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Prevalence of Cerebral Venous Thrombosis in COVID-19 Patients: A Systematic Review

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Abstract

Background: COVID-19 is a novel coronavirus that has been rapidly transmitted between individuals globally. COVID-19 has been associated with thrombotic events. A cerebral venous thrombosis is a rare form of stroke with a most common site of origin believed to be the junction of larger sinuses and cerebral veins. So, it is important to identify the prevalence and incidence of cerebral venous thrombosis among COVID-19 patients. **Aim:** To assess the prevalence of cerebral venous thrombosis in COVID-19 patients by reviewing the previous studies reported on this subject. **Method:** We searched for articles focused on our subject through PubMed and Google scholar databases. The included searching terms included "CVT, COVID-19, Prevalence, Complications, and Effect." The inclusion criteria were studies conducted on COVID-19 patients, English articles, available full-text articles, and original articles. **Result:** We got 1178 articles; only six articles were eligible for the inclusion criteria. The included articles involved a total number of 551,727 participants with a mean age ranging between 34 years and 53.3 years and covered seven countries. The incidence of CVT among COVID-19 was reported as well as risk factors and symptoms. **Conclusion:** The incidence of CVT is high among COVID-19 patients compared to the general population, patients with influenza, and those who received the mRNA vaccine, whereas the prevalence requires further studies for precise data. A management strategy or treatment regimen should be established based on the severity of CVT patients, as the mortality rate among those patients was high.

Keywords

Prevalence, CVT, COVID-19

1. Introduction

Stroke is one of the major causes of mortality and long-term disability which is usually caused by hemorrhage or arterial occlusion [1]. Cerebral venous thrombosis (CVT) is a rare form of stroke and accounts for 0.5% of all stroke cases; CVT is associated with an increased mortality rate [2] [3]. The incidence of CVT is ranging from 0.22 to 1.32 per 100,000 annually [4]. CVT is more frequent in young adults and children [4] [5] and more common among females compared to males [4]. CVT can present with a multitude of symptoms and signs, and this makes it hard to distinguish it from other neurological conditions [2]. The early identification of symptoms and management improves the overall outcomes of CVT patients [2]. The risk factors of CVT are divided into genetic risks such as inherited thrombophilia and acquired risks such as trauma, surgery, cancer, exogenous hormones, pregnancy, and puerperium [6].

The SARS-CoV-2 virus that belongs to the corona family viruses caused COVID-19 disease. It was first isolated in December 2019 [7]. The patients with COVID-19 were suffering symptoms such as fever, lack of air, dry cough, headache, diarrhea, fatigue, and throat pain [8]; however, there have been reports of multisystemic manifestations, including neurologic and thrombotic complications [9].

In this context, thrombosis following COVID-19 infection can be related to inflammation, plaque activation, endothelial dysfunction, and blood stasis [10]. There were many risk factors that have been hypothesized to contribute to thrombosis among COVID-19 patients; these factors include prothrombic events caused by cytokines storm, immobility, and reduced activity of thromboprophylaxis [11]. A study from Italy showed thrombotic events occurred in 7.7% of closed cases [12], whereas another study reported that the incidence of thrombotic complications among COVID-19 patients in intensive care unit was 31% even with prophylaxis [13].

Although attention has been given to cerebrovascular thrombotic events, few reports have addressed the risk of CVT among COVID-19 patients. The large majority of these reports are case reports, so we performed this systematic review to assess the prevalence of CVT among COVID-19 patients by reviewing previous studies that reported such subject.

2. Method and Search Strategy

This systematic review follows the PRISMA checklist guidance for systematic review and meta-analysis [14]. We revised two databases for research, including PubMed and Google scholar databases.

We used several keywords for the searching process, including "CVT, COVID-19, Prevalence, Complications, and Effect." We used these keywords in different combinations to get all articles related to our subject. All obtained titles from this primary exploration were revised, and all the studies which didn't include CVT and COVID-19 were excluded. The findings were then explored to

choose only full-text articles written in English and reporting CVT among COVID-19 patients.

3. Eligibility Criteria

We reviewed the remaining full-text articles written in English language and reported CVT among COVID-19 patients. Each of the case reports, review articles, and duplicate articles were all excluded. The inclusion criteria were original articles conducted on COVID-19 patients and experienced CVT, written in the English language, and not case reports. We showed the full description of the search strategy in Figure 1.

4. Data Review and Collection

We reviewed the abstracts of eligible articles, as well as the full article text. A pre-designed excel sheet was used to extract data of interest from the eligible

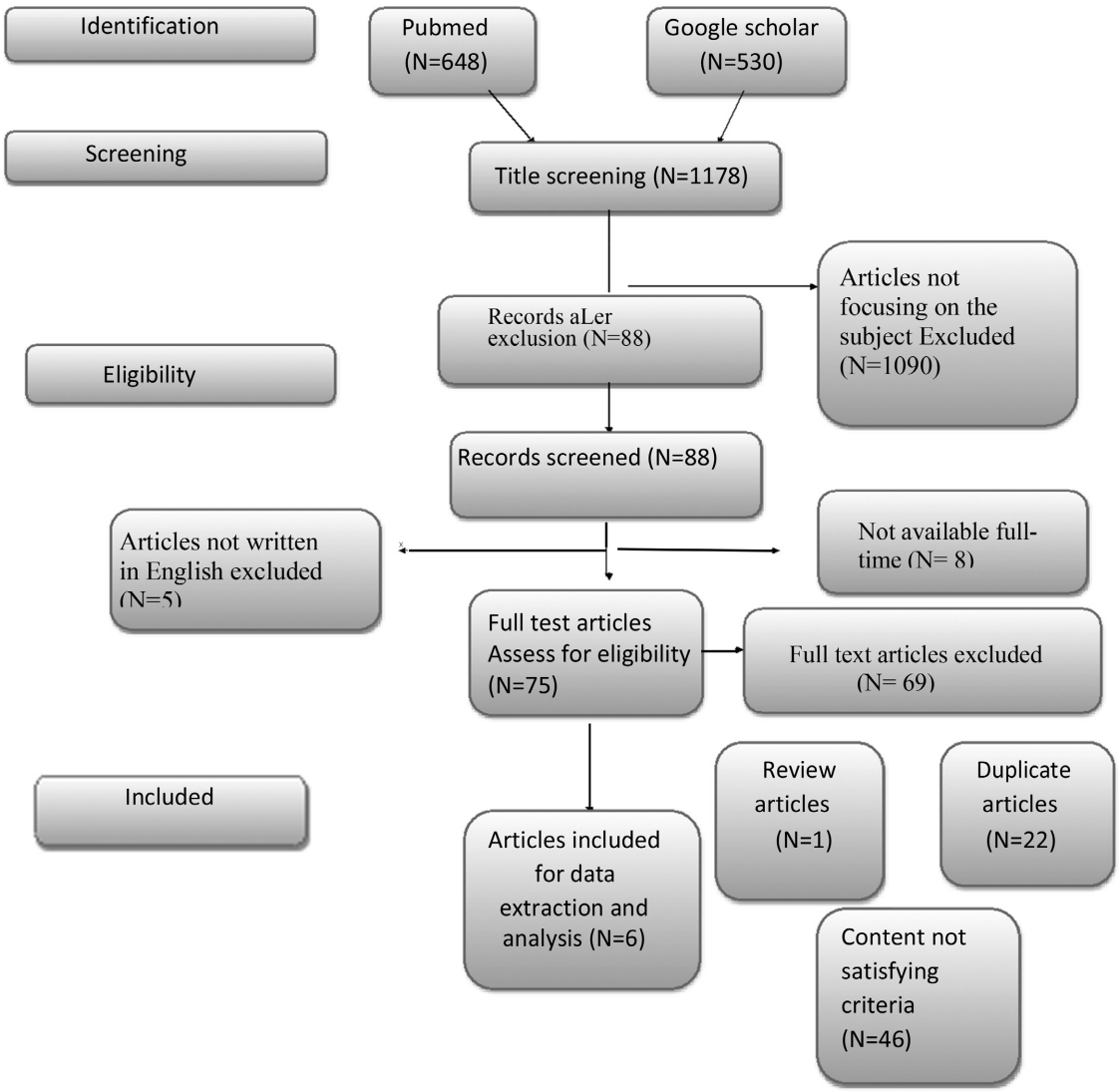

Figure 1. Planning of eligible criteria.

studies. We then revised the extracted data. We transferred the selected data to a pre-designed table to summarize the main findings.

5. Results

This systematic review included six articles that met the eligible criteria [15]-[20] (**Table 1**). There were three studies published in 2021 [15] [16] [17] and three studies published in 2020 [18] [19]. One study was case series [20], one study was an observational study [16], whereas the remaining four studies were retrospective [15] [17] [18] [19]; two studies were retrospective cohort [15] [17], one study was retrospective observational [18], and one was a retrospective study [19]. There were two multinational studies from different counties [16] [19]; one study included patients from ten centers in four countries (Egypt, Pakistan, Singapore, UAE) [16], whereas the other multinational study included patients from nine centers from three countries (Iran, USA, Singapore) [19]. Regarding the settings and strategy of the other four studies, the first study was from the USA and included two cohorts of influenza patients and individuals who received the mRNA vaccine [15]. The second study was conducted in the USA at six different tertiary care centers [17], third study was from Wuhan, China [18], and the fourth one was case series from the USA.

The total number of participants was 551,727. Male gender was predominant in three studies [16] [18] [20], whereas it did not state the gender of participants in one study [17], and in the other two studies, there was female dominance [15] [19]. The mean age of patients ranged between 34 years [20] and 53.3 years [18]. the first study reported 23 patients with CVT out of 537,913 patients with COVID-19 [15]. Another study reported 20 patients had CVT and recent COVID-19 [16]. One study reported 13 patients with CVT and COVID-19 and 57 patients with CVT and without COVID-19 [19]. The case series included three patients who developed CVT with COVID-19 [20].

The findings of the included studies were various, so we could summarize the main findings into main points. Regarding the occurrence of CVT among COVID-19 patients, there were four studies reported that point [15] [17] [18] [19]; one study reported the incidence of CVT to be 42.8/million individuals after COVID-19 diagnosis, and the incidence of CVT was higher among COVID-19 patients compared to those with influenza or received mRNA COVID-19 vaccine

The same study also reported the incidence of portal vein thrombosis (PVT), which was higher compared to CVT. The incidence of PVT after COVID-19 diagnosis was 392.3/million individuals, which was also higher compared to a matched cohort of individuals with influenza or received mRNA vaccine [15].

Another study reported that only 12 patients out of 13,500 COVID-19 patients had imaging-proved CVT. The incidence of CVT was 8.8/10,000 during three months, and the incidence of CVT was found to be higher compared to the incidence of CVT among the general population, which is 5 per million annually [17]. In the third study, the prevalence of CVT, cerebral hemorrhage, and acute

Table 1. Systematic review studies of prevalence of cerebral venous thrombosis in COVID19 patients.

Author and Publication year	Study design	Population, Sample size and Age of participants	Settings/ Strategy	Results and main < findings
Taquet *et al.* 2021 [15]	Retrospective cohort	-537,913 patients diagnosed with COVID-19 -Male:45.1% -Mean age = 46.2 years -Patients with COVID-19 and CVT: 23 (100%) -Male: 30.4% -Mean age = 46.5 years	-USA -Compared with two cohorts of influenza patients and individuals received mRNA vaccine	*The incidence of CVT in the two weeks after a COVID-19 diagnosis was 42.8 per million people *The incidence of CVT among COVID-19 patients was significantly higher than in a matched cohort of people who received an mRNA vaccine and patients with influenza *The incidence of PVT after COVID-19 diagnosis was 392.3 per million people; this was significantly higher than in a matched cohort of people who received an mRNA vaccine and patients with influenza *COVID-19 is associated with a markedly increased incidence of CVT compared to patients with influenza, people who have received BNT162b2 or mRNA-1273 vaccines and compared to the best estimates of the general population incidence. compared to previously reported non-COVID-19
Hameed *et al.* 2021 [16]	Multicenter and multinational observational study	-20 patients with symptomatic CVT and recent COVID-19 -Male: 70% -Mean age = 42.4 years	-Ten centers from 4 countries participated; Egypt, Pakistan, Singapore, UAE	*Headache (85%) and seizures (65%) were the common presenting symptoms *CVT was the presenting manifestation in 13 cases (65%), 7 (35%) patients developed CVT while being treated for COVID-19 *Respiratory symptoms were absent in 45% of the patients. *The most common imaging finding was infarction (65%), followed by hemorrhage (20%). *The superior sagittal sinus (65%) was the most common site of thrombosis. *Acute inflammatory markers were raised, including elevated serum D-dimer (87.5%), erythrocyte sedimentation rate (69%), and C-reactive protein (47%) levels. *Homocysteine was elevated in half of the tested cases. *The mortality rate was 20% (4 patients); mortality is high, but functional neurological outcome is good among survivors. *COVID-19-related CVT is more common among males at older ages when compared to previously reported non-COVID-19.

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Al-Mufti *et al.* 2021 [17]	Retrospective multicenter cohort	-13,500 patients with COVID-19 -Male: -Mean age = 48 years	Six different New York tertiary care centers	*12 patients (%) had imaging-proved CVT *The incidence of CVT was 8.8 per 10,000 during 3 months *The incidence of CVT is considerably higher than the reported incidence of cerebral venous thrombosis in the general population of 5 per million annually. *There was a male preponderance (8 men, 4 women) and an average age of 49 years (95% CI, 36 - 62 years; range, 17 - 95 years). *1 patient (8%) had a history of thromboembolic disease *Neurologic symptoms secondary to cerebral venous thrombosis occurred within 24 hours of the onset of the respiratory and constitutional symptoms in 58% of cases, and 75% had venous infarction, hemorrhage, or both on brain imaging *Management consisted of anticoagulation, endovascular thrombectomy, and surgical hematoma evacuation. *The mortality rate was 25%. *Early evidence suggests a higher-than-expected frequency of cerebral
Li *et al.* 2020 [18]	Retrospective observational	-221 patients with COVID-19 -Male: 59.3% -Mean age = 53.3	Union Hospital, Wuhan, China	*11 (5%) developed acute ischemic stroke, 1 (0·5%) cerebral venous sinus thrombosis (CVST), and 1 (0.5%) cerebral hemorrhage. *COVID-19 with new onset of CVD were significantly older (71.6 ± 15.7 years vs 52.1 ± 15.3 years; p<0·05), and more likely to present with severe COVID-19 (84.6% vs. 39.9%, p < 0.01) *COVID-19 with new onset of CVD were significantly more likely to have cardiovascular risk factors, including hypertension, diabetes, and previous medical history of cerebrovascular disease (all p<0·05). *COVID-19 with new onset of CVD were more likely to have increased inflammatory response and hypercoagulable state as reflected in C-reaction protein and D-dimer *Of 11 patients with ischemic stroke, 6 received antiplatelet treatment with Aspirin or Clopidogrel and 3 of them died. The other 5 patients received anticoagulant treatment with Clexane and one of them died. *The mortality rate was

Continued

Mowala *et al.* 2020 [19]	Multinational retrospective study	Two groups; Group one: -13 patients with CVST and COVID-19 -Male:38.5% -Mean age = 50.9 Group two (control): -57 CVST patient without COVID-19 -Male: 33.3% -Mean age = 36.7	Nine centers in three countries. Eleven patients from seven centers in Iran, one patient from the United States and one patient from Singapore were recruited	*of 13 patients with CVST and COVID-19; Six patients were discharged with good outcomes (mRS ≤ 2) and three patients died in hospital. *Compared to the control group, the SARS-CoV-2 infected patients were significantly older, had a lower rate of identified CVST risk factors, had more frequent cortical vein involvement, and a non-significant higher rate of in-hospital mortality *CVST should be considered as potential comorbidity in COVID-19 infected patients presenting with neurological symptoms. *Compared to non-SARS-CoV-2 infected patients, CVST occurs in older patients, with lower rates of known CVST risk factors and might lead to a poorer outcome in the COVID-19 infected group.
Cavalcanti *et al.* 2020 [20]	Case series	-3 patients developed profound neurologic injury secondary to CVT with COVID-19 -Male: 2 (66.66%) -Mean age = 34 years	USA	*One patient had thrombosis in both the superficial and deep systems; another had involvement of the straight sinus, vein of Galen, and internal cerebral veins; and a third patient had thrombosis of the deep medullary veins. *Two patients presented with hemorrhagic venous infarcts. The median time from COVID-19 symptoms to a thrombotic event was 7 days (range, 2 - 7 days). *Two patients were managed with both hydroxychloroquine and azithromycin; one was treated with lopinavirritonavir. *All patients had a fatal outcome *Severe and potentially fatal deep cerebral thrombosis may complicate the initial clinical presentation of COVID-19. *No conclusions can be drawn other than that these cases provide hints as to the accumulating evidence that COVID-19 is a serious contributor to hypercoagulation, increasing the fatality of the disease. *Heightened awareness of this atypical but potentially treatable complication of the disease.

ischemic stroke among 221 patients with COVID-19 was 0.5%, 5%, and 0.5%, respectively [18]. The last study reported the inclusion of 13 patients with CVT and COVID-19 and compared this group with another group with CVT and without COVID-19. However, the number of patients with CVT and COVID-19

was 13 patients, and it was lower than the other group with CVT and without COVID-19, which included 57 patients [19].

The risk factors associated with developing CVT among COVID-19 patients were reported in three studies [16] [18] [19]. These risk factors include elder patients [16] [18] [19], male gender [16] and severe COVID-19 [18].

The symptoms associated with the presentation of CVT among COVID-19 patients were reported in three studies [16] [17] [20]. They included headache (85%), seizure (65%), and 45% had respiratory symptoms without neurological manifestations. The major imaging findings were infarction (65%) and hemorrhage (20%). Superior sagittal sinus was the most common site of thrombosis [16]. Another study reported 58% of patients had neurological symptoms in first 24 hours of the onset of respiratory symptoms. The main radiological findings were venous infarction, hemorrhage, or both [17]. In the case series, two patients out of three had hemorrhagic venous infarction [20].

The findings regarding diagnostic markers of CVT among COVID-19 patients were reported in first study [16]. Elevation of acute inflammatory markers was found, including D-dimer (87.5%), erythrocyte sedimentation rate (69%), C-reactive protein (47%), and homocysteine (50%) [16]. Third study reported markers regarding cardiovascular disease in general; also, there was an increase in the inflammatory response and an increase in D-dimer and C-reactive protein [18].

The management of patients was reported in two studies [17] [18]. One study reported that the management was done through anticoagulation, endovascular thrombectomy, and surgical hematoma evacuation [17]. Another study reported that six patients received antiplatelet treatment with aspirin or clopidogrel, but three patients died, whereas the remaining five patients received anticoagulation treatment, and only one died [18]. The mortality rate was reported in five studies [16] [17] [18] [19] [20], and it was 20% [16], 25% [17], and 38% [18].

6. Discussion

In our review, we found there is an association between COVID-19 disease and CVT. For instance, the incidence of CVT among COVID-19 patients was 8.8 per 10,000 compared to the general population, patients with influenza, and individuals who received mRNA vaccine [17]. In the general population, the risk factors of CVT were females, young age and malignancy in elderly patients [5] [6] [21] [22]. In our review, older age and male gender were the major risk factors for CVT among COVID-19 patients. This can be attributed to the impact of COVID-19, which may change the susceptibility of patients to develop CVT.

The most common presentation of CVT in COVID-19 patients was headache, followed by seizure [16]. Thus, COVID-19 patients can have CVT without neurological manifestations. Laboratory wise, COVID-19 with CVT showed elevation in D-dimer and markers of inflammation, such as C-reactive protein [16] [18]. We found that the elevation in D-dimer levels was associated with an in-

crease in the rate of vascular complications [23].

Also, we found that the antiplatelet therapy such as aspirin and clopidogrel wasn't effective in the treatment of CVT patients. Three patients out of six patients who received that regimen died, whereas, among five patients who received anticoagulation treatment, only one patient died [18]. However, this may be attributed to the severity of CVT, and anti-platelets may be not appropriate for the conditions of patients and lead to death, which was not mentioned in the study. Another study reported using anticoagulation, surgical hematoma evacuation, and endovascular thrombectomy for CVT patients; the mortality rate reported was 25% among 12 patients [17].

7. Conclusion

The accurate incidence and prevalence of CVT among COVID-19 patients is hard to report due to the lack of the number of studies and variations between the studies and included populations. However, we could conclude that the incidence of CVT is high among COVID-19 patients compared to the general population, patients with influenza, and those who received the mRNA vaccine. This warns us and encourages us to make attention to the development of CVT among COVID-19 patients, so CVT should be suspected and expected in COVID-19 patients. Older age was the major risk factor reported. A management strategy or treatment regimen should be established based on the severity of CVT patients as the mortality rate among those patients was high.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Behrouzi, R. and Punter, M. (2018) Diagnosis and Management of Cerebral Venous thrombosis. *Clinical Medicine*, **18**, 75-79. https://doi.org/10.7861/clinmedicine.18-1-75

[2] Idiculla, P.S., Gurala, D., Palanisamy, M., Vijayakumar, R., Dhandapani, S. and Nagarajan, E. (2020) Cerebral Venous Thrombosis: A Comprehensive Review. *European Neurology*, **83**, 369-379. https://doi.org/10.1159/000509802

[3] Bousser, M.-G. and Ferro, J.M. (2007) Cerebral Venous Thrombosis: An Update. *The Lancet Neurology*, **6**, 162-170. https://doi.org/10.1016/S1474-4422(07)70029-7

[4] Coutinho, J.M., Zuurbier, S.M., Aramideh, M. and Stam, J. (2012) The Incidence of Cerebral Venous Thrombosis: A Cross-Sectional Study. *Stroke*, **43**, 3375-3377. https://doi.org/10.1161/STROKEAHA.112.671453

[5] Ferro, J.M. and Canhao, P. (2014) Cerebral Venous Sinus Thrombosis: Update on Diagnosis and Management. *Current Cardiology Reports*, **16**, Article No. 523. https://doi.org/10.1007/s11886-014-0523-2

[6] Saposnik, G., Barinagarrementeria, F., Brown Jr., R.D., Bushnell, C.D., Cucchiara, B., Cushman, M., Deveber, G., Ferro, J.M. and Tsai, F.Y. (2011) Diagnosis and Management of Cerebral Venous Thrombosis: A Statement for Healthcare Profes-

sionals from the American Heart Association/American Stroke Association. *Stroke*, **42**, 1158-1192. https://doi.org/10.1161/STR.0b013e31820a8364

[7] Zicarelli, C.A., Martins, J.V., Doni, W.V., Rodrigues Pinheiro dos Santos, R., Rampazzo, A.C.M., Ramos do Nascimento, M., *et al.* (2021) Cerebral Venous Thrombosis and Covid 19: Literature Review. *Journal of Neurology & Stroke*, **11**, 57-68. https://doi.org/10.15406/jnsk.2021.11.00457

[8] Seyed, E., Riahi, N. and Nikzad, H. (2020) The Novel Coronavirus Disease-2019 (COVID-19): Mechanism of Action, Detection and Recent Therapeutic Strategies. *Virology*, **551**, 1-9. https://doi.org/10.1016/j.virol.2020.08.011

[9] Koralnik, I.J. and Tyler, K.L. (2020) COVID-19: A Global Threat to the Nervous System. *Annals of Neurology*, **88**, 1-11. https://doi.org/10.1002/ana.25807

[10] Manolis, A.S., Manolis, T.A., Manolis, A.A., Papatheou, D. and Melita, H. (2021) COVID-19 Infection: Viral Macro- and Micro-Vascular Coagulopathy and Thromboembolism/ Prophylactic and Therapeutic Management. *Journal of Cardiovascular Pharmacology and Therapeutics*, **26**, 2-24. https://doi.org/10.1177/1074248420958973

[11] Baldini, T., Asioli, G.M., Romoli, M., Carvalho Dias, M., Schulte, E.C., Hauer, L., Aguiar De Sousa, D., Sellner, J. and Zini, A. (2021) Cerebral venous Thrombosis and Severe Acute Respiratory Syndrome Coronavirus-2 Infection: A Systematic Review and Meta-Analysis. *European Journal of Neurology*, **28**, 2478-3490. https://doi.org/10.1111/ene.14727

[12] Lodigiani, C., Iapichino, G., Carenzo, L., Cecconi, M., Ferrazzi, P., Sebastian, T., *et al.* (2020) Venous and Arterial Thromboembolic Complications in COVID-19 Patients Admitted to an Academic Hospital in Milan, Italy. *Thrombosis Research*, **191**, 9-14. https://doi.org/10.1016/j.thromres.2020.04.024

[13] Klok, F.A., Kruip, M.J.H.A., van der Meer, N.J.M., Arbous, M.S., Gommers, D., Kant, K.M., *et al.* (2020) Incidence of Thrombotic Complications in Critically Ill, ICU Patients with COVID-19. *Thrombosis Research*, **191**, 148-150. https://doi.org/10.1016/j.thromres.2020.04.041

[14] Liberati, A., Altman, D.G., Tetzlaff, J., Mulrow, C., Gøtzsche, P.C., Ioannidis, J.P., *et al.* (2009) The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. *PLoS Medicine*, **6**, Article ID: e1000100. https://doi.org/10.1371/journal.pmed.1000100

[15] Taquet, M., Husain, M., Geddes, J.R., Luciano, S. and Harrison, P.J. (2021) Cerebral Venous Thrombosis and Portal Vein Thrombosis: A Retrospective Cohort Study of 537,913 COVID-19 Cases. *eClinicalMedicine*, **39**, Article ID: 101061. https://doi.org/10.1016/j.eclinm.2021.101061

[16] Hameed, S., Wasay, M., Soomro, B.A., Mansour, O., Abd-Allah, F., Tu, T., Farhat, R., Shahbaz, N., Hashim, H., Alamgir, W. and Iqbal, A. (2021) Cerebral Venous Thrombosis Associated with COVID-19 Infection: An Observational, Multicenter Study. *Cerebrovascular Diseases Extra*, **11**, 55-60. https://doi.org/10.1159/000516641

[17] Al-Mufti, F., Amuluru, K., Sahni, R., Bekelis, K., Karimi, R., Ogulnick, J., Cooper, J., Overby, P., Nuoman, R., Tiwari, A. and Berekashvili, K. (2021) Cerebral Venous Thrombosis in COVID-19: A New York Metropolitan Cohort Study. *American Journal of Neuroradiology*, **42**, 1196-1200. https://doi.org/10.3174/ajnr.A7134

[18] Li, Y., Li, M., Wang, M., Zhou, Y., Chang, J., Xian, Y., Wang, D., Mao, L., Jin, H. and Hu, B. (2020) Acute Cerebrovascular Disease Following COVID-19: A Single

Center, Retrospective, Observational Study. *Stroke and Vascular Neurology*, **5**, 279-284. https://doi.org/10.1136/svn-2020-000431

[19] Mowla, A., Shakibajahromi, B., Shahjouei, S., Borhani-Haghighi, A., Rahimian, N., Baharvahdat, H., Naderi, S., Khorvash, F., Altafi, D., Ebrahimzadeh, S.A. and Farahmand, G. (2020) Cerebral Venous Sinus Thrombosis Associated with SARS-CoV-2; a Multinational Case Series. *Journal of the Neurological Sciences*, **419**, Article ID: 117183. https://doi.org/10.1016/j.jns.2020.117183

[20] Cavalcanti, D.D., Raz, E., Shapiro, M., Dehkharghani, S., Yaghi, S., Lillemoe, K., Nossek, E., Torres, J., Jain, R., Riina, H.A. and Radmanesh, A. (2020) Cerebral Venous Thrombosis Associated with COVID-19. *American Journal of Neuroradiology*, **41**, 1370-1376. https://doi.org/10.3174/ajnr.A6644

[21] Einhaupl, K., Stam, J., Bousser, M.-G., De Bruijn, S.F.T.M., Ferro, J.M., Martinelli, I., *et al.* (2010) EFNS Guideline on the Treatment of Cerebral Venous and Sinus Thrombosis in Adult Patients. *European Journal of Neurology*, **17**, 1229-1235. https://doi.org/10.1111/j.1468-1331.2010.03011.x

[22] Stam, J. (2005) Thrombosis of the Cerebral Veins and Sinuses. *New England Journal of Medicine*, **352**, 1791-1798. https://doi.org/10.1056/NEJMra042354

[23] Vidali, S., Morosetti, D., Cossu, E., Luisi, M.L.E., Pancani, S., Semeraro, V., *et al.* (2020) D-Dimer as an Indicator of Prognosis in SARS-CoV-2 Infection: A Systematic Review. *ERJ Open Research*, **6**, 00260-02020. https://doi.org/10.1183/23120541.00260-2020