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High incidence of venous and arterial thrombo embolic high complications in specific COVID-19 pandemic areas: are there clusters of populations carrying an hereditary predisposition to assess?

Abstract

Coagulopathy in COVID-19 pneumonia is a deleteroius complication which has lead to a high rate of deaths in several populations world wide like in Northern Italy Red Zone during pandemic time in March 2020. Due to an high incidence of thrombo embolic (TE) events among several clusters of involved populations, a suspect of an hereditary predisposition due to polymorphisms in several genes involved in the caoagulation process could be formulated and investigated.

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Coagulopathy in patients with COVID-19 is associated with an increased risk of death. Furthermore, the relevance of COVID-19-coagulation abnormalities are becoming increased recording a substantial proportion of patients with severe COVID-19 developing sometimes unrecognized, venous and arterial TE complications. There is a growing body of evidences to this concern showing a wide pictorial fashion of features getting from an increased D-dimer concentration, thrombocytopenia, prolonged prothrombin time, reduction of fibrinogen and increased D-dimer suggestive of DIC to a diffuse and life-threatening thrombotic microangiopathy.[1]

Recently in an Italian paper by Lodigiani C et al., authors described the rate and characteristics of TE complications in hospitalized symptomatic patients with laboratory-proven COVID-19 admitted to their hospital in Milan, (Italy), belonging to the Red Zone during February and March 2020 pandemy.[2] They showed that, despite the use of anticoagulant prophylaxis and therapy, the rate of venous and arterial thrombo embolic complications in hospitalized COVID-19 patients was approximately 8% and hypothesized that this already high value could be underestimated. These results were compared with other groups studies (Dutch, Chinese, French) obtaining substantial high different percentages. While their data resulted to be much higher than Dutch study, Chinese and French studies provided much more increased rate of symptomatic thrombo embolism regardless the use of anticoagulant therapy or thromboprophylaxis.[3-5]

Given these controversial results among different Covid-19 populations in different countries, several considerations should be examined in light of two key points. The former is related to the recent advances in the COVID-19 invasion mechanism knowledge due to the Spike protein's activity on ACE 2 receptors expressed in a wide manner also in the endothelial cells, leading to a vasculitis and TE events specific in the alveolar-capillary barrier.[6] The latter could be a genetic predisposition for TE complications triggered by the Covid-19 pneumonitis in mutations carriers of factors which interact in determining the risk of TE. This hypothesis may explain the magnitude of TE events in these groups and nevertheless the impact of COVID-19 TE on different "ethnicity" among them. In fact, several polymorphisms in genes linked to coagulative process may induce a high risk of coagulopathy. Thus, it is reasonable to hypothesize a high incidence of TE COVID-19 complications in unaware population clusters carrying an undetected specific mutation.

For example, the risk of coagulopathy associated with the polymorphic variants factor V Leiden (FVL), of prothrombin (PT20210A), methylene-tetrahydrofolate-reductase (C677TOR/A1298C- MTHFR) genes have been widely investigated in many studies.[7] In particular the MTHFR gene polymorphisms have been linked to a related hereditary risk factor for elevated serum homocysteine levels as in case of MTHFR- C677T and A1298C which lead to decreased enzyme activity and therefore to an elevation of serum homocysteine level and in turn to TE events.[8] An elevated homocysteine level is associated with an increased likelihood of having a blood clot in the veins and enhanced risk for developing atherosclerosis, which can in turn lead to coronary artery disease, heart attack, and stroke. Predisposing associated factors have been found as older age, smokers and male sex and pregnancy. Taken collectively all these factors bring our mind to the typical coagulopathy features recorded in a poor prognosis population affected by severe Covid-19 infection of the Italian Red Zone pandemic in the beginning of March 2020. Although these evidences, any mention or any investigations have been done to this concern in the published papers to explain the high percentage of TE in this population during Covid-19 pandemic time.Probably a genetic predisposition or "ethniticity" may reflect the different incidence of various TEevents in different populations as confirmed in several studies.[9]

Thus there is the impression of a limitation in all published studies reporting a high incidence of coagulopathy in several clusters of populations without assessing at an individual patient level a possible role of an heredithary condition or "ethnicity" linked to polymorphisms in genes involved in the coagulation process in order to customize an efficacious anthrombotic therapy.[10]

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None.

Conflicts of interest

The authors declare that there is no conflict of interest.

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