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ESTABLISHING POPULATION-SPECIFIC CLINICAL REFERENCE INTERVALS IN NIGERIA: CHALLENGES AND A PROPOSED 3-PHASE ROADMAP

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Abstract

Background: Most laboratories in Nigeria still use reference intervals (RIs) copied from textbook manuals or equipment/reagent inserts, most of which were derived from Caucasian populations. This can lead to misclassification of results, unnecessary referrals, and poor clinical decisions. Despite these known limitations, Nigeria does not yet have a coordinated national effort to establish its own population-specific RIs.

Objective: To identify the key challenges to establishing population-specific clinical RIs in Nigeria and to propose a practical 3-phase roadmap for their development, validation, and integration into the national health system.

Methods: We searched PubMed, Scopus, African Journal Online (AJOL), and Google Scholar for Nigerian studies on RIs published from 2000 to 2025. We also reviewed national and international guidelines on RI establishment. Data on study populations, methods, reported intervals, and stated challenges were extracted. From these findings, we developed a 3-phase roadmap to guide the establishment of Nigerian RIs. Meta-analysis was not conducted because of differences in study methods.

Results: The review identified major gaps including limited funding, lack of standardized methods, insufficient multi-center data, and weak policy integration. Most published studies were single-center and

covered only a few analytes. No national compendium of RIs currently exists.
Conclusion: Establishing population-specific RIs in Nigeria is feasible but requires a coordinated, phased approach. We proposed a 3-phase roadmap focused on standardization, multi-center data generation, and policy integration. Prioritizing Phase 1 is recommended to begin the process. Implementing this roadmap will improve diagnostic accuracy and patient care across Nigeria

Keywords: Reference Intervals, Nigeria, Population-specific, Laboratory Standardization, Clinical Laboratory, Health Policy, Implementation Roadmap

INTRODUCTION

Laboratory medicine forms the basis of more than 70% of medical decisions, including diagnosis, treatment, and monitoring. To interpret laboratory results, clinicians compare patient values to a RI, defined by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) as the central 95% range between the 2.5th and 97.5th percentiles of values from healthy individuals.[1] In Nigeria and most low-and middle-income countries, laboratories routinely adopt RIs from Western textbooks or reagent manufacturers. These intervals are often established using data from North American, European, and Asian populations. This assumption of biological uniformity is not supported by evidence from African populations. Differences in haemoglobin, white blood cell counts, creatinine, and liver enzymes have been documented in Nigerian studies.[2-5] Giving the substantial biological and environmental diversity in Nigeria, direct transfer of foreign intervals may lead to misclassification of patients, inappropriate clinical decisions, over-investigation, and resource waste.[6,7] Despite recommendations by the Clinical and Laboratory Standards Institutes (CLSI) and World Health Organization (WHO) that each country or region should establish its own RIs,[1] Nigeria still lacks a coordinated national effort to generate population-specific data. Challenges such as inadequate funding, lack of harmonization of analytical methods, and limited research capacity have slowed progress.[8] Consequently, this review identifies the key barriers to establishing population-specific clinical RIs in Nigeria and proposes a pragmatic 3-phase roadmap for their development and implementation.

RATIONALE

Human physiology is influenced by genetic background, ethnicity, and environmental exposures.[9] This is reflected in notable variations in haematological and biochemical profiles between African and Caucasian populations, including lower mean haemoglobin concentrations and neutrophil counts in some African groups, higher creatinine levels in others, and distinct patterns in glucose metabolism. Using foreign RIs can cause healthy Nigerians to be misclassified as abnormal or can mask true pathology, leading to over-investigation, under-diagnosis, or inappropriate treatment.[10-12]

Nigeria's unique environment, diet, and disease burden also alter physiological baselines.[13] Tropical climate, endemic malaria and helminth infections, diets low in animal protein, and biomass fuel exposure may affect liver enzymes, kidney function tests, and inflammatory markers.[14,15]In addition, the high prevalence of G6PD deficiency and sickle cell trait in Nigeria affects bilirubin levels and indices of haemolysis.[16] These population-specific factors are not captured in Western-derived RIs, underscoring the need for local data.

REGULATORY

Adherence to international quality standards is essential for reliable laboratory results.[17,18] ISO 15189: 2022, the global standard for medical laboratories, requires each laboratory to verify that the RIs in use are

appropriate for the population it serves, or establish its own.[19,20] The Medical Laboratory Science Council of Nigeria (MLSCN, 2022), in its guidelines for laboratory practice and accreditation, also emphasizes the need for locally derived or verified RIs.[21] Similarly, the WHO-AFRO SLIPTA (World Health Organization Regional Office for Africa, 2015) checklist identifies the use of population-specific RIs as a key element for achieving and maintaining accreditation.[21] Consequently, the routine adoption RIs from textbooks, reagent package inserts, or Western populations without validation is no longer acceptable. Laboratories that fail to address this requirement risk producing clinically misleading results and may not meet national and international accreditation standards.

DATA GAP

Despite the known limitations of foreign RIs, there remains a substantial data gap for the Nigerian population.[22] To date, most available studies on Nigerian RIs are limited in scope. They are typically single-center, have small sample sizes, and often use analytical or statistical methods that are no longer recommended.[22] As a result, they lack the power and generalizability required for national application. To address this, a coordinated, multi-center national study is needed. Such a study should generate robust RIs stratified by age, sex, and geopolitical region, in accordance with the CLSI guidance. This approach would ensure that intervals are statistically valid and clinically relevant. Beyond the immediate clinical benefit, a national RI project would also create an opportunity to establish a well-characterized biobank. Such a resource could support future research in genomics, biomarker discovery, and precision medicine tailored to Africans.[23]

CHALLENGES

Despite the clear need, establishing RIs in Nigeria is constrained with systemic barriers. A CLSI-compliant RI study requires testing a large number of samples across multiple analytes and partitions, which is expensive. [1,6] Reagent costs, personnel, quality assurance, and logistics place a major burden on laboratories. Infrastructure costs are further compounded by the need for stable power to support phlebotomy, sample processing, centrifugation, and storage. Reagent stock-outs, cold-chain failures, and absence of dedicated grants from agencies such as Tertiary Education Trust Fund (TETFUND) or Federal Ministry of Health (FMoH) can result in sample wastage and incomplete studies.

Nigeria also has a limited medical laboratory scientist with formal postgraduate training in chemical pathology and even fewer with deep exposure to CLSI guidelines. The statistical techniques needed for indirect methods, including outlier detection, and non-parametric percentiles estimation, are often not taught in sufficient depth in undergraduate curricula.[7] As a result, some studies rely on basic spreadsheet calculations, which may compromise validity.

Recruiting healthy individuals is also difficult: Strict CLSI exclusion criteria are challenging to apply in a setting with high disease burden and untreated hypertension, malaria parasitaemia, or undisclosed herbal medication use. Cultural resistance may further slow recruitment because of fear of blood donation, rumours of blood commercialization, and lack of participant compensation. In addition, ethics approval from the National Health Research Ethics Committee and Institutional Ethics Committees may take several months and often requires proof of funding before clearance.

Fragmentation, instrument heterogeneity, and lack of coordination further limit progress: Most Nigerian RI studies published to date are single-center,[2-5,9-12,14,16] which limits sample size and increases uncertainty. Different hospitals use different analytical platforms, making results difficult to compare without harmonization. There is also no central body to collate national data. In contrast to South Africa's National Health Laboratory Service, Nigeria lacks a coordinated national laboratory network. The MLSCN has the

mandate but not always the funding or database infrastructure needed to support a national effort.

Poor data systems also limit the use of indirect methods: Although Laboratory information systems exist in some Nigerian tertiary hospitals, paper records are still common. Even digital systems frequently have important demographic and clinical variables. Age may be recorded only as "adult," sex may be missing, and diagnosis codes may not be linked to laboratory results. These shortcomings make indirect data mining difficult, even though it is one of the most economical and sustainable approaches for Nigeria.[13]

EVIDENCE

Evidence from single-center studies across Nigeria suggests that laboratory reference values differ from Western standards. In Ibadan, studies of healthy adults reported mean haemoglobin concentrations and total white blood cell counts lower than Western reference ranges. In Kano, investigators observed a predominance of microcytic and anisocytic red blood cells, a pattern possibly linked to the high prevalence of thalassemia trait in the region. Data from Port Harcourt showed sex-based differences in haematological parameters, with overall platelet counts also lower than Western standards. In Zaria, healthy adults had higher mean serum creatinine levels, indicating that foreign RIs may misclassify healthy individuals as having renal impairment. Similarly, in Enugu, the use of kidney function equations derived from Caucasian populations led to overdiagnosis of kidney disease among healthy Nigerians.[2-4,9-11]

Data for special populations remain limited. A paediatric study in Ibadan showed that foreign haemoglobin cut-offs could underdiagnose anemia in children. In Ile-Ife, studies in women in the third trimester reported haemoglobin levels below those recommended by Western obstetric guidelines. In Ilorin, lipid profile studies suggested that healthy adults have lower high-density lipoprotein cholesterol and higher triglyceride levels than Western populations, possibly reflecting dietary and lifestyle differences.[2-4,9-12,14,16] Collectively, these studies indicate that Nigeria RIs may differ meaningfully from imported standards, and reliance on foreign intervals can contribute to diagnostic error, unnecessary testing, and patient anxiety.

ROADMAP

The paucity of nationally derived RIs remains a critical gap in Nigerian laboratory medicine and contributes to misdiagnosis, inappropriate treatment, and poor monitoring of patients. While the challenges of funding, infrastructure, human capacity, and lack of standardization are well documented, they are not insurmountable. To move from problem description to action, we propose a pragmatic, 3-phase roadmap tailored to the Nigerian health system context.

Phase 1 should focus on coordination and policy development. The MLSCN, working with the FMoH and relevant partners, should establish a National RI Committee. This body should develop a national protocol, provide technical guidance, and ensure that all studies follow international standards. Ethical approval templates should be standardized to reduce delays, and RI verification should become part of laboratory accreditation.[20] Sustainable funding may be secured through government research grants and strategic partnerships.

Phase 2 should focus on data generation: Robust RIs will require a combination of direct sampling of healthy individuals and indirect data-mining from existing laboratory databases.[7] For the direct approach, reference centers should be established across the geopolitical zones to recruit healthy participants and capture ethnic, dietary, and environmental variation. For the indirect approach, hospitals with functional laboratory information systems should analyze existing patient data to derive reference values.[10] This method is cost-effective and can include age groups that are difficult to recruit directly, but it requires adequate training for laboratory scientists and biostatisticians to ensure data quality and proper analysis.[12]

Phase 3 should focus on harmonization and implementation: data from all zones should be harmonized and

validated across common analyzer platforms.[13] The National Committee should then publish the first edition of Nigerian national RIs. These should be made freely available through an open-access database and a mobile application for clinicians and laboratories.[14] Adoption of national intervals should be required for accredited laboratories, and reagent manufacturers should be encouraged to include Nigerian-specific RIs in product literature. A system for periodic review should be established so that intervals remain relevant as population health and laboratory technology evolve.

CONCLUSION

The use of manufacturer-derived RIs in Nigeria continues to compromise diagnostic accuracy and patient care. Challenges such as ethnic and environmental diversity, lack of standardization, resource constraints, and poor data coordination have hindered the development of population-specific RIs. This review proposes a practical 3-phase roadmap as a pathway to address these gaps. Phase 1 focuses on foundation and standardization, phase 2 on multi-center data generation across Nigeria's geopolitical zones, and phase 3 on validation and integration into national health policy. Implementation of this roadmap will require coordinated efforts from the FMoH, MLSCN, Nigeria Centre for Disease Control and Prevention (NCDC), National Health Insurance Authority (NHIA), tertiary hospitals, and professional bodies. Establishing nationally validated RIs is not just a technical laboratory exercise but a critical step towards health-system strengthening, improved diagnostic accuracy, and achievement of universal health coverage in Nigeria. Stakeholders should prioritize funding for phase 1 within the next 12 months, while future studies should generate the data required for phase 2 to support a sustainable and regularly updated national compendium of RIs.

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