

# Life-Threatening Spontaneous Hematoma in Unusual Sites in Patients with COVID-19 on Anticoagulant Therapy: A Case Series

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## Abstract

*Thromboembolic manifestations are a common phenomenon in patients affected by corona virus (SARS CoV-2). Recent studies have shown that patients with acute renal failure are also at a greater risk of venous and arterial thromboembolism, 15-30% in ICU, and 7% inpatient care. However, frequently unjudicial use of anticoagulants may develop severe life-threatening hematoma. In our hospital settings we had a dedicated COVID Unit with a Hemodialysis facility. Our Nephrology department had managed 381 patients being COVID positive along with renal impairment from March 2020 to January 2022. Among these patients, four patients developed spontaneous non traumatic hematoma in unusual sites. On admission all the patients received treatment according to our national guidelines for COVID-19. Cases: It is a retrospective analysis in a single-centered hospital. Four cases with confirmed COVID-19 with acute kidney injury and on anticoagulant therapy had developed sudden concealed bleeding. These patients had no previous history of anticoagulant therapy before admission. Case 1 developed hemorrhage in Right lower anterior paramedian deep parietal wall of abdomen,*

*Case 2 had hematoma in retroperitoneal space and in lower third of Iliopsoas, Case 3 developed hemorrhage in left cerebral hemisphere, Case 4 had Intramuscular Hematoma in left rectus abdominis. Out of these four patients two of them required Hemodialysis and one of them went into shock. All patients included were male. The mean age was 57±19.64years. All the four patients were initially managed conservatively with keen monitoring and with proper volume resuscitation, blood transfusion and discontinuation of the anticoagulants. Three of the patients survived with conservative management and one patient died due to sudden massive cardiac arrest. The use of therapeutic anticoagulant can increase the risk of bleeding in atypical sites and may exhibit higher patient death with COVID-19 if not identified at early stage. So a risk-benefit ratio of usage of anticoagulants should be kept in mind and further clinical trials needed to justify its random use in COVID-19.*

*Keywords: Spontaneous Hematoma, COVID-19 Pandemic, Anticoagulant Therapy, Covid 19 complication, Hematoma in unusual site.*

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## Introduction

COVID-19 is caused by the encapsulated, single-stranded RNA virus SARS-CoV-2. It has an alarming mortality rate and is easily spread via the air by droplets released by sick persons. On January 30, 2020, the World Health Organization labeled the epidemic a public health emergency of worldwide significance. It was announced in March of 2020 that the virus has reached Bangladesh. Since then, the pandemic has steadily increased in severity and afflicted population throughout the country. The intensity of sickness ranges from asymptomatic to severe, with a high percentage of individuals with clinically evident infection experiencing severe illness. Individuals with preexisting illnesses including diabetes, hypertension, or chronic kidney disease are more likely to have complications with COVID-19. Patients with chronic renal disease who are on anticoagulant treatment represent a subgroup of the general population who are prone to non-traumatic, spontaneous bleeding.

The corona virus prefers to infect the lung. The endothelial dysfunctions, thrombosis, and dysregulated inflammation typically observed in this unique disease have, however, drawn attention to a vasculocentric explanation of COVID-19. Anticoagulant medication is used with some COVID-19 patients to reduce the risk of pulmonary embolism and venous thrombosis.[1] Muscular hematomas and arterial bleeding are two new consequences of anticoagulant therapy in COVID-19 patients. In people with COVID19 infection, thromboembolic events have been observed to be as high as 21% with a death rate of 74%.[2] Anticoagulants are often used to avoid thrombosis in cases of severe COVID-19 infection, and it has been demonstrated that doing so lowers mortality.[3] However, due to the lack of clear guidelines up to this point, there is still considerable debate regarding the dosage, timing, and duration of anticoagulation as well as the best drug to use. Additionally, using anticoagulants carries some risk. The effects of bleeding complications might be slight, substantial, or even life-threatening. Our goal of this study was to unveil the risk of bleeding due to use of anticoagulants in COVID-19 patients.

### Methods:

It was a Retrospective study in the Department of Nephrology in Anwer Khan Modern Medical College Hospital(AKMMCH) from March 2020 to January 2022. Four cases selected by purposive sampling from 381 laboratory confirmed COVID-19 positive patients with renal impairment who developed spontaneous non traumatic hematoma in unusual sites.

### Case series

#### Case 1

A 69-yr old male patient, known case of diabetes mellitus, hypertension, ischemic heart disease and chronic kidney disease presented with symptoms of covid with positive RT-PCR for Covid-19. On admission his temperature was 100F , blood pressure 140/80mmHg, heart rate-96 beats/minute, respiratory rate-22 breaths/min,oxygen saturation(SPO2)- 92% with 10L of oxygen through N/ M and 80% in ambient air (Table I). Chest computed tomography(CT) on admission revealed ground glass opacities in bilateral peripheral lung fields approx. 80% lung involvement and the laboratory findings are given in Table-II.

**Table-I**

<i>Clinical presentation of the patients of our study</i>				
Variable	Case 1	Case 2	Case 3	Case 4
Age	69 years	65 years	32 years	63 years
Sex	Male	Male	Male	Male
Medical History	DM, HTN, IHD, CKD 3b	DM, HTN, ESRD	RPGN	DM, HTN, Post Kidney Transplant
Presenting complaints	Fever, SOB, Dry cough	Fever, Cough, SOB	Fever, SOB, Decreased Urine output, B/L leg swelling	Fever, cough, loose motion
COVID-19 Diagnostic test RT PCR	Positive	Positive	Positive	Positive
Pneumonia	Yes	Yes	Yes	Yes
Intubation required	No	No	No	Yes
Treatment of COVID-19	Tocilizumab, Enoxaparin, Methylprednisolone	Dexamethasone, Remdesivir, Enoxaparin	Favipiravir, Enoxaparin, Frusemide, Methylprednisolone Rivaroxaban	Favipiravir, Remdesivir, Enoxaparin, Hydrocortisone

**Table-II***Laboratory values at presentation*

Variable	Case 1	Case 2	Case 3	Case 4
Hb(g/dl)	12.9g/dl	9.90 g/dl	10.4 g/dl	14.0g/dl
ESR	—	20mm/hr	98mm/hr	65mm/hr
WBC(L/mm <sup>3</sup> )N/L	10k95%/3%	25K90%/4%	6.3K72%/22%	5K87%/7%
platelet	276K	111K	180K	160K
S Electrolytes	S.Na-140mmol/L K-4.8mmol/L	Na-127 mmol/L K-5.3mmol/L	Na-123 mmol/L K- 6.5 mmol/L	Na- 128mmol/L K-4.6mmol/L
S urea	52mg/dl	157 mg/dl	268mg/dl	—
S creatinine	2.7 mg/dl	7.3 mg/dl	25 mg/dl	1.4 mg/dl
SGPT	39 U/L	38U/L	15U/L	22U/L
S.LDH	385U/L	247U/L	—	210
PT with INR	16s/1.31	16s/1.66	14s/1.15	13s/1.13
D Dimer	0.3 mg/L	1.44 mg/L	0.32 mg/L	0.21mg/L
S.Ferritin	400ng/ml	58.2 ng/ml	1339 ng/ml	664 ng/ml
CRP	30mg/L	44mg/L	55.9mg/L	13 mg/L
IL 6	16pg/ml	29.7pg/ml	—	—
Troponin I	447 pg/ml	4543 pg/ml	—	—
Therapeutic	Enoxaparin	Enoxaparin 40IU	Enoxaparin 40IU	Enoxaparin 60IU
Anticoagulation	40IU BD/Day-7/	BD/Day 5/NSTEMI+	OD/ Day-4/ Covid 19	OD/
used/Dose/Day/In	NSTEMI + Cov-19	Covid 19	Hypercoagulability	Day-10/ Covid 19
dication	Hypercoagulability	Hypercoagulability		Hypercoagulability
Variable	Case 1	Case 2	Case 3	Case 4
Site of Bleeding/ Hematoma size	Right lower ant paramedian deep parietal wall	Hematoma in retroperitoneal space and in lower third of rectus abdominis	Hemorrhage in left cerbral hemisphere	Intramuscular Hematoma in left rectus abdominis
Day of Hospitalization corresponding to bleeding	Day 11	Day 9	Day 16	Day 10
Imaging used for diagnosis	Non contrast CT scan lower abdomen	Non Contrast CT of whole abdomen including pelvis	CT scan of Brain	Non contrast CT scan of lower abdomen
Treatment for Bleeding	PRBC and Conservative	PRBC and FFP Conservative	PRBC Conservative	PRBC Conservative

The patient was prescribed injectable Enoxaparin 40IU BID, Dexamethasone 5mg/ml intravenously along with antiviral drugs – Remdesivir (200 mg single dose followed by 100 mg).

Despite initial treatment and with 10L of oxygen supplementation, the patient's saturation decreased so he was shifted to ICU on 3<sup>rd</sup> day of admission. Hence Tocilizumab (8mg/kg) was administered in ICU and he

was kept with NIV support and did not require intubation. After 5 days of ICU stay his general condition improved gradually from acute respiratory failure and was shifted to cabin on day 8. To prevent thrombosis he received low molecular weight Heparin, Enoxaparin 40mg/0.4ml subcutaneously BID for 10 days.

On 11<sup>th</sup> day the patient complained of sudden pain in right lower abdomen. Initially it was dull aching pain

and had no radiation or had any relation with movement and subsided with analgesic. However his intensity of pain increased the following day. His blood pressure and heart rate were 110/80mmHg and 112 beats/min respectively. A noncontrast abdominal and pelvic CT was done which showed a hematoma (10cm X 4.5cm) in the right lower anterior paramedian deep parietal wall (figure-1). His other laboratory findings at the time of bleeding were included in Table-II.

The patient was managed conservatively and his Enoxaparin was stopped meanwhile. He received 3 units of packed red blood cell (PRBC) and 6 units of Fresh frozen plasma for 3 consecutive days with antibiotics and intravenous fluid. The Hematoma size did not increase in size and showed signs of regression and since patient's vitals were stable with conservative management he was discharged from the hospital on day 29.



**Figure 1:** CT scan of Lower Abdomen shows Large Heterogenous soft tissue density mass lesion along right lower anterior para median deep parietal wall.

### Case-2

A 65yrs old male, known case of diabetes mellitus, hypertension, was admitted with COVID-19 and was also diagnosed with Septicaemia and with acute left ventricular failure. On arrival at our hospital his vital signs- heart rate 100 beats/minute, blood pressure-110/70mmHg, temp-38.4 C, SPO<sub>2</sub>- 82% in ambient air, peripheral edema was 3+. Initial laboratory findings were given in Table II. The patient received SLED hemodialysis for first 3 consecutive days followed by every alternative day.

He received Antiviral Remdesivir (200mg loading dose followed by 100mg once daily for 5days), injectable

Enoxaparin 40IU once daily and injectable dexamethasone (7.5mg once daily). The patient general condition improved gradually and his oxygen saturation was maintained at 96% in room air.

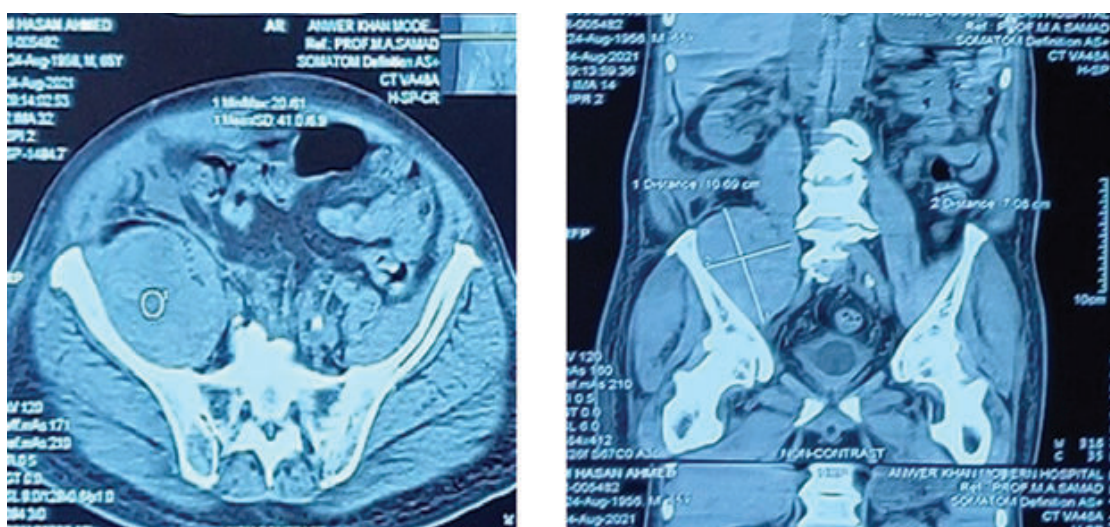
On Day 9 of admission suddenly patient complained of dragging pain and discomfort in right iliac region with radiation to right leg which subsided upon taking oral analgesics. However on the following day the patient was groaning with pain with decreased GCS level (Glasgow coma scale) E3V4M4 with acute urinary retention. On general examination his vital signs were- heart rate-112beats/min, blood pressure-130/80mmHg, SPO<sub>2</sub>- 98% in room air. On abdominal examination a lump of approx. 7cm X3cm was palpated on right iliac region with an extension to right inguinal ligament. There was slight bulging of abdomen on right side and local temperature was raised slightly. It was mild tender, firm, fixed. His right thigh was kept in flexed position. A differential diagnosis of Psoas abscess or appendicular lump were made and a consultation from General Surgeon were taken and was advised for conservative management.

Since the mass was slowly growing in size we decided to aspirate aseptically through Fine needle. However on syringe insertion frank blood came out so we carried out a Computed tomography of abdomen including pelvis which revealed hematoma in retroperitoneal space with an extension to the attachment to iliopsoas muscle (Figure 2).

### Case-3

A 32year old male patient normotensive, nondiabetic with no prior history of kidney disease got admitted with the complaints of respiratory distress, generalized body swelling and diminished urine output. He came out RT PCR positive for COVID-19 with acute renal failure. His vital signs were as follows- heart rate-78 beats/min, blood pressure-160/85mmHg, temperature-101F, oxygen saturation (SPO<sub>2</sub>)-88% with 12L of oxygen through rebreather mask, moderate peripheral edema, respiratory rate was 24 breaths/min. The laboratory values after admission given in Table II.

He received injectable Enoxaparin 40IU OD for 10days, injection Methylprednisolone (1000mg for 3days), tab Favipiravir (1600 mg for 5 days), Remdesivir (loading



**Figure 2:** CT abdomen: Large soft tissue density mass extending from retroperitoneal space to the attachment of iliopsoas muscle

dose 200mg on day 1 followed by 100mg once daily for 5days). The patient received acute hemodialysis with standard dosage of Heparin during dialysis.

On 14<sup>th</sup> day of admission he was discharged with Rivaroxaban 10mg once daily after being COVID negative. However after 2 days of discharge he revisited with convulsion and with right sided hemiparesis and poor GCS level. Immediate CT scan of brain was done which revealed left sided hematoma with midline shifting (Figure:3). The patient deteriorated over 24hrs and required intubation and ventilator support and was transferred to ICU. The laboratory values at the time of bleeding is given in Table-III.



**Figure 3:** CT scan of Brain: Left cerebral hemorrhage with midline shifting

Table III shows the laboratory values of the patients at the time of bleeding episode and the outcome of each patient

**Table-III**

<i>Laboratory values at the time of bleeding episode</i>				
Variable	Case 1	Case 2	Case 3	Case 4
CBC	Hb- 8.3 g/dl	7.2 g/dl	8.1 g/dl	11.3 g/dl
	Platelet- 239k	Platelet-90K	Platelet-121K	Platelet- 115K
S creatinine	1.7 mg/dl	6.2 mg/dl	6.4mg/dl	1.5mg/dl
PT with INR	16s/1.33	16s/1.31	14s/1.15	15s/1.43
APTT	36.8s	38s	—	36s
Prior History of bleeding	No	No	No	No
Trauma	No	No	No	No
Outcome	Discharged	Discharged	Discharged	Expired

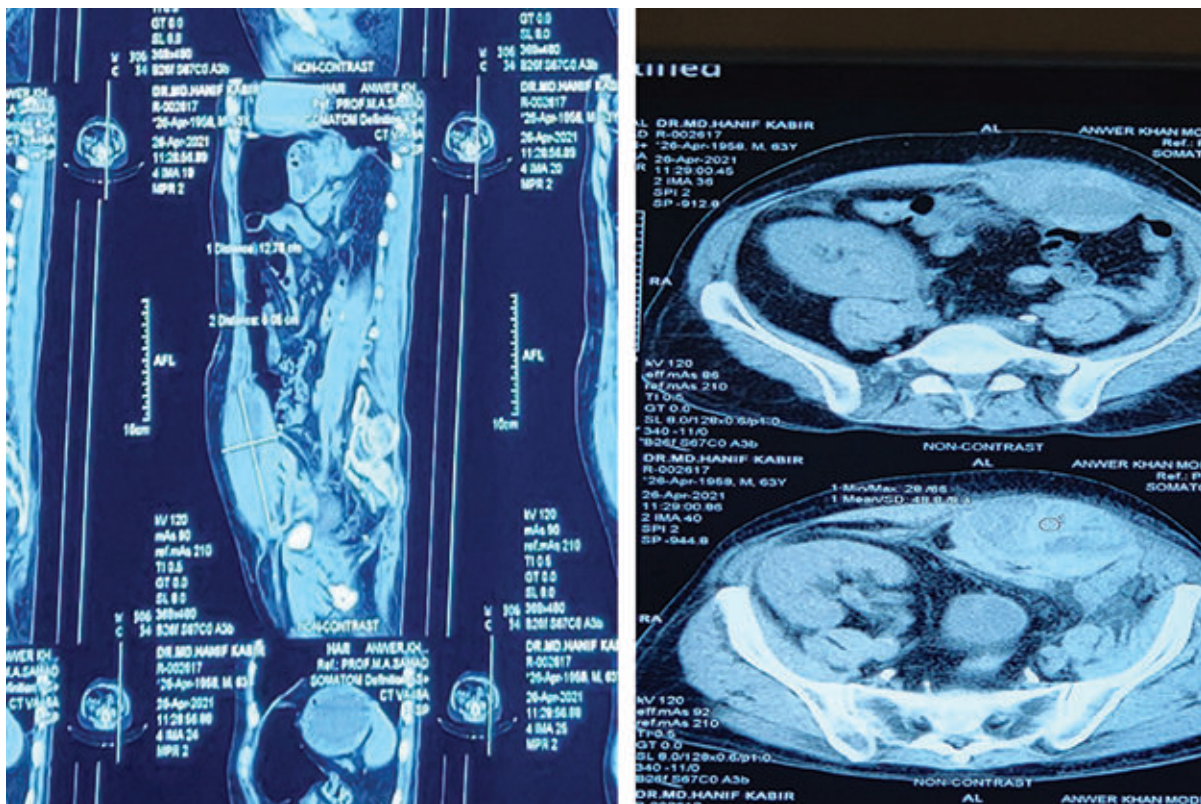
**Case-4**

This patient was a 63-year old man with hypertension, diabetes and post-renal transplant 19 years back got admitted with COVID-19. On admission the patient was oriented, afebrile and respiratory rate was 16 breaths/min and oxygen saturation of 96% in room air. Since the patient had excruciating cough he got admitted in hospital. HRCT chest revealed ground glass opacities involving multiple lung segment. Other laboratory findings are given in Table II and III.

The patient was on regular Prednisolone, mycophenolate mofetil and cyclosporine after transplant. In addition he received LMWH injectable Enoxaparin 60IU OD, Favipiravir and Remdesivir subsequently. His sputum culture revealed growth of *Kleibsellia sp* and according to sensitivity pattern antimicrobial broad spectrum therapy was given. The patient’s vitals were stable throughout the duration except oxygen was required at 8L/min which maintained oxygen saturation at 97%.

On 12<sup>th</sup> day of admission, the patient complained of mild pain in left lower abdomen which decreased upon taking oral analgesics. On palpation a lump was felt in left paramedian region extending to iliac fossa, whereas in right transplanted kidney was palpable. A noncontrast computed tomography of whole abdomen revealed intramuscular hematoma in left rectus abdominis (Figure:4). The patient was clinically stable and size of hematoma did not increased over 2 days.

On 14<sup>th</sup> day of admission and 3<sup>rd</sup> day of hematoma formation around late midnight he complained severe pain in left iliac region for which opioid analgesic was given which subsided the pain. Around early morning the following day he became restless with pain so he was shifted to surgery unit for urgent surgical exploration. However on the way of shifting he developed sudden shock and was transferred to intensive care unit and was kept on ventilator support where he developed sudden cardiac arrest and upon 40mins of CPR he failed to revive and was declared death.



**Figure 4:** Intramuscular Hematoma in Left rectus abdominis

**Discussion:**

Hyper coagulation and thrombosis are common in COVID-19 patients and can occur in different areas of body leading to death in some cases. For this reason guidelines recommend thromboprophylaxis with anticoagulant in all patients hospitalized with COVID-19. However, less frequently it can result in major bleeding in unusual sites. Worldwide such unusual bleeding manifestations due to use of low-molecular weight heparin in COVID-19 patients had also been notified and similar cases were reported in different journals<sup>4,5</sup>.

Here we have presented four such cases of hematoma in unusual sites that we observed among 381 COVID-19 positive with renal impaired patients who had received anticoagulant particularly LMWH. Therefore we should also be cautious about these rare and serious complications of spontaneous bleeding so that they can be detected earlier and manage accordingly.

The understanding of COVID-19, a novel disease with systemic involvement, is constantly expanding. The actions of the virus are defined as typical events resulting in vascular injury and deregulation of the immune response, often known as “cytokine storms”. [1,6] According to clinical research, people with COVID-19 have elevated levels of fibrinogen, fibrin-degradation products, and D-dimer, and these increases have been linked to the severity of the disease. [6] Numerous clinical studies in COVID-19 patients have demonstrated that venous and arterial thromboembolisms increase the risk of morbidity and mortality, indicating that early anticoagulant therapy administration is crucial to avert these events. [6] On the other hand, recent research has indicated that muscle hematomas or arterial bleeding could result after anticoagulant medication<sup>7,8</sup>.

Retroperitoneal, adrenal gland, and cerebral hemorrhagic problems have also been reported<sup>9</sup>. A COVID-19 patient with an immediate onset of hemoptysis and alveolar bleeding was described by Peys et al. [10]. But only a small number of studies have mentioned spontaneous hemothorax as a potential side effect of anticoagulant therapy in COVID-19 patients<sup>11</sup>.

The attachment of the SARS-CoV-2 virus to the endothelial cells' angiotensin-2 receptor, which results in the production of proinflammatory cytokines, endothelial dysfunction, and systemic inflammation, has

been hypothesized to be the cause of the risk of developing thrombosis in COVID-19. Anticoagulant administration has been linked to bleeding events even if it may be helpful in COVID-19 infection. According to a research by Al-Samkari et al. [12], major bleeding rates (WHO Grade 3-4) were 2.3%, with overall bleeding incidence rates in COVID-19 patients being 4.8% and 7.6% in non-critically ill and critically ill patients, respectively. Recently, several papers have reported retroperitoneal hemorrhage as a COVID-19 complication with a similar presentation.

Hemostasis is often achieved by stopping or altering anticoagulant treatment and volume resuscitation with fluids and blood products. Small hematomas with minimal symptoms that don't require blood transfusions such as any small retroperitoneal bleeding can be managed conservatively. For patients with severe abdominal pressure symptoms and hemodynamic instability, additional therapy options such surgical exploration combined with hematoma evacuation or selective arterial embolization using interventional radiology are reserved. [13] Concerning the treatment of hematomas, there is no clear agreement. A better result would come from early discovery and rapid intervention. We hypothesize that prompt treatment will lessen the hematoma's growth and cut down on the time the surrounding tissues are compressed. Since in our setting, in Covid period, there were no facilities of selective arterial embolization or routine surgical exploration, we had to manage all the cases conservatively.

**Conclusion:**

The use of therapeutic anticoagulant can increase the risk of bleeding in atypical sites and may exhibit higher patient death with COVID-19 if not identified at early stage. So a risk-benefit ratio of usage of anticoagulants should be kept in mind and further prospective case control clinical trials needed to justify its random use in COVID-19.

**Conflict of interest:** None declared.

**References:**

1. Sakr Y, Giovini M, Leone M, et al. Pulmonary embolism in patients with coronavirus disease-2019 (COVID-19) pneumonia: a narrative review. *Ann Intensive Care* 2020;10: 124–213.

2. Malas MB, Naazie IN, Elsayed N, Mathlouthi A, Marmor R, Clary B. Thromboembolism risk of COVID-19 is high and associated with a higher risk of mortality: a systematic review and meta-analysis. *EClinicalMedicine*. 2020;29:100639.
3. Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost* 2020;18:1094–9.
4. Al Jumaan MA, Alahmari N, Elnour A, Alshahrani S, Mattoo A, Alghamdi M. Post-COVID-19 non-traumatic iliopsoas hematoma: A case report. *J Taibah Univ Med Sci*. 2023 Feb;18(1):61-64. doi: 10.1016/j.jtumed.2022.07.001. Epub 2022 Jul 19. PMID: 35875171; PMCID: PMC9293483.
5. Elikowski W, Fertala N, Zawodna-Marszałek M, Karoń J, Skrzywanek P, Mozer-Lisewska I, Szczepaniak P, Łazowski S, Źytkiewicz M. Retroperitoneal hematoma in COVID-19 patients - case series. *Pol Merkur Lekarski*. 2022 Apr 19;50(296):118-123. PMID: 35436275.
6. Kaur S, Tripathi DM, Yadav A. The enigma of endothelium in COVID-19. *Front Physiol* 2020;11:989.
7. Mattioli M, Benfaremo D, Fustini E, et al. Atypical spontaneous hematomas in a patient with severe coronavirus disease 2019 (COVID-19). *Semin Thromb Hemost* 2020;46: 856–858.
8. Conti CB, Henchi S, Coppeta GP, et al. Bleeding in COVID19 severe pneumonia: The other side of abnormal coagulation pattern? *Eur J Intern Med* 2020;77:147–149.
9. Mousa-Ibrahim F, Berg S, Od'TPDetola O, et al. Intracranial hemorrhage in hospitalized SARS-CoV-2 patients: a case series. *J Stroke Cerebrovasc Dis* 2021;30:105428.
10. Peys E, Stevens D, Weygaerde YV, et al. Haemoptysis as the first presentation of COVID-19: a case report. *BMC Pulm Med* 2020;20:275–284.
11. Desnos C, Boussouar S, Hekimian G, et al. Spontaneous hemothorax in 4 COVID-19 ARDS patients on VV-ECMO revealing pulmonary artery aneurysms. *Crit Care* 2020;24: 638–642.
12. Al-Samkari H, Karp Leaf RS, Dzik WH, Carlson JCT, Fogerty AE, Waheed A, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. *Blood*. 2020;136:489–500.
13. Chan YC, Morales JP, Reidy JF, Taylor PR. Management of spontaneous and iatrogenic retroperitoneal haemorrhage: conservative management, endovascular intervention or open surgery? *Int J Clin Pract* 2008;62:1604–13.