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Blood coagulation parameter abnormalities in hospitalized patients with confirmed COVID-19 in Ethiopia

--Manuscript Draft--

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Full Title:	Blood coagulation parameter abnormalities in hospitalized patients with confirmed COVID-19 in Ethiopia
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Corresponding Author:	Shambel Araya, MSc Addis Ababa University Addis Ababa, ETHIOPIA
Keywords:	COVID-19; Prothrombin time; activated partial thromboplastin time; international normalized ratio; platelet; Addis Ababa; Ethiopia
Abstract:	Background : Coagulopathy and thromboembolic events are among the complications of Corona Virus disease 2019 (COVID-19). Thus, abnormal coagulation profiles in COVID-19 patients are taken as important prognostic factors of COVID-19 disease severity. The aim of this study was to analyze coagulation profiles of hospitalized COVID-19 patients in Addis Ababa, Ethiopia. Methods : This cross-sectional study was conducted among 455 Covid-19 patients admitted at Millennium COVID-19 treatment center, Addis Ababa, Ethiopia from July 1- October 23, 2020. Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT) and International normalized ratio (INR) were ~~estimated by~~ HUMACLOT DUE PLUS coagulation analyzer (Wiesbaden, Germany) . In all tests, $p<0.05$ was defined as statistically significant. Result : A prolonged prothrombin time was found ~~among~~ 46.8% of study subjects with COVID-19 . ~~P~~rolonged prothrombin time and high INR were seen among 53.3% severe and 51% critical patients with COVID-19 manifestation. Thrombocytopenia was detected in 22.1% of COVID-19 patients. 50.5% and 51.3% of COVID-19 patients ~~aged~~ older than 55 years had thrombocytopenia and prolonged APTT respectively. Conclusion : In this study, prolonged prothrombin time and high INR were found ~~among~~ severe and critical COVID-19 patients. Thrombocytopenia and prolonged APTT were dominant in COVID-19 patients older than 55 years. Thus, we recommend emphasis to be given for monitoring of platelet count, PT, APTT and INR in hospitalized COVID-19 patients ~~management~~.
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Response to Reviewers:	Cover letter Shambel Araya Addis Ababa University Addis Ababa, Ethiopia

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Date: January 1, 2021
To: PLOS ONE Journal
Dear Editorial:
We are glad to write this response that our paper entitled “Blood coagulation parameter abnormalities among patients with confirmed COVID-19 in Ethiopia” (Submission ID: PONE-D-20-35898) has been requested to review for publication in PLOS ONE journal. We are pleased to have an opportunity to make our paper revised and we have greatly appreciated the reviewers’ and editor’s comments and suggestions were very helpful overall. In revising the paper, we have carefully considered reviewers’ and editor’s comments and suggestions on our revised submission. As instructed, we have attempted to succinctly explain changes made in reaction to all comments and reply to each comment in point-by-point fashion as follows:

Response to Editor’s comments
Additional Editor comments
Comment. “This is an important and timely paper to consider the abnormalities of haematological parameters in an African context and in COVID-19 disease. There are, however, unfortunately significant numbers of typographical errors and word omissions which make the sense of the paper difficult to follow in some cases. For example, the authors refer to a "prolonged" but do not indicate which parameter. There are, in addition, a number of references which need to be included (especially in the discussion).”
Response: As suggested by the editor we thoroughly went through the manuscript and revised the typographical, grammatical, editorial, and word omissions.
Journal requirements
When submitting your revision, we need you to address these additional requirements.
Comment #1. “Please ensure that your manuscript meets PLOS ONE's style requirements, including those for file naming.”
Response #1: we strictly followed PLOS ONE's style requirements during preparation and revision of our manuscript as suggested by the editor.
Comment #2. “Thank you for submitting the above manuscript to PLOS ONE. During our internal evaluation of the manuscript, we found significant text overlap in the Discussion, Abstract, and other sections, between your submission and the following previously published works:
- https://applications.emro.who.int/emhj/v26/09/1020-3397-2020-2609-999-1004-eng.pdf
- https://www.hematology.org/COVID-19/COVID-19-and-coagulopathy
- https://pubmed.ncbi.nlm.nih.gov/32702124/

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Please revise the manuscript to rephrase the duplicated text, cite your sources, and provide details as to how the current manuscript advances on previous work. Please note that further consideration is dependent on the submission of a manuscript that addresses these concerns about the overlap in text with published work.”
Response #2. As per the suggestion of the editor, we have revised different sections of manuscript to reduce text overlap with the mentioned previous studies and cite the utilized sources as follows:
•Abstract, Background section: ‘Infection with corona virus disease 2019 (COVID-19) could be complicated with coagulopathy and high risk of thromboembolic events.’ Revised as “Coagulopathy and thromboembolic events are among the complications of Corona Virus disease 2019 (COVID-19).”

	•Abstract, conclusion section: 'We found an abnormal pattern of coagulation parameters and association of advanced age and co-morbidities with a high rate of mortality in severe COVID-19 patients, which should be taken into consideration in their hospital management. Revised as "In this study, prolonged prothrombin time and high INR were found among severe and critical COVID-19 patients. Thrombocytopenia and prolonged APTT were dominant in COVID-19 patients older than 55 years. Thus, we recommend emphasis to be given for monitoring of platelet count, PT, APTT and INR in hospitalized COVID-19 patients management." •Discussion part first paragraph: 'COVID-19, which is caused by SARS-CoV-2, has spread across the globe. Although most patients recover within 1 to 3 weeks, COVID-19 has already caused >1.2 million deaths worldwide and more than 1400 in Ethiopia as of October 30,2020 according to WHO report (15). Dysregulation of coagulation produces a coagulopathy associated with hyper coagulability as evidenced by venous and arterial thrombosis and multi-organ dysfunction. Up to 20% of affected patients require hospitalization, and the mortality rate in such patients is high (16, 17). Coagulopathy is one of the most significant prognostic factors in patients with COVID-19 and is associated with increased mortality and admission to critical care (14, 18). Most commonly observed coagulopathy in patients hospitalized with COVID-19 (COVID-19-associated coagulopathy) is characterized by increased coagulation parameters like PT, APTT and INR levels (19, 20).' Revised as "The COVID-19 pandemic has brought major impact on health care globally. It has already caused >1.2 million deaths worldwide and more than 1400 in Ethiopia as of October 30,2020 according to WHO report(15). Coagulation abnormalities are indicated as frequent findings in COVID-19 patients and associated with poor prognosis and survival(7). Similarly, it is also indicated that coagulopathy which is resulted due to dysregulation of coagulation and associated with hypercoagulability as evidenced by venous and arterial thrombosis and multiorgan dysfunction(16); is one of the most significant prognostic factors in patients with COVID-19 and associated with increased hospitalization, admission to critical care, and mortality(14, 17-19). Previous studies indicated that coagulopathy in patients hospitalized with COVID-19 is characterized by increase in coagulation parameters such as PT, APTT and INR levels(20, 21)." •Discussion part 3rd Paragraph: "As for all coagulopathies, treatment of the underlying condition is paramount. Experience to date suggests that COVID-19 infection infrequently leads to bleeding despite abnormal coagulation parameters (23,24). Supportive care including blood product transfusion should be individualized (24, 25). Blood component therapy should not be instituted on the basis of laboratory results alone, but reserved for those who are bleeding requires an invasive procedure, or who are otherwise at high risk for bleeding complications (25)." Revised as "Treatment of the underlying condition is suggested to be paramount in coagulopathies. It is shown that bleeding is not common clinical manifestation in COVID-19 infections despite abnormal coagulation parameters (23,24). Along these, it is suggested that supportive care including blood product transfusion should be individualized in COVID -19 patients (25, 26). Laboratory findings alone should not be taken as basis for instituting blood transfusion therapy, rather it should be reserved for those who are bleeding, require an invasive procedure, or who are otherwise at high risk for bleeding complications(26, 27)" Discussion part 4th Paragraph: "Considerable evidence indicates that COVID-19 is associated with a hyper-coagulable state. Thus, despite anticoagulant thrombo-prophylaxis, different studies have reported that rates of venous thromboembolism (VTE) and arterial thrombosis ranging from 15% to 30% in critically ill patients with COVID-19 and ~7% in those admitted to medical wards (26-28). Clotting of access catheters, dialysis membranes, and extracorporeal circuits has also been reported. Furthermore, in patients dying from COVID-19, autopsy studies reveal unsuspected deep vein thrombosis and multiple thrombi in the vessels of the lungs, kidneys, and other organs (9, 27). These findings have prompted some clinicians to use treatment doses of heparin or low- molecular-weight heparin instead of prophylactic doses in critically ill COVID-19 patients (12,25, 29). Revised as "Evidences indicate that COVID-19 is associated with a hyper-coagulable state. Venous thromboembolism (VTE) and arterial thrombosis ranging from 15% to 30% were found in critically ill patients with COVID-19 and about 7% in those admitted to medical wards (28-30). Clotting is reported from different medical devices used,

deep vein thrombosis and multiple thrombi in the vessels of the lungs, kidneys and other organs from autopsy of patients died of Covid-19 (9, 29). These indicate clinicians to use therapeutic doses of heparin or low-molecular-weight heparin instead of prophylactic doses in critically ill COVID-19 patients (12, 26, 31).
•Conclusion part: “We recommend monitoring platelet count, PT, APTT and INR. Worsening of these parameters indicates progressive severity of COVID-19 infection and predicts that more aggressive critical care will be needed; experimental therapies for COVID-19 infection might be considered in this setting. Improvement of coagulation parameters along with improving clinical condition provides confidence that stepping down of aggressive treatment may be appropriate.”
Revised as “In this study, prolonged prothrombin time and high INR were found among severe and critical COVID-19 patients. Thrombocytopenia and prolonged APTT were dominant in COVID-19 patients older than 55 years. Thus, we recommend emphasis to be given for monitoring of platelet count, PT, APTT and INR in hospitalized COVID-19 patients management.
Comment #3. “Please state whether you validated the questionnaire prior to testing on study participants. Please provide details regarding the validation group within the methods section.”
Response #3. Not applicable. We did not used questionnaire in this study.
Comment #4. We note that you have indicated that data from this study are available upon request. PLOS only allows data to be available upon request if there are legal or ethical restrictions on sharing data publicly. For information on unacceptable data access restrictions, please see http://journals.plos.org/plosone/s/data-availability#loc-unacceptable-data-access-restrictions.
Response #4. All the available data were included in the manuscript.
Comment #5. ” PLOS requires an ORCID iD for the corresponding author in Editorial Manager on papers submitted after December 6th, 2016. Please ensure that you have an ORCID iD and that it is validated in Editorial Manager. To do this, go to ‘Update my Information’ (in the upper left-hand corner of the main menu), and click on the Fetch/Validate link next to the ORCID field. This will take you to the ORCID site and allow you to create a new iD or authenticate a pre-existing iD in Editorial Manager. Please see the following video for instructions on linking an ORCID iD to your Editorial Manager account: https://www.youtube.com/watch?v=_xcclfuvtxQ”
Response #5. “Already linked”
Comment #6. “Please amend the manuscript submission data (via Edit Submission) to include author Moges Wordofa.”
Response #6. Comment accepted and author included
Comment #7. “We note you have included a table to which you do not refer in the text of your manuscript. Please ensure that you refer to Table 1 in your text; if accepted, production will need this reference to link the reader to the Table.”
Response #7. Comment accepted and corrected accordingly.

Response to comments and suggestions inserted in the PDF format Manuscript
Comment # 1: in the abstract section. A prolonged (insert analytical parameter that was prolonged) was present in 48.8% of study subjects with COVID-19?
Response 1: Parameter inserted and and revised as “A prolonged prothrombin time was found among 46.8% of study subjects with COVID-19”
Comment # 2: In the abstract section. The comment to remove the interpretation and conclusion.
Response #2. Comment accepted and modified accordingly.
Comment #3. On Title. “Blood coagulation parameter abnormalities among in hospitalized patients with confirmed COVID-19 in Ethiopia”
Response #3: Accepted and modified as: “Blood coagulation parameter abnormalities in hospitalized patients with confirmed COVID-19 in Ethiopia”
Comment#4: in the abstract, method part: ‘…were estimated by auto analyzer.” ‘Which parameter?’.
Response to #5. Although the comment was to indicate which parameter, since the parameter are already mentioned we perceived it as to mean which auto analyzer and inserted the specific analyzer used as_”…..HUMACLOT DUE PLUS coagulation analyzer (Wiesbaden, Germany)”
Comment #6. In the introduction part. “ ….WHO. Write out abbreviation in full the first time it is used”.

	Response #6. Corrected as suggested. …..World Health Organization(WHO). Comment #7. In the laboratory analysis part, "…HUMACLOT DUE PLUS.. Insert trademark symbol e.g. R or TM." Response #7. Accepted and modified as "…HUMACLOT DUE PLUS coagulation analyzer (Wiesbaden, Germany) Comment #8. In the laboratory analysis part, "…Beckman coulter DxH 600 automated hematology analyzer.. Insert trademark symbol e.g. R or TM." Response #8. Accepted and modified as "…Beckman coulter DxH 600 automated hematology analyzer Comment #9. "Thrombocytopenia and abnormal coagulation parameters (PT, APTT and INR) could be considered as important indicators of COVID-19 disease severity. This statement belongs in the discussion section of the article." Response # 9: Accepted and removed as suggested. Comment #10. In discussion part. 'Thrombocytopenia, defined as platelet count less than 100×10^9 cells per L were independently associated with severity. Insert reference.' Response #10: Comment accepted; reference inserted as suggested. "Thrombocytopenia, defined as platelet count less than 100×10^9cells/L were independently associated with COVID-19 severity(34)" Comment 11. Discussion Part. "As many studies reported that the coagulopathy associated with COVID-19 is characterized by thrombocytopenia, prolongation of the prothrombin time, high levels of D-dimer, and elevated levels of fibrinogen, factor VIII, and von Willebrand factor. Insert reference" Response #11. Comment accepted; reference inserted as suggested. "Many studies reported that coagulopathy associated with COVID-19 is characterized by thrombocytopenia, prolongation of the prothrombin time, high levels of D-dimer, and elevated levels of fibrinogen, factor VIII, and von Willebrand factor(3, 11, 16)." Comment #12. Conclusion part. "We recommend monitoring platelet count, PT, APTT and INR. ...in patients hospitalized COVID-19 patients. Response #12. Comment accepted and modified as "We recommend monitoring platelet count, PT, APTT and INR in hospitalized COVID-19 patients." Looking forward to hearing from you. Thank you again for your consideration! Sincerely, Shambel Araya (BSc, MSc) Corresponding author
Additional Information:	
Question	**Response**
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NO authors have competing interests Enter: *The authors have declared that no competing interests exist.* **Authors with competing interests** Enter competing interest details beginning with this statement: *I have read the journal's policy and the authors of this manuscript have the following competing interests: [insert competing interests here]* * typeset	
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Format for specific study types **Human Subject Research (involving human participants and/or tissue)** • Give the name of the institutional review board or ethics committee that approved the study • Include the approval number and/or a statement indicating approval of this research • Indicate the form of consent obtained (written/oral) or the reason that consent was not obtained (e.g. the data were analyzed anonymously) **Animal Research (involving vertebrate animals, embryos or tissues)** • Provide the name of the Institutional Animal Care and Use Committee (IACUC) or other relevant ethics board that reviewed the study protocol, and indicate whether they approved this research or granted a formal waiver of ethical approval • Include an approval number if one was obtained • If the study involved *non-human primates*, add *additional details* about animal welfare and steps taken to ameliorate suffering • If anesthesia, euthanasia, or any kind of animal sacrifice is part of the study, include briefly which substances and/or methods were applied **Field Research** Include the following details if this study involves the collection of plant, animal, or other materials from a natural setting: • Field permit number • Name of the institution or relevant body that granted permission	
Data Availability Authors are required to make all data underlying the findings described fully available, without restriction, and from the time of publication. PLOS allows rare exceptions to address legal and ethical concerns. See the PLOS Data Policy and FAQ for detailed information.	Yes - all data are fully available without restriction

A Data Availability Statement describing where the data can be found is required at submission. Your answers to this question constitute the Data Availability Statement and **will be published in the article**, if accepted. **Important:** Stating 'data available on request from the author' is not sufficient. If your data are only available upon request, select 'No' for the first question and explain your exceptional situation in the text box. Do the authors confirm that all data underlying the findings described in their manuscript are fully available without restriction?	
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and contact information or URL). • This text is appropriate if the data are owned by a third party and authors do not have permission to share the data. * typeset	
Additional data availability information:	

Blood coagulation parameter abnormalities in hospitalized patients with confirmed COVID-19 in Ethiopia

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Abstract

Background: Coagulopathy and thromboembolic events are among the complications of Corona Virus disease 2019 (COVID-19). Thus, abnormal coagulation profiles in COVID-19 patients are taken as important prognostic factors of COVID-19 disease severity. The aim of this study was to analyze coagulation profiles of hospitalized COVID-19 patients in Addis Ababa, Ethiopia. **Methods**: This cross-sectional study was conducted among 455 Covid-19 patients admitted at Millennium COVID-19 treatment center, Addis Ababa, Ethiopia from July 1- October 23, 2020. Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT) and International normalized ratio (INR) were estimated by HUMACLOT DUE PLUS coagulation analyzer (Wiesbaden, Germany). In all tests, $p<0.05$ was defined as statistically significant.

Result: A prolonged prothrombin time was found among 46.8% of study subjects with COVID-19. Prolonged prothrombin time and high INR were seen among 53.3% severe and 51% critical patients with COVID-19 manifestation. Thrombocytopenia was detected in 22.1% of COVID-19 patients. 50.5% and 51.3% of COVID-19 patients aged older than 55 years had thrombocytopenia and prolonged APTT respectively.

Conclusion:
In this study, prolonged prothrombin time and high INR were found among severe and critical COVID-19 patients. Thrombocytopenia and prolonged APTT were dominant in COVID-19 patients older than 55 years. Thus, we recommend emphasis to be given for monitoring of platelet count, PT, APTT and INR in hospitalized COVID-19 patients management.

Key words: COVID-19, Prothrombin time, activated partial thromboplastin time, international normalized ratio, Platelet, Addis Ababa, Ethiopia.

Introduction

Coronavirus disease 2019 (COVID-19) is caused by a novel beta corona virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)(1). COVID-19 has become a pandemic that has heavily affected the global population. As of November 8, 2020, there have been 49,578,590 confirmed cases of COVID-19 and 1,245,717 deaths, reported to World Health organization (WHO). Similarly, there have been 99,204 confirmed cases of COVID-19 with 1,518 deaths in Ethiopia(2).

The severity of COVID-19 varies considerably from asymptomatic to life threatening, lung injury being the main clinical manifestation. Most of the patients have a favorable prognosis, but some rapidly progress to severe and critical cases with respiratory distress syndrome, coagulation dysfunction and multiple organ failures (3, 4). Although the pathophysiology and the underlining mechanisms of clinical manifestations remain unclear, thrombo-inflammation and cytokine storm are clearly established components in Severe Acute Respiratory Distress Syndrome (SARS) of COVID-19(5-8).

Coagulopathy and abnormal coagulation profiles were indicated among the most significant markers of poor prognosis in COVID-19 patients (9-11). A retrospective cohort study conducted in Spain Madrid ~~showed~~, COVID-19 non-survivors had significantly lower prothrombin activity, abnormal coagulation parameters like prolonged PT, APTT, higher D- dimer and higher fibrinogen levels compared to survivors indicating coagulation parameters could be an efficient measure for ~~improving the clinical management and~~ predicting the prognosis of patients with SARS COV-2(7). Similarly, Long et al has reported that occurrence of coagulation dysfunction is more likely in severe and critically ill patients. The study also showed that D-dimer and prothrombin time could be considered as main indicators in predicting the mortality of COVID-

19 patients(3). Different studies also support that COVID-19 patients are at high risk of developing disseminated intravascular coagulation (12, 13).

It is also indicated that comparison of reports from various populations related to the clinical course, outcome of COVID-19 and blood coagulation profile in these patients are necessary to help the management and treatment of the disease (12, 14). Moreover, this routine coagulation parameter tests could be used as potential indicators for COVID-19 in individuals having typical clinical manifestations that would be inputs for prompt patient management especially in resource limited settings where the high-tech gold standard RT-PCR is not widely available, like Ethiopia. However, data on coagulation profiles among Ethiopian COVID-19 patients is scarce. Thus, the aim of this study was to find out the coagulation profile of COVID-19 patients admitted at Millennium COVID-19 treatment center, Addis Ababa, Ethiopia.

Methods

Ethical consideration: The study was approved by Addis Ababa University College of Health Sciences, department of Medical Laboratory Sciences research ethics review committee (DRERC/538/20/MLS) and it was in accordance with the principles of the Helsinki II declaration. Laboratory test results were communicated to the responsible clinicians working at the treatment center. Written informed consent was obtained from the study participants. All the information obtained from the study participants were kept confidential.

Study population

In this study, we have included 455 consecutive patients with confirmed SARS-CoV-2 infection and admitted to Millennium COVID-19 treatment center, Addis Ababa, Ethiopia from July 1-October 23, 2020. The treatment center is the first referral center of COVID-19 patients in

Ethiopia, since May 02, 2020. None of the study participants ~~was~~ ~~taking~~ anticoagulant medications before blood drawing. Diagnosis of SARS-CoV-2 infection was made ~~according to~~ real time PCR.

Sample collection and coagulation profile analysis

2.6. Laboratory Analysis

~~Eight milliliters of v~~enous blood ~~were~~ collected by professional nurses working in the treatment center: ~~five milliliters~~ in EDTA for platelet count, ~~three milliliters in~~ 3.2% sodium citrated anti-coagulated tube for analysis of coagulation parameters. The samples for coagulation tests were collected at hospital admission. The prothrombin time (PT), activated partial prothrombin time (APTT), and international normalized ratio (INR) were analyzed using HUMACLOT DUE PLUS® coagulation analyzer (Wiesbaden, Germany). Platelet count was performed using UniCel® DxH 800 Coulter®Cellular Analysis System (Beckman Coulter, Inc. 4300 N. Harbor Blvd. Fullerton, CA 92835). The coagulation parameters were compared with the manufacturer cut off normal range of PT = 11.7- 15 seconds, APTT = 23.8- 37.9 seconds, INR = 1.0- 1.2 and PLT= 159-386/µ.l. The coagulation parameters above the cut off range were considered as a prolonged time and thrombocytopenia in the case of lower than cut off value for platelet. All laboratory tests and its interpretation were done following the manufacturers' recommendation and standard operating procedures.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) software version 25.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Chi-square test was used to determine association

among categorical variables. The quantitative data were expressed as Mean ± SD. P value < 0.05 was considered as statistically significant.

Results

Socio-demographic and Clinical characteristics of Study participants

In this study, 455 patients diagnosed with COVID-19 were included. Among the study participants, 289 (63.5%) were males. The study participants were between the age of 4 and 90 years with a mean of 49.9 ±18.3 years. From the total 455 case, there were 297 mild cases, 90 severe cases, and 68 critical cases based on disease severity of COVID-19 (Table 1).

Table 1: Socio-demographic characteristics of study participants ~~Addis Ababa, Ethiopia, 2020~~

Variables		Frequency	Percent
Gender	Male	289	63.5%
	Female	166	36.5%
Age group	0-18 years	15	3.2%
	18-35 years	101	22.1%
	36-55 years	158	34.7%
	>55 years	181	39.7%
Disease severity	Moderate	297	65.2%
	Severe	90	19.8%
	Critical	68	15%

The median time from the disease onset to admission was 4 days (2-8 days). Severe and critical groups showed differences in sex ratio and age distribution. In severe and critical groups, majority were ~~males and elderly~~ (Table 2).

Table 2: Socio-demographic characteristics and disease severity of COVID-19 patients admitted to Millennium COVID-19 treatment center Addis Ababa, Ethiopia

Variables		Disease Severity			P-value
		Moderate, n (%)	Severe, n (%)	Critical, n (%)	
Age(year)	0-18, n= 15	10(66.7)	4(26.7)	1(6.7)	0.283
	18-35, n=101	65(64.35)	22(21.78)	14(13.8)	
	36-55, n=158	107(67.7)	31(19.6)	20(12.65)	
	>55, n=181	115(63.5)	33(18.2)	33(8.2)	
Sex, N=455	Male, n=289	187(64.7)	56(19.3)	46(15.9)	0.045
	Female, n=166	110(66.2)	34(20.4)	22(13.2)	

Magnitude of coagulation abnormalities

In this study, 209 COVID-19 patients (46%) showed prolonged PT and higher INR values. Among those patients with prolonged PT, 51.3% were above 55 years of age. Prolonged PT value ~~was found~~ among males (49.8%) than females (41%) and ~~it has a significant association with gender~~ (P = 0.045). Similarly, 51.4% and 53.3% of ICU (critical) and severe patients had prolonged PT values. Notably, prolonged APTT values were found among 43.1% of individuals, and from these 47%, 45% and 41% were among ICU (critical), severe and moderate patients, respectively. 57.2% of female patients had prolonged APTT; and 51.3% of patients aged older than 55 years had a prolonged APTT.

Thrombocytopenia was detected in 22.1% (101 out of 455)~~22.1% individuals~~. 50.5% (50 out of 99) patients aged older than 55 years had thrombocytopenia. ~~Thrombocytopenia~~ was higher among male (23.8%) than female (18%) ICU patients (Table 3).

Table 3: Coagulation parameters in patients with severe COVID-19 ~~according to different variables~~

Coagulation Parameters		***Variables***								
		Age				***Sex***		***Disease Severity***		
		0-18 n(%)	***19-35 n(%)***	***36-55 n(%)***	***>55 n(%)***	***Male n(%)***	***Female n(%)***	***Moderate n(%)***	***Severe n(%)***	***Critical n(%)***
PT	High n=213	9(4.2)	50(23.47)	61(28.6	93(43.6)	144(67.6)	69(32.4)	130(61)	48(22.5)	35(16.4)
	Normal n=220	6(2.7)	45(20.45)	89(40.4)	80(36.3)	131(59.5)	89(40.4)	149(67.7)	40(18.1)	31(14.1)
	Low=22	0	6(27.2)	8(36.3)	8(36.3)	14(63.6)	8(36.3)	18(81)	2(9)	2(9)
APTT	High=196	6(3)	46(23.4)	68(34.7)	76(38.77)	101(51.5)	95(48.5)	115(58.67)	41(21)	42(21.4)
	Normal n=193	6(3.1)	38(19.7)	70(36.2)	79(41)	136(70.4)	57(29.5)	137(71)	36(18.6)	21(10.8)
	Low n=66	3(4.5)	17(25.7)	20(30.3)	26(39.3)	52(78.7)	14(21)	45(68)	13(19.7)	5(7.5)
PLT	High n=65	4(6.1)	11(17)	24(37)	26(40)	43(66)	22(33.8)	39(60)	8(12.3)	8(12.3)
	Normal n=289	8(3)	70(24.2)	105(36.3)	105(36.3)	175(60.8)	114(39)	214(74)	44(15)	31(10.6)
	Low n= 101	3(2.9)	20(20)	28(27.7)	50(49.5)	69(69.70	30(30.3)	33(32)	38(37.6)	30(29.7)
INR	High n=210	9(4.2)	50(24.7)	60(28.5)	91(43.3)	141(67)	69(32.8)	127(60.4)	50(23.8)	33(15.7)
	Normal =224	5(2.2)	44(19.6)	93(41.5)	82(36.6)	115(51)	75(33.4)	113(50.4)	45(20)	32(14.2)
	Low n=21	1(4.7)	7(33.3)	5(23.8)	8(38)	14(66.6)	7(33.3)	15(71)	3(14.5)	3(14.5)

PLT=platelet; PT= prothrombin time; APTT=activated partial thromboplastin time; INR=international normalized ratio.

Discussion

The COVID-19 pandemic has brought major impact on health care globally. COVID-19 has already caused >1.2 million deaths worldwide and more than 1400 in Ethiopia as of October 30,2020 according to WHO report(15). Coagulation abnormalities are indicated as frequent findings in COVID-19 patients and associated with poor prognosis and survival(7). Similarly, it is also indicated that coagulopathy which is resulted due to dysregulation of coagulation and associated with hypercoagulability as evidenced by venous and arterial thrombosis and multiorgan dysfunction(16); is one of the most significant prognostic factors in patients with COVID-19 and is associated with increased hospitalization, admission to critical care, and mortality(14, 17-19). Previous studies indicated that coagulopathy in patients hospitalized with COVID-19 is characterized by increase in coagulation parameters such as PT, APTT and INR levels (20, 21).

Patients with serious infection are more likely to have COVID-19 associated coagulopathy than patients with a mild infection (21,22). In our study, prolonged PT, APTT an INR was found among severe and critical COVID-19 patients than moderate ones. Similarly, studies also reported that thrombotic complications are common among COVID-19 patients admitted to intensive care unit (ICU) (9.5%-47%)(22-24).

Treatment of the underlying condition is suggested to be paramount in coagulopathies. It is shown that bleeding is not common clinical manifestation in COVID-19 infections despite abnormal coagulation parameters (23,24). Along these, it is suggested that supportive care including blood product transfusion should be individualized in COVID -19 patients(25, 26). Laboratory findings alone should not be taken as basis for instituting blood transfusion therapy, rather it should be reserved for those who are bleeding, requires an invasive procedure, or who are otherwise at high risk for bleeding complications (26, 27).

Evidences indicate that COVID-19 is associated with a hyper-coagulable state. Venous thromboembolism (VTE) and arterial thrombosis ranging from 15% to 30% were found in critically ill patients with COVID-19 and about 7% in those admitted to medical wards (28-30). Clotting is reported from different medical devices used, deep vein thrombosis and multiple thrombi in the vessels of the lungs, kidneys and other organs from autopsy of patients died of Covid-19 (9, 29). These indicate clinicians to use therapeutic doses of heparin or low-molecular-weight heparin instead of prophylactic doses in critically ill COVID-19 patients (12, 26, 31). In the current study, thrombocytopenia was observed among males (23.8%) than females (19.8%) and older people (27.6%). Severe (42.68%) and critical (42%) patients also had thrombocytopenia and this was in line with studies conducted in different countries (20, 22, 32, 33). Thrombocytopenia, defined as platelet count less than 100×10^9 cells/L were independently associated with COVID-19 severity(34). Studies across suggested that routine coagulation tests can be considered as a significant marker to help clinicians assess prognosis and severity of patients with COVID-19. In critically ill patients, thrombocytopenia correlates with multi-organ failure and death, and a decline in platelet count, even in the absence of overt thrombocytopenia, portends a worse outcome (9, 12, 13). In patients who are not bleeding, there is no evidence that correction of laboratory parameters with blood products improves outcomes. Replacement might worsen disseminated thrombosis and further deplete scarce blood products (28, 35).

Many studies reported that coagulopathy associated with COVID-19 is characterized by thrombocytopenia, prolongation of the prothrombin time, high levels of D-dimer, and elevated levels of fibrinogen, factor VIII, and von Willebrand factor (3, 11, 16). The degree of coagulation abnormalities correlates with disease severity and predict the risk of thrombosis, the need for ventilator support, and mortality. COVID-19-associated coagulopathy is however

unique with a much decreased platelet count (9, 36-38) Patients with critical COVID-19 infection and a cytokine storm have an extreme hyper-coagulable state. Even though the reason for this life-threatening condition is not known, this might be due to an uncontrolled hyper-inflammatory response without previous immunity (39, 40).

Conclusion: In this study, prolonged prothrombin time and high INR were found among severe and critical COVID-19 patients. Thrombocytopenia and prolonged APTT were dominant in COVID-19 patients older than 55 years. Thus, we recommend emphasis to be given for monitoring of platelet count, PT, APTT and INR in hospitalized COVID-19 patients management.

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Availability of data and material

All the available data are included in the manuscript.

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Blood coagulation parameter abnormalities ~~among~~ in hospitalized patients with confirmed COVID-19 in Ethiopia

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Abstract

Background: ~~Infection with~~ Coagulopathy and thromboembolic events are among the complications of C~~c~~orona V~~v~~irus disease 2019 (COVID-19). ~~could be complicated with coagulopathy and high risk of thromboembolic events. Currently~~ Thus, ~~a~~ abnormal coagulation profiles in COVID-19 patients are taken as ~~an~~ important prognostic factors of disease severity. The aim of this~~e~~ study was to analyz~~eing~~ coagulation profiles of ~~admitted~~ hospitalized COVID-19 patients~~, with COVID-19 from~~ in Addis Ababa, Ethiopia. **Methods**: This cross-sectional study was conducted among 455 Covid-19 patients admitted at Millennium COVID-19 treatment center, Addis Ababa, Ethiopia from July 1- October 23, 2020~~June 2020 to October 2020~~. Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT) and International normalized ratio (INR) were estimated by HUMACLOT DUE PLUS coagulation analyzer (Wiesbaden, Germany) ~~auto analyzer~~. In all tests, $p<0.05$ was defined as statistically significant. **Result**: A prolonged prothrombin time ~~has been reported in up to~~was found among 46.8% of study subjects with COVID-19. ~~clinical conditions.~~ Prolonged prothrombin time and high INR ~~was~~ were seen among 53.3% severe and 51% critical patients with COVID-19 manifestation. ~~An increase in coagulation parameters is the most significant change in coagulation parameters in severe COVID-19 patients, and progressively increasing values can be used as a prognostic parameter indicating a worse outcome in older peoples (93 patients aged >55 years had a coagulopathy).~~ Thrombocytopenia was detected in ~~around 101/455 (~~22.1%~~)~~ of ~~individuals~~COVID-19 patients. 50.5% and 51.3%. ~~individual's~~ of COVID-19 ~~aged~~patients aged older than 55 years had thrombocytopenia and ~~,~~prolonged APTT respectively.

Conclusion:

In this study, prolonged prothrombin time and high INR were found among severe and critical COVID-19 patients. Thrombocytopenia and prolonged APTT were dominant in COVID-19 patients older than 55 years. Thus, we recommend emphasis to be given for monitoring of platelet count, PT, APTT and INR in hospitalized COVID-19 patients management.

~~We found an abnormal pattern of coagulation parameters and association of advanced age and co-morbidities with a high rate of mortality in severe COVID-19 patients, which should be taken into consideration in their hospital management.~~

Key words: COVID-19, Prothrombin time, Activated partial thromboplastin time, international normalized ratio, Platelet, Addis Ababa, Ethiopia.

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Introduction

Coronavirus disease 2019 (COVID-19) is caused by a novel beta corona virus called ~~as~~ severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)(1). COVID-19 has become a pandemic that has heavily affected the global population. As of November 8,2020, there have been 49,578,590 confirmed cases of COVID-19 and 1,245,717 deaths, reported to World Health organization (WHO). Similarly, there have been 99,204 confirmed cases of COVID-19 with 1,518 deaths in Ethiopia(2).

The severity of COVID-19 varies considerably from asymptomatic to life threatening, lung injury being the main clinical manifestation. Most of the patients have a favorable prognosis, but some rapidly progress to severe and critical cases with respiratory distress syndrome, coagulation dysfunction and multiple organ failures(3, 4). Although the pathophysiology and the underlining mechanisms of clinical manifestations remain unclear, thrombo-inflammation and cytokine storm are clearly established components in Severe Acute Respiratory Distress Syndrome (SARS) of COVID-19(5-8).

Coagulopathy and abnormal coagulation ~~factors~~profiles were indicated among the most significant markers of poor prognosis in COVID-19 patients (9-11). A retrospective cohort study conducted in Spain Madrid showed COVID-19 non-survivors had significantly lower prothrombin activity, abnormal coagulation parameters like prolonged PT, APTT, higher D-dimer and ~~,~~ higher fibrinogen levels compared to survivors indicating coagulation parameters could be an efficient measure for improving the clinical management and predicting the prognosis of patients with SARS COV-2(7). Similarly, Long et al has reported that occurrence of coagulation dysfunction is more likely in severe and critically ill patients. The study also showed that D-dimer and prothrombin time could be considered as ~~a~~ main indicators in predicting the

mortality of COVID-19 patients(3). Different studies also support that COVID-19 patients ~~infected by COVID-19~~ are at high risk of developing disseminated intravascular coagulation (12, 13).

It is also indicated that comparison of ~~-~~reports from various populations related to the clinical course, outcome of COVID-19 and blood coagulation profile in these patients are necessary to help the management and treatment of the disease(12, 14). Moreover, this routine coagulation parameter tests could be used as potential indicators for COVID-19 in individuals having typical clinical manifestations that would be inputs for prompt patient management especially in resource limited settings where the high-tech gold standard RT-PCR is not widely available, like Ethiopia. However, data on coagulation profiles among Ethiopian COVID-19 patients is scarce. Thus, the aim of this study was to find out the coagulation profile of COVID-19 patients admitted at Millennium COVID-19 treatment center, Addis Ababa, Ethiopia.

Methods

Study population

In this study, we have included 455 consecutive patients with confirmed SARS-CoV-2 infection and admitted to Millennium COVID-19 treatment center, Addis Ababa, Ethiopia from July 1-October 23, 2020. The treatment center is the first referral center of COVID-19 patients in Ethiopia, since May 02, 2020. ~~Blood samples were collected by nurse professional in the treatment center and transported to Millennium COVID-19 treatment center.~~ None of the study participants was taking anticoagulant ~~drugs~~ medications before blood drawing. Diagnosis of SARS-CoV-2 infection ~~COVID-19~~ was made according to real time PCR.

Sample collection and coagulation profile analysis

2.6. Laboratory Analysis

Eight milliliters of venous blood ~~were~~ was collected by professional nurses working in the treatment center: five milliliters in EDTA for platelet count, three milliliters in 3.2% sodium citrated anti-coagulated tube for analysis of coagulation parameters. The samples for coagulation tests were collected at hospital admission. The prothrombin time (PT), activated partial prothrombin time (APTT), and international normalized ratio (INR) were analyzed using HUMACLOT DUE PLUS coagulation analyzer (Wiesbaden, Germany). Platelet count was performed using Beckman coulter DxH 600 automated hematology analyzer. The coagulation parameters were compared with the manufacturer cut off normal range of PT = 11.7- 15 seconds, APTT = 23.8- 37.9 seconds, INR = 1.0- 1.2 and PLT= 159-386/µ.l. The coagulation parameters above the cut off range were considered as a prolonged time and thrombocytopenia in the case of lower than cut off value for platelet. All laboratory tests and its interpretation were done following the manufacturers' recommendation and standard operating procedures.

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Ethical Consideration. The study was approved by Addis Ababa University College of H~~h~~ealth S~~s~~cience~~s~~, department of M~~m~~edical L~~l~~aboratory Sciences research ethics ~~and research~~review committee. Informed consent was taken from each of the study participants. Laboratory test results were communicated to the responsible clinicians working at the treatment center. All the information obtained from the study participants were kept confidential.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) ~~statistical~~ software ~~package~~ version 25.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Chi-square test was used to

determine association among categorical variables. The quantitative data were expressed as Mean ± SD. P-value < 0.05 was considered as statistically significant.

Results

Socio-demographic and Clinical characteristics of Study participants

In this study, 455 patients diagnosed with COVID-19 were included. Among the~~y~~ study participants, 289 (63.5%) were males. The study participants were between the age of 4 and ~~-~~90 years with a mean of 49.9 ±18.3 years. From the total 455 case, there were 297 m~~M~~ild cases, 90 severe cases, and 68 critical cases based on disease severity of COVID-19 ~~. These cases were divided into three groups based on the disease severity and the rate of critical cases was 15%~~(Table 1).

Table 1: Socio-demographic characteristics of study participants Addis Ababa, Ethiopia, 2020

Variables		Frequency	Percent
Gender	Male	289	63.5%
	Female	166	36.5%
Age group	0-18 years	15	3.2%
	18-35 years	101	22.1%
	36-55 years	158	34.7%
	>55 years	181	39.7%

Disease severity	Moderate	297	65.2%
	Severe	90	19.8%
	Critical	68	15%

The median time from the disease onset to admission was 4 days (2-8 days). Severe and critical groups showed ~~statistically significant~~ differences in sex ratio and age distribution. In severe and critical groups, majority were males and elderly (Table 2)~~1~~

Table 2: Socio-demographic characteristics and disease severity of COVID-19 patients admitted to Millennium COVID-19 treatment center Addis Ababa, Ethiopia

Variables		Disease Severity			P-value
		Moderate, n(%)	Severe, n(%)	Critical, n=68	
Age(year)	0-18, n= 15	10	4	1	0.283
	18-35, n=101	65	22	14	
	36-55, n=158	107	31	20	
	>55, n=181	115	33	33	
Sex, N=455	Male, n=289	187	56	46	0.045
	Female, n=166	110	34	22	

Magnitude of coagulation abnormalities

In this study, 209 COVID-19 patients (46%) showed prolonged PT and higher INR values. Among those patients with prolonged PT, 51.3% ~~are~~ were above ~~-~~55 years of age. Prolonged PT value was found among males (49.8%) than females (41%) and ~~prolonged PT~~it has a significant association with gender (P ~~-value~~ 0.045). Similarly, 51.4% and 53.3% of ICU (critical) and severe patients had ~~a~~ prolonged PT values. Notably, prolonged APTT values were found among ~~196/455~~43.1% of ~~-~~individuals, and from these 47%, 45% and 41% were ~~the distribution~~ among ICU (critical), ~~s~~Severe and moderate patients, respectively. 57.2% of ~~95/166~~ female patients had prolonged APTT; and 51.3% of patients aged older than 55 years had a prolonged APTT. ~~Thrombocytopenia and abnormal coagulation parameters (PT, APTT and INR) could be considered as important indicators of COVID-19 disease severity.~~

Thrombocytopenia was detected in 22.1%(101 out of 455)~~around 101/455 (~~22.1%~~)~~ ~~of~~ individuals. 50.5%(50 out of 99)~~/99~~ ~~(50.5%)~~ ~~individual's~~ patients aged older than 55 years had thrombocytopenia. Thrombocytopenia was higher among male (23.8%) ~~ICU patients~~ than female (18%) ICU patients.

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Table 3: Coagulation parameters in patients with severe COVID-19 according to different variables

Coagulation Parameters		***Variables***								
		Age				***Sex***		***Disease Severity***		
		0-18 n=15	***19-35 n=101***	***36-55 n=158***	***>55 n=181***	***Male n=289***	***Female n=166***	***Moderate n=297***	***Severe n=90***	***Critical n=68***
PT	High	9	50	61	93	144	69	130	48	35

	Normal	6	45	89	80	131	89	149	40	31
	Low	0	6	8	8	14	8	18	2	2
APTT	High	6	46	68	76	101	95	115	41	42
	Normal	6	38	70	79	136	57	137	36	21
	Low	3	17	20	26	52	14	45	13	5
PLT	High	4	11	24	26	43	22	39	8	8
	Normal	9	70	107	105	177	114	130	44	31
	Low	2	20	27	50	69	30	128	38	29
INR	High	8	52	60	92	140	68	96	49	33
	Normal	6	39	88	77	105	65	106	38	32
	Low	1	10	10	12	44	33	95	3	3

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158 PLT=platelet; PT= prothrombin time; APTT=activated partial thromboplastin time;
159 INR=international normalized ratio.

160 **Discussion**

161 The COVID-19 pandemic has brought major impact on health care globally. ~~, which is caused by~~
162 ~~SARS-CoV-2, has spread across the globe. Although most patients recover within 1 to 3 weeks,~~
163 COVID-19 has already caused >1.2 million deaths worldwide and more than 1400 in Ethiopia as
164 of October 30,2020 according to WHO report(15). Coagulation abnormalities are indicated as

frequent findings in COVID-19 patients and associated with poor prognosis and survival(7). ~~Dysregulation of coagulation produces a coagulopathy associated with hyper coagulability (7)as evidenced by venous and arterial thrombosis and multi organ dysfunction. Up to~~Similarly, it is also indicated that coagulopathy which is resulted due to dysregulation of coagulation and associated with hypercoagulability as evidenced by venous and arterial thrombosis and multiorgan dysfunction(16); is one of the most significant prognostic factors in patients with COVID-19 and is associated with increased hospitalization, admission to critical care, and mortality(14, 17-19) ~~20% of affected patients require hospitalization, and the mortality rate in such patients is high(18, 19). Coagulopathy is one of the most significant prognostic factors in patients with COVID-19 and is associated with increased mortality and admission to critical care(14, 17)~~. Previous studies indicated that ~~Most commonly observed~~ coagulopathy in patients hospitalized with COVID-19 ~~(COVID-19 associated coagulopathy)~~ is characterized by increase in ~~d~~ coagulation parameters ~~like~~ such as PT, APTT and INR levels(20, 21).

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Patients with ~~a~~ serious infection are more likely to have COVID-19 associated coagulopathy than patients with a mild infection (21,22). In our study, prolonged PT, APTT an INR was found among s~~S~~evere and critical COVID-19 patients than moderate ~~clinical manifestations~~ones. ~~and~~ Similarly, ~~many~~ studies also report~~ed~~ ~~–~~that thrombotic complications are common among COVID-19 patients admitted to ~~the~~ intensive care unit (ICU) ~~for COVID-19~~ (~~reported in~~ 9.5%-47%)(22-24).

~~As for all coagulopathies,~~ T~~t~~reatment of the underlying condition is suggested to be paramount in coagulopathies. It is shown that bleeding is not common clinical manifestation in ~~Experience to date suggests that~~ COVID-19 infections ~~infrequently leads to bleeding~~ despite abnormal coagulation parameters (23,24). ~~–~~Along these, it is suggested that s~~S~~upportive care including

blood product transfusion should be individualized in COVID -19 patients(25, 26). ~~Blood component therapy should not be instituted on the basis of~~ L~~l~~aboratory ~~results~~ findings alone should not be taken as basis for instituting blood transfusion therapy, ~~but~~ rather it should be reserved for those who are bleeding, require an invasive procedure, or who are otherwise at high risk for bleeding complications(26, 27).

~~Considerable~~ E~~evidence indicate~~vidences indicate~~s~~ that COVID-19 is associated with a hyper-coagulable state. ~~Thus, despite anticoagulant thrombo-prophylaxis, different studies have reported that rates of~~ V~~v~~enous thromboembolism (VTE) and arterial thrombosis ranging from 15% to 30% were found in critically ill patients with COVID-19 and ~~~~about 7% in those admitted to medical wards(28-30). Clotting is reported from different medical devices used, deep vein thrombosis and multiple thrombi in the vessels of the lungs, kidneysand other organs from autopsy of patients died of Covid-19 ~~Clotting of access catheters, dialysis membranes, and extracorporeal circuits has also been reported. Furthermore, in patients dying from COVID-19, autopsy studies reveal unsuspected deep vein thrombosis and multiple thrombi in the vessels of the lungs, kidneys, and other organs~~(9, 29). These ~~findings have prompted some clinicians~~indicate clinicians to use ~~treatment~~ therapeutic doses of heparin or low-molecular-weight heparin instead of prophylactic doses in critically ill COVID-19 patients(12, 26, 31).

In ~~this~~ the current study, thrombocytopenia was observed among males (23.8%) than ~~males~~females (19.8%) and older people~~s~~(27.6%). Severe (42.68%) and critical (42%) patients ~~had also~~also had ~~shown~~ thrombocytopenia and this was in line with studies conducted in different countries (20, 22, 32, 33). Thrombocytopenia, defined as platelet count less than 100×10^{9} cells/~~ per~~ L were independently associated with COVID-19 severity(34). Studies across suggested that routine coagulation tests can be considered as a significant marker to help

clinicians assess prognosis and severity of patients with COVID-19. In critically ill patients, thrombocytopenia correlates with multi-organ failure and death, and a decline in platelet count, even in the absence of overt thrombocytopenia, portends a worse outcome(9, 12, 13). In patients who are not bleeding, there is no evidence that correction of laboratory parameters with blood products improves outcomes. Replacement might worsen disseminated thrombosis and further deplete scarce blood products(28, 35).

~~As~~ M~~m~~any studies reported that ~~the~~ coagulopathy associated with COVID-19 is characterized by thrombocytopenia, prolongation of the prothrombin time, high levels of D-dimer, and elevated levels of fibrinogen, factor VIII, and von Willebrand factor(3, 11, 16). The ~~levels of coagulation~~degree of coagulation abnormalities ~~–~~correlate with disease severity and predict the risk of thrombosis, the need for ventilator support, and mortality. ~~Although the features of~~ COVID-19-associated coagulopathy ~~have been considered~~is however ~~–~~unique with a very decreased platelet count (9, 36-38)~~. However, in P~~patients with critical COVID-19 infection and a cytokine storm, have an ~~an~~ extreme hyper-coagulable state. ~~was reported.~~ Even though the reason for this life-threatening condition is not known, ~~but~~ this might be due to an uncontrolled hyper-inflammatory response without previous immunity(39, 40).

Conclusion: In this study, prolonged prothrombin time and high INR were found among severe and critical COVID-19 patients. Thrombocytopenia and prolonged APTT were dominant in COVID-19 patients older than 55 years. Thus, ~~We~~ we recommend emphasis to be given for monitoring of platelet count, PT, APTT and INR in hospitalized COVID-19 patients management. ~~Worsening of these parameters indicates progressive severity of COVID-19 infection and predicts that more aggressive critical care will be needed; experimental therapies~~

~~for COVID-19 infection might be considered in this setting. Improvement of coagulationparameters along with improving clinical condition provides confidence that stepping down of aggressive treatment may be appropriate~~

Ethical Clearance: Ethical clearance was obtained from Addis Ababa University, College of Health Science, Department of Medical Laboratory Sciences, Research ethics ~~ethical~~ review committee and it was in accordance with the principles of the Helsinki II declaration.

Consent for publication: Not applicable

Availability of data and material

~~The data sets used or analyzed during the current study are available from the corresponding author on reasonable request.~~All the available data were included in the manuscript.

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