Section: Clinical Haematolgy

Original Research Article

OBSERVATIONAL STUDY ON TREATMENT AND PROGNOSIS OF COVID-19 RELATED THROMBOCYTOPENIA

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Abstract

Background: The haematological spectrum of Covid 19 varies from a prothrombotic state to bleeding diathesis. Thrombocytopenia in COVID infection is reported to be a poor prognostic marker. As it is multifactorial with variable presentation, critical treatment decisions are challenging and individually tailored. **Aim:** The study aims to analyze the clinical relevance, treatment, and prognosis and assess the response of thrombocytopenia in COVID illness. **Materials and Methods:** All covid positive patients presenting with thrombocytopenia (<50000/µl) within 45 days for Hematology consultation were included in the study. The data regarding bleeding symptoms, comorbidities, CBC, peripheral smear, coagulation profile, viral markers, LDH, CRP, S. Ferritin, RFT, LFT, Covid severity, treatment, response, and follow-up data were obtained. **Result:** Total of 19 cases with a mean age of 50.6 years and an M: F ratio of 0.9 were studied. Nadir's platelet count was below 10x103/µl in 57.9% of cases. 47.4% of cases had thrombocytopenia in the early phase of illness (day1-day15). Covid infection was mild, moderate, and severe in 47.4%, 31.6%, and 21.1%, respectively. Elevated inflammatory markers correlated significantly with poor response to steroids and overall mortality (p=0.001) but not with platelet counts. Intravenous immunoglobulin was administered as second-line therapy in 9 patients with critical platelet count, organ-related bleeding, and poor response to steroids (>5 days). A favourable response was observed in 78.9% of cases. Relapse after 8 months was noted in one case (5.3%). Mortality (day 26) was observed in a young male who initially presented with thrombocytopenia (day 1) and rapidly progressed to MODS, ARDS, and coagulopathy. **Conclusion:** Thrombocytopenia in COVID can occur both in the early and late phases. Close monitoring and timely intervention with IVIG in severe thrombocytopenia may be life-saving. Severe thrombocytopenia during early active infection confers poor survival.

INTRODUCTION

Covid-19, caused by the SARS-CoV-2 virus, is a highly infectious disease affecting millions worldwide. The haematological spectrum of Covid-19 varies significantly among patients, with some experiencing a prothrombotic state while others may have a bleeding diathesis. Thrombocytopenia, or a decrease in the number of platelets in the blood, is one of the most common haematological complications of Covid-19. Platelets play a vital role in clotting and preventing bleeding. Therefore, a decrease in their number can lead to an increased risk of bleeding. Mild thrombocytopenia is present in about 5-10% of patients with SARS-CoV-2 infection and is considered a poor prognostic marker, indicating a more severe form of the disease.[1] The cause of thrombocytopenia in Covid-19 is

multifactorial and can be due to several factors, including viral infection, immune response, and secondary infections. The virus directly infects and kills platelets, leading to a decrease in their number. The immune response to the virus can also lead to an increase in the destruction of platelets.[2] Secondary infections, such as sepsis, can further contribute to thrombocytopenia. The variable presentation of the disease also makes it challenging to make critical treatment decisions. For example, in some cases, thrombocytopenia may resolve independently; in others, it may progress and require more aggressive treatment. Treatment of thrombocytopenia in Covid-19 patients depends on the underlying cause and the severity of the condition.[3] In mild cases, supportive care such as platelet transfusions may be sufficient. In more severe cases, antiviral or immunomodulatory therapy may be necessary. Antiviral therapy, such as remdesivir, effectively reduces the viral load and improves platelet counts. Immunomodulatory therapy, such as the use of corticosteroids, can also be used to suppress the immune response and reduce the destruction of platelets. In addition, it is important to monitor and manage any co-existing conditions such as hypertension, diabetes, and heart disease, as these can also contribute to developing thrombocytopenia.[4] The management of thrombocytopenia also requires close monitoring of platelet counts, bleeding symptoms, and other laboratory parameters such as clotting times. Therefore, thrombocytopenia is a common complication of Covid-19 and is considered a poor prognostic marker.[5] The multifactorial nature of the disease makes treatment decisions challenging and requires an individualized approach. Further research is needed to understand the underlying mechanisms of thrombocytopenia in Covid-19 and develop more effective treatment strategies. In addition, it is important to monitor and manage any co-existing conditions. Closely monitoring platelet counts, bleeding symptoms, and other laboratory parameters such as clotting times are crucial in the management. We conducted a retrospective study at our COVID care centre to analyze the clinical relevance, treatment, and prognosis and assess the response of thrombocytopenia in COVID illness.

MATERIALS AND METHODS

A hospital-based, single-centre, prospective observational study was conducted at Rajiv Gandhi Government general hospital from (January 2021 to July 2021). All covid positive patients presenting with thrombocytopenia (<50000/µl) within 45 days of Hematology consultation during the peak of the covid pandemic were included in the study. In addition, 19 cases of severe thrombocytopenia attributed to COVID infection (RTPCR positive) were enrolled for the study. Patients with the alternate cause of thrombocytopenia like HIV, HBV, HCV, HIT, TTP, Aplastic anaemia, or MDS were excluded. All the patients were initially treated with steroids depending on the severity of thrombocytopenia (Either pulse of Methylprednisolone 1g/kg for 2-3 days/low dose Dexamethasone/oral Prednisolone). Intravenous immunoglobulin was administered as second-line therapy in patients with critical platelet count, organ-related bleeding, or poor response to steroids (>5 days). Thrombopoietin receptor agonists were not administered, considering the cumulative risk of thrombosis during COVID illness. Platelet transfusions were given during acute bleeding. The data regarding bleeding symptoms, comorbidities, Complete blood count, peripheral smear, coagulation profile, viral markers, Lactate dehydrogenase, C-reactive protein, Serum Ferritin, Renal function test, Liver function test, Covid severity, treatment, response, and 1-year follow-up data were obtained from medical records and OPD visit records.

The data were tabulated and analyzed using IBM SPSS version 21.0 software. The Chi-square test and sample t-test were used to compare categorical and continuous variables.

RESULTS

Out of 220 haematological consultations for COVID positive patients, 34 cases of severe thrombocytopenia during covid infection were identified. We excluded cases of thrombocytopenia secondary to any other cause like aplastic anaemia, known ITP, MDS, and secondary to other viral infections like HIV, Hepatitis B, and Hepatitis C. 19 cases of severe thrombocytopenia attributed to COVID infection (RTPCR positive) were enrolled for the study. This population had a mean age of 50.6 years and an M: F ratio of 0.9. Nadir platelet count was below 10000/µl in 57.9% of cases. None of the cases showed thrombotic complications. Hypertension, diabetes, hypothyroidism, and CAD were present in 36.8%, 15.8%, 5.3%, and 5.3%, respectively. 47.4% of cases had thrombocytopenia in the early phase of illness (day1-day15). Table 1 shows the relevant clinical and treatment profile of the study population. Covid infection was mild, moderate, and severe in 47.4%, 31.6%, and 21.1%, respectively.

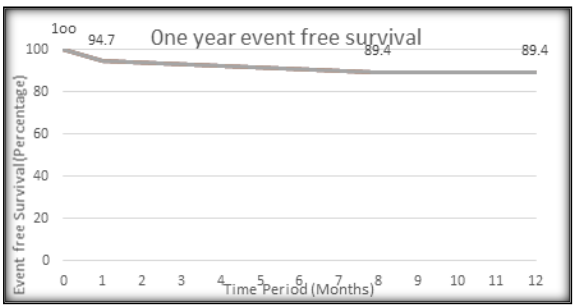

Figure 1: The curve represents the treatment response over one year

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Table 1: Demographic data of the study

Variable		No of patients
Gender	Male	9
	Female	10
Age group	30-50	11
	50-70	7
	>70	1
ICU admission	Yes	3
	No	16
Comorbidity	SHTN, T2DM	3
	SHTN	3
	SHTN, Hypothyroid	1
	SHTN, T2DM, CAD	1
	Nil	12
Severity	Mild	9
	Moderate	6
	Severe	4

Table 2: Condition and treatment among patients

		No of patients
Simultaneous/Post covid (>15 days)	Simultaneous	9
	Post-Covid	10
Inflammatory marker	Elevated	4
	Normal	15
Treatment	IVIG + Steroids	9
	Steroids	10

A favourable response was defined as a platelet count above 25x103/µl and resolution of bleeding. It was observed in 78.9% of cases. One year of event-free survival was 89.4%. Figure 1 shows the treatment response of these patients for a one-year follow-up. Relapse after 8 months was noted in one case (5.3%). Mortality (day 26) was observed in a young male who initially presented with severe thrombocytopenia (day 1) and rapidly progressed to MODS, ARDS, and coagulopathy. The noteworthy point was the young patient had no comorbidity.

DISCUSSION

Thrombocytopenia in COVID infection is considered to carry a bad prognosis.[6] COVID-19 thrombocytopenia could be postulated secondary to direct platelet-viral interaction via pathogen recognition receptors (PRR). This might lead to platelet activation and clearance through the reticuloendothelial system.[7] It could also be related to sepsis.

Treatment of thrombocytopenia during COVID illness can be treated like any other Immune thrombocytopenia. However, amidst the procoagulant and autoinflammatory state of COVID, critical platelet count appears prohibitive and challenging. Timely decisions and close monitoring become imperative. The administration of steroids is common in COVID and thrombocytopenia management, hence the first choice among physicians.[8] Intravenous immunoglobulin is a life-saving and immediate second choice as advocated by guidelines.[8]

Anticoagulation required for COVID management becomes challenging with critical platelet count. It must be tailored according to individual risk-benefit basis. None of our cases had thrombosis, but western literature suggests a higher risk of thrombosis in cases of COVID vaccine-associated thrombocytopenia and cases of pre-existing ITP with COVID infections.[9,10] However, the risk of thrombosis in ITP is not hypothetical and remains even with anticoagulation.[11,12]

In this setting, the administration of thrombopoietin receptor agonists is not advocated like in other ITPs. Platelet transfusions are, however, administered as necessary. In addition, the chronicity of immune thrombocytopenia is not emphasized much. Our one-year follow-up data reveals thrombocytopenia to be a short-lived immune event. However, relapse is also not impossible, as was noted in one case. This is similar to the observation by EJ Lee et al.[11]

The initial nadir platelet count was noted to be below 10000 in a maximum of cases. This is similar to the French series, which predominantly focussed on de novo ITP rather than pre-existing ITP.[13] The temporal relation of thrombocytopenia and covid illness varied across studies and case reports.[14] We observed that patients presenting within the first week of COVID illness had severe thrombocytopenia and milder covid illness. However, this correlation did now show statistical significance. In addition, there was a mortality observed in our study due to respiratory failure and multiorgan dysfunction secondary to COVID. However, the overall treatment response of COVID-induced thrombocytopenia to conventional steroids and IVIG holds a favourable outlook.

Ongoing studies and experiences from various countries must be published to create more awareness and guidance for treating physicians and haematologists. To our knowledge, this is the first and largest series of COVID-induced thrombocytopenia reported from our country. Although severe thrombocytopenia during acute

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covid infection appears frightening, the appropriate treatment promises a good response. The caveat is timely diagnosis after excluding other causes, appropriate treatment, and close monitoring.

CONCLUSION

In conclusion, thrombocytopenia, a decreased number of platelets in the blood, has been strongly associated with poor prognosis in COVID-19 patients. Although studies have found that treatment with corticosteroids and IVIG is effective in treating severe ITP, achieving a critical platelet count can be difficult due to COVID-19's procoagulant and autoinflammatory state. Therefore, close monitoring and timely intervention with IVIG may be life-saving, and further research is needed to establish the efficacy of this treatment in other populations.

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