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# Vascular complications in adult patients with COVID-19 infection in Margan Hospital, Babylon Governorate, Iraq: (January of 2020 to June of 2021)

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## Abstract

This study has been performed for assessment of clinical course and risk factors for vascular thrombotic events in adult inpatients with coronavirus 2019 infection (COVID-19). This infection has become a serious global challenge affect large number of population world wide lead to significant morbidity and mortality specially from vascular disorders. Our study included 900 patients admitted to Margan hospital in Babylon Governorate, Iraq from January of 2020 to June of 2021. 551 (61.2%) was male and 349 (38.8%) was female. Fifty-eight (6.5%) of all patients had vascular complication of different forms. The most frequent type of vascular complications was cerebrovascular accidents involved 23 patients (39.7%) and other types include coronary artery diseases, peripheral vascular diseases and deep venous thrombosis. The mean age of the affected patients with vascular complications was (64 years) while for patients with no vascular complications was (53.17 years). The most frequent associated symptom in affected patients is chest pain (N=15, 25.9%), other symptoms include disturb level of consciousness, lower limb pain, lower limb swelling, side body weakness and shortness of breath. For all 58 patient, the mean SPO2% on admission was 89% and mean of lowest SPO2% was 80% . In this study we perform comparison in certain variables between affected group with vascular complication(N=58) and other non-affected group and this comparison showed that (58.6%) of affected group were smoker and 72.4% with comorbidity while just (5.3%) of non-affected group were smoker and 43.2% with comorbidity, the mean lung involvement by Chest CT-scan was 62% for affected patients group and 45% for other, C-reactive protein(CRP) was positive in 86.2% of affected group and 65.8% of non-affected group. Only 166( 18.4%) of 900 patients were died [18% of them with vascular complications] while the majority of patients (707) ( 78.6%) get complete cure[only 1.5% of them with vascular complications ].

According to this study our findings demonstrate that:

- Smoking, older age and presence of comorbidity increase risk of vascular complications in patients with COVID-19 infection.
- In cases of COVID-19 infection, the positive CRP and lung involvement (by CT scan of chest) is significantly more in patient with vascular complications.
- Vascular complications is significantly present more in died patients in this study than in cure patients, so this can make the vascular disorders an important mortality factor.

**Keywords**
COVID-19 infection, study, vascular, complications, comorbidity

In December 2019, an outbreak of respiratory symptoms of unclear cause was appeared in Wuhan, Hubei Province, China. Further studies led to the isolation of a novel respiratory virus whose genome assessment showed it to be a novel coronavirus related to SARS-CoV, and therefore called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is a betacorona-virus related to the subgenus Sarbecovirus. The global spread of SARS-CoV-2 and a lot of deaths caused by coronavirus disease (COVID-19) made the World Health Organization to declare a pandemic on 12 March 2020.

Genomes analysis and comparison with previously known coronavirus genomes indicate that SARS-CoV-2 presents unique features that distinguish it from other coronaviruses: optimal affinity for angiotensin converting enzyme 2 (ACE2) receptor and a polybasic cleavage site at the S1/S2 spike junction that determines infectivity and host range (Andersen et al., 2020; Nao et al., 2017).

Patients with SARS-CoV-2 infection may present symptoms ranging from mild to severe with a large portion of the population being asymptomatic carriers. The most common reported symptoms include fever (83%), cough (82%) and shortness of breath (31%) (Wang et al., 2020). In patients with pneumonia, chest X-ray usually shows multiple mottling and ground-glass opacity (Wang et al., 2020; Zhu et al., 2020).

Gastrointestinal symptoms such as vomiting, diarrhea, and abdominal pain are described in 2–10% of the patients with COVID-19 (Chen et al., 2020; Wang et al., 2020), and in 10% of patients, diarrhea and nausea precede the development of fever and respiratory symptoms (Wang et al., 2020).

One of the important causes of morbidity and mortality after COVID-19 infection is vascular thrombosis venous and arterial. Many researches showed that the patients with COVID-19 infection were associated with abnormal coagulation parameters and increase risk of thrombotic events. This is particularly important because of the poor clinical outcomes occur with this complication in critically-ill patients (Klok et al., 2020; Tang et al., 2020).

The serious vascular complications in patient with COVID-19 infection include acute coronary syndrome and MI. The main causes of that are remain unknown, but could be due to the elevated myocardial demand because of the infection, akin to type 2 MI, cytokine-induced atherosclerotic plaque instability and rupture, or non-plaque thrombosis (Bangalore et al., 2020; Libby et al., 2018; Tavazzi et al., 2020).

Indeed, a common manifestation in patients with COVID-19 is the presence of coagulation abnormalities and instances of thromboembolism, which has been associated with disease severity and a higher incidence of mortality (Tang et al., 2020), whilst also increasing the risk of MI and stroke. The endothelium plays an important role in the prevention of thromboembolic events by regulating the coagulation cascade, achieved, in part, via inhibition of various tissue factors by a Kunitz-type protease inhibitor, known as the tissue factor pathway inhibitor (TFPI) that resides on the endothelial cell surface (van Hinsbergh, 2012). The transmembrane protein tissue factor is required for in vivo coagulation by the binding and activation of various tissue factors (i.e., activation of factor Xa) promoting prothrombin conversion to thrombin, and thus the conversion of fibrinogen to fibrin (van Hinsbergh, 2012; White et al., 2010), inhibiting TFPI and promoting clot formation. TFPI is predominantly bound to the microvasculature (Osterud, Bajaj, & Bajaj, 1995), however, it has been demonstrated to play a role in the regulation of arterial thrombosis in mice (White et al., 2010).

Marked coagulation derangements have been reported in a single-center cross-sectional study by Goshua et al. (2020) who assessed markers of endothelial cell and platelet activation, namely circulating von Willebrand factor (vWF), soluble P-selectin and soluble thrombomodulin, in critically and non-critically ill COVID-19 patients. They

observed that endotheliopathy is present in COVID-19 and is associated with increased mortality, with a suggestion that soluble thrombomodulin concentrations may predict mortality and clinical outcomes in COVID-19 patients. It was suggested that the coagulopathy observed in their data was distinctly separate from disseminated intravascular coagulation (DIC) and should be considered an endotheliopathy (Goshua et al., 2020).

## Discussion

- **Method**

In this research 900 patients; 551 males (61.2%) and 349 females (38.8%) have been involved with mean age of 56 years(table 1) , all of them were admitted to Margan University Hospital, Babylon Governorate in Iraq from January of 2020 to June of 2021.

**Table 1: The Distribution of patients according to socio-demographic characteristics (N=900)**

| Study variables | | |
|---|---|---|
| **Age (years)** | (53.87 ± 15.01) | (16.0 - 96.0) |
| **Gender** | | |
| Male | 551 | 61.2% |
| Female | 349 | 38.8% |
| Total | 900 | 100.0% |
| **Smoking** | | |
| Smoker | 79 | 8.8% |
| Non smoker | 821 | 91.2% |
| Total | 900 | 100.0% |

In this study different parameters or variables were applied during assessment of involved patients and these include: complete blood count, C-reactive protein, monitoring of SPO2%, CTscan of chest, ----- --- --- --- . All patients underwent follow-up until discharge from hospital or until death.

**-Results**

The vascular complications affect 58 of all patients **[**34males (58.6%), 24females (41.4%)**]** and these include: Cerebrovascular accidents which is the most frequent, Coronary artery diseases, Peripheral vascular diseases and Deep venous thrombosis (tab. 2).

**Table 2: The Distribution of patients according to vascular complications (N=900)**

| Study variables | Number | % |
|---|---|---|
| **Vascular complications** | | |
| Present | 58 | 6.5% |
| Absent | 842 | 93.5% |
| Total | 900 | 100.0% |
| **Type of vascular complications** | | |
| Cerebrovascular accidents | 23 | 39.7% |
| Peripheral vascular diseases | 11 | 18.9% |
| Coronary artery diseases | 19 | 32.8% |
| Deep venous thrombosis | 5 | 8.6% |
| Total | 58 | 100.0% |

Associated symptoms in patients with vascular complications include: chest pain, disturb level of consciousness, Lower limp pain, Lower limp swelling, Side body weakness, Shortness of breath (tab. 3). They are treated with anti-ischemic drugs and other therapeutic methods.

**Table 3 : The Distribution of patients with vascular complication according to intervention need and associated symptoms (N=58)**

| Study variables | Number | % |
|---|---|---|
| **Intervention** | | |
| Anti-ischemic drugs | 19 | 32.8% |
| Nonspecific treatment | 39 | 67.2% |
| Total | 58 | 100.0% |
| **Associated symptoms** | | |
| Chest pain | 15 | 25.9% |
| DLOC | 13 | 22.4% |
| Lower limp pain | 11 | 19.0% |
| Lower limp swelling | 5 | 8.6% |
| Side body weakness | 10 | 17.2% |
| Shortness of breath | 2 | 3.4% |
| No symptoms | 2 | 3.4% |
| Total | 58 | 100.0% |

In this study we perform comparison in certain variables between affected group with vascular complication (N=58) and other non-affected group and this comparison showed that :

The mean age of patients with vascular complications (64 years) is more than other patients (53years) so the older age group more liable for vascular disorders. For all 58 patient, the mean SPO2% on admission was 89% and mean of lowest SPO2% was 80% .There is significant difference in the lowest Spo2% between patients with vascular complications (affected group) and other. The chest CT-scan involvement is significantly more in affected group(62% while 45% in non-affected group)(tab.4)

Regarding smoking 58.6% (No.34) of affected group were smokers while just 5.3%(No.45) of non-affected group were smokers. Comorbidity present in 72.4% of affected patients and in 43.2% of other group. C-reactive protein(CRP) was positive in 86.2% of affected group and 65.8% of non-affected group (tab.5). The mean platelet count was lower in affected group and there was non-significant difference regarding PCV (tab.6).

**Table 4: The mean differences of study variables according to vascular complications**

| Study variables | Vascular complications | N | Mean | SD | t-test | P-value |
|---|---|---|---|---|---|---|
| Age (years) | Present | 58 | 64.00 | 10.54 | **7.322** | **<0.001*** |
| | Absent | 842 | 53.17 | 15.03 | | |
| SPO2 on admission (%) | Present | 58 | 0.89 | 0.03 | -0.253 | 0.801 |
| | Absent | 840 | 0.89 | 0.09 | | |
| Lowest SPO2 (%) | Present | 58 | 0.80 | 0.05 | **-2.962** | **0.004*** |
| | Absent | 839 | 0.83 | 0.13 | | |
| CT involvement (%) | Present | 58 | 0.62 | 0.12 | **9.091** | **<0.001*** |
| | Absent | 805 | 0.45 | 0.22 | | |

*P value ⩽ 0.05 was significant.

Table 4 : The mean differences of study variables including (age, SPO2 on admission, lowest SPO2 and CT involvement) according to vascular complications including (present and absent). There were significant differences between means of age, lowest SPO2 and CT involvement according to vascular complications.

**Table 5 Association between study variables and vascular complications**

| Study variables | Vascular complications | | Total | $X^2$ | P-value |
|---|---|---|---|---|---|
| | Present | Absent | | | |
| **Gender** | | | | | |
| Male | 34 (58.6) | 517 (61.4) | 551 (61.2) | | |
| Female | 24 (41.4) | 325 (38.6) | 349 (38.8) | | |
| Total | 58 (100.0) | 842 (100.0) | 900 (100.0) | 0.177 | 0.674 |
| **Smoking** | | | | | |
| Smoker | 34 (58.6) | 45 (5.3) | 79 (8.8) | | |
| Non smoker | 24 (41.4) | 797 (94.7) | 821 (91.2) | | |
| Total | 58 (100.0) | 842 (100.0) | 900 (100.0) | **192.34** | **<0.001*** |
| **Comorbidities** | | | | | |
| Present | 42 (72.4) | 364 (43.2) | 406 (45.1) | | |
| Absent | 16 (27.6) | 478 (56.8) | 494 (54.9) | | |
| Total | 58 (100.0) | 842 (100.0) | 900 (100.0) | **18.66** | **<0.001*** |

| Study variables | Vascular complications | | Total | $X^2$ | P-value |
|---|---|---|---|---|---|
| | Present | Absent | | | |
| **C-reactive protein** | | | | | |
| Positive | 50 (86.2) | 554 (65.8) | 604 (67.1) | | |
| negative | 8 (13.8) | 288 (34.2) | 296 (32.9) | | |
| Total | 58 (100.0) | 842 (100.0) | 900 (100.0) | **10.24** | **0.001*** |
| **Associated symptoms** | | | | | |
| Yes | 56 (96.6) | 34 (4.0) | 90 (10.0) | | |
| No | 2 (3.4) | 808 (96.0) | 810 (90.0) | | |
| Total | 58 (100.0) | 842 (100.0) | 900 (100.0) | **516.02** | **<0.001*** |
| **Respiratory rate** | | | | | |
| 12-18 | 3 (5.2) | 25 (26.0) | 28 (18.2) | | |
| 18-30 | 33 (56.9) | 49 (51.1) | 82 (53.2) | | |
| >30 | 22 (37.9) | 22 (22.9) | 44 (28.6) | | |
| Total | 58 (100.0) | 96 (100.0) | 154 (100.0) | **11.74** | **0.003*** |
| **Interventions** | | | | | |
| Yes | 58 (100.0) | 35 (4.2) | 93 (10.3) | | |
| No | 0 (0.0) | 807 (95.8) | 807 (89.7) | | |
| Total | 58 (100.0) | 842 (100.0) | 900 (100.0) | **537.95** | **<0.001*** |

*P value ⩽ 0.05 was significant.

Table 5 shows the association between study variables including (gender, smoking habit, comorbidities, C-reactive protein, respiratory rate, associated symptoms and interventions required) and vascular complications including (present and absent). There was significant association between smoking habit, comorbidities, C-reactive protein, respiratory rate, associated symptoms and interventions required and vascular complications.

Table 6: The mean differences of study variables according to vascular complications

| Study variables | Vascular complications | N | Mean | SD | t-test | P-value |
|---|---|---|---|---|---|---|
| Platelet count | Present | 58 | 286.79 | 113.01 | | |
| | Absent | 253 | 239.77 | 128.85 | **2.561** | **0.011*** |
| PCV (HCT) | Present | 58 | 40.46 | 4.98 | | |
| | Absent | 265 | 38.81 | 6.06 | 1.932 | 0.054 |

*P value ⩽ 0.05 was significant.

Table 6 : The mean differences of study variables including (Platelet count and PCV (HCT)) according to vascular complications including (present and absent). There were significant differences between means of platelet count according to vascular complications.

Only 166(18.4%) of 900 patients were died [18% of them with vascular complications] while the majority of patients (707) ( 78.6%) get complete cure[only 1.5% of them with vascular complications ](Fig.1).

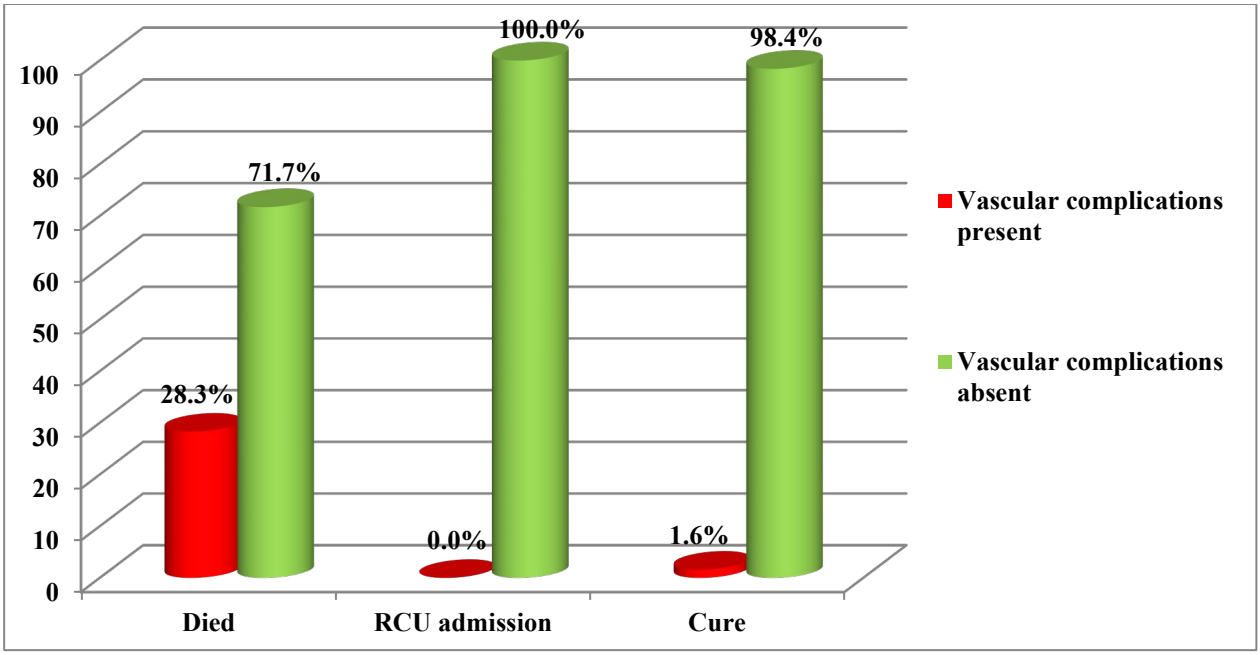


Figure 1: The association between fate of patients and vascular complications (N=900)

Figure 1 : shows the association between fate of patients including (died, RCU admission and cure) and vascular complications (present and absent).There was significant association between fate of patients and vascular complications.
)X2= 161.55, P <0.001(*

## Data Analysis

Statistical analysis was carried out using SPSS version 25. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as (Means ± SD). Student t-test was used to compare means between two groups. Pearson chi-square and Fisher's exact test were used to find the association between categorical variables. A *p*-value of ⩽ 0.05 was considered as significant.

## Conclusion

- Smoking, older age and presence of comorbidity increase risk of vascular complications in patients with COVID-19 infection.
- In cases of COVID-19 infection, the positive CRP and lung involvement (by CT scan of chest) is significantly more in patient with vascular complications.
- In this study vascular complications is significantly present more in died patients than in cure patients, so this can make the vascular disorders an important mortality factor.

## Recommendations

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