

Analysis of Thrombocytopenia in Critically ill COVID-19 Patients: A Single Centre Retrospective Study**Amudhavalli Singaram¹, Premalatha Sundarasan², Babiya Infant Arockiasamy³, Arunbabu Chinnadurai⁴, Amitesh Krishna S⁵**¹Assistant Professor, Department of Pathology, KAPV Government Medical College, Tiruchirappalli²Professor, Department of Pathology, Government Ariyalur Medical College, Ariyalur³Assistant Professor, Department of Pathology, KAPV Government Medical College, Tiruchirappalli⁴Associate Professor, Department of Surgery, Government Stanley Medical College, Chennai⁵3rd year MBBS Student, Government Omandurar Medical College and Hospital affiliated to The Tamil Nadu Dr M.G.R Medical University, Chennai

Received: 25-08-2023/ Revised: 28-09-2023 / Accepted: 30-10-2023

Corresponding author: Dr. Arunbabu Chinnadurai

Conflict of interest: Nil

Abstract:

Introduction: In 2019, the world witnessed the outbreak of a group of viruses known as corona virus, mainly affecting lungs and the disease is termed as COVID-19. To correlate with the severity of illness, many potential biological markers are being analysed in Covid-19 patients, chiefly haematological parameters. Among this thrombocytopenia seem to be of more significance and a prognostic marker for critically ill patients. This study aims to analyse the meticulous relation between critically ill Covid-19 patients and thrombocytopenia.

Materials and Methods: A retrospective observational cohort study was conducted in the Department of Pathology, Government Medical College and Hospital, Omandurar Government Estate, Chennai, Tamil Nadu. COVID positive cases admitted in Government Omandurar Medical College Hospital during the month of October 2020 were included for the study. Clinical and demographic details like age, sex, comorbidities (Hypertension, diabetes mellitus, cardiovascular disease), clinical manifestations and CBC reports were collected from medical records. A total of 1176 cases were included, comprising 803 males and 373 females.

Observation and Results: Among 803 males, 186 had thrombocytopenia and among 373 females, 45 had thrombocytopenia. The age group ranges from 7- 98 years, with peak age group at 51-60 years followed by 61-70 years. Among the comorbid illnesses, diabetes mellitus is more commonly seen compared to Systemic Hypertension. The hematological abnormalities observed in our study are Lymphopenia (34.12%), Raised NLR (27.72%), thrombocytopenia (19.6%), neutrophilia(20.49%) and leukocytosis (17.51%).

Conclusion: Compared with clinical symptoms, platelet count changes occur earlier and can be easily determined, so clinicians should pay more attention to the changes to personalize the therapeutic interventions and treatment procedures.

Keywords: COVID-19 patients, Thrombocytopenia, Neutrophil to leukocyte ratio, Corona virus.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

In 2019, the world witnessed the outbreak of a novel virus. This virus is found to be a new strain of a group of viruses known as coronavirus, mainly affecting lungs and the disease is termed as COVID-19 [1]. COVID-19 initially originated as an epidemic in Wuhan of China, continued to progress to become a pandemic.

Though most people develop only mild to moderate respiratory illness and recover without any special treatment, elderly people and people with other comorbid conditions are seen to develop severe illness. To correlate with the severity of illness, many potential biological markers are being analysed in Covid-19 patients, chiefly haematological

parameters [2]. It is found that high haemoglobin value, leukopenia, neutropenia and thrombocytopenia are observed in patients [3]. Among this thrombocytopenia seem to be more significant and a prognostic marker for critically ill patients [4]. This study aims to analyse the meticulous relation between critically ill Covid-19 patients and thrombocytopenia and the role played by it in recovery of Covid-19 patients.

Aims and Objective

- To observe and analyse the Total platelet count value in the Complete Blood Count (CBC) tests performed in Covid-19 patients.

- To record the values and categorise thrombocytopenia accordingly.
- To correlate Thrombocytopenia with clinical severity of the illness in COVID19 patients.

Materials and Methods

A retrospective observational cohort study was conducted in the Department of Pathology, Government Medical College and Hospital, Omandurar Government Estate, Chennai, Tamil Nadu.

COVID positive cases admitted in Government Omandurar Medical college Hospital during the

month of October 2020 were included for the study. Clinical and demographic details like age, sex, comorbidities (Hypertension, diabetes mellitus, cardio vascular disease), clinical manifestations and outcomes were collected from medical records. The total platelet count is collected from the CBC reports, from the records in the Pathology Central Laboratory. The platelet count value is then categorised accordingly. The categorised values are further studied using statistical analysis. The collected data is then analysed using SPSS software.

Classification of Thrombocytopenia[5]

Table 1: Classification of Thrombocytopenia

Platelet count	Category
100,000 – 150,000/micro litre of blood	Mild
50,000 – 100,000/ micro litre of blood	Moderate
<50,000/ micro litre of blood	Severe

Inclusion Criteria: Patients of all ages and both sexes with Diagnosis of Covid 19 confirmed either with RT-PCR or COVID pattern on CT chest.

Exclusion Criteria: Patients with other Hematological disorders (Leukemia, Hypersplenism and Idiopathic Thrombocytopenic Purpura.) Patients with auto immune diseases, Patients with other infective conditions like AIDS and TB.

Observation and Results

During the period of October 1 to October 31, 2894 number of patients were admitted in Government Omandurar Medical College Hospital, Chennai. Those cases with demographic details like age, sex, associated illness, presenting complaints and hematological parameters were recruited. A total of 1176 cases were included, comprising 803 males (68.3%) and 373 females (31.7%). Among 803 males, 186 had thrombocytopenia and among 373 females, 45 had thrombocytopenia as depicted in Table no 2 and Chart no 1.

Table 2: Incidence of Thrombocytopenia in Males and Females

Sex	Non thrombocytopenia	Thrombocytopenia	Total
Male	617 (65.29%)	186(80.51%)	803 (68.3%)
Female	328 (34.71%)	45(19.49%)	373 (31.7%)
Total	945	231	1176

The age group ranges from 7- 98 years, with peak age group at 51-60 years (29.7 %) followed by 61-70 years (21 %)

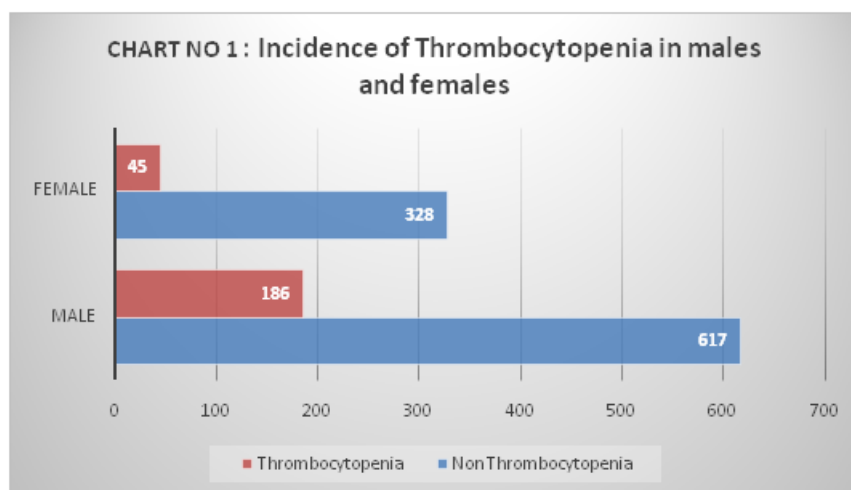


Figure 1: Incidence of Thrombocytopenia in Males and Females

The presenting complaints observed were fever in 593 cases (50.4%), cough in 465 cases (39.5%), Dyspnea in 341 cases (28.9%), Myalgia in 80 cases(6.8%), diarrhea in 29 cases(2.4%), Sore throat in 28 cases (2.3%), Anosmia in 17 cases (1.4%) as depicted in figure 2

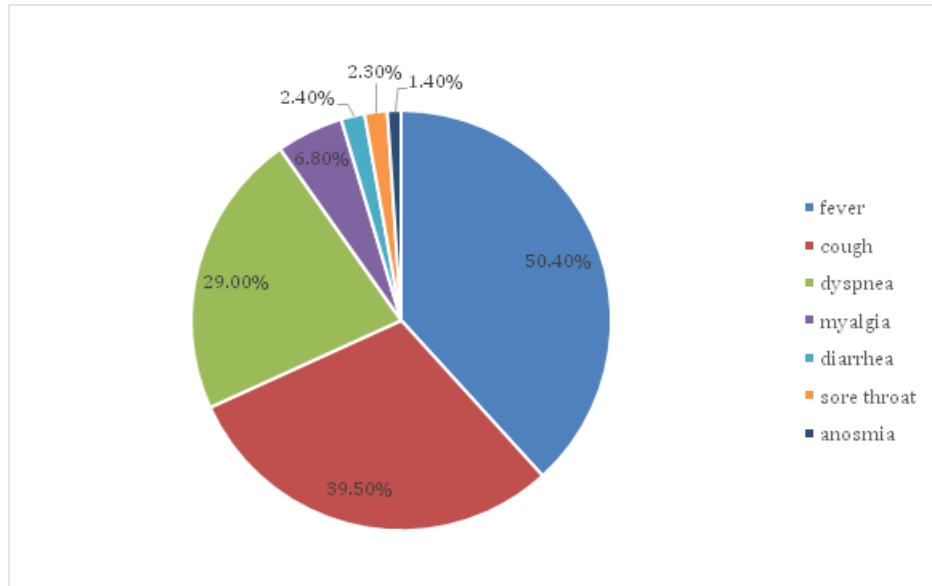


Figure 2: Various Presenting Complaints in Covid Affected Patients

Out of the total 1176 cases, 452 cases(38.4%) had comorbid illnesses, that include 251 cases (30.1%) of diabetes mellitus, 181 cases (21.3%) of Systemic Hypertension and 20 cases (1.3%) of Coronary artery disease and 15 cases of COPD and thrombocytopenia is more seen in Diabetic patients compared to others as depicted in Table no 3 and figure no 3.

Table 3: Various Comorbidities in Covid Affected Patients

Co Morbidity	Total	Non Thrombocytopenia	Thrombocytopenia
COPD	15	2	13
Hypertension	181	63	118
Diabetes	251	60	191
Cardiovascular disease	20	10	10

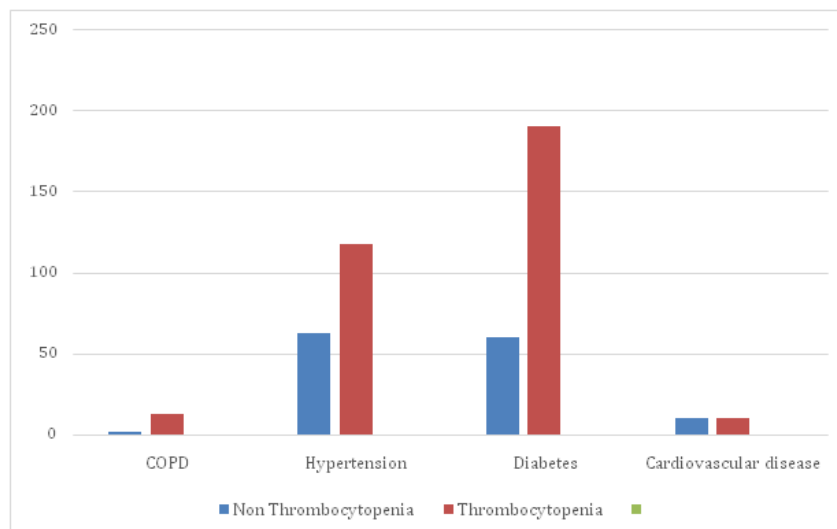
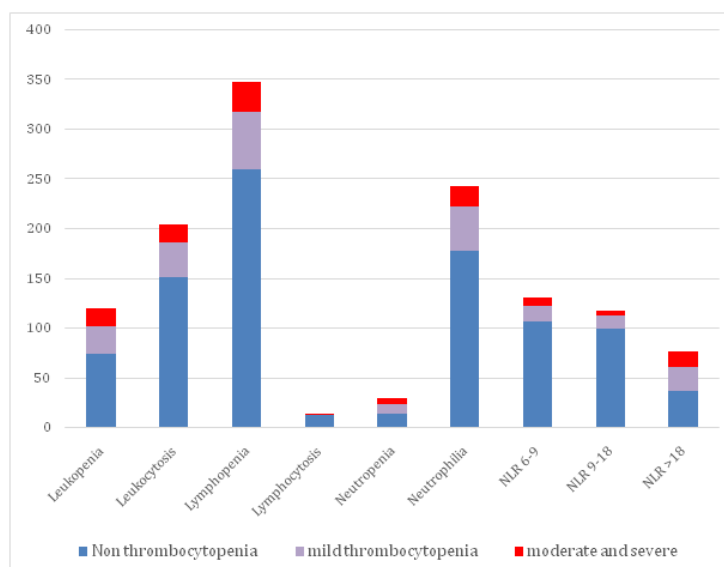


Figure 3: Various Comorbidities in Covid Affected Patients

Other hematological abnormalities were compared with thrombocytopenia and it was found that thrombocytopenia is more commonly associated with lymphopenia, neutrophilia and increased NLR- neutrophil to lymphocyte ratio as depicted in Table no 4 and Figure no 4. Hence these markers can be also be used for risk assessment.

Table 4: Incidence of Other Hematological Abnormalities and its Coincidence with Thrombocytopenia

Hematological Abnormalities	Non Thrombocytopenia	Mild Thrombocytopenia	Moderate And Severe Thrombocytopenia
Leukopenia (WBC <4000/mm ³)	75	27	18
Normal Leukocyte (WBC 4000- 11000/mm ³)	718	100	33
Leukocytosis (WBC >11000/mm ³)	152	35	18
Lymphopenia (less than 1000/mm ³)	260	58	30
Normal Lymphocyte (1000-4000/mm ³)	672	104	38
Lymphocytosis (> 4000/mm ³)	13	0	1
Neutropenia (less than 1500/mm ³)	15	9	6
Normal Neutrophil count (1500- 8000/mm ³)	752	108	43
Neutrophilia (> 8000/mm ³)	241	45	20
NLR- neutrophil to lymphocyte ratio (6-9)	124	16	8
NLR (9-18)	119	13	5
NLR (more than 18)	83	24	16

**Figure 4: Incidence of other Hematological Abnormalities and its Coincidence with Thrombocytopenia**

Discussion

Corona virus is a highly contagious virus found in humans and several domestic animals causing a variety of acute and chronic diseases. COVID- 19 presents with a wide variability in the severity of disease ranging from asymptomatic to critical disease.

Platelet count may be a simple biomarker which could aid in identifying the severe infection [6].

In this study a total of 1176 cases were included, comprising 803 male (68.3%) and 373 female (31.7%) and it is similar to the study by Xiaoboyang et al [7] where 52.6% were male, 47.4% were females, and in study of Wei-liu et al [8] 50% were males, 50% were females. The age group ranges from 7- 98 years, with peak age group at 51-60 years

(29.7%) followed by 61-70 years (21%) This in line with Yanli liu et al [9] where 46 years was the median age .

In our study the presenting complaints observed were fever in 593 cases (50.4%), cough in 465 cases (39.5%), Dyspnea in 341 cases (28.9%), Myalgia in 80 cases (6.8%), diarrhoea in 29 cases (2.4%), Sore throat in 28 cases (2.3%), Anosmia in 17 cases (1.4%). In Wei-liu et al [8] study, the most common symptoms were fever on admission and cough. Diarrhoea was uncommon (3.8%).

Out of the total 1176 cases, 452 cases (38.4%) had comorbid illnesses, that include 251 cases (30.1%) of diabetes mellitus, 181 cases (21.3%) of Systemic Hypertension and 20 cases (1.3%) of Coronary artery disease and 15 cases of COPD. Danying Liao

et al [10] study showed 48% patients had comorbidities, with hypertension being the most common, followed by diabetes, coronary heart disease, and carcinoma. SARS-CoV-2 can bind to its target cells through angiotensin-converting enzyme 2 (ACE2), which would facilitate infection with COVID-19, while hypertension and diabetes mellitus were linked to ACE2 polymorphisms, specifically in Asian populations. According to xiaofangzhao et al [11], the non-surviving group had a higher proportion of hypertension and diabetes than the surviving group.

Abnormal coagulation is a common complication of COVID-19 and is manifested by intravascular thrombosis, pulmonary vascular leakage and disseminated intravascular coagulation. Thrombocytopenia is also a common clinical manifestation associated with poor outcome in patients with community acquired pneumonia. In addition, SARS-CoV-2 induces disseminated intravascular coagulopathy state characterized by increased consumption of platelets leads to thrombocytopenia, elevation of fibrinogen and D-dimers level [6].

Other possible mechanism is CD 13 and CD66a are expressed on bone marrow CD34 + cells. SARS-CoV-2 may induce the growth inhibition by binding to CD13 or CD66a of hematopoietic cells and bone marrow stromal cells, resulting in abnormal hematopoiesis and immunodeficiency. This leads to immune-mediated hematopoietic stem cell damage, thereby further leading to thrombocytopenia. Increased IL-1 β , IL-6, IL-2, IL-2R, IL-7, IL-10, and TNF α observed in covid 19 patients which cause different degrees of coagulation disorders. Inflammatory factors and lymphocyte function tests have been suggested for assessing severity of disease. According to Danying Liao et al [10] study high neutrophil to lymphocyte ratio, which might be a result of excessive inflammation and immune suppression in sepsis triggered by SARS-CoV-2 infection, can be useful for predicting severity and mortality. In sepsis, neutrophils are hyperactivated with delayed apoptosis disorder, along with the depletion and exhaustion of CD4 and CD8 T cells as a result of apoptosis, lymphocytopenia is also common in SARS-CoV and MERS-CoV infection. So neutrophil to lymphocyte ratio appears to be an efficient and practical indicator for risk of COVID-19 mortality.

The hematological abnormalities observed in our study are Lymphopenia (34.12%), Raised NLR (27.72%), thrombocytopenia (19.6%), neutrophilia (20.49%), leukocytosis (17.51%), Among 1176 cases, 945 cases(80.35%) had normal platelet count value and 231 cases (19.64%) had low platelet count. 162 (13.77%) cases had mild thrombocytopenia, 59 (5.01%) cases had moderate thrombocytopenia, and 10 (0.85%) cases severe

thrombocytopenia. According to xiaofangzhao et al [11], compared with survivors, non-survivors had higher white blood cell count, neutrophil count, and lower lymphocyte count, which may be related to disorders of inflammatory and immune responses in non-survivors. According to Xiaobo yang et al [7], thrombocytopenia was more likely to occur in non-survivors 72.7% than in survivors 10.7%.

Conclusion

Furthermore, virus infection cause immune damages to platelets by inducing auto-antibodies and immune complexes. The use of immunomodulators and short courses of corticosteroids at low-to-moderate dose may potentially be helpful for critically ill patients with COVID-19, using essentially, very personalized attitude towards each particular patient. Platelet count dynamically shows pathophysiological changes in body, which can act as an early warning index for the early treatment of COVID-19. It can also serve as a simple and repeatable clinical indicator. Compared with clinical symptoms, platelet count changes occur earlier and can be easily determined, so clinicians should pay more attention to the changes to personalize the therapeutic interventions and treatment procedures.

References

1. World Health Organisation overview on coronavirus: <https://www.who.int/health-topics/coronavirus#tab=tab 1>.
2. Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KGE, Tan GB, Mucheli SS, Kuperan P, Ong KH. Hematologic parameters in patients with COVID-19 infection. *Am J Hematol.* 2020 Jun;95(6):E131-E134.
3. Usul E, Şan İ, Bekgöz B, Şahin A. Role of hematological parameters in COVID-19 patients in the emergency room. *Biomark Med.* 2020 Sep;14(13):1207-1215.
4. Khurana D, Deoke SA. Thrombocytopenia in Critically Ill Patients: Clinical and Laboratorial Behavior and Its Correlation with Short-term Outcome during Hospitalization. *Indian J Crit Care Med.* 2017 Dec;21(12):861-864.
5. Erkurt, Mehmet & Kaya, Emin & Berber, İlhami & Koroglu, Mustafa & Kuku, Irfan. Thrombocytopenia in Adults: Review Article. *Journal of Hematology.* 2012;1:44-53.
6. Liu W, Tao ZW, Wang L, Yuan ML, Liu K, Zhou L, Wei S, Deng Y, Liu J, Liu HG, Yang M. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chinese medical journal.* 2020 May 1;133(09):1032-8.
7. Yang X, Yang Q, Wang Y, Wu Y, Xu J, Yu Y, Shang Y. Thrombocytopenia and its association with mortality in patients with COVID-19. *Journal of Thrombosis and Haemostasis.* 2020 Jun 1;18(6):1469-72.

8. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DS, Du B. Clinical characteristics of coronavirus disease 2019 in China. *New England journal of medicine*. 2020 Apr 30;382(18):1708-20.
9. Liu Y, Sun W, Guo Y, Chen L, Zhang L, Zhao S, Long D, Yu L. Association between platelet parameters and mortality in coronavirus disease 2019: Retrospective cohort study. *Platelets*. 2020 May 18;31(4):490-6.
10. Liao D, Zhou F, Luo L, Xu M, Wang H, Xia J, Gao Y, Cai L, Wang Z, Yin P, Wang Y. Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study. *The Lancet Haematology*. 2020 Sep 1; 7(9): e671-8.
11. Zhao X, Wang K, Zuo P, Liu Y, Zhang M, Xie S, Zhang H, Chen X, Liu C. Early decrease in blood platelet count is associated with poor prognosis in COVID-19 patients—indications for predictive, preventive, and personalized medical approach. *EPMA Journal*. 2020 Jun;11:139-45.