Original Article

Assessment of Nigerian Blood Transfusion Centers' Capacity for Provision of Convalescent Plasma for Treatment of SARS-CoV-2 Infected Patients

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Abstract

Background and Objectives: With the data from small clinical trials leading to the emergency authorization of convalescent plasma (CP) as one of the treatment options of coronavirus disease 2019 (COVID-19) in the United States, countries across the world are likely to key in as the race toward discovering evidence-based treatment and vaccines continues. We assessed Nigerian blood transfusion services' preparedness to provide CP support for patients with moderate-to-severe acute respiratory syndrome coronavirus 2 infection. **Materials and Methods:** We conducted an online survey using a questionnaire designed to assess the Nigerian blood centers' existing capacity. Forty-two tertiary facilities were selected, and a questionnaire was E-mailed to the selected blood bank staff of each center. Responses were collated and analyzed using descriptive statistics. **Results:** The majority of the facilities had neither apheresis (73.5% [25 of 34]) nor cold centrifuge (55.9% [19 of 34]) for blood components collection or preparations. Family replacement blood donors contributed 51%–90% of the donations in 70.6% (24 of 34) of the centers. Only 2.9% of the centers had an existing capacity for using nucleic acid to screen transfusion transmissible infections, and only one center reported the capacity for pathogen inactivation of blood components. None of the centers provide leukodepletion for blood components. **Conclusion:** At the current state, Nigerian blood transfusion services are incapable of providing adequate and safe CP for COVID-19 treatment. Efforts should be made to invest in this critical health service area to take advantage of the readily available CP to reduce mortality and morbidity associated with the COVID-19 pandemic, and other disorders.

Keywords: Blood donation, convalescent plasma, coronavirus disease 2019, severe acute respiratory syndrome coronavirus 2

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Introduction

Emerging and reemerging infectious diseases have continued to pose a threat to the global public health agenda.[1] The 21st century has seen the emergence of highly virulent zoonotic infections, crossing over to humans, with a pandemic propensity. Severe acute respiratory syndrome (SARS) was first reported in 2002 and the Middle East Respiratory Syndrome (MERS) in 2012.[1] In late 2019, another outbreak of severe flu-like illness was reported in Wuhan (the capital city of Hubei province) in China.[2] The organism causing the infection was initially named novel coronavirus 2019, but later rechristened SARS-coronavirus 2 (SARS-CoV2),-whereas the disease was named coronavirus disease 2019 (COVID-19).[1,2]

For the first time in over a century since Spanish Flu, COVID-19 quickly attained the status of a pandemic that affects nearly all continents.[2]

Globally, about 24 million confirmed cases of COVID-19 and over 800,000 deaths had been reported by August 2020.[3] Despite limited testing sites, Nigeria has recorded over 50,000 confirmed cases with >1000 deaths, by the same period.[4] The

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combination of SARS-CoV2 highly infectious nature and its significant morbidity and mortality make evidence-based treatment strategies (which are currently lacking) a priority.[5] Thus, several ongoing clinical trials have been launched with existing drugs that are being repurposed for the treatment of COVID-19.[5] Convalescent plasma (CP) is considered as one of such effective treatment options, and evidence of its safety and relative benefits came mainly from observational studies and small clinical trials.[6-8] Based on public health emergency, the United States (US) Federal Foods and Drug Administration (FDA) issued emergency authorization for the use of CP as a treatment option; in anticipation of favorable results from the phase III clinical trials assessing the efficacy and effectiveness of CP in patients with moderate and severe COVID-19.[9]

Although CP appears to be easy to produce locally by licensed blood banks, resource-limited countries like Nigeria have peculiarities that may affect their preparedness in utilizing this readily available treatment option. The Nigerian blood transfusion service is mainly hospital-based, significantly driven by family replacement blood donors (FRBD), and sometimes commercial donors disguising as FRBD.[10] These donors are considered unsafe by the World Health Organization (WHO) standard, which recommends only centrally coordinated blood transfusion service dependent entirely on voluntary nonremunerated blood donors (VNBD).[11] In Nigeria, the central National Blood Transfusion Services (NBTS) contribution to the blood supply is negligible.[10] Moreover, the rigorous conditions of a large clinical trial with a blood component would require an effective and efficient centrally coordinated and standardized transfusion service. In the absence of an effective NBTS, regional and hospital-based transfusion services would be the only systems to fall back. This study was aimed to discern the existing capacity and practices of the blood centers in the Nigerian tertiary health institutions, as the first step toward the provision of safe CP for the treatment of patients with COVID-19.

Materials and Methods

We conducted a cross-sectional survey over 3 months (May to July 2020), the peak of COVID-19 restrictions, using an online structured questionnaire. The questionnaire was sent out via an E-mail to selected representatives of each blood center attached to a tertiary health facility in the 36 states of Nigeria, including the Federal Capital Territory. The sampling was based on a convenient technique. We also separately sent an E-mail to the coordinator of the NBTS to get a comprehensive self-reported assessment of the existing capacity of Nigeria's transfusion services. The responders selected for this survey were either the blood facilities directors, biomedical scientists coordinating operations of the blood facilities, or physicians working as transfusion medicine specialists in the blood facilities. Their responses were collated online via a "Google Form" and downloaded as a comma-separated values file. We selected only the blood facilities attached to tertiary health centers because they represent the highest level of sophistication in Nigeria's health-care system. We E-mailed weekly reminders to the respondents as a strategy to improve the questionnaire return rate.

To ascertain the pandemic's impact on blood donations, we retrieved the records of blood donors in Aminu Kano Teaching Hospitals (one of the tertiary health facilities in Nigeria) for 4 months (March to June) for the year 2019 and 2020. This period coincides with when restrictive measures and lockdowns were at their peak in Kano, Nigeria.

The data collected were analyzed using STATA version 13 (STATA Corp, College Station, TX, USA). The Chart was done with Microsoft Excel (2010), and the trend comparison for the blood donation patterns of 2019 and 2020 was made using Chi-square statistics. The alpha level of significance was pegged at <0.05. All dichotomous and categorical variables were summarized as numbers and percentages. We designed the map using the ArcGIS version 10.7.

Results

We report the results of a survey from 34 blood banks and blood donor centers of tertiary health facilities across Nigeria, including the NBTS. Of the 42 online survey questionnaires E-mailed, 34 were returned with appropriate responses, giving us an approximate 81% return rate [Figure 1]. The majority (79.4% [27 of 34]) of the respondents were hematologists/transfusion medicine specialists [Table 1]. Half of the blood banks (50% [17 of 34] had an approximate storage capacity of ≤200 units of blood, and 61.8% (21 of 34) of blood banks issue out (daily cross-match) <50 units of blood. Over half of the blood banks (55.9% [19 of 34]) had no cold centrifuge for blood fractionation. None of the facilities had the capacity for leukodepletion or used bedside leukocytes filters routinely. The majority 76.5% (26 of 34) had a −20°C freezer and 58.8% (20 of 34) had −70°C freezer for blood product

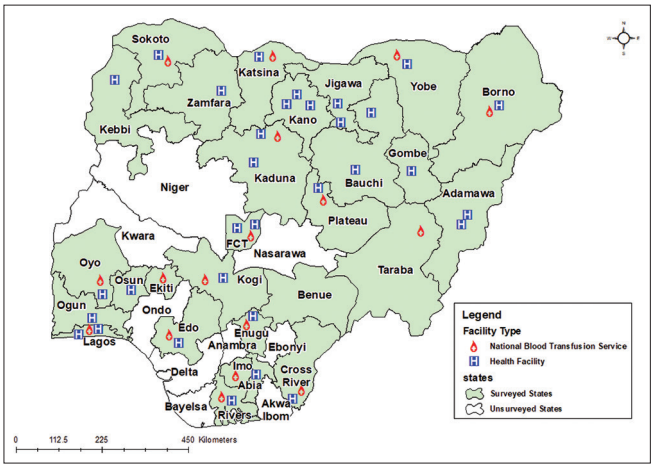

Figure 1: Nigeria's map with 36 states and the Federal Capital Territory, including the health facilities that participated in the survey. A total of 34 out of 42 centers responded (including NBTS), which gave a return rate of approximately 81%. Some states had more than one response

storage. Almost all of the facilities (97.1% [33 of 34]) had no capacity for pathogen inactivation.

In terms of automated methods of collecting blood components, most of the facilities (73.5% [25 of 34]) had no apheresis machine, Table 2. In the blood centers where an apheresis machine exists, its utilization is limited, and (66.7% [6 of 9]) reported using it rarely for blood components collection or therapeutic purposes. The majority (70.6% [24 of 34]) of the blood centers relied on FRBD, which constituted about 51%–90% of their regular donors, whereas VNRBD constituted <5% in 72.7% (24 of 34) centers. Only a single blood center (NBTS headquarters, Abuja) could use nucleic acid testing to screen for transfusion transmissible infections (TTIs). Even though SARS-CoV2 is not classified as a TTI, only 2.9% (1 of 34) could implement routine testing of SARS-CoV2 using nucleic acid testing because of inadequately trained personnel and lack of PCR equipment.

Table 1: Baseline data of blood processing and storage capacity in the Nigerian blood banks across 28 states, including the National Blood Transfusion Service

	n (%)
Blood centers (responders)	34 of 42 (80.9)
Qualification of the respondents	
Physician/hematologist	26 (76.5)
Laboratory scientist	7 (20.5)
Laboratory technologist	1 (3)
Storage capacity of the facility (units)	
≤100	8 (23.5)
101-200	9 (26.5)
201-400	10 (29.4)
401-500	5 (14.7)
500	2 (5.9)
Average number of daily cross-match (units)	
<50	21 (61.8)
50-100	12 (35.3)
NA	1 (2.9)
Availability of cold centrifuge	
Yes	15 (44.1)
No	19 (55.9)
Availability of platelet incubator for storage	
Yes	11 (32.4)
No	23 (67.7)
Leukodepletion for component preparation/ leukocytes filters	
Yes	0.0
No	34 (100)
Availability of-20 refrigerator	
Yes	26 (76.5)
No	8 (23.5)
Availability of -70 refrigerator	
Yes	14 (41.2)
No	20 (58.8)
Capacity to do pathogen inactivation	
Yes	1 (2.9)
No	33 (97.1)

NA: Not applicable

None of the blood centers could measure the COVID-19 IgG titer as a prerequisite for emergency authorization to use CP in the treatment of COVID-19.

Blood donations in Aminu Kano Teaching Hospital, over the period of nationwide lockdown in Nigeria (March to June), significantly dropped when compared to the same period in 2019 (P <.001) [Figure 2]. There was a sharp drop in the blood donations in April when the lockdown was at its peak.

Discussion

CP is a promising treatment strategy for COVID-19, which if successful could likely pave the way for the development of commercially prepared immunoglobulins for COVID-19 treatment. We report here the findings of the first survey from Nigeria, which assessed the country's blood transfusion services' preparedness to key into the expanding indications of CP for COVID-19 treatment. Our results show that Nigeria's blood transfusion service is largely hospital-based and is driven mainly by the FRBD. The NBTS, which is saddled with the central coordination of safe blood provision in Nigeria, has 18 regional centers, including the federal capital. This lack of spread means that accessing the service of the NBTS by all the 36 states will require an efficient transport system. This lack of widespread presence and delivery challenges to the local centers contribute to the difficulty in standardization and most likely, to the high rate of FRBD and even commercial donors. FRBD have been reported to be unsafe because of the high rate of TTIs compared to VNRBD, leading to the preference of VNRBD by the WHO as a more dependable source of blood.[12,13] However, this conclusion is influenced by the status of the donors. First-time blood donors have a higher TTIs rate than repeat VNBD (who have been hitherto screened and counseled on risky behaviors.[12] Indeed it is documented that the difference in TTIs rate appears to be similar between FRBD and VNBD when the data are controlled for the first-time donation status.[13] The centrally coordinated blood transfusion services also come with significant financial

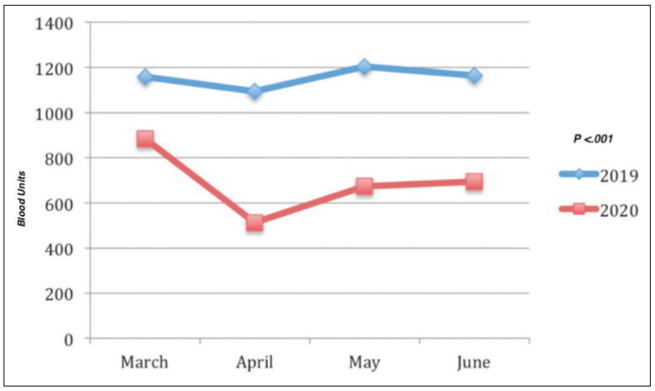

Figure 2: The impact of COVID-19 on blood donation patterns in Aminu Kano Teaching Hospital for March to June 2020 compared to the same period in 2019, $P < 0.001$. There was a sharp drop in April 2019 before the donation pattern stabilizes in May and June

Table 2: Baseline data on blood donation patterns and screening capacity of the foremost Nigerian blood centers across 28 out of 36 states, including the National Blood Transfusion Services

	n (%)
Availability of apheresis machine	
Yes	9 (26.5)
No	25 (73.5)
Average monthly utilization of donor apheresis	
Rarely used	6 (66.7)
1-3 per month	2 (22.2)
80 per month	1 (11.1)
Average monthly utilization of therapeutic apheresis	
0 per month	6 (66.7)
1 per month	3 (33.3)
Proportion of voluntary blood donors (%)	
<5	24 (75.0)
5-15	6 (18.8)
50	1 (3.1)
100	1 (3.1)
Proportion of family replacement blood donors (%)	
5-20	5 (14.7)
50	3 (8.8)
51-90	24 (70.6)
>90	2 (5.9)
Capacity to screen donors routinely for SARS-COV2	
Yes	1 (2.9)
No	33 (97.1)
Nucleic acid test for TTI screening	
Yes	1 (2.9)
No	33 (97.1)
SARS-CoV2 IgG measurement	
Yes	0.0
No	34 (100)
Other challenges, *n*=11	
No constant electricity	1 (9.1)
Lack of pediatric bags	1 (9.1)
Rapid tests and ELISA	4 (36.4)
Others	5 (45.4)

SARS-CoV2: Severe acute respiratory syndrome coronavirus 2, TTI: Transfusion transmissible infection, ELISA: Enzyme-linked immunosorbent assay

commitment relative to the regional or hospital-based transfusion services due to the numerous logistics involved in recruiting VNRBD and the distribution of blood and products to the various centers.[13] Thus, resource-limited countries with poor budgetary allocation to health like Nigeria, will have significant challenges in maintaining an effective, centrally coordinated blood transfusion service and are unlikely to meet the WHO criteria for blood sufficiency. These data suggest that for Nigeria to be eligible for CP therapy serious efforts must be made to shore up the number of VNRBD or a waiver should be given to the hospital-based FRBD to be the main drivers in this campaign. The latter approach will likely be affected by blood shortages.

Screening for TTIs is a key step toward safe blood transfusion. Our survey finds that only NBTS in Nigeria has the capacity for nucleic acid testing, which is the gold standard for TTIs screening. Over the past few years, countries like Nigeria had received external funding, particularly through the US-funded President's Emergency Plan for AIDS Relief (PEPFAR), to improve blood transfusion safety.[12,13] Such external funding has led to an improvement in the number of TTIs screened. However, due to such programs' central nature, much of the funds were spent on creating NBTS and neglecting the general hospital-based transfusion services that are the major drivers of blood supply in Nigeria.[12,13] The prevailing practice of TTI screening in Nigeria is based on rapid test kits for HIV, hepatitis B and C, and syphilis.[10] Rapid test kits have been shown to have low sensitivity and specificity, and are grossly limited in identifying early infections during the window period.[10,13] Therefore, improvement in the screening capacity for TTIs as a prerequisite for CP treatment in patients with COVID-19 is necessary.

In standard practices, plasma and plasma products undergo a pathogen inactivation process to reduce the likelihood of TTIs during transfusion. Leukodepletion also helps in reducing the incidence of adverse effects related to blood transfusion. Our survey shows that none of the facilities, including the NBTS, has the capacity for leukodepletion or offers bedside leukocytes filter for blood transfusion. Only the NBTS has the minimal capacity for pathogen inactivation at its headquarters. In addition, the blood centers are unable to quantify SARS-CoV2 IgG. Measuring the SARS-CoV2 IgG level in the CP is a prerequisite in the FDA's emergency authorization.[9] These deficiencies will affect the CP's safety, hence the need to be addressed before authorizing the CP for COVID-19 treatment in Nigeria.

The capacity for collection, preparation, and storage of CP is critical to the product's supply sustainability. More than 50% of Nigeria's blood donor centers do not have a cold centrifuge for blood components preparation. For a more efficient and safer CP collection, the availability of apheresis is also desirable. Our results show that two-thirds of the blood centers do not have an apheresis machine. Even for the few centers that possess it, its utilization for both blood component donation and therapeutic purposes is very poor. This finding implies that a sustainable supply of CP in Nigeria cannot be guaranteed due to its inadequate plasma collection capacity. However, most centers have −20°C freezers, and a substantial number have −70°C freezers. The availability of these resources will help to maintain ideal storage for blood components provided the perennial problem of epileptic electricity supply is addressed through alternative energy sources.

Globally, COVID-19 has affected blood supplies due to initial lockdowns and scaling down of other clinical services in the hospitals.[14] Almost 73% of the surveyed blood centers reported having VNRBD usually as low as <5%, thus relying mainly on FRBD or commercial donors. The effect of COVID-19 on the

blood supply chain in Nigeria was dramatic. Our data shows that when COVID-19 restrictive measures were in full effect in Nigeria, blood donations were reduced significantly to as low as half of what was documented for the same period in 2019. The reduction in blood supply has implications not only for COVID-19 treatment but other diseases such as obstetric hemorrhages, severe malarial anemia, and sickle cell anemia that will require blood transfusion support.

Our study has several strengths. The survey has covered the largest number of significant blood centers across the country, including the NBTS, with a very high return rate. The study design is straightforward and easy to replicate. The survey's approach that emphasized self-assessment is also unlikely to be affected by observer bias. Most of the respondents are well versed in blood transfusion; our findings are not likely confounded by knowledge asymmetry. The study's weaknesses include a lack of onsite physical assessment and fewer responses from the centers in southeastern Nigeria compared to other geopolitical regions.

Conclusion

We have demonstrated that the Nigerian blood transfusion service is unprepared to take full advantage of the CP in COVID-19 treatment. The country's policymakers need to quickly and decisively develop a concerted effort toward improving the country's transfusion services.

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Conflicts of interest

There are no conflicts of interest.

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