REPUBLIC OF LEBANON
MINISTRY OF PUBLIC HEALTH

Lebanese Committee of Blood Transfusion

Program of COVID-19 convalescent plasma collection and transfusion guidance on collection, testing, processing, storage, distribution and monitored use

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Contents

1. Introduction

While this document is not legally binding, it aims to facilitate a common approach across blood transfusion services in Lebanon to the donation, collection, testing, processing, storage, distribution and monitoring of convalescent plasma for the treatment of COVID-19.
This document is without prejudice to the requirements of the "Good transfusion practice guidelines" MOPH, which continue to apply.
This guidance is updated as needed, in line with scientific developments.
Because the safety and efficacy of convalescent COVID-19 plasma as a treatment for COVID19 are unproven at this time, clinical use of this product should be managed as an experimental therapy consistent with ethical and legal safeguards (informed consent of donors and patients, institutional approval, special labeling as an investigational product)

2. Background

Plasma collected from patients that have recovered from an infectious disease has been transfused over many decades for the prophylaxis and/or treatment of various infectious diseases although the evidence of its effectiveness and safety is mostly limited to empirical reports. During a rapidly expanding outbreak of a viral infection, large populations of susceptible persons may become ill early in the event, prior to availability of effective vaccines and antiviral therapies.
As highlighted by the WHO Blood Regulators Network , an organized program to collect convalescent plasma or serum from disease survivors could provide a potentially valuable empirical intervention while data on effectiveness and safety of its use are being gathered through structured clinical trials. The COVID-19 pandemic is a clear situation where plasma from recovered patients might be a valuable resource to support the disease treatment within randomized or case-control clinical trials or observational studies of plasma transfusion and in the development of a plasma-derived medicinal products. The use of convalescent plasma for prophylactic treatment of 'at-risk' population groups is also a possibility in the future but is not addressed in this document.

3. Authorization of convalescent plasma collection, testing, processing, storage and distribution

Blood establishments holding a license for blood bank from MOPH and complying with "good transfusion practice guidelines" for donation, collection, processing and testing are authorized by Ministry of public health to proceed.

4. Donor eligibility

Convalescent plasma donors should be recruited directly by the use of national registries of patients that were infected with COVID-19 and recovered. Alternatively, potential donors should be identified through collaboration with public health bodies or treating hospitals or through targeted donor recruitment strategies including, but not restricted to, (social) media calls.
In addition to standard donor criteria for blood or plasma donation, the following criteria should be applied:

a. Confirmation of previous infection with SARS-CoV-2 by a record of a validated diagnostic test at the time of illness or a positive test for antiSARS-CoV-2 antibodies, whether the individual had symptoms or not.
NAT and serology tests should be CE marked or FDA approved.

b. An interval of at least 28 days after full recovery.

c. Standard selection criteria for whole blood or plasma donation according to local requirements and standards (age, weight, collection frequency, vital signs, freedom from deferral criteria) in line with "Good transfusion practice guidelines" MOPH

d. Non-reactivity of blood samples for transfusion transmitted infections including HIV, HBV, HCV, syphilis (for whole blood) and locally transmitted infections using approved serological tests, consistent with local requirements for collection of blood components for transfusion.

e. To avoid the risk of Transfusion Related Acute Lung Injury (TRALI) preference should be given to use of plasma from male donors or from female donors who have never been pregnant including abortions. This measure lowers the possibility of presence in the plasma of the antibodies to HLA or granulocyte antigens that cause TRALI. TRALI occurs within 6 hours after transfusion of implicated plasma and can be severe. (3)

f. Informed consent in line with MOPH policies and preferably addressing the existing uncertainties in the antibody level dynamics in convalescent plasma donors.

g. Recovery from COVID-19 infection should be confirmed through:

- Physical examination of the donor to establish good health including absence of fever and respiratory symptoms
- If plasma is collected prior to 28 days after full recovery from illness, then confirmation of the resolution of the infection should be obtained through demonstration of two non-reactive Nucleic Acid Tests (NAT) for SARS-CoV-2 performed at an interval of at least 24 hours on nasopharyngeal swabs
- The approximate date of COVID-19 infection, history of symptoms, treatments received and date of resolution of all symptoms documented and traceable
- When feasible, the total and neutralizing titers of anti-SARS-CoV-2 antibodies should be determined as part of product characterization before use. Current data suggest that donations with a minimal titre by end-point dilution of 1:80 or preferably 1:160 should

be selected. Absent a test for neutralizing antibodies, and where feasible, donations also can be selected based on high reactivity in a serologic assay for anti-SARS-CoV-2 antibodies. When antibodies are not detected in the collected plasma, it cannot be considered for COVID-19 therapeutic purposes

- Furthermore, donor blood/serum/plasma samples should be saved frozen at -80°C for retrospective testing and further scientific investigations.

5. Criteria for collection of COVID-19 plasma

a. Performed in certified blood establishments by appropriately trained staff.
b. Use only of approved blood collection or plasmapheresis equipment under standard operating procedures.
c. Supervision of the collection process by trained staff.
d. Volume of plasma to be collected: at least 200 to 600 mL (without anticoagulant) based on the procedure.
e. Plasma units intended for use as convalescent plasma should be clearly labeled as COVID-19 Convalescent Plasma/Blood and stored in a dedicated location.
f. The first plasma donation can be followed by further donations at a frequency taking into full account the health status of the donor and the interval between 2 plasma donations.
For donors that donate more than once, antibody titers should generally be measured at every donation and donors should be deferred if there is evidence of potentially detrimental antibody depletion.

NB: Donors will ideally donate plasma by plasmapheresis, but where that is not possible, whole blood can also be collected, with plasma separation in the blood establishment.

6. Post-donation treatment of plasma

a. Freezing as soon as possible at -20°C or preferably colder and stored frozen until administration
b. Plasma samples aliquots should be taken for archiving at -80°C and future potential scientific investigations
c. Plasma obtained by plasmapheresis should be split before freezing into 2-3 separate units (e.g. 3x200 ml).

7. Recommendations for plasma transfusion

a. Follow standard hospital procedures and recommendations for thawing and transfusion of plasma
b. It is crucial to ensure ABO compatibility between the donor and the recipient
c. Transfusion of plasma from at least two donors may be therapeutically beneficial to achieve more effective immune protection from delivery of diverse antibodies.

d. In the absence of published peer-reviewed reports of transfusion of convalescent COVID-19 plasma, patients could receive one or 2 initial doses of COVID-19 convalescent plasma of 200 to 240 mL each in IV injection at J8 +/- 2 from the onset of clinical symptoms followed by 1 or 2 additional doses of 200 ml after 24h according to disease severity and tolerance to infusions) so a total of 2 to 4 units / patient in 2 episodes at a slow transfusion rate of 200 mL/hour (3,5 mL/mn)
e. Blood/serum/plasma samples of the recipient prior to and after transfusion should be taken for future potential scientific investigations.

NB: Patients having a previous history of severe allergic reactions to plasma transfusion are not eligible to transfusion by convalescent plasma

8. Distribution of COVID-19 convalescent plasma Convalescent plasma should be distributed by blood establishments in the following circumstances

- The specific patient has laboratory confirmed COVID-19.
- The patient has been hospitalized.
- The patient has a scale of severity of at least grades 4 et 5 as described in WHO until the 10th day after the onset of clinical symptoms. For grades higher than 5 or transfusion to be done more than 10 days after the onset of symptoms, the decision is for the treating physician.

- A special attention should be given to cardiac patients during transfusion due to increased risk of circulatory overload (TACO : Transfusion Acute Circulatory Overload).

- The patient, or their legal representative, has given informed consent to transfusion with COVID-19 convalescent plasma. The uncertainty about the efficacy of convalescent plasma in treating people with COVID-19 should be communicated to potential recipients or their legal representatives, whether they are part of a clinical trial or of monitored use, to avoid fostering unfounded expectations and to ensure that prospective recipients or their legal representatives make informed decisions regarding treatment.

- Blood services should aim to issue the components with the highest antibody titers available.

9. Patient outcome data

The patient outcome date should at least include the following parameters:

1. Gender
2. age range
3. co-morbidities
4. Date of onset of symptoms
5. Date of hospitalization

2. Transfusion time point (in days from disease onset)
3. Number, volume and antibody titre (if evaluated) of transfused unit(s)
4. Therapies administered to the patient in parallel (other than supportive care)
5. Clinical symptoms and laboratory parameters– according to the disease progression scale (Annex 1) at the following time points:
• Prior to transfusion
• > 5 days after transfusion15
• At discharge (if the patient survives)
6. Any serious adverse reactions or events possibly linked to the transfusion
7. Length of hospitalisation (if no death).
8.Date of clinical cure (end of symptoms)

10. References

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11. Annexes

ANNEX 1: WHO Ordinal Scale for COVID-19 Clinical Improvement[17]

Ordinal Scale for Clinical Improvement

Patient State	Descriptor	Score
Uninfected	No clinical or virological evidence of infection	0
Ambulatory	No limitation of activities	1
	Limitation of activities	2
Hospitalized Mild disease	Hospitalized, no oxygen therapy	3
	Oxygen by mask or nasal prongs	4
Hospitalized Severe Disease	Non-invasive ventilation or high-flow oxygen	5
	Intubation and mechanical ventilation	6
	Ventilation + additional organ support – pressors, RRT, ECMO	7
Dead	Death	8