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Impact of Specimen Referral Network to Rapidly Scale-Up CD4 Testing in Nigeria

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ABSTRACT

Background. Regular, efficient and quality CD4 testing is vital to track disease progression in people living with human immunodeficiency virus (HIV). The lack of sample referral networks resulted in unacceptably long turnaround times (TAT) for laboratory results. The major objective of this study is to assess the contribution of integrated specimen referral network to rapidly scale up CD4 testing to accelerate progress towards the UNAIDS 90–90–90 treatment target for HIV. **Methods.** This is a retrospective study conducted on the reported activities of all 3PL service providers from March 2018 to March 2019. Information was obtained from all the approved CD4 diagnostic centres across all the 36 states and the Federal Capital Territory (FCT) of Nigeria. Tracking records and reports of all centres were also obtained. The total number of specimens rejected was obtained from each centre from the data extraction tool set up by Axios Foundation. Data from bi-monthly quality indicator reports, which included specimen rejection and workload statistics, were included. The data obtained were inputted and analyzed with IBM-SPSS version 25.0. **Results.** The total number of samples transported in the 13 months was 17,629 with the highest number of samples (17.4%) transported in Cross River state. Exactly 15.0% of these samples were transported in Rivers state and FCT had the third-largest sample movement of 12.9%. Cross River, Rivers, and FCT also recorded the highest number of reported results of 87%, 68%, and 64% respectively. There was a steady increase in the number of samples and results transported until July 2018 where the highest peak (2,085) was recorded. Two other peaks were observed in November 2018 (1,979) and February 2019 (1,889). There were 54 (0.31%) rejected samples recorded in the entire 13 months. Although the highest number of transported samples were recorded in Cross River and Rivers states, no sample rejection was recorded in these states. **Conclusion.** The integrated specimen referral network has significantly scaled-up specimen referral and results-reporting networks by increasing access to CD4 count testing that has significantly contributed to ART-related monitoring. This integrated service is very important for enhancing the specimen referral system and increasing access to quality laboratory services in Nigeria. The successful implementation of the integrated system may be relevant to other areas of laboratory services other than sample referrals.

RÉSUMÉ

Contexte. Un dépistage régulier, efficace et de qualité du CD4 est essentiel pour suivre la progression de la maladie chez les personnes vivant avec le virus de l'immunodéficience humaine (VIH). L'absence de réseaux d'aiguillage d'échantillons a entraîné des délais d'exécution inacceptablement longs (TAT) pour les résultats de laboratoire. L'objectif principal de cette étude est d'évaluer la contribution du réseau intégré d'aiguillage des échantillons pour accroître rapidement le dépistage du CD4 afin d'accélérer les progrès vers l'objectif de traitement du VIH 90-90 pour l'ONUSIDA. **Méthodes.** Il s'agit d'une étude rétrospective menée sur les activités déclarées de l'ensemble des prestataires de services 3PL de mars 2018 à mars 2019. Des informations ont été obtenues auprès de tous les centres de diagnostic CD4 approuvés dans les 36 États et du Territoire de la capitale fédérale (FCT) du Nigéria. Des dossiers de suivi et des rapports de tous les centres ont également été obtenus. Le nombre total de spécimens rejetés a été obtenu à partir de chaque centre à partir de l'outil d'extraction de données mis en place par la Fondation Axios, données tirées des rapports semestriels sur les indicateurs de qualité. **Résultats.** Le nombre total d'échantillons transportés au cours des 13 mois était de 17 629, le plus grand nombre d'échantillons (17,4 %) transportés dans l'État de Cross River. Exactement 15,0 % de ces échantillons ont été transportés dans l'État de Rivers et FCT a eu le troisième mouvement d'échantillon en importance de 12,9 %. Cross River, Rivers et FCT ont également enregistré le plus grand nombre de résultats déclarés, soit 87 %, 68 % et 64 % respectivement. Le nombre d'échantillons et de résultats transportés a augmenté régulièrement jusqu'en juillet 2018, où le pic le plus élevé (2 085) a été enregistré. Deux autres pics ont été observés en novembre 2018 (1 979) et en février 2019 (1 889). Il y en avait 54 (0,31 %) échantillons rejetés enregistrés au cours des 13 mois. Bien que le plus grand nombre d'échantillons transportés ait été enregistré dans les États de Cross River et de Rivers, aucun rejet d'échantillon n'a été enregistré dans ces États. **Conclusion.** Le réseau intégré d'aiguillage des échantillons a considérablement élargi les réseaux d'aiguillage et de rapport des résultats en augmentant l'accès aux tests de comptage des CD4 qui ont contribué de façon significative à la surveillance liée au TAR. Ce service intégré est très important pour améliorer le système de référence des spécimens et accroître l'accès aux services de laboratoire de qualité au Nigéria. La mise en œuvre réussie du système intégré peut être pertinente pour d'autres secteurs de services de laboratoire autres que les références d'échantillons

INTRODUCTION

Developing countries currently bear the brunt of HIV and AIDS infection, in addition to the burden of economic hardship and other diseases (1). Regular, efficient and quality CD4 testing is vital to track disease progression in people living with human immunodeficiency virus (HIV). The poor and fragmented specimen referral system in sub-Saharan Africa is uncovered by AIDS (2). The lack of sample referral networks resulted in unacceptably long turnaround times (TAT) for laboratory results. Patients samples are being referred to higher-tiered laboratories with better testing facilities due to lack of or inadequate facilities in the lower-tier laboratories to carry out all necessary tests, (2). Authors have described the timely access to HIV and diagnosis, treatment, and monitoring services as the key requirements to improving and prolonging the lives of people living with HIV, as well as a right direction towards actualizing the goal of an AIDS-free generation (1,3).

Laboratories are essential infrastructure for early detection and reporting of disease (4), and are most effective when organized into an integrated, multi-level network, enabling timely access to appropriate diagnostic tools at each level (5). Tiered laboratory networks facilitate sequential diagnostic testing to identify or confirm the etiological agent(s) causing disease (4). Authors have explained that the laboratory network requires a formal structure for the referral and transport of diagnostic specimens, which will minimize transfer steps and improve rapid diagnosis and laboratory confirmation, thereby reducing the time for reporting of new cases, or an emerging outbreak, and also facilitate safe and secure sample management (2,6,7). The prompt diagnosis and commencement of Antiretroviral therapy (ART) among patients with HIV/AIDS reduces transmission, morbidity, and mortality (8). The laboratory has an important role in ensuring that quality results are available on time to enable care providers to initiate treatment (2).

Several obstacles to an effective sample referral system have been described. Louis identified important challenges limiting widespread access to CD4 cell count testing in Sub-Saharan Africa as inconsistent supplies of electricity and water, poor physical infrastructures, shortage of skilled technicians, irregular and unstable supply-chain for consumables and reagents, and poor equipment handling (8). Standley *et al* described developing an effective and sustainable specimen referral system as an obstacle to the requirement for coordination in establishing a fully integrated and tiered laboratory system, with facilities and staff equipped and trained at each level of the network to manage samples appropriately, safely, and securely (4). According to Kebede *et al.,* non-standardized sample referral system, inadequate staff, the problem of non-standard sample containers, and unacceptably long turnaround time (TAT) impedes testing services (2).

Many of the general challenges to expanding access to CD4 testing in developing countries are explicitly relevant in Nigeria. However, conventional efforts and investment have led to a drastic scale-up of care and treatment for people living with HIV/AIDS in resource-limited countries over the last decade (8). According to Louis, the need to increase the availability of CD4 testing in Africa has driven the development of an array of cost-efficient and technically simple CD4 cell count testing platform. He further mentioned possible approaches to expansion of access to CD4 tests as (1) establishment of decentralized testing using these platforms and (2) development of testing networks that will fast track the movment of specimens from the collection centres to the approved testing laboratories.

In 2018, to expand access to quality CD4 cell count testing, the Federal Ministry of Health (MOH) established a National Integrated Specimen Referral Network (NISRN) with the major objective of attaining a cost-effective, productive, safe and secure referral system involving third-party logistics providers (3PLS) being supervised by Global Health Supply Program (GHSC-PSM). Due to the lack of a standard sample referral system, Nigeria was faced with a high cost of CD4 testing and long TAT. The NISRN was therefore saddled with the responsibility of oversing specimen transportation services around the country. The services of the 3PL include returning concluded result/reports from reference laboratories to the sample collection health facilities (9). This study assessed the impact of specimen referral network to rapidly scale-up CD4 testing in Nigeria.

METHODOLOGY

This is a retrospective study conducted on the reported activities of all 3PL service providers from March 2018 to March 2019. Information was obtained from all the approved CD4 diagnostic centres across all the 36 states and the Federal Capital Territory (FCT) of Nigeria. Tracking records and reports of all centres were also obtained. The total number of specimens rejected was obtained from each centre from the data extraction tool set up by Axios Foundation. Data from bi-monthly quality indicator reports, which included specimen rejection and workload statistics, were included. The data obtained were inputted and analyzed with IBM-SPSS version 25.0. The analysis done include descriptive statistic; frequencies and proportions. The results were presented to show the contribution sample referral network in scaling up CD4 diagnosis in Nigeria.

RESULTS

Table 1 shows the distribution of samples referred and the results pick up in 13 months of National integrated sample referral network services. The total number of samples transported in the 13 months was 17,629 with over three thousand samples within Cross River state (3075, 17.4%). Exactly 15.0% of these samples were transported in Rivers

state and FCT had the third-largest sample movement. Cross River, Rivers, and FCT also recorded the highest number of results picked up which accounted for 87%, 68% and 64% of the total samples transported in the respective states. Though the number of samples transported in Niger (419), Borno (69) and Edo (36) states were small, the total number of results picked-up in these states were higher than 90% of the total samples transported while the number of results picked up in Plateau 62 (477%) and Kwara states were far 46 (128%) more than the number of samples transported (13, 36) across all reference laboratories in these states. Figure 2 shows the monthly movement of samples and results. There was a steady increase in the number of samples and results transported until July 2018 where the highest peak (2,085) was achieved. Two other peaks were observed in November 2018 (1979) and February 2019 (1889). Low sample movement was recorded in December and January.

Table 1: Viral load sample transported and results obtained from referral centres in 13 months

State	CD4 Samples	% Sample	CD4 Results	Result Uptake
Cross River	3075	17.4%	2673	87%
Rivers	2645	15.0%	1804	68%
FCT	2266	12.9%	1454	64%
Benue	2045	11.6%	1828	89%
Akwa Ibom	1836	10.4%	1581	86%
Bayelsa	846	4.8%	462	55%
Lagos	717	4.1%	489	68%
Kaduna	543	3.1%	308	57%
Ondo	483	2.7%	193	40%
Sokoto	426	2.4%	360	85%
Niger	419	2.4%	392	94%
Anambra	357	2.0%	254	71%
Zamfara	354	2.0%	204	58%
Adamawa	351	2.0%	284	81%
Kebbi	324	1.8%	266	82%
Nasarawa	176	1.0%	40	23%
Gombe	159	0.9%	21	13%
Kogi	90	0.5%	64	71%
Ekiti	70	0.4%	42	60%
Borno	69	0.4%	68	99%
Bauchi	59	0.3%	46	78%
Katsina	37	0.2%	24	65%
Edo	36	0.2%	35	97%
Kwara	36	0.2%	46	128%
Delta	35	0.2%	19	54%
Ogun	35	0.2%	16	46%
Taraba	34	0.2%	29	85%
Jigawa	29	0.2%	0	0%
Kano	20	0.1%	7	35%
Imo	14	0.1%	2	14%
Plateau	13	0.1%	62	477%
Osun	12	0.1%	5	42%
Enugu	10	0.1%	10	100%
Oyo	8	0.0%	2	25%
Abia	0	0.0%	0	0%
Ebonyi	0	0.0%	0	0%
Yobe	0	0.0%	0	0%
Total	**17629**	100.0%	**13090**	74%

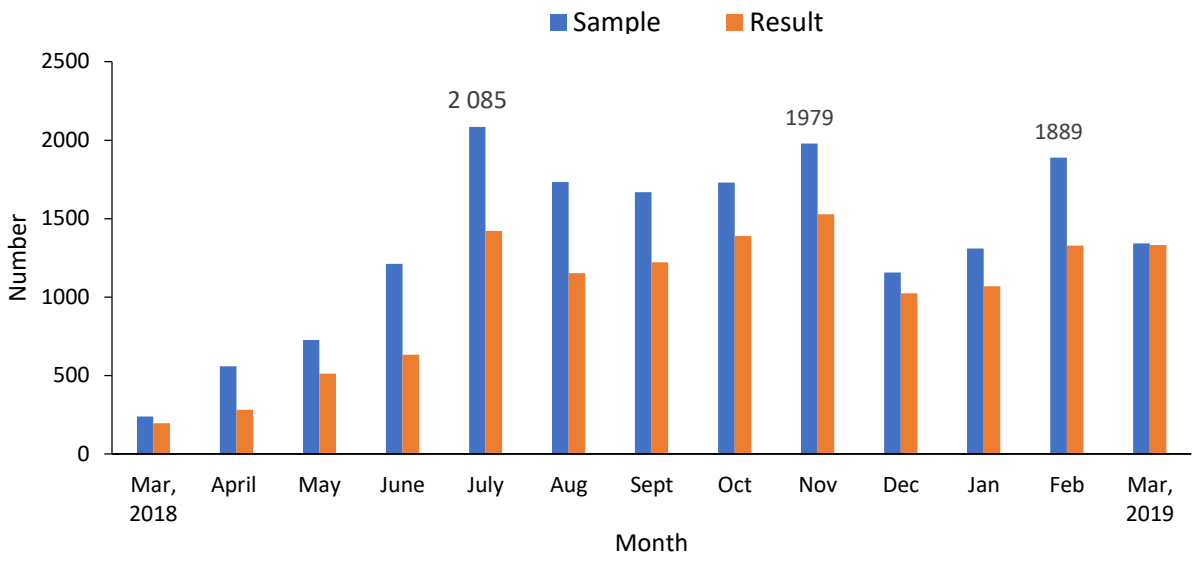

Figure 1: Monthly number of samples and results transported

There were 54 rejected samples recorded in the entire 13 months. This number accounted for 0.31% of the total 17,629 samples transported. Over half of the rejected samples (29, 53.7%) were from Jigawa state, 7 (13.0%) from Akwa Ibom and 4 (7.4%) from FCT. Although the highest number of transported samples were recorded in Cross River and Rivers states, no sample rejection was recorded in these states (Figure 2).

Figure 2: Number of rejected samples per state

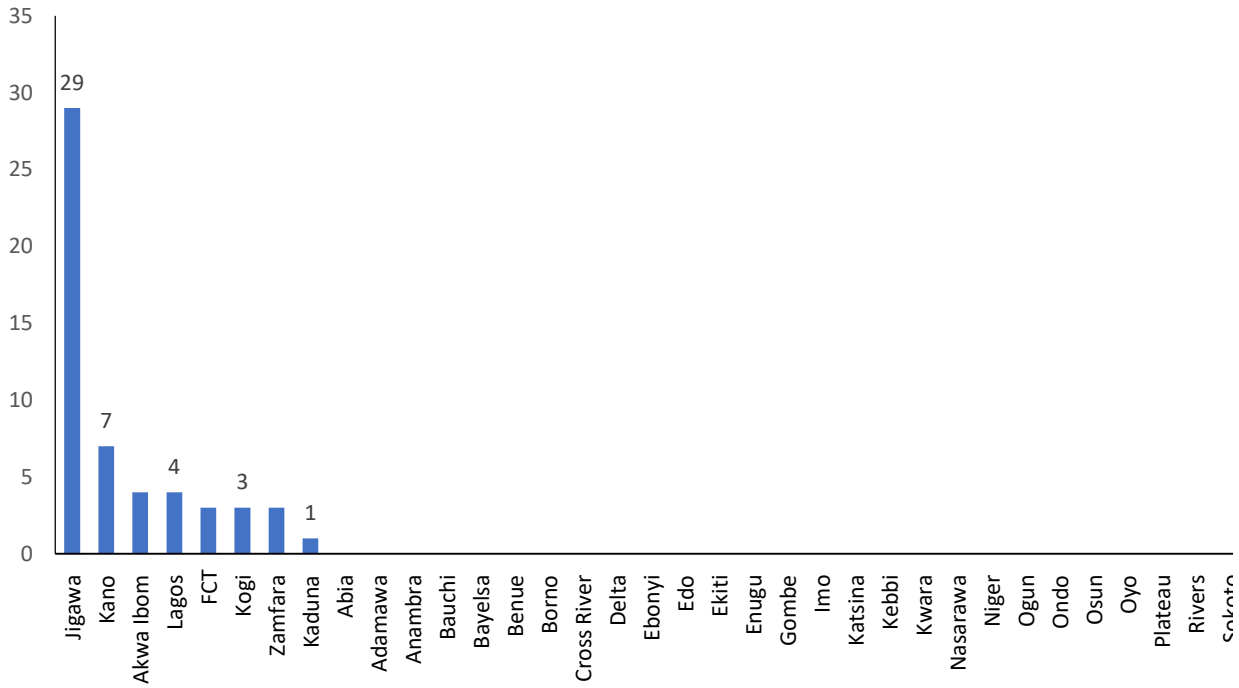

Figure 2: Number of rejected samples per state

DISCUSSION

We report in this study the successful implementation of a national integrated specimen referral network with decentralized access to laboratory testing as reported by Louis *et al* and (8) in Haiti and suggested by Nkengasong (2009). Though there is no previous reliable data on the number of CD4 samples analyzed in Nigeria before this study, however, 17629 samples were transported through the integrated 3PL services in Nigeria with a result pick up of 74%. Such rapid expansion of CD4 testing was observed in Haiti where the 91% success was recorded in 3 years (8). The rapid monthly increase in the number of referred samples and result pick up can be attributed to the increase in the number of new patients being enrolling or using the integrated 3PL services in the country. This might also be due to the efficiency, short turnaround time, and cost reduction of the 3PL services though we did not do a formal cost analysis, the major aim of establishing NISRN was to reduce the cost of sample testing across the country.

Several other countries, both in Africa and other parts of the world have successfully established well-coordinated integrated sample referral networks. For example, the sample referral network in Zambia was successfully implemented to enrol and monitor HIV positive pregnant women (11). Successful piloting and roll-out of an efficient sample referral system were also reported in Ethiopia through the private-public partnership initiated by the Ethiopia Ministry of Health (2).

Since the inception of the national integrated specimen referral network, Nigeria has shown steady progress on increasing access to treatment for people living with HIV, with the adoption of a test and treat policy in 2016 with the integrate sample referral system in 2018. This has further accelerated referrals to treatment facilities for people who test positive for the virus (12). UNAIDS reported that the number of people living with HIV having access to antiretroviral therapy (ART) in Nigeria almost tripled from 2010 to 2017 and the number increased from 360 000 people in 2010 to more than 1 million people in 2018 (12). They further confirmed that the new data are more accurate as they are based on an expanded surveillance system and a revised and enhanced methodology and the significant expansion in the country's response to HIV in recent years (12).

The impact of the integrated system has also contributed to the tremendous increase in the number o testing laboratories and the testing centres. The fining of this study revealed that only three states (Abia, Ebonyi, and Yobe) did not show any sample movement. The report of the USAID/MOH that 'the number of sites providing treatment has more than tripled, the number of sites providing services to prevent mother-to-child transmission of HIV has increased eightfold and the number of HIV counselling and testing sites has increased fourfold' (12) further corroborates our claim.

A similar report was documented in Kenya where 35% upsurge in the number of patients enrolled on ART was seen just after five months of implementing a sample referral system and in Uganda where successful implementation of a specimen transport system resulted in increased access to early infant diagnosis of HIV from 36% to 51% (6,13).

One of the important challenges limiting widespread of CD4 cell count testing in Sub-Saharan Africa is sample rejection. African Society of Laboratory Medicine described an efficient specimen transportation system as the one that has fewer specimen rejections at laboratories, as specimens are transported appropriately and promptly (14). This study recorded only 54 rejected samples which accounted for 0.31% of the total 17,629 samples transported. The sample rejection rate of <0.5% shows the efficiency and effectiveness of the 3PL services in sample transportation. In one of the few studies that recorded sample rejection rate of CD4 count testing, the rejection rate of 0.7% was seen in Ethiopia in 2018 (15) while another study in India reported the rejection rate of 5.3% samples across all laboratories in North India. These values are far greater than the values seen in this study.

The major limitation of this study is that the data used were secondary data from the specimen tracking and monthly quality indicators report in from Axios Foundation. The recorded data could underestimate the magnitude of specimen rejection. Also, other parameters such as information on the training of staff (sample transporters e.g. the couriers and drivers) on sample management, handling and safety were not available.

Summarily, the NISRN has significantly scaled-up specimen referral and results-reporting networks by increasing the number of samples referring sites, increased access to CD4 count testing and decreasing TAT that has significantly contributed to ART-related monitoring. This integrated service is very important for enhancing the specimen referral system and increasing access to quality laboratory services in Nigeria. The successful implementation of the integrated system may be relevant to other areas of laboratory services other than sample referrals.

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