenia during the critical care stay. This number is high considering the complications it can be associated with. In our study, only patients with severe thrombocytopaenia developed bleeding.

SARS-CoV-2 is associated with hypercoagulability state. This may manifest as thrombosis in deep veins, cerebro-vascular accidents, and myocardial infarctions. We also noticed that some of our patients developed deep vein thrombosis despite low platelet count. In such background one of the differential diagnosis would be Heparin Induced thrombocytopaenia. Performing heparin–PF4 antibody testing would help in differentiating HIT and COVID induced hyercoagulability.[17] This testing is not available in Sri Lanka and therefore , differentiation was not possible.

According to our study, patients with thrombocytopaenia are likely to die, when compared to patients who have normal platelet count. Same has been shown in COVID-19 patients from other countries and this has been studied as a prognostic factor. Not only that thrombocytopenia is considered as a bad prognostic factor in non-COVID patients too. However one must exclude other possible causes of thrombocytopenia before coming into conclusions. 31.7% of patients had other identifiable cause for thrombocytopenia in our cohort. Most patients had sepsis related thrombocytopaenia.

Considering the burden of critically ill patients with SARS-CoV-2 infection on the demand for ICU needs in a country, it is important to know the factors that could affect prognosis. This study can help by adding valuable information to the available literature in patients with thrombocytopaenia.

Recommendations

Considering all the factors, the future studies can be concentrated on developing these parameters as prognostication factors. It will help patient selection when the demand for the ICUs are high.

Conclusions

Thrombocytopenia may arise due to multiple aetiologies in critically ill patients. Our study shows that at least 1/3 of the critically ill patients with COVID-19 infection develop thrombocytopenia at some point of their course of illness. It is important to have an insight on the progression of the illness and the outcome in order to plan discharge and follow up for these patients.

Consent

Not applicable, The study was done as a retrospective study .

Ethical approval (where ever applicable)

Ethical review was obtained from ethical review committee of National Hospital Kandy- Sri Lanka. (NO NHK/ERC/17/2021)

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