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Incidence of Thrombo-embolic conditions in covid 19 patients .

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(وَيَسْأَلُونَكَ عَنِ الرُّوحِ ۖ قُلِ الرُّوحُ مِنْ أَمْرِ رَبِّي وَمَا أُوتِيتُم مِّنَ الْعِلْمِ إِلَّا قَلِيلًا)

سورة الاسراء
اية ٨٥

الاهـــــــداء

اهدي هذا العمل الى روح والدي العزيز رحمه الله والى جنة الله في الارض امي الغالية والى سندي بعد أبي عمامي والى اخوتي والى جميع من تلقيت منهم النصحية والدعم من الاصدقاء والاقارب واساتذتي الافاضل

الـــشـــكـــر والـــتـــقـــديـــر

الشكر لله اولاً واشكر الاستاذ الدكتور شكر محمود ياسين

كان بمثابة الانسان الواعظ الحكيم الذي ساعدني كثيراً في انجاز

هذا البحث اسأل من الله ان يوفقه

وقبل ان انتهي من كلامي

اود ان اشكر كل شخص وقف معي وساندني على طول

مسيرتي الدراسية ممن تلقيت منهم العلم والمعرفة والنصح

واخص بالذكر (والدي)

List of Content

Abstract:

Corona virus infection has emerged as a global health crisis.The incidence of thromboembolism has been increasingly reported.Incidence of thromboembolic disease is reported to be high in COVID-19 patients ranging from cutaneous thrombosis to pulmonary embolism, stroke and coronary thrombosis.The role of thromboembolism and hypercoagulability may be due to over production of proinflammatory cytokines .we also discussed the pathophysiology and risk factor of thromboembolic disease and give a framwor for management of anticoagulant based on the current evidence.Our study reviewed the the incidence of venous and arterial thromboembolism in COVID-19 patients requiring hospitalization and receiving recommended anticoagulant strategies.

Introduction:

The severe acute respiratory distress syndrome-associated coronavirus-2 (SARS-CoV-2), causing Coronavirus disease 2019 (COVID-19), was initially identified in Wuhan, Hubei, China in December 2019 [1]. It has emerged as pandemic by the WorldHealth Organization in early March 2020, [2] and by early April there were over 1.5 million cases worldwide, with over 90,000 deaths[3].Progressive respiratory failure and a generalized coagulopathy are associated with the highest mortality[1,4,5]. The symptoms range from asymptomatic or mild constitutional symptoms to bilateral pneumonia, sepsis , endothelial dysfunction, coagulation activation, severe acute respiratory distress syndrome (ARDS) requiring hospitalization and intensive care unit (ICU) admission and multiorgan failure as a key features of severe COVID-19[6,7,8]. The role of thrombo- inflammation and endothelial injury in the pathogenesis of the disease is being increasingly recognized[9]. The mechanism is that coronavirus infection could activate multiple systemic coagulation and inflammatory responses. Host inflammatory responses result in increased proinflammatory cytokine production including tumor necrosis factor (TNF), Interleukin (IL)-6, IL-8 and IL-1B which leads to activation of coagulation and consumptive coagulopathy[10,11]. This overproduction of cytokine response may lead to multiorgan failure and eventually death in some patients[11]. Coagulopathy associated with COVID-19 may be explained by the ‘two way activation’ theory, as seen by thrombocytopenia in critically ill patients (TICP) and inflammatory and microthrombogenic responses that occur when endothelial insult takes place[12]. In addition to the factors mentioned above, these patients have additional risk factors for increased thrombosis most notable among those being hypoxia, and immobility which made worse by frequent use of prone positioning[13,14]. Several studies demonstrated a higher incidence of venous

thrombotic events in patients diagnosed with COVID-19 admitted to the intensive care unit (ICU) compared with those from historical data[15,16]. It has been premised that the high mortlity observed mong COVID-19 ptients may be due to unrecognized pulmonry embolism (PE) and pulmonary in situ thrombosis. Estimtes of the risk of arterial and in particular venous thromboembolic complictions still preliminry and depend on local diagnostic snd pharmacological preventivestra-tegies[17,18]. Since the beginning of the COVID-19 pandemic serious thrombotic complications have been reported in infected patients especially those that are critically ill[17]. Lung autopsies from patients who died of COVID-19 revealed diffuse alveolar edema, thrombosis, formation of hyaline membrane resembling an ARDS like pattern[14,19]. Several studies reported a wide range of thromboembolic complications including venous (PE, DVT) and arterial thrombosis. Microthrombosis in lungs noted as high as 80% in autopsy of fatal COVID -19[20]. The researches found that patients of of COVID-19 to have significant increases in fibrinogen degradation products(FDP), d-dimer levels and prolongation of prothrombin time (PT) with 71.4% meeting diagnostic criteria for DIC [21]. It must be noted that fibrinogen levels may increase initially as an acute phase reactant and this elevations may not necessarily be specific for COVID-19[22]. Reports of elevated d-dimer levels and fibrinogen are increasingly prevalent in COVID-19 affected patients leading many hospitals to routinely monitor these values. These elevations appear to correlate with increased levels of inflammatory markers and may be indicators for disease severity in addition to thrombotic risk[23,24]. A new information becomes available it appears increasingly important to routinely monitor platelet count, PT/aPTT, d-dimer, and fibrinogen to assist and managing thrombotic complications. It has been reported that d-dimer levels of 1.5 µg/mL for predicting venous thromboembolic events has a sensitivity and specificity rate of 85% and 88.5% respectively and a negative predictive value of

94.7%[25]. The findings suggest ultrasound is surveillance tool for early detection of patients at higher risk for thrombotic events [26]. The approach to management of anticoagulation in these patients remains unclear in absence of well conducted trials[9]. The Current strategies are heavily influenced by observational reports and empirical hospital protocols. In asymptomatic and mildly symptomatic patients do not require hospital admission, ambulation should continue to be the mainstay of thromboprophylaxis. It is advisable to prophylactic anticoagulation in admitted patients without clinical contraindications [17,27]. Unfractionated heparin and low molecular weight heparin (LMWH) have been successfully used in patients both prophylactically and therapeutically[28,29].Higher doses should be considered for those with higher risk patients (eg, obese, active malignancy, prolonged immobility or recent surgery). It must be noted a high incidence of VTE has been noted on patients on either prophylactic and therapeutic anticoagulation which makes routine surveillance extremely important[15,30]. ICU patients positive for COVID-19 with elevated d-dimer levels and/or clinico-radiological suspicion for thrombosis should be considered for therapeutic anticoagulation only after careful assessment of their bleeding risk. Choice of agent should be discussed with interdisciplinary team and agents selected based on availability, end organ function and administration techniques with minimization of nursing contact. Active surveillance for thrombosis should continue even after initiation of therapeutic anticoagulation as clot progression has been demonstrated in patients with therapeutic levels of anticoagulation[9]. Patients with COVID-19 who experience a major thromboembolic event such as PE without any additional risk factors should be considered to have had a provoked thromboembolic event and may need 3-6 months of anticoagulation[31]. Minor episodes of DVTs should continue anticoagulation therapy for 2-6 weeks post hospital discharge[32]. Antiviral therapies which may be utilized in certain COVID-19 patients are potent enzymes inhibitors and can slow

down metabolism and prolong duration of action of many medications including direct oral anticoagulants so caution should be exercised regarding their dosing [27,33]. Prophylactic anticoagulation should be considered in patients presenting with elevated d-dimer levels but with no suspicion or evidence of thrombosis[9]. Better understnding of COVID-19 thromboembolic risk will help to optimize diagnostic strategies and randomized controlled trials on VTE prevention[34]. The aim of study The present study aims to determine the incidence of thromboembolic events and complications in hospitalized COVID-19 patients.

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The articles review

The available recent articles related to incidence of thromboembolic events in patient with COVID-19 patients[34,35,36] have been discussed the rate of venous and arterial thrombosis in patients with confirmed COVID-19 requiring hospitalization.Theses researches investigated coagulation markers in COVID-19 patients during the course of disease and the diagnosis of thromboembolic events during their hospitalization. The outcome of venousthromboembolism (VTE) included pulmonary embolism (PE) and deep vein thrombosis (DVT).The outcome of arterial thrombosis included ischemic stroke,myocardial infrarction and limb ischemia.[34,35,36]. Patient's settings in theses studies including ICU or non-ICU settings. The following parameters were used age ,sex ,D-dimer ,fibrinogen level ,prothrombin time , platelet count, patient category (ICU and non-ICU)and type of anticoagulant (LMWH,UF)[34,35,36]. The diagnosis of COVID-19 in most studies required the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time polymerase chain reaction. They found that rate of

thromboembolic event in hospitalized COVID-19 patients was remarkable despite use of anticoagulant prophylaxis. These two studies [34,35] found that the incidence of DVT in confirmed COVID-19 patients was higher than incidence of PE in both ICU and non-ICU. While in this study [36], found that PE was higher than DVT on both ICU and non-ICU settings. They found that D-dimer and fibrinogen level in hospitalized patients which reflected the hypercoagulability state in. COVID-19 was elevated. The incidence of these thromboembolic events was multifactorial including corona virus induces cytokines that activates coagulation,fibrinolytic system is suppressed,platelets are activated by the cytokines and endothelial damage due to inflammation binds platelets and accelerates the thrombotic reaction. So due to increased risk of thromboembolism in hospitalized COVID-19 , the interventional and managment trials should should be conducted to improve the prevention , diagnosis and treatment of thrombotic complications in these patients. In addition , among these studies that used anticoagulant prophylaxis , the criteria for anticoagulant prophylaxis and the dosage are varied. It has been suggested that the use of higher prophylaxis dosages may improve the outcome of COVID-19 patientsThe administration of low molecular weight heparin during the earlier phases of disease may exert positive effect on the terms of thrombosis prevention and decreasing systemic and pulmonary inflammation and limiting viral invasionWe also found the incidence of thromboembolism in COVID-19 patients may influenced by other factor such as ethnicity showed that European have significantly higher incidence of VTE compared with Maori , Pacific Island and Asian populations[35].

Conclusion:

We observe coagulation alteration in COVID-19 patients indicating significant hypercoagulability.Systemic thrombosis is commonly associated wih critically ill COVID-19 patients and may lead to fatal outcomes if not diagnosed and and managed correctly.Thrombotic risk present despite antithrombotic treatment.VTE including DVT and PE was higher than arterial thromboembolism in these patients.These patients may even have higher D-dimer level.This could be arguments for prolongation of thromboprophylaxis and for increased dose in critically ill patients and patients with additional thrombotic risk factor.

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