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COLLEGE OF HEALTH AND MEDICAL SCIENCE

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PATTERNS OF ANTICOAULATION AND OUTCOME IN COVID -19 PATIENTS ADMITTED TO TASH ISOLATION CENTER , ADDIS ABABA ETHIOPIA, RETROSPECTIVE STUDY (June 2020-June 2021)

Research proposal to be submitted to Addis Ababa University, College Of Health And Medical Sciences, School Of Medicine in partial fulfillment of the requirement of certificate of internal medicine

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Abbreviations

AAU: Addis Ababa University

AIDS: Acquired immune deficiency syndrome

ARDS: acute respiratory distress syndrome

CNS: Central Nervous System

COVID -19: Coronavirus disease 2019

DOAC: direct oral anticoagulants

ESR: erythrocyte sedimentation rate

FMoH: Federal Ministry of Health

GI: Gastrointestinal

Hb: Hemoglobin

HIV: Human Immune-deficiency Virus

ICU: Intensive care unit

IDSA: infectious disease society of America

LDH: Lactate Dehydrogenase

LMWH: low molecular weight heparin

MRN: Medical Record Number

MV: mechanical ventilator

PTE: Pulmonary thromboembolism

SARS-CoV-2: Severe acute respiratory syndrome Coronavirus -2

TASH: Tikur Anbesa Specialized Hospital

UFH: unfractionated heparin

US: United States

VTE: Venous thromboembolism

WHO: World Health Organization

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ABSTRACT

Background

Earlier reports of high prevalence of thrombosis and related mortality has led to use of anticoagulants being part of the main treatment with varying results. Despite current large scale data showing credible benefits there are no studies done to determine the pattern of anticoagulation use and outcome in COVID patients in Ethiopia.

OBJECTIVE

To assess patterns of anticoagulation and outcome, of COVID-19 patients admitted to TASH isolation ward June2020- June 2021.

METHODOLOGY

Facility based retrospective cross-sectional study using secondary data analysis, was conducted. Records were retrieved using TASH, isolation log book. 126 patients were included. Data was analyzed using descriptive and binary logistic regression analysis

Result

Of the total 126 cases, Anticoagulation was used in 94 pts 74.6%. Therapeutic dose anticoagulation was used in 13(13.8%) pts of which 8 had severe disease. Prophylactic dose 79(84%), intermediate dose in two pts. UFH was used in 78(82.9%), LMWH 13(13.8%), DOAC 2(2.2%). only 58.8% of the patients received the full dose of prescribed anticoagulation. Pulmonary Thrombo-Embolism occurred in 9 pts of which 8 had severe disease and nearly half were on anticoagulation. Venous thrombosis occurred in 7 pts among those 5 had severe disease. Three out of the seven pts were on anticoagulation. In Hospital mortality was (n=14, 11.8%).

Conclusion

In conclusion, majority of patients received anticoagulation with UFH in prophylactic dosage. Anticoagulation use was not associated with diseases severity, in hospital mortality or 3 months outcome. Complications of anticoagulation were rare and minor. Complications were not associated with poor outcome.

CHAPTER ONE: INTRODUCTION

1.1 Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has quickly become the one of the direst international pandemic crises since the 1918 Spanish flu. Different viral factors resulted in emerging variants with different virulence factors that has allowed the pandemic to persist. Ethiopia was not an exception with recorded total cases of nearly half a million.

Infection referred to as coronavirus disease 2019 (COVID-19) primarily characterized by cough, fever, shortness of breath, muscle pain, loss of taste or smell, and/or no symptoms at all. Management of COVID-19 is similar to many viral respiratory illnesses in that therapy is largely supportive, but respiratory failure from acute respiratory distress syndrome (ARDS) is the leading cause of mortality.

Many patients with known or suspected COVID-19 have mild disease that does not warrant hospital-level care. For hospitalized patients many treatment options have been suggested, utilized, and are in trials for their effectiveness against SARS COV- 2, but the level of evidence varies between these therapies.

Earlier reports show high prevalence of pulmonary microvascular thrombosis and altered coagulation. Although less frequently reported arterial thrombosis were also observed largely in patients with predisposing comorbidities with alarming reports in young and healthy patients with COVID -19.The observation led to use of anticoagulants being part of the main treatment with varying results. The lack of high quality evidence regarding type dosage and net benefit of anticoagulation is a large area of interest. The National comprehensive COVID guideline issued in early 2020 indicated use of anticoagulation for prevention of VTE only in mechanically ventilated patients.

Large scale randomized trials have shown futility and possible harm of therapeutic coagulation in critical and severe illness. but intrim analysis indicated reduction of organ support free days. The data on anticoagulation of symptomatic outpatients is even sparse. How evere a small scale trial indicated no benefit to anticoagulation or antiplatelet treatments. Overall the potential harm or benefits of anticoagulation remain sparse and continue to be explored. Hardly any data is available in the practice and outcome of anticoagulation use in COVID -19 patients in Africa let alone Ethiopia

1.2 Statement of the problem

COVID 19 patients diagnosed in tertiary hospitals have a higher likelihood of comorbidities. Patients with multiple comorbidities have higher predisposition of developing severe disease, associated with high risk of thrombosis, related complications and mortality. The use of anticoagulation in this group is compounded by underlying factors that predispose to bleeding, thrombosis or both. To the authors knowledge there are no published studies regarding use of anticoagulants in this high risk groups.

1.3 Significance of the study

The study will identify patterns of anticoagulation use and their outcomes. It contributes in understanding clinical and other risk profiles of COVID patients, pattern of anticoagulation use, and associated impact on outcome especially in the presence of comorbidities. This initial study may serve as springboard for further study conducted on COVID to follow long term outcomes of patients which largely remains unknown at early stage.

CHAPTER TWO: LITRATURE REVIEW

The newly discovered beta coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has quickly become one of the most dire international pandemic with more than 120 million confirmed cases over the world. Ethiopia is one of the 5 African courtiers registering the highest COVID numbers with 261,580 confirmed cases and 4332 deaths (1)

Overall higher rates of infection in Africa are associated with high population density, urbanization, and transport connectivity, high volume of tourism and international trade, and high level of economic and political openness. Limited or poor access to healthcare are also associated with higher COVID-19 infection rates (26). Similarly earlier reports in Ethiopia showed COVID infection in youths, males and patients that had travel history of abroad were more infected with Coronavirus disease (27).

In addition to community transmission failure to segregate potentially infected patients has resulted in documented nosocomial outbreak in Durban, South Africa involving 80 staff members and 39 patients with mortality in 15 infected patients. In contrary strict application of infection prevention protocols meant rare nosocomial infections in high resource countries (29, 30).

Mild (no or mild pneumonia) was reported in 81 percent, Severe disease in in 14 percent and Critical disease (e.g., with respiratory failure, shock, or multi organ dysfunction) was reported in 5 percent. Comorbidities and other conditions that have been associated with severe illness and mortality include Cardiovascular disease, Older age, Diabetes mellitus, Hypertension, Chronic lung disease, Cancer (in particular hematologic malignancies, lung cancer, and metastatic disease), Chronic kidney disease, Obesity, Smoking (18-24)

In Africa Older people and individuals with chronic conditions such as HIV, tuberculosis and anemia experience severe forms COVID-19 leading to hospitalization and death. Similarly, high burden of chronic obstructive pulmonary disease, high prevalence of tobacco consumption and low levels of expenditure on health and low levels of global health security score contribute to COVID-19 related deaths (26). In Ethiopia Hypertension, age older than 25 years, and HIV/AIDS were significantly associated with symptomatic infection ;More than one-third of cases were recovered and overall case fatality rate was around two percent at the earlier period of the pandemic (27,28)

COVID-19 infection has been associated with increased risk of pulmonary embolism and strongly associated with in hospital mortality COVID-19 is associated with a hypercoagulable state associated with acute inflammatory changes and laboratory findings of altered coagulation parameters. The pathogenesis of these abnormalities is incompletely understood. Risk for venous thromboembolism (VTE) was markedly increased, especially during the early stages of the pandemic in patients in the intensive care unit (ICU), with early case series reporting prevalence of 25 to 43 percent in ICU

patients, often despite prophylactic-dose anticoagulation. Later studies have reported risks in the range of 5 to 10 percent in ICU patients and <5 percent in hospitalized medical patients. (32) Later studies done after standard use of steroids as treatment regimen reported much lower prevalence of thromboembolism. If the observed decrease is related with use of steroid resulting in decreased thrombosis remains to be confirmed.

Based on the observations several expert organizations have recommended prophylactic anticoagulation for patients admitted with covid-19, who do not have a contraindication to this treatment, to reduce the risk of thromboembolism. Multiple observational cohort studies have shown early initiation of prophylactic anticoagulation compared with no anticoagulation among patients admitted to hospital with covid-19 was associated with a decreased risk of 30 day mortality and no increased risk of serious bleeding events (33). In contrary later open label randomized trials failed to show net benefit of intermediate dose heparin(INSPIRE), and therapeutic dose rivaroxaban anticoagulation. The interim analysis of largest multiplatform randomized control trial on the subject (ACTIV-4, REMAP-CAP and ATTACC) indicates patients with moderate COVID-19 (defined as hospital admitted but not initially requiring ICU care)therapeutic anticoagulation with UFH on LMWH is superior to prophylactic dose regarding the reduction of primary endpoint of organ support free days to days 21. The same regimen has shown futility and possible harm in severe COVID-19 infection (receiving organ support or ICU care). The conners et al paper evaluating outcomes of in symptomatic COVID outpatients randomized to aspirin, apixaban 2.5 mg po bid / apixaban 5 mg po bid and placebo found no significant difference in outcome. (34,35). In conclusion the benefit of anticoagulation in COVID-19 has not been clearly established, the data on which agents to use and the optimal dosing strategy is ongoing. So far studies favor LMWH and UFH and discourages rivaroxaban.

In response to the Pandemic TASH the largest tertiary referral hospital in the country integrated isolation and COVID treatment services with continued routine care .Studies show (6.5%) TASH admissions in the 2010-2013 were due to DM with 21% of those having cardiovascular disease and older age. Hypertension and nephropathy contributed majority of coexisting illness (24). TASH is the Primary referral center for oncology/hemato-oncology patients with indicated annual incidence of 64,000 new cases annually.(24,25).For reasons mentioned above admitted patients to the hospital are expected to be at higher risk to COVID infection, severe disease, high risk of VTE and worse outcomes.

As the largest tertiary hospital and teaching center in the country treatment responses are expected to quickly follow the rapidly evolving COVID treatment protocols. The employment of such acquired understandings in line with the medical and economic profile of each patient ultimately determine better treatment outcomes.

Currently there is scarce data regarding COVID 19 infection in patients with multiple comorbidities and possibility of nosocomial acquired disease in hospitals providing integrated care in Ethiopia. The prevalence of VTE in this high risk patients, patterns of anticoagulation use and outcome are largely not studied.

CHAPTER THREE: OBJECTIVE

3.1 General Objective

- To assess patterns of anticoagulation and outcome, l of COVID-19 patients admitted to TASH isolation ward June2020- June 2021.

3.2 Specific Objectives

Primary objective

- To describe patterns of use, dosage and type of anticoagulation in TASH isolation center from June 2020 until June 2021
- To identify prevalence of VTE in COVID -19 patients admitted to TASH Isolation center during the study period

Secondary Objectives

- To describe the socio-demographic and clinical characteristics of COVID 19 patients admitted TASH Isolation during the study period center from June 2020 until June 2021
- To assess prevalence pf bleeding complications associated with anticoagulation use COVID-19 patients in TASH isolation center during the study period
- To evaluate outcome of hospitalized COVID-19 patients in TASH isolation center during the study period

CHAPTER FOUR: METHODOLOGY

4.1 Study Area

The study was conducted in TASH in Addis Ababa. TASH Isolation ward was established as a vital response to the evolving pandemic. The ward was established with 7 ward beds and 5 ICU beds but was later expanded .The ward is attended by 3 residents supervised by designated consultants with consultations available from all subspecialties in the hospital. Admitted patients are tested with qualitative COVID-19 PCR test at least once. Patients who have tested negative and was transferred to their respective wards. Patients who have tested positive are treated at TASH COVID center or transferred to assigned COVID treatment center.

4.2 Study Period

It's a one year study starting from June2020 until June 2021.

4.3 Study Design

Facility based retrospective cross-sectional study through secondary data analysis from the hospital logbook. Secondary data was collected using structured questionnaire using ODK software from the retrieved charts. Patients were also communicated through their contact address to complete the necessary data. Post discharge status was registered after the phone interview.

4.4 Source Population

All laboratory confirmed COVID 19 patients admitted to TASH isolation ward from June- June 2021.

4.5 Study Population

All patients admitted to TASH isolation ward from June- June 2021.

4.6 Sampling Technique & Sample Size Determination

NO sampling technique was required. All eligible cases during the study period was included.

4,7 Inclusión & Exclusion Criteria

Inclusion Criteria: pts. Admitted to isolation ward with presumed symptoms of COVID for which COVID PCR test is done and the result is positive and concurrent clinical data can be found

Exclusion Criteria: patients who have indeterminate results, unregistered results or incomplete patient record

4.8 Study Variables

Independent Variables:

- age,
- sex,
- underlying comorbidity,
- presence of symptoms at presentation,
- Severity of disease at presentation
- Oxygen requirement
- Anticoagulation use

  (1) treatment-dose anticoagulation, defined as ever having received treatment-dose anticoagulation (for prophylactic intent) while hospitalized;

  (2) prophylactic-dose anticoagulation, defined as only receiving prophylactic-dose anticoagulation while hospitalized;

  (3) No anticoagulation, defined as receiving neither treatment nor prophylactic anticoagulation while hospitalized and;

  (4) intermediate anticoagulation, defined as receiving doses between therapeutic and prophylactic regimens

- Treatment modalities used
  - Corticosteroid – dexamethasone
  - Empiric antibiotics

Dependent Variables:

- Primary outcome
  - VTE events including PTE and DVT
  - Death
  - Discharge
- Secondary outcome
  - Three month VTE events including PTE and VTE
  - Three month post discharge status
  - major and clinically relevant non-major bleeding

4.9 Data Collection Methods and Tools

Admitted patients in the time June 2020- June 2021 who fulfil the inclusion criteria was included in the study. COVID ward registry books was used to obtain patient ID Cards. A structured questionnaire was employed to collect data on demographics, clinical manifestations, comorbidities, laboratory values, inpatient medications, treatments (including invasive mechanical ventilation and kidney replacement therapy), and outcomes (including length of stay, discharge, readmission, and mortality, VTE and bleeding) of the study subjects. Supervised physician collected data from the chart. The questionnaire was tested, and revisions were made before data collection started. Additional data was collected from patient previous and/or current records and phone interview was done to assess post discharge 3 months status.

4.10 Data Processing and Analysis

The collected data was cleaned, coded and finally analyzed by SPSS version 26 statistical package. The results was expressed in frequency and proportions for categorical variables and mean and standard deviation for continuous variables with normal data and median and interquartile range for non‐normal data. The difference between proportions was assessed with the $\chi 2$ test and Fisher exact test for expected frequency <5 in univariate analysis was used to make a comparison between groups. The difference between means by the independent samples t‐test. A p value < .05 was considered statistically significant. To determine the predictor of disease severity (non-severe versus severe) and COVID-19 outcome (alive or dead during hospital stay) a binary logistic regression model was used independently. In the univariate analysis, variables with $p < 0.05$ were used to identify potential significant factors for the final models. Adjusted odds ratio with a 95% confidence interval and p-value < 0.05 was used as statistically significant.

4.12 Ethical Consideration

Ethical clearance was obtained from the Addis Ababa University College of Health and Medical sciences ethical Clearance Committee and official letter was written to TASH to secure permission.

4.13 Dissemination Plan

After completion of the result was copied and given to TASH Library, Department of internal medicine, pulmonary and critical care division and infectious diseases for possible publication in different journals and Magazines.

CHAPTER FIVE: RESULT

Based on the Isolation ward Log book data during the study period there was total admission of 644 admissions listed. Among these admitted 437 listed as having the positive COVID PCR test were selected. Patient records were retrieved and 261 were found from the listed records. 135 of retrieved records were excluded due to incomplete or absent records. Based on our inclusion and exclusion criteria 126 patients were eligible for our study.

Patient socio-demographic characteristics

The study population included patient's age in range from 14 to 95 years. The median age in the study was 46 years. Except the age group of 56-65 males comprise a larger number of participants. Majority of the patients were from Addis Ababa (58.7%) followed by Oromya (18.3%) and Amhara (11.9%).patients were admitted from every region of the country.

Clinical characteristics

Majority of the patients 78.5% of pts(n=99) are transferred from other wards. Emergency (N=18, 18.8%), orthopedics (N=16 16.1%),B5(11.8%) B8(10.4%) Contribute bulk of the patients. Transferred patients make up 76.4% of severe COVID patients. Average duration prior to transfer is 9.36 days CI (7.48-11.25) and median is 6 days. Duration of stay ranges from 1 day to 45 days.

Significant number (61.8%) of admitted patients had at least one symptom on admission. The remaining patients were admitted solely based on positive COVID PCR tests. Shortness of breath in 82.1%, cough in 78.2% ,Fever 64.1%, chest pain 56.4%, myalgia 32.1%, loss of taste 20.5%, vomiting/nausea 20.5%, Headache 16.7% were the most common presenting symptoms.

Supportive imaging investigations were done for 26 patients. Three patients had CT SCANS that showed bilateral peripheral GGO and 25 patients had chest x-ray with characteristic COVID bilateral lower lung opacities.

Out of the admitted patients 11.9% were critical, 29.4% severe, 13.5% had moderate disease and the remaining 45.2% had mild disease. Larger share of admitted patients (73.8% n=93) had at least one comorbidity; hypertension (23.8%), coexisting malignancy (19%), cardiac disease (16.9%) hematologic disorders(16.7%) diabetes (15.9%) were the five most common comorbidities.

Treatment

Oxygen therapy was provided for 71 (56.3%) pts. Nasal prongs were used in 33(46.6%)pts., Facemask with reservoir in 19(26.7%), facemask without reservoir in 12(9.5%), Non-invasive ventilation was used in 4pts, 3 pts required intubation and invasive ventilation. Vasopressors were used in 6 pts., Renal replacement Therapy was required in 2 pts. Steroids were administered to 85(67.4%), antibiotics 87 (67.9%), Asprin/ Clopidogril was given to 13(10.3%) pts.

Anticoagulation was used in 94 pts 74.6%. Therapeutic dose anticoagulation was used in 13(13.8%) pts of which 8 had severe disease. Prophylactic dose 79(84%), intermediate dose in two pts. UFH was used in 78(82.9%), LMWH 13(13.8%), DOAC 2(2.2%)

Outcome

The most common complications were seizure (n=5, 4%), ARDS (n=17,13.5%) both only in pts with severe disease. Shock (n=8, 6.3%) 5 due to septic shock and 3 had Hemorragic shock, cardiac arrest (n-=5), Acute Kidney Injury (n=12,9.5%), Severe electrolyte imbalance(n=4),Other complications(n= 10,7.9%)

Pulmonary Thrombo-Embolism occurred in 9 pts of which 8 had severe disease .4 were on anticoagulation . Venous thrombosis occurred in 7 pts of which 5 had severe disease. 3 out of the 7 pts were on anticoagulation. Bleeding occurred in 9 pts of which 7 had severe disease and were on anticoagulation. HIT was suspected in 3 pts all with severe disease and on UFH. Transfusion was required in 7 patients of which 5 was transfused for conditions related with other comorbidities while not on anticoagulation.

In Hospital mortality was (n=14, 11.8%), the remaining pts were discharged from the ward alive of which (34, 20.5%) were transferred back to ward(63, 38%) were transferred to other covid facility(15,9%). Cause of death was refractory septic shock in 4 pts, respiratory failure in 3 pts , Multiple Organ Failure In 2 pts and cardiac arrest in 3, massive PTE in 1 , massive cardio embolic stroke in 1 pt.

At discharge 45 (40.17%) pts were discharged with anticoagulation. Of which 9 were on therapeutic dose anticoagulation, four was for treatment of PTE, three for treatment of VTE and two for thrombosis elsewhere. The remaining 35 patients were discharged with prophylactic doses of anticoagulation. thirty patients (26.7%) were discharged with steroids.

Out of the 89 pts whose outcome at 3 months were assessed (n=75, 84.2%) were alive. 14 pts died. Only one pt was readmitted after discharge for due to bleeding the patient was previously discharged on therapeutic anticoagulation with Dual anti Platelet for ischemic heart disease with intra-cardiac thrombus.

Ability to self-care at 3 months versus before illness was worse in 9 pts(10.4%) of those assessed . The remaining patients reported better or same ability to self-care.1 patient is diagnosed with Long COVID; 55 yr old female with prior bronchiectasis and cor-pulmonale, and complains persistent fatigue.

A chi-square test result revealed a statistically significant difference in disease severity across patient groups based on Age, Glasgow coma scale at admission ($P<0.0001$), hypertension, diabetes , other chronic pulmonary disease ($p<0.05$).Independent t test showed a statistically significant difference in disease severity Respiratory rate at admission , oxygen saturation on room air($p<0.0001$)
A chi square test and fisher exact test indicated statistically significant difference in outcome across patient groups based on, presenting symptoms (cough, shortness of breath, chest pain), requirement of oxygen therapy antibiotic use, pulmonary thromboembolism ($p<0.05$). Severity of COVID, use of vasopressor and development of any complications (shock, seizure, AKI, ARDS) ($p<0.0001$). Independent t test showed a statistically significant difference in disease severity oxygen saturation on room air and on oxygen support ($p<0.05$)
Use of anticoagulation was not associated with in hospital mortality or 3 months outcome. Chi square test showed no association between anticoagulation use and PTE or VTE.

Significant difference in outcome at 3 months was observed based on, presenting symptoms (cough, shortness of breath, chest pain), requirement of oxygen therapy antibiotic use, pulmonary thromboembolism, transfusion requirement, suspected HIT ($p<0.05$). Severity of COVID, use of vasopressor and development of any complications (shock, seizure, AKI, ARDS) ($p<0.0001$). Independent t test showed a statistically significant difference in disease severity based on oxygen saturation on room air and on oxygen support, maximum oxygen flow requirement ($p<0.05$).

Only oxygen saturation on room air and with support were significantly associated with COVID-19 severity in the multivariable binary logistic regression. The odds of having severe disease compared with non-severe disease 8.8 times greater (AOR-=8.855,95 CI 2.434,32.208 P- VALUE 0.001) in the saturation below 90% group in the oxygen

saturation at room air and and 28 times greater on support (AOR=28.342, 95% CI1.329 ,304.337, p-value 0.032) respectively presence of malignancy (AOR = 4.64, 95% CI 1.32, 16.33, p-value 0.017).
The presence of ARDS and shock during admission, use of of facemask oxygen and severity of COVID were statistically significantly associated with outcome. Having severe covid was 29 times more likely to result in death greater (AOR-=29.34,95CI 1.12,67.208 P- VALUE 0.042). odd s of mortality increased by 7.4 times with requirement of facemask ventilation greater (AOR-=7.49,95CI 1.26-44 P- VALUE 0.026)b. complicating with ARDS had greater odds of mortality by 13.85 times (AOR-=13.85 95CI 2.75-69 P- VALUE 0.0001). group of patients who complicated with shock had 119 times more odds of mortality (AOR-=119 95CI 4.349-528.3 P- VALUE 0.005)

CHAPTER SIX: DISCUSSION

This study investigated the patterns of anticoagulation clinical manifestations, treatment, outcomes, and factors related to the severity and mortality of COVID 19. It was undertaken on patients who were admitted to TASH isolation center from June 2020 to June 2021 in the pre-vaccine era. Majority of participants were males with a median age of 46 years, nearly 30% over 65. Cough, SOB, chest pain, fever, and headaches were the commonest symptoms. Hypertension, malignancy, cardiac disease and diabetes were the most frequent comorbidities.
Overall, age ≥ 45, HTN , and SOB were found to be significant predictors of disease severity whereas older age (≥ 60), malignancy, SOB, and vomiting were significantly associated with in-hospital mortality.

Although definitive prevalence of bacterial infection couldn't be ascertained, greater than 85%, of patients received antibiotics in this study. This looks to be consequence of high prevalence of transferred patients from inpatient wards and the universal recommendation of antibiotics in moderate to critical disease conditions in the previous national guidelines. Steroids were given to 85% of the patients as recommended.

Anticoagulants were used in three fourth of the patients majority received prophylactic doses and using UFH. Therapeutic anticoagulation doses were used in suspected or proven venous/ pulmonary thromboembolism or in critical cases only. This varies from the initial international recommendations of using therapeutic anticoagulation in all hospital admitted patients. national guideline recommendation did not clarify the dosage to be used and only indicated use in mechanically ventilated paients. The decision seems to be threaded in fear of bleeding complications in ill patients with poly-pharmacy.the lack of d- dimer and fibrinogen studies that could be used to classify patients who could benefit from therapeutic anticoagulation may also have limited the use. In the later stages the uniform use of prophylactic anticoagulation was concurrent

with the developing understanding of anticoagulation use in COVID in different stages. Noticeably anticoagulation was avoided in hematologic malignancy patients instead pro-thrombotic agents like tranexamic acid were used to treat bleeding. Interesting finding was only 58.8% of the patients received the full dose of prescribed anticoagulation. Almost a fourth of the patients received less than a third of their prescribed anticoagulation. This may be due to high cost of medications and Scarcity. Only a quarter of the patients were given anticoagulation on discharge. Majority of those are patients who recovered from severe disease who were expected to be incumbent. Prophylactic dose anticoagulation was given to the majority. This is consistent with evolving understanding of anticoagulation use in recovering patients.

Only 7% and 6% of the total patients developed PTE or VTE during admission which might be underestimated due to lack of investigations. The low event rate is also compounded by small sample size. Intriguingly only half of this patients received anticoagulation and none had received the full recommended dose of anticoagulation. Yet the observations are too small to make associations.HIT was suspected in three patients and anticoagulation was switched. Transfusion due to bleeding was required for only one patient who was on anticoagulation

Nearly three fourth of the patients have at least one comorbidity. Hypertension, , coexisting malignancy, cardiac disease, hematologic disorders, diabetes were the five most common comorbidities .which varies significantly with other reports reflecting the high proportion of patients transferred from inpatient wards.

On Multivariate analysis patients with higher respiratory rate and lower oxygen saturation had more severe disease. No other significant associations were found among other clinical parameters. This may be due to inclusion of patients with multiple comorbidities and less representation of patients with mild disease On the other hand, COVID-19 in-hospital mortality was also associated with disease severity, requirement of face mask oxygen, and development of ARDS and Shock. Comorbidities were not associated with in hospital mortality. This may be due to smaller sample size.

This study is limited by relatively small scale, very low event rates the lack of confirmatory imaging .The cross-sectional nature of the study design made it difficult to make the cause-effect relationship between the various factors and disease severity or treatment outcome. Being a single-center and hospital-based study, the findings may not be generalizable.

In conclusion, older age, the presence of PTE, and shortness of breath were associated with severe COVID-19 and in-hospital mortality. Anticoagulation use was not associated with in- hospital mortality or 3 month outcome.

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Crosstab		sum	
Age Mean SD 53.9 (38-69.8)	<15	2	2%
	15-25	17	13%
	26-35	28	22%
	36-45	15	12%
	46-55	21	17%
	56-65	26	21%
	66-75	14	11%
	>75	3	2%
Sex of the participant	female	58	46%
	male	68	54%
Region	Addis Ababa	74	59%
	Amhara	15	12%
	Dredawa	2	2%
	Harari	1	1%
	Oromia	23	18%
	SNNPR	9	7%
	Somali	1	1%
	Tigray	1	1%
Was there any sign and/or symptom on admission?	No	48	38%
	Yes	78	62%
History of fever	No	17	13%
	Yes	50	40%
Cough	No	17	13%
	Yes	61	48%
Sore throat	No	68	54%
	Yes	10	8%
Muscle aches (myalgia)	No	53	42%
	Yes	25	20%
Vomiting/nausea	No	62	49%
	Yes	16	13%
Joint pain	No	70	56%
	Yes	8	6%
Abdominal pain	No	68	54%
	Yes	10	8%

Shortness of breathing	No	14	11%
	Yes	64	51%
Chest Pain	No	34	27%
	Yes	44	35%
Wheezing	No	74	59%
	Yes	4	3%
comoribidities			0%
Diabetes	No	106	84%
	Yes	20	16%
Hypertension	No	96	76%
	Yes	30	24%
Other chronic cardiac disease (not including HTN)	No	105	83%
	yes	1	1%
	Yes	20	16%
Asthma	No	121	96%
	Yes	5	4%
Tuberculosis	No	116	92%
	Yes	10	8%
Other chronic pulmonary disease	No	118	94%
	Yes	8	6%
Chronic kidney disease	No	117	93%
	Yes	9	7%
Chronic liver disease	No	121	96%
	Yes	5	4%
any malignancy	No	83	66%
	yes	43	34%
Coexisting Malignancy		24	19%
Hematologic malignancy		21	17%
Diagnosis of VTE at presentation	No	120	95%
	Yes	6	5%
Current or previous thromboembolic events	Arterial Thrombosis	7	6%
	Arterial Thrombosis & Pulmonary embolism	1	1%

	Pulmonary embolism	3	2%
	Venous thrombosis	6	5%
	Venous thrombosis & Pulmonary embolism	1	1%
	Other thrombosis	2	2%
	No event	106	84%
Corticosteroid	No	41	33%
	Yes	85	67%
Antibiotic	No	39	31%
	Yes	87	69%
Antiplatelet	No	113	90%
	Yes	13	10%
Systemic anticoagulation	No	32	25%
	Yes	94	75%
Dosage of anticoagulation	Therapeutic anticoagulation	13	10%
	Intermediate anticoagulation	2	2%
	Prophylactic anticoagulation	79	63%
Type of anticoagulation	warfarin	1	1%
	DOAC	2	2%
	LMWH	13	10%
	UFH	78	62%
Oxygen therapy?	No	55	44%
	Yes	71	56%
Inotropes/vasopressors?	no	121	96%
	Yes	6	5%
Renal replacement therapy (RRT) or dialysis?	no	124	98%
	Yes	2	2%
Shock	No	118	94%
	Yes	8	6%
Seizure	No	121	96%
	Yes	5	4%

9.6 Cardiac arrest	No	121	96%
	Yes	5	4%
9.7 Acute renal injury	No	114	90%
	Yes	12	10%
9.8 ARDS	No	109	87%
	Yes	17	13%
PTE	No	117	93%
	yes	9	7%
Venous thrombosis	No	119	94%
	yes	7	6%
Bleeding	No	117	93%
	yes	9	7%
transfusion	Yes	7	6%
	No	119	94%
	Yes	9	7%
Suspected HIT	No	117	93%
	Unknown	6	5%
	Yes	3	2%
Readmission	No	68	76%
	Yes	1	1%
Outcome from Isolation	Alive	112	89%
	Death	14	11%
Ability to self-care at discharge versus before illness		17	13%
	Better	24	19%
	Same as before illness	40	32%
	Unknown	1	1%
	Worse	44	35%
Outcome at 3 months	contacted	89	71%
	Alive	75	60%
	Death	14	11%
Ability to self-care at 3 months versus before illness		80	63%
	Better	16	13%
	same as before illness	1	1%
	Same as before illness	23	18%

	Worse	6	5%
medications at discharge		0	0%
Corticosteroid/dexamethasone 6 mg iv/d or higher and equivalent other corticosteroids		1	1%
	No	87	69%
	Unknown	9	7%
	Yes	29	23%
Antibiotic		0	0%
	No	80	63%
	Unknown	8	6%
	Yes	37	29%
Antiplatelet		0	0%
	No	100	79%
	Unknown	11	9%
	Yes	14	11%
Systemic anticoagulation		17	13%
	No	53	42%
	Yes	42	33%
	UFH	11	9%
	DOAC	7	6%
	LMWH	2	2%
	warfarin	1	1%
	Unknown	11	9%
Dosage of anticoagulation	Therapeutic anticoagulation	9	8%
	Intermediate anticoagulation	1	1%
	Prophylactic anticoagulation	34	30%
Readmission	Yes	1	1%
Readmission for PTE	yes	0	0%
Readmission for bleeding	Yes	1	
Respiratory rate Median – 24 IQR (20-28)			
Oxygen saturation on atm 92 IQR(85-93)			
GCS MEAN 14.74(14.09-14.95)			

Table 2: Demographic, comorbidity, and symptom characteristics; comparison based on disease severity and factors associated Severity

variable	P VALLUE	COR	COR 95% RANGE		P VALUE	AOR	AOR 95% CI range	
Age in years	<0.0001	1.043	1.019	1.067	0.474	1.021	0.965	1.079
Sex of the participant(1)	0.667	1.178	0.558	2.486				
Respiratory rate	<0.0001	1.222	1.113	1.338	0.05	1.034	0.999	1.071
Oxygen saturation on atmospheric Air	<0.0001	0.794	0.723	0.873	0.001			
Saturation<90	<0.0001	16.25	5.146	51.317	0.001	8.855	2.434	32.208
Saturation >90								
Oxygen saturation on support	0.02	0.785	0.612	1.007				
Saturation<90	0.032	5.895	1.162	29.906	0.032	28.342	1.329	304.337
GCS	<0.0001	0.342	0.138	0.851	0.830	0.904	0.361	2.269
Hypertension	0.022	2.692	1.156	6.271	0.302	3.147	0.357	27.762
Other chronic cardiac disease (not including HTN)	0.553	1.343	0.508	3.550	0.395	2.431	0.314	18.812
Diabetes	0.006	3.983	1.478	10.732	0.557	0.431	0.026	7.157
Other chronic pulmonary disease	0.020	7.114	1.369	36.982	0.102	9.340	0.639	136.434
Asthma	0.718	1.402	0.225	8.733				
Tuberculosis	0.601	1.423	0.379	5.350				
Chronic kidney disease	0.434	1.730	0.439	6.816				
Chronic liver disease	0.549	0.506	0.055	4.679				
Coexisting Malignancy	0.695	0.824	0.312	2.176				
Hematologic malignancy	0.553	1.343	0.508	3.550				
Diagnosis of VTE at presentation	0.966	1.038	0.182	5.915				
History of fever	0.443	1.562	0.500	4.881				
Loss of taste	0.062	0.046	0.944	9.828				

Headache	0.919	0.940	0.285	3.103				
Cough	0.291	0.556	0.187	1.653				
Seizures	0.999		0.000					
Sore throat	0.862	1.125	0.298	4.245				
Muscle aches (myalgia)	0.064							
Vomiting/nausea	0.430	1.561	0.516	4.724				
Shortness of breathing	0.170							
Chest Pain	0.332	1.565	0.634	3.862				
Bleeding / hemorrhage at presentation	0.999	0.000	0.000					

Table 3: Demographic, comorbidity, treatment and symptom characteristics; comparison based on outcome

variable	Chi p value	P VALLUE	COR	COR 95% RANGE		P value	AOR	AOR 95% CI range	
Age in years	0.411	0.129	1.025	0.993	1.057				
Sex of the participant(1)	0.381	0.752	1.196						
Hypertension	0.08								
Other chronic cardiac disease (not including HTN)		0.614	1.424						
Diabetes	0.168	0.178	2.400			0.999			
Coexisting Malignancy	0.336	0.341	1.840	0.524	6.463				
Hematologic malignancy	0.8	0.800	0.816	0.169	3.946				
HIV		0.285	2.500	0.465	13.429				
Diagnosis of VTE at presentation	0.657	0.660	1.646	0.178	15.200				
Cough	0.021	0.030	0.214	0.054	0.858	0.263	10.750	0.168	687.230
Shortness of breathing	0.0001	0.001	0.089	0.021	0.384	0.998			
Chest Pain	0.022	0.048	8.486	1.019	70.697	0.942	1.119	0.055	22.742
Muscle aches (myalgia)	0.111	0.142	0.204	0.024	1.706				
Vomiting/nausea	0.456	0.431	1.813	0.412	7.977				
Steroids during admission	0.117	0.135	3.250	0.692	15.264				
Antibiotic/in patient/	0.039	0.070	6.767	0.853	53.703	0.91	8.216	0.916	53.68
Systemic anticoagulation/in patient	0.658	0.464	1.707	0.407	7.155				
Dosage of anticoagulation		0.162	1.722	0.804	3.686				
Percent of doses received		0.001	0.966	0.946	0.986	0.997			
Max severity of COVID	0.0001	0.003	6.532	1.907	22.375	0.042	29.340	1.121	67.605
Oxygen therapy required	0.002	0.011	4.721	1.423	15.662				
Any complication	<0.0001					0.003			
Pulmonary thrombosis after	0.008	0.025	9.238	1.319	64.717	0.226			

admission									
Venous thrombosis after admission	0.130								
Bleeding after admission	0-07	0.583	1.343	0.468	3.852				
Transfusion required	0078					0.50			
Suspected HIT	0.078	0.736	1.334	0.249	7.140				

Table 4: Demographic, comorbidity, treatment and symptom characteristics; comparison based on 3 months outcome and factors associated outcome 3 month outcome

variable		P VALLUE	COR	COR 95% RANGE		P value	AOR	AOR 95% CI range	
Age in years	0.207	0.342	1.011	0.988	1.035				
Sex of the participant	0.381	0.383	0.684	0.291	1.605				
Length of hospital stay		0.001	0.855	0.779	0.937	0.020	0.727	0.555	0.952
Oxygen saturation on atmospheric air	0.005	0.040	2.857	1.050	7.772	0.124	12.823	0.499	329.782
Oxygen saturation on support	0.021	0.291	3.562	0.337	37.687	0.774			
Hypertension	0.375	0.092	0.328	0.090	1.198	0.078	0.001	0.000	2.118
Other chronic cardiac disease (not including HTN)	0.936	0.936	0.951	0.278	3.255				
Diabetes	0.138	0.589	1.380	0.430	4.433				
Other chronic pulmonary disease	0.301	0.342	0.355	0.042	3.012				
Coexisting Malignancy	0.054								
Hematologic malignancy	0.117	0.123	2.248	0.803	6.295				
Chronic liver disease	0.03	0.066	8.667	0.864	86.885	0.58			
Diagnosis of VTE at presentation	0.743	0.744	1.339	0.232	7.722				
Cough	0.01	0.014	0.206	0.058	0.731	0.376	2.184	0.071	115.117
Shortness of breathing	0.027	0.033	0.250	0.070	0.897	0.086	0.676	0.014	31.840
Chest Pain	0.008	0.011	4.600	1.417	14.937				
Steroids / during admission	0.01	0.013	3.818	1.322	11.030				
Systemic anticoagulation/ during admission	0.179	0.720	0.844	0.335	2.129				
Dosage of anticoagulation	0.117	0.022	4.714	1.254	17.717				
max severity		0.007	3.389	1.394	8.236	0.049	7.63	1.01	58.131

Oxygen therapy required	0.179	0.003	3.653	1.576	8.467				
O2 flow(max required)	0.093	0.010	1.189	1.043	1.356				
Interface/Facemask/Mask with reservoir		0.102	2.470	0.836	7.300	0.814	0.625	0.012	31.342
Venous thrombosis after admission	0.004	0.007	19.500	2.236	170.083	0.068			
Pulmonary thrombosis after admission	0.001	0.004	10.139	2.139	48.063	0.025	38.79	1.594	324.44
Transfusion required		0.122	0.234	0.037	1.475	0.044	0.012	0.000	0.888
Bleeding		0.021	2.825	1.170	6.818	0.176			