SciMedCentral

Journal of Hematology & Transfusion

Commentary

Thrombotic Thrombocytopenia Induced by Cov-2 Infection and Some Components of Vaccines: Is it Related to Host Prethrombotic State?

Jerard Seghatchian*

International Consultancy in Innovative Manufacturing and Quality/Safety of Blood-Derived Bioproducts. UK

***Corresponding author**

Jerard Seghatchian, International Consultancy in Innovative Manufacturing And Quality/Safety of Blood-Derived Bioproducts. London, England, UK, Email: jseghatchian@btopenworld.Com

Submitted: 18 May 2021

Accepted: 26 May 2021

Published: 28 May 2021

ISSN: 2333-6684

Copyright

© 2021 Seghatchian J

OPEN ACCESS

Abstract

CoV-2 infection-induced thrombotic thrombocytopenia purpura [TTP] is life-threatening event often observed amongst critically ill CoV-2 patients and intriguingly subsequent to vaccination, as a rare event, with an incidence about 10 cases per million vaccinated individuals, as characterised by blood clot combined with low platelet count. Nevertheless, it is unclear how vaccines that are not infective and based mainly on the characteristic of the viral spike proteins, could lead selectively to thrombotic event, unless a host predisposition to thrombotic events is already in place. Nevertheless this rare event open the door of Pandora box to a series of other important questions that remains to be fully investigated: i] Why the physiological responses to CoV-2 infection and the vaccine' spike proteins are age- dependent and appears predominantly occurs in young female below the age 50?; ii] Why the type of blood clot forms by differing infection differs and only severely affects the unvaccinated populations? and how these events should be accurately diagnosed ?; iii] Where we stands on the balance the overall benefit of the vaccination, in building a solid protection barrier against infection versus the negligible rare risk of thrombotic even in certain predisposed groups?. The main objective of this invited commentary is to provide a personal viewpoint on the CoV-2 infection or vaccines- induced TTP and to explore the planed remedial action to survive COVID and to save some lives. While the race between, the emergence of fast spreading mutated virus, versus the limited therapeutic values of slow acting of vaccines therapy continue, the use of some innovative and safer alternative booster therapies for the immediate delivery of some multivariate -targeted neutralising antibodies is considered to be the best preventative and therapeutic strategies intervention that we do need right now urgently. In short while efforts in developing multivariate types of vaccines are still progressing, but because of the delayed mode of action of passive immunotherapy, taking up to 3-4 weeks to develop real protection against infection, and vaccines effectiveness not being 100%, vigilance is still the key element in the advancement of mass vaccination rollout to survive COVID.

BACKGROUND

Since the COVID-19 pandemic began a plethora of research carried out in order to better understanding CoV-2 infection-induced activation of hemostasis and infection induced prethrombotic states and immune reactions, where the use artificial tools in big data and patterns analysis combined with new technologies were extremely useful to put in place some appropriate interventional therapy to save lives [1-12].

Initially attention focussed on CoV-2 infection – induced activation of haemostatic components and severe thrombotic events in some predisposed groups and delayed immune reactions[1-4]. Some armada of anti-inflammatory and anti- infective drugs, identified through the use of artificial intelligence, were applied, with partial beneficial outcome [5-12]. Meanwhile continual efforts were made in the use of coronavirus convalescent plasma, [CCP] and to improve its safety using modern blood purification technologies [13]. Moreover using some innovative and practical tools to obtain CCP – derived neutralising antibodies hyperconcentrate as purer and safer products for direct mode of the delivery of antibody for the purpose of immunotherapy in particular in vaccine non-responder individuals [7-12], while In parallel attentions were focussed on the development further candidates vaccines, based on the characteristic profile of the viral spike proteins, as vaccine supply found to be the rate limiting step in mass vaccination programme [8].

Conceptually the dual application of vaccine in combination with purer neutralising polyclonal antibody hyperconcentrate, obtainable by affinity adsorption bead technologies, will prove to be the best strategy for individuals that are vaccine' non-responders or poor responders, as vaccine effectiveness is not 100% or when the circulating neutralsing antibodies are clearing rapidly from circulation. The objective being not only to standardised the use convalescent plasma but also remove some toxic elements [i.e. altered coagulation factors, activated complements, cytokines [12-16] as well as to provide a balanced levels antibody in either SD plasma or normal pool viral inactivated plasma or cryosupernatant to compensate for deficiency of albumin often observed subsequent to severe infection of such interventional therapy [9]. Some studies in this direction are still in planning stages for clinical trials [12].

NEW DOMINATE VARIANTS IN THE UK AND POTENTIAL RISK OF TTP

Recently some new cases of fast spreading 'Indian variant', B.1.617.2, that is still causing enormous devastation in India, has emerged and almost 3 time faster each week locally in the UK, with considerable ramifications for the rest of the world.

Based on the UK genetic finger printing analyses here are at least three closely related variants that are originated in India: B.1.617, B.1.617.2, and B.1.617.3 , accounting for the 50 per cent of all cases reported worldwide and 30 per cent of deaths. Moreover evidence is accumulating that B.1.617.2 has a mutation on the spike protein which the coronavirus uses to latch onto human cells called L452R. This receptor was also detected in a variant spreading in California variant identified earlier this year and is thought to explain why the variant spreads more easily. However unlike the other variants in the B.1.617 family, it does not have the E484Q mutation, which may help the virus evade some types of antibodies, hence current vaccine in use may prove effective if we could delay it transmissibility to unvaccinated individual. Nevertheless the presence of these two mutations, among many others, are why the Indian variant family has a transmission advantage, spread three times faster than previous imported variants of concern, such as that from South Africa and the two other Indian variants still remaining under investigation. Interestingly across the four nations, England has reported the bulk of cases – 1,255 of B.1.617.2, compared to 35 in Scotland, 11 in Wales and 12 in Northern Ireland, possibly reflecting both the traveling link and localised community related association. Intriguingly in the UK there was no travelling restriction for India, though were put in place earlier for Pakistan and neighbouring countries.

In India, where most health workers were vaccinated early, the Indian variant looked like being less of a problem for immune evasion than the Brazilian or South African variants but there are some early positive signs as an on-going study of healthcare workers nationally has suggested there is no signal of an increase in reinfections and as it stands possible reinfections detected nationally appear approximately proportionate to the prevalence of this variant. It is less likely, therefore to cause a reinfection than the South Africa variant, B.1.351, because more than 40 per cent of the country have not been vaccinated yet and only 30 per cent have had both jabs - although the hope is that the oldest and most vulnerable are protected because they were vaccinated first.

Some experts are worrying if this variant could lead to another big spike in hospitalisations and deaths. The best-case scenario is that infections stay under control thanks to the UK's speedy vaccine rollout, and the variant has, ultimately, little impact. But the more worrying scenario is that the new variant takes hold among the communities with low vaccine uptake, where it could cause a major rise in cases and, subsequently, deaths; the nightmare scenario is that the new variant takes hold in countries which have been unable to access vaccinations, driving severe new waves, hence more collaborative works, teams working is essential as no one is safe until everyone is safe and the best line of defence is to get vaccinated asap and encourage everyone to do the same well in advance as in the long term vaccines are the most important preventative measure. No data on infection induced TTP is yet available and the use of pooled convalescent plasma or serum for recovering polyclonal antibody a against this variant, as the most effective booster antibody therapy, as explored from other strains[5-13].

In short apart from the Indian variant some others most fearful fast spreading mutated RBD of spike proteins variants have been identified earlier in the UK enbodying: The UK- Kent valiant that still spreading fast all over the world but is originated from travelling to Spain; the South African variant that target the younger population and creating chaos all over the world, as some vaccines in use appear to be less effective than the others; and the two fearful Brazilian variants, that are capable to reinfect some individuals who recovered and have developed antibody against the main strain; and the California variants that still developing in limited number in the Europe and the UK.

Today the above variants have being well characterized in terms of transmissibility; pathogenicity; risk of immune scape and inducing activation of the complements and inflammatory factors and cytokine storms leading to thrombotic events. In fact a collection of recombinant antigens for these variants, are currently available commercially, covering critical mutations such as K417N/T, E484K, N501Y and D614G on Spike protein and R203G, G204R and P13L on Nucleocapsid protein. These reagents reportedly can be used to evaluate the efficacy of the antibodies and vaccination, as CoV-2 like all the other viruses constantly undergo changes in their size and charges some accounting for their fast transmissibility and severity and the effectiveness of vaccines and the appropriate therapeutics intervention.

Where We Stands Now And Where We Might Be Going

To start with the good news, the 17th May coincides with the first day that the restriction due to lock down in the UK is coming to end finally, in view of the successful interim results on mass vaccination in the UK, as more than 60% of population beguining with those most in risk- the older age and most of front line staffs are already vaccinated, using the two available and approved vaccines [the Pfizer and AstraZeneca]that provided highly promising outcome in highly severe cases by reducing the rate hospitalization, viral transmissibility and saving live.

Unfortunately, come the news of a very rare event of blood clot, identified with the use AstraZeneca types vaccines, mostly in young female, first by some European countries and later with the use of the newly developed single dose Johnson and Johnson type of vaccines, mainly in the age below 50 in the USA, hence contributing further to vaccine hesitancy despite being very rare potential side effect of vaccine. It remains still unclear whether these events might be related the host predisposing to prethrombotic event, or to some unkown components of these types of vaccines that remains amongst the challenging issues to be resolved as highlighted below. Adding to these dilemma is the appearance of the emerging new Indian variant identified in the UK genetic surveillance locally and spreading at least 3

time faster that other variants. Fortunately the early laboratory indication in Oxford indicates that the current vaccines are fully effective of this variant, hence the rush for the vaccinating the younger generation is continuing with rigors to slow done the rate of this fast spreading infection. Nevertheless there are many promises and pitfalls associated with COVID infection requiring further in depth analyses:

Firstly all the regulatory agencies after reviewing all data on blood clots by vaccines available to them came to conclusion that these highly rare events of blood clot for now should be considered as the rare side effect of vaccination and for cautionary safety measures, the individual concerned should be given a choice for the appropriate choice of the available vaccines with a lower rare side effect until further data on the topic become available as a rare risk factor. This recommendation accordingly has been currently adopted in the UK and the Pfizer vaccine is the second choice vaccine as has been in use for the younger ages, with the proven safety efficacy for mass vaccination in both USA and Israel and also validated for the use in pregnancy that are known to be associated with hypercoagulability [2-4].

Secondly an alternative to this proposal is that we should introduce a simple hypercoagulability pre-screening test for the under age of 50 female before vaccination. In this context many factors are known to predispose certain groups of females to hypercoagulability, including the rare congenital factor V Leiden or acquired hypercoagulability such as the presence/ development of some rare autoantibodies and the presence of lupus anticoagulant [1], and other conditions i.e. the use of the oral contraceptives, hormone therapy, pregnancy amongst some other contributory factors. Moreover a deficiency of a vWF multimers cleaving protein, ADAMTS13 might be the cause of this condition as within the vascular circulation there are ultra large von Will Factor multimers, having receptor sites for platelet to bound and aggregate, causing local inflammation and injury and leading thrombotic events and organ failure and DIC as a synonym for death is coming [1-4]. Therefore such a pre-screening test Will prove useful in establishing the cause for concerns on the evidence based.

In context the development of purer convalescent plasma-derived neutralizing antibodies hyperconcentrates, as the booster antibody to deployment approved vaccines, in view of the fact that the effectiveness of vaccines are not 100% considerable ongoing studies are still in progress to ensure the optimal safety and minimize the potential side effects all interventional therapy, where the use artificial intelligence in the big data and patterns analyses were instrumental [5, 6]. Of particular relevance to current practice are the rare untoward toxic side effect of the convalescent plasma in view of infection induced activation complements and inflammatory pathways and development of autoantibodies and some thrombotic events in some individual that should preferentially removed before usage as previously described [13- 18].

Thirdly the recent the pitfalls of very rare thrombotic adverse effects [less than one per million] in association with the use of the AstraZeneca and Johnson and Johnson vaccines, has raised some public alarm regarding the vaccine-induced immune thrombotic thrombocytopenia (VITT). Interestingly there are some pathological and clinical similarity between the well-established negatively charged heparin-induced thrombocytopenia (HIT), that we are familiar with and VITT, that mostly occurs in some young predisposed female below the age of 30 but it is worthy to highlight that the potential for vaccine-inducing blood clot is comparatively at least 6-10 times lower than by the infection – induced thrombotic events, by the on-going coronavirus variants.

Meanwhile as a cautionary measure VITT has been listed as a very rare side the zero risks in any therapeutic intervention against CoV-2 variants do not exist and furthermore considerable variability observed in the host physiological response to both vaccines and to CoV-2 infection –induced hypercoagulability.

Moreover on the basis of the benefit versus risk analysis, the use of the approved AstraZeneca- types of vaccines, including Janssen, justify their use in all age group without of any question. In fact, in this context there is a change of policy in the USA as after a week of fears and hesitation, they finally opted to pursue again the successful rollout of the Janssen vaccine, the first one dose vaccine design, and it is now back for use as a new armature to BEAT COVID but intriguingly the unused stored AstraZeneca vaccine was distributed to Canada, South America and I in view of their urgent need for more transmissible variant . hence USA is pressing on to recalibrate the condition helping others in need in parallels to their own national need.

Expectedly there is no changes in the UK rollout protocols are made due to fear of very rare potential side effects as almost 50 million doses of the types vaccines have been administered to the UK population without any major severe side effects, while French' stored AstraZeneca vaccines either wasting or offered to younger than 55 aged groups . in view of the fact that there is still a believe this vaccine is not suited to older aged that 55 aged group, despite the large scale interim data from UK, Clearly politicians should be honest and open with public and when come to vaccine and fast spreading variants the objective should be to vaccinate the world as the safest approach as no one safe until everyone safe as we are witnessing with the emerging Indian variant , with divesting impacts all over the world, in 18 countries so far, predominately targeting the unvaccinated groups as put in evidence by the UK hospitals' records .

Clearly while the development of a clot, at the early stages of the inflammatory thromboembolism can be easily contained but severe infection-induced organ injury with fatal outcome, without the use of vaccines as preventative or therapeutic intervention, are often beyond clinical repair. Therefore the use of more effective communication skills are essential to overcome high levels of vaccine hesitancy that still exist in some part of the world, despite the enormous progresses that we are witnessing that have been made with success on passive immunotherapy to survive CoV-2 variants and to save lives. Meanwhile the race between the CoV-2 mutated variant strains and the targeted vaccines development to save life is still on and

many investigators are focusing on the development of targeted vaccines against variants and some booster bio- products, free from autoantibodies, activated complements and cytokines, as a safer and more effective coronavirus convalescent plasma-derived alternative therapies[1]. The journey in this direction is already begun but we need some urgent clinical trials to clearly establish their usefulness in the current health care system with more certainty, in particular in areas of poor economic infrastructure [18]

Another unresolved challenges is to establishing, with certainty, what are the deriving causes behind the platelet clot, mainly young female individuals?

In fact several host epidemiological and environmental factors could contribute to the ongoing recurrences of clotting events narratives, that need to be explored with some certainty. These include: a] infection- induced the inflammatory processes before vaccination? ; b] physiological responses subsequent the early phases immune response that known to be associated on the evidence based with the activation of the complement systems? ; c] is it in response to the formation of the immune complexes formation with viral antigens that could triggers the localized activation coagulation factors and subsequently to platelet consumption in certain individuals, who might be already predisposed to pre-thrombotic events or having some genetic or acquired hypercoagulability?; d] finally what are the agents in the vaccines that might be responsible for the initiation of he reported blood clot consisting of platelet clot in some unusual sites such as the brains of mainly young female individuals?

Moreover there are several other precipitating factors predisposing to thrombotic complications and include: infection-induced inflammation; activation of complements in the early defence mechanism; and activation of the coagulation systems and platelet and its immobilization, all contributing to diffuse intravascular coagulation. Since in the majority cases blood clot appeared mainly in female below the age 30, it raises the pertinent question whether some host factor [i.e. being potentially on the oral contraceptive, hormone therapy, pregnancy, or other conditions etc.], specifically predisposing them to thrombotic events. Therefore it is therefore important to understand the overall clinical benefit of vaccination in older population at risk of severe infection such as the over 60 aged male have a higher benefit than young female with less than 30 years, who are less prone to be infected by coronavirus infection.

In fact the recent study, on more than 3 million hospitalized COVID-19 patients, the ratio of benefit of vaccination versus the potential risk of the blood clot, was used as the marker of venous and arterial thrombotic complications. It was observed that only a negligible numbers [79 in total in all age group] with the ratio of "14.1:0.2" for the over the age of 60 male as compared to female under the age of 30 with a ratio of" 0.8:1.1" respectively. This clearly confirms that the notions that vaccine immunotherapy is truly of benefits to all ages, even the younger population, where there is a higher risk of blood clot, for what ever might be the reasons might be.

The relationship between the types of infections, as causative agents and the nature of thrombotic events and stroke

In another independent recent report, comparing admitted hospitalized influenza patients with patients admitted with COVID-19, it was found that a 10 folds increased risk for thrombotic complications occurred, by day 30 in the COVID group, particularly in patients admitted to the ICU, as driven by a difference in venous thrombotic complications 3.6% in influenza group compared with 23% in COVID-19 group. Moreover, in the influenza respiratory viruses a two fold transient increase in vascular complications in respiratory tract infections with an increase for venous thrombotic disease and an even fivefold increase for ischemic heart disease. Moreover the arterial thrombotic complications and in particular myocardial infarction, occurred more in patients with influenza than in patients with COVID-19. Moreover strokes occurred in the ratio of 0.2/1.6% and 0.8/1.7 in the patients with influenza patients with COVID-19 , all pointing out that the types of thrombotic events in Covid infection quite different than other respiratory infections. Surprisingly, in a Chinese community study no difference in VTC rates were observed overall in younger populations. However the risk of venous thrombosis is known to be lower in East Asians than in white Caucasians, which limits generalizing these findings to others geographical populations. Therefore, both mechanisms likely play a role in the pathophysiology of COVID-19–associated thrombosis, and further research in this field is needed.

From diagnostic standpoints it is important to recall that thrombotic risks in COVID-19 due to in situ immuno thrombosis could have been underestimated, since this diagnosis is often established only after death in pathology reports. In fact from diagnostic stand point, evidence is accumulating that the improved D Dimmer test is highly effective to discriminate to identify hospitalized patients with COVID-19 as low, moderate, and high VTE risk, with potential to individualize thrombo prophylactic strategies. However so far no clear approach exists to discriminate high-risk hospitalized patients with coronavirus disease for venous thromboembolism within a multihospital health system and the IMPROVE-DD VTE risk score classified approximately 45% of the population into high VTE risk showing some potential to individualize strategies to prevent VTE in this population.

While it is now firmely believed that the activation of the early phase of inflammatory - coagulation systems do occur in both the viral pneumonias such as influenza virus and in severe acute respiratory syndrome of the CoV-2 variants but in patients with influenza there is a high risk of arterial thrombotic complications, whereas the virus-specific COVID features on site specific immuno thrombosis, leading to COVID-19–associated alveolar injury and an extreme inflammatory response on situ, contributing to small-vessel thrombus formation in the lungs, as are often corroborated in autopsy studies supporting this the presence of platelet-fibrin thrombi in small arterial vessels of the lungs and a higher incidence of DVT upon screening, which is compatible with the conventional thromboembolic origin of PE

and the possibility of the white platelet clot reflecting the low platelet count in brain of some patients.

CONCLUSION

It has been two years since the COVID-19 pandemic began and plethora of research into CoV-2 has led to deployment of vaccines as the most effective approved therapeutics intervention. Recently, however some limited cases of blood clot, in unusual sites, predominantly in the young female in the age ranges below 30, has been reported not only by using the approved AZCV but also others approved vaccines in the current use, including the new generation vaccine, Johnson and Johnson, one shot vaccine [approximately one case per million], currently in use in the USA.

Interestingly there is a technical similarity between Oxford, Johnson and Johnson and Russian vaccines all three are using the adenovirus technologies. While this is a very rare event but Perhaps it would be more appropriate that a simple pre-screening test for hypercoagulability embodying the familial history of acquired hypercoagulability of the females under 50 should be introduced as an additional safety measures if such a rare side effects in new generation of vaccines predominately in young female persist .

Clearly today it will be difficult to guarantee people will get the same vaccine soon or latter that they had originally promised as it is becoming practically impossible task because once you've completed a course of one of the two dose validated vaccines the in the future it could be quite difficult to guarantee again you get the same type of vaccine, even with the shorter delays between the two dose to make vaccine available to all while diluting its effectiveness, as newer generation of more effective and more practical one dose and multivariate targeted vaccines are already on the table and there will be a mix and match types vaccines for second or a third or fourth vaccination, over the next few years. Not forgetting the most useful strategy of the booster types of fast acting by nature of neutralizing polyclonal antibodies hyper concentrate that considered to be the best fit product for use in vaccine' no- responders and or poor- responders , at real time, not mentioning the young female as such a product considered to be highly effective without delay in building up the immunity against variants and being by nature highly toxic free.

Meanwhile as we are still gathering further evidence –based information to discriminate CoV-2 hospitalised patients at high risk even with an universal thrombo prophylactic strategy and a more targeted multiple variants - based vaccines in parallel with validated and approved purer and safer alternative booster bio products , that must be supported by clinical trials, we must wait and see there might be a clear approach to what we need to, as the high priority.

However for sure instead of fighting, like some rats in the sack, who is getting first delivery of the highly scarce supply of vaccine nationally and over amplifying the minimal risk of side effect of some highly in demands vaccines that unfortunately is happening in Europe, despite having plenty of such vaccine in store even without usage. Surely facilitating mass vaccination as the main objective should be and helping the others to vaccinate the world globally as we are witnessing with the currently emerging Indian variant, supporting the concept that no one is safe until every one is safe and some countries with poor economic [18] , should joint the other as a team to help not only by Covax approach but also be supportive to help with the appropriate know- how to build appropriately targeted vaccine production and the alternative therapy locally to support each other with close collaboration and team working to benefit of all concerned.

Meanwhile the message to take home is to stay tune with the evidence –based life saving benefits of the global vaccines as side effects all approved vaccine so far is negligible and very rare and can even be prevented with proposed plan of action. Interestingly ISTH has come up with a very thoughtful diagnostic flow chat [updated 20 April, 2021], with a comprehensive VITT treatment, a highly recommended SDP chart for use to fill up this gap in the thrombotic events or the antithrombotic guidance statements for hospitalized patients with coronavirus disease.

REFERENCES

1. Amiral J, Vissac AM, Seghatchian J. Covid-19, induced activation of hemostasis, and immune reactions: Can an auto-immune reaction contribute to the delayed severe complications observed in some patients? Transfus Apher Sci. 2020; 59: 102804.
2. Seghatchian MJ. Sammama MM . Hecker SP. H percoagulable states; fundamental aspects, acquired disorders and congenital thrombophilia by CRC Press Inc. 1996.
3. Seghatchian MJ, Savidge GF[Edi]. Factor VIIIvon Willebrand factor-[Vol II] Clinical aspects of deficiency states by CRC Press Inc. 1989.
4. Stirling Y, Woolf L, North WRS, Seghatchian J, Meade TW. Haemostasis in normal pregnancy. Thromb Haemost. 1984; 52: 176-182.
5. Seghatchian J. An introductory commentary on the use of artificial intelligence, machine learning and TQM, as novel computational tools in big data patterns or procedural analysis, in transfusion medicine. Transfus Apher Sci. 2020: 59: 102985.
6. Alessandro DA. Benford's law and metabolomics: a tale of numbers and blood. Transfus Apher Sci. 2020: 59: 103019.
7. Seghatchian J. New generation of vaccines and convalescent plasma therapy for the management of CoV-2, in the global pandemic. Transfus Apher Sci. 2021: 103064.
8. Seghatchian J. Editorial. Facts and challenges on global deployment of vaccines for the immunotherapy of the evolving SARS Cov-2 variants: What a new year, with a fast spreading South African and the most fearful Brazilian variants, as the unwanted gifts, imposing enormous crises to surmount. Transfus Apher Sci. 2021; 60: 103091.
9. Seghatchian J, Acker JP, Putter JS. Update on newer approaches to prevent or treat COVID-19 infection: what we all need the most right now. Transfus Apher Sci. 2020; 59: 102933.
10. Seghatchian J, Lanza F. Convalescent plasma, an apheresis research project targeting and motivating the fully recovered COVID 19 patients: A rousing message of clinical benefit to both donors and recipients alike. Transfus Apher Sci 2020; 59 : 102794.
11. Lanza F, Agostini V, Monaco F, Passamonti F , Seghatchian J . Therapeutic use of convalescent plasma in covid-19 infected patients with concomitant hematological disorders. IACH. 2021.
12. Putter JS, Seghatchian J. An update on COVID-19 infection

control measures, plasma-based therapeutics, corticosteroid pharmacotherapy and vaccine research. Transfus Apher Sci. 2020; 59: 102934.

13. Gang Chen, Yangzhong Zhou, Jie Ma, Peng Xia, Yan Qin et al. Is there a role for blood purification therapies targeting cytokine storm syndrome in critically severe COVID-19 patients? Renal Failure, 2020; 42: 483-488.

14. Alessandro DA, Tiffany T, Dzieciatkowaska, M, Hill RC, Richado F et al. Serum proteomics in COVID-19 patients: altered coagulation and complement status as a function of IL-6 level. Journal of proteome research. 2020. 19: 4417-4427.

15. Picchianti Diamanti A, Rosado MM, Pioli C, Sesti G, Laganà B. Cytokine release syndrome in COVID-19 patients, a new scenario for an old concern: The fragile balance between infections and autoimmunity. Int J Mol Sci. 2020; 21: 3330.

16. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020; 395: 1417-1418.

17. Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. J Thromb Haemost. 2020; 18: 1559-1561.

18. Smit Sibinga C Th, Abdella YE, Seghatchian J. Poor economics - Transforming challenges in transfusion medicine and science into opportunities. Transfus Apher Sci. 2020: 59: 102752.

Cite this article

Seghatchian J (2021) Thrombotic Thrombocytopenia Induced by Cov-2 Infection and Some Components of Vaccines: Is it Related to Host Prethrombotic State? J Hematol Transfus 8(1): 10901