RESEARCH ARTICLE

Adult Hematology and Clinical Chemistry Laboratory Reference Ranges in a Zimbabwean Population

Wadzanai P. Samaneka†‡*, Gibson Mandozana‡‡, Willard Tinago‡‡, Nehemiah Nhando¹, Nyaradzo M. Mgod¹, Mutsawashe F. Bwakura-Dangarembizi², Marshall W. Munjoma¹,6☯, Zvenyika A. R. Gomo⁴☯, Zvavahera M. Chirenje⁴,6☯, James G. Hakim¹,5,7☯

¹ University of Zimbabwe-University of California San Francisco Collaborative Research Programme, Harare, Zimbabwe, 2 Department of Community Medicine, University of Zimbabwe College of Health Sciences, Harare, Zimbabwe, 3 Department of Pediatrics, University of Zimbabwe College of Health Sciences, Harare, Zimbabwe, 4 Department of Chemical Pathology, University of Zimbabwe College of Health Sciences, Harare, Zimbabwe, 5 Department of Medicine, University of Zimbabwe College of Health Sciences, Harare, Zimbabwe, 6 Department of Obstetrics and Gynecology and Reproductive Health Sciences, University of Zimbabwe College of Health Sciences, Harare, Zimbabwe, 7 University of Zimbabwe Clinical Research Centre, Harare, Zimbabwe

♦ These authors contributed equally to this work.
‡ These authors also contributed equally to this work.
* wsamaneka@uzcrc.co.zw

Abstract

Background

Laboratory reference ranges used for clinical care and clinical trials in various laboratories in Zimbabwe were derived from textbooks and research studies conducted more than ten years ago. Periodic verification of these ranges is essential to track changes over time. The purpose of this study was to establish hematology and chemistry laboratory reference ranges using more rigorous methods.

Methods

A community-based cross-sectional study was carried out in Harare, Chitungwiza, and Mutoko. A multistage sampling technique was used. Samples were transported from the field for analysis at the ISO15189 certified University of Zimbabwe-University of California San Francisco Central Research Laboratory. Hematology and clinical chemistry reference ranges lower and upper reference limits were estimated at the 2.5th and 97.5th percentiles respectively.

Results

A total of 769 adults (54% males) aged 18 to 55 years were included in the analysis. Median age was 28 [IQR: 23–35] years. Males had significantly higher red cell counts, hemoglobin, hematocrit, and mean corpuscular hemoglobin compared to females. Females had higher white cell counts, platelets, absolute neutrophil counts, and absolute lymphocyte counts compared to males. There were no gender differences in eosinophils, monocytes, and
Males had significantly higher levels of urea, sodium, potassium, calcium, creatinine, amylase, total protein, albumin and liver enzymes levels compared to females. Females had higher cholesterol and lipase compared with males. There are notable differences in the white cell counts, neutrophils, cholesterol, and creatinine kinase when compared with the currently used reference ranges.

Conclusion
Data from this study provides new country specific reference ranges which should be immediately adopted for routine clinical care and accurate monitoring of adverse events in research studies.

Background
Laboratory reference ranges are used to guide the interpretation of laboratory results and for the proper management of patients in clinical and research settings. Reference values are established from a sample of the reference population and selected on the basis of criteria such as age, gender, dietary habits, ethnicity, and the environment [1, 2, 3]. For the correct interpretation of laboratory results and safety of study participants, it is imperative that reference ranges are appropriate for the relevant population. A Nigerian study reported remarkable differences in normal reference ranges compared to those of other countries [4].

Laboratory reference ranges currently used in clinical and research settings in Zimbabwe such as the University of Zimbabwe-University of California San Francisco (UZ-UCSF) collaborative research program are derived from several sources, including textbooks and local studies of varying rigor, many of which are over a decade old [5, 6, 7, 8, 9, 10]. Textbook reference ranges are often based on Western populations and significant differences have been observed from those of African origin [1, 3]. The Clinical Laboratory and Standards Institute (CLSI) guidelines recommend that reference ranges be descriptive of a specific population and ideally are to be verified every 5 years [11].

This study was therefore conducted to determine current adult hematology and clinical chemistry reference ranges for a Zimbabwean population.

Materials and Methods
Study Settings
The UZ-UCSF is a Zimbabwe based United States National Institutes of Health (NIH) funded Clinical Trials Unit (CTU) which has been conducting Phase I/II and III multicenter HIV clinical trials since 1994. Participants were derived from the general population within the UZ-UCSF research catchment areas of Harare, Chitungwiza, and Mutoko. Harare is the capital and largest city of Zimbabwe with a population of 1.5 million; Chitungwiza is a dormitory city for Harare with 350,000 inhabitants located 30 km southeast of the capital and Mutoko is a rural community of 40,000 inhabitants located 140 km northeast of Harare [12].

Study Design
A cross-sectional study of a representative sample of the adult population of Harare, Chitungwiza, and rural Mutoko was used to determine reference ranges for hematology and chemistry parameters.
Sampling Strategy

The administrative units in Zimbabwe comprise provinces, districts, and wards. In cities and towns, a ward is a division created for administrative or legislative purposes, while in rural areas, wards are comprised of villages. Community sensitization in the wards was conducted by experienced outreach workers prior to commencement of the study. Multistage sampling technique was used to select the areas from which participants were drawn. The first-stage sampling unit was the ward. We randomly selected 38 of 52 wards in Harare, 8 of 24 in Chitungwiza, and 3 of 8 in Mutoko. The second stage was household sampling, where households were systematically selected from a randomly selected reference point. After identifying a household, the head of the household or any other adult household representative described the household composition. A research assistant stratified household members according to age, which was verified by proof of national identification document. In households with more than one person of the same age group and/or sex, a Kish grid was used to randomly select the participant. However, in order to have approximately equal numbers of males and females, the research assistant alternately chose a male or female from one household to the next.

Participants

This analysis is part of a larger study to determine Zimbabwean hematology and clinical chemistry laboratory ranges in children, adolescents and adults that was conducted between May and September 2011. A total of 2359 participants aged 0–55 years were recruited into the study; divided into pediatric (0–<12 years), adolescent (12–<18 years) [13] and adult (18–55 years) cohorts. This paper is based on the 769 adult cohort. Participants were healthy volunteers with no history, clinical or laboratory evidence of chronic disease (hypertension, diabetes, liver or renal disease) and were human immunodeficiency virus infection (HIV) and hepatitis B surface antigen (HBsAg) negative on laboratory testing. Participants were on no medications for acute illness (or were one week past completion of a course of medication) with no abnormal findings on clinical and laboratory examination.

Ethical considerations

The protocol was approved by the Joint Research Ethics Committee of the University of Zimbabwe and Parirenyatwa Teaching Hospital and the Medical Research Council of Zimbabwe. Each participant provided a written informed consent.

Specimen collection and handling

All samples were collected by a clinician using standard phlebotomy procedures as described elsewhere [13]. Blood was collected as follows: 10 mL in a plain tube for chemistries, 10 mL in a purple EDTA tube for full blood counts, and 4 mL in a grey sodium fluoride tube for glucose testing. The sodium fluoride tubes were immediately placed on ice pack at collection. All samples were transported to the UZ-UCSF Central Laboratory in temperature controlled bags maintained at 15–25°C and were processed on average 6 hours after sampling [13].

Laboratory procedures

All samples were delivered to the ISO 15189 certified UZ-UCSF Central Laboratory on the day of collection. Processing was completed after specimen verification at the Central Laboratory’s specimen management section and all samples were analyzed on the day of collection. All samples were entered into the electronic database (DISA Laboratory Information system, Laboratory System Technologies, version 16.03).
Hematology

With whole blood collected in the EDTA tube, white cell count, hemoglobin, automated five-part differential, platelet count, mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), red blood cell count and hematocrit were determined using Sysmex XT2000i (Symex Europe D-22848 Nordersted, Germany) operated in the manual mode.

Clinical chemistry and Serology

Using the blood sample collected in the plain tubes, biochemical analysis, HIV and Hepatitis B (HBV) screening were determined. Samples were centrifuged at 1100×g for 10 minutes and serum kept at 2–8°C pending testing. HIV screening was performed using Determine (Abbott Diagnostics, Wiesbaden, Germany) and oral quick (Orasure Technologies, Inc, Bethlehem, PA, USA). HBsAg was tested in serum using an enzyme immune assay manufactured by Bio-Rad Laboratory, (Redmond, WA, USA). Those testing HIV positive or HBsAg positive were excluded from the analysis. The chemistries assayed were: sodium, potassium, chloride, phosphate, creatinine, creatinine kinase, calcium, urea, aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), albumin, total protein, gamma glutamyl transferase (GGT), total bilirubin, direct bilirubin, bicarbonate, triglycerides, lipase, cholesterol, high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C) and glucose. All tests were analyzed using the Hitachi 902 (Hitachi, Roche diagnostics D-68292 Mannheim Germany) according to manufacturer specifications. Methods for all analysis were traceable to International Federation of Clinical Chemistry (IFCC) standards.

Quality Control

To perform quality control on the hematology measures, three levels of E-Check controls (low, normal and high level) (Sysmex Corporation 1-5-1 Wakinohama-Kaigandori Chuo-ku Kobe Japan) were run daily. Quality control for the biochemical assays was performed by running daily assays for two analytes, precinorm and precipath, (Roche Diagnostics GmbH, Sandhofer Strasse 116, and D-68305 Mannheim) prior to sample testing. Each analyte performance was tracked using real-time Levey Jennings QC plots monitored within 2 standard deviation of the laboratory established control mean. The UZ-UCSF Central laboratory also participates in External Quality Assurance (EQA) programs provided by the College of American Pathologists and monitored by Patient Safety Monitoring in International Laboratories (SMILE) for both Hematology and Clinical Chemistry. The EQA performance was acceptable for all panels processed over the study period.

Data Management and Statistical analyses

Demographic data were entered into a Microsoft Access 2007 database and laboratory data into DISA Laboratory Information System (Laboratory System Technologies, version 16.03). Demographic and laboratory data were merged and analyzed in STATA 12.1 (College Station, Texas, USA) and the Reference Value Advisor version 2.1 (Microsoft, Radmond, WA, USA). All calculations for determining reference intervals were based on the CLSI guidelines [11]. The Reference Value Advisor uses non-parametric statistical methods to determine the 95% reference limits, with the lower limit defined as the 2.5th percentile and the upper limit as the 97.5th percentile. Ninety percent confidence limits around the lower and upper confidence estimates were determined using a nonparametric bootstrap method, (not reported). Our underlying assumption was that the 2.5% and 97.5% centiles contain 95% of the distribution of normal
values of the reference population. Extreme values were handled as described in the CLSI guidelines by performing a range check and the methods of Dixon (Dixon’s Test). Mann-Whitney U tests were used to analyze differences by gender. The reference intervals were calculated separately for men and women and then combined, both are reported. A two-sided p-value of <0.05 was considered significant.

**Participant safety**

All results were reviewed by study clinicians. The study team communicated all results to participants; those with abnormal results were informed accordingly and referred to the nearest health care centers for appropriate management.

**Results**

Of the 998 adult (18 to 55 years) participants screened, 229 were excluded; 25 (2.5%) due to missing data, (14 had no demographic information, 11 had no laboratory information), 139 (13.9%) were HIV positive, 3 (0.3%) had unknown HIV status, 38 (3.8%) were HBsAg positive and 24 (2.4%) had no HBsAg results. Complete data from 769 adults were included in this analysis. Of these, 588 (76.5%) were from Harare, 128 (16.6%) from Chitungwiza and 53 (6.9%) from Mutoko. The median age of the participants was 28 [IQR: 23–35] years and 412 (54%) were male. There were 242 (98 females, 144 males) in the 18–24 years age-band; 328 (139 females, 189 males) in the 25–34 years age-band; 148 (86 females, 62 males) in the 35–44 years age-band and 51 (34 females, 17 males) in the 44–55 years age-band. The majority of the participants had attained at least secondary education level, 706 (91.8%).

**Hematological indices**

The median values and 2.5<sup>th</sup>—97.5<sup>th</sup> percentile ranges of hematology parameters stratified by gender are presented in Table 1.

Compared with women, men had significantly higher red cell count, hemoglobin, hematocrit, and mean corpuscular hemoglobin while women had significantly higher white cell count, platelets, absolute neutrophil count and absolute lymphocyte counts. The median WBC was 4.6 × 10<sup>3</sup> cells/μL and 5.2 × 10<sup>3</sup> cells/μL for males and females respectively (p<0.001). The combined WBC reference range was 2.9–7.9 × 10<sup>3</sup> cells/μL. The reference range for hemoglobin was 13.2–18.3 g/dL for males and 10.2–15.9 g/dL for females with significantly different medians of 15.9 g/dL and 13.5 g/dL, respectively (p<0.001). The median platelet count for males was 229.0× 10<sup>3</sup> cells/μL compared to 268.5× 10<sup>3</sup> cell/μL for females (p<0.001). The combined reference range was 138–384.8 ×103 cell/μL. The lower limit of neutrophils for males was 772.7 cells/μL, reference range 772.7–3967.3 compared to 1112.0 cells/μL, reference range 1112.0–4440.1 cells/μL for females with a combined reference range of 939.2 to 4252.3 cells/μL.

**Biochemistry**

The median values and 2.5<sup>th</sup>—97.5<sup>th</sup> percentile ranges of hematological parameters stratified by gender are presented in Table 2.

We established chemistry reference ranges for 24 analytes; renal function tests (urea, creatinine), serum electrolytes (ALP, ALT, AST, total bilirubin, direct bilirubin, total protein, albumin, GGT), non-fasting lipid profile (triglycerides, total cholesterol, LDL cholesterol, HDL cholesterol), pancreatic enzymes, (lipase, amylase), creatinine kinase and random glucose. Males had higher levels of urea, sodium, potassium, calcium, creatinine, amylase, total protein,
albumin, and liver enzymes levels compared to females (p<0.001). Females had higher total cholesterol and LDL-cholesterol compared to males. The median total cholesterol for males was 149 mg/dL compared to 163 mg/dL for females (p<0.001). The combined reference range was 99.1–237 mg/dL. The median LDL-cholesterol values were 82 mg/dL for males and 100mg/dL for females (p<0.001). No sex differences were observed for HDL-cholesterol and triglycerides. Creatinine kinase was significantly higher in males with a median of 197.5 IU/L compared to 149 IU/L in females. The combined reference range was 76–437.2 IU/L.

**Discussion**

This is the first population-based study in Zimbabwe to comprehensively study a wide range of hematological and biochemical laboratory indices using internationally accepted CLSI guidelines [11]. Results from this study showed several differences with the existing reference ranges.
Table 2. Chemistry, 95% Reference Intervals.

| Analyte/Unit | RI: Female | RI: Male | RI: Combined | Current in Use |
|--------------|------------|----------|--------------|----------------|
|              | n | Median | Mean (sd) | Range | Median | Mean (sd) | Range | Median | Mean (sd) | Range |
| *Sodium, mmol/L | 357 | 141 | 141.3 (3.1) | 135–148 | 412 | 143 | 142.7(3.2) | 136–149 | 769 | 142 | 142(3.2) | 136–149 |
| *Potassium, mmol/L | 357 | 4.2 | 4.3(0.4) | 3.5–5.2 | 412 | 4.4 | 4.4(0.4) | 3.6–5.3 | 769 | 4.3 | 4.3(0.4) | 3.6–5.2 |
| *Chloride, mmol/L | 357 | 102 | 102(2.9) | 96–107 | 412 | 101 | 101(4.5) | 95–107 | 769 | 101 | 101(2.9) | 96–107 |
| *Bicarbonate, mmol/L | 357 | 22.4 | 22.5(3.1) | 16.1–29.1 | 412 | 24.3 | 24.5(3.0) | 18.8–31.6 | 769 | 23.4 | 23.6(3.2) | 17.2–30.9 |
| *Urea, mg/dL | 357 | 8.7 | 8.9(2.7) | 3.9–15.4 | 412 | 9.8 | 9.9(2.8) | 4.8–15.4 | 769 | 9.9 | 9.5(2.9) | 4.1–15.4 |
| *Creatinine, mg/dL | 357 | 0.7 | 0.7(0.1) | 0.5–1.1 | 412 | 0.9 | 0.9(0.2) | 0.7–1.3 | 769 | 0.8 | 0.8(0.2) | 0.6–1.2 |
| *ALP, IU/L | 357 | 69 | 72.6 (23.1) | 39–131 | 412 | 80 | 84.2(24.4) | 49–149 | 769 | 75 | 78.7(24.5) | 42–144.3 |
| *ALT, IU/L | 357 | 15 | 16.9(7.5) | 5–35 | 412 | 21 | 23.5(11.9) | 9.0–58.8 | 769 | 18 | 20.5(10.4) | 7–51 |
| *AST, IU/L | 357 | 23 | 23.3(6.3) | 12.0–40.0 | 412 | 28 | 30.3(9.8) | 17.0–57.0 | 769 | 25 | 25.8(6.7) | 14–41 |
| *GGT, IU/L | 357 | 0.5 | 0.5(0.2) | 0.2–1.1 | 412 | 0.6 | 0.7(0.3) | 0.3–1.6 | 769 | 0.6 | 0.64(0.3) | 0.3–1.5 |
| *T. Bilirubin, mg/dL | 357 | 9.1 | 9.1(0.7) | 7.9–10.8 | 412 | 9.4 | 9.5(0.7) | 8.2–11.4 | 769 | 9.3 | 9.3(0.7) | 8.1–11.2 |
| *Phosphatase mg/dL | 357 | 3.4 | 3.4(0.6) | 2.3–4.7 | 412 | 3.3 | 3.3(0.6) | 2.3–4.5 | 769 | 3.3 | 3.4(0.6) | 2.3–4.6 |
| *Creat. Kinase, IU/L | 357 | 149 | 168.7 (73.7) | 76–389.8 | 412 | 197.5 | 221.9(101.5) | 83.5–504.5 | 769 | 173 | 196.5 (89.9) | 76–437.2 |
| *Lipase, IU/L | 357 | 32 | 36.7 (15.9) | 16.7–81.0 | 412 | 30 | 32.6(12.2) | 15.0–62.7 | 769 | 31 | 34.3 (13.9) | 16–67 |
| *Amylase, IU/L | 357 | 90 | 93.5 (29.4) | 43.9–159.6 | 412 | 102 | 107(33.6) | 53.2–186.7 | 769 | 96 | 100.8 (31.8) | 49–176 |
| T. Chol./HDL Ratio | 357 | 3.3 | 3.4(0.9) | 2.1–5.6 | 412 | 3.0 | 3.1(0.9) | 1.7–5.4 | 769 | 3.1 | 3.2(0.9) | 1.8–5.6 |
| Triglycerides, mg/dL | 357 | 68 | 75.5(33) | 33.8–159.5 | 412 | 69 | 76.1(30.8) | 37.0–156.1 | 769 | 69 | 75.3(31) | 35–155.4 |
| *Total Chol., mg/dL | 357 | 163 | 166.2 (35.2) | 100.9–240.0 | 412 | 149 | 152.4 (33.7) | 99–232 | 769 | 156 | 159.1 (35.6) | 99.1–237 |
| LDL-Chol., mg/dL | 357 | 100 | 102 (28.6) | 52–160 | 412 | 82 | 85.5(29.3) | 40.9–159.3 | 769 | 90 | 92.5 (28.5) | 47–154.3 |
| HDL-Chol., mg/dL | 357 | 49.5 | 51.9 (13.3) | 31.9–85.0 | 412 | 49 | 51.4(14.1) | 31–87 | 769 | 49 | 51.7 (13.7) | 31–85 |

*parameters with statistically significant gender differences

ALP-Alkaline Phosphatase; ALT-Alanine Aminotransferase; AST-Aspartate Aminotransferase; GGT-Gama Glutamyl transferase

T. Bilirubin-Total Bilirubin; D. Bilirubin-Direct Bilirubin; Gluc. Random- Random Glucose; Creatinine Kinase; Total Chol-Total Cholesterol; LDL-Chol-Low Density Lipoprotein Cholesterol; HDL-Chol-High Density Lipoprotein Cholesterol.

Reference ranges for WBC, neutrophil counts and platelets reported in this study were noted to be lower than those currently in use at the UZ-UCSF (for patient care and research). LDL
cholesterol, HDL cholesterol and direct bilirubin from this study were higher compared to the existing reference ranges. We observed very high creatinine kinase reference range of 76–437 IU/L compared to the current range of 0–145 IU/L. Our study also showed higher lipase and amylase compared to the existing reference ranges.

The reference range values for hemoglobin, hematocrit, and red blood cells are comparable to those established by the International AIDS Vaccine Initiative (IAVI) at seven clinical centers in four sub-Saharan African countries; Rwanda, Uganda, Kenya and Zambia [14]. Several hematological indices including hemoglobin, hematocrit, and red blood cell count reference ranges for both males and females from our study are comparable to those from previous African studies [8, 15, 16, 17]. The reference range for neutrophils for males in our study was 773–3967 which was lower than that observed among South Africans, Tanzanian and Ugandan males [15, 16, 18]. However our female reference ranges were comparable to those of other African countries [16, 17].

The finding of low white cell counts and low neutrophil counts among African populations has been frequently reported and thought to be constitutional [1,2,19,20]. Our data showed higher platelet counts in females, a finding previously reported in other studies [1, 21].

Higher reference ranges for urea, sodium, potassium, calcium and creatinine in males compared to females have been reported in studies done in Tanzania, Uganda and Kenya [16, 18, 22]. High creatinine in males compared to females is expected and in many international settings is explained by a greater skeletal, muscle and bone mass in males [23].

Combined male and female reference ranges for sodium, potassium and chloride were comparable to those reported in an Ethiopian study [24]. However we found higher phosphate ranges than those from this study.

Total cholesterol, HDL cholesterol and LDL cholesterol levels were higher when compared with results from Tanzanian and Kenyan, studies [16, 22]. In comparing males and females our study showed higher HDL cholesterol in females than males similar to findings in a Botswana study [25].

In using reference ranges to grade adverse events in international research settings we have observed occasional differences between ranges provided by the sponsor and those of the local population. In our setting the UZ-UCSF implements NIH sponsored studies and uses DAIDS (Division of AIDS, National Institute of Allergy and Infectious Diseases, NIH) toxicity grading scales to identify possible adverse events [26]. The DAIDS toxicity table grades ANC as grade 1 (1000–1300 cells/mm$^3$), grade 2 (750–999 cell/mm$^3$), grade 3 (500–749/mm$^3$) and grade 4 (<500 cells/mm$^3$). A male in our setting with a neutrophil count of 773 cells/mm$^3$ would be regarded as having a grade 2 adverse event yet this is normal according to the reference ranges we have established in this study. Moreover the lower limit of the combined neutrophil reference range of 939 cells/mm$^3$ would still be a grade 2. Similar discrepancies are also observed in cholesterol and phosphate. In the research setting this discrepancy between normal references ranges in our population and the toxicity levels provided in the sponsors table may impact patient management.

One of the limitations of our study is that the glucose and lipid samples were non-fasting. Most references values for serum lipids are established on fasting blood samples when used for cardiovascular risk assessment according to most national and international guidelines [27]. Some studies suggest that the variation between fasting and non-fasting LDL-Cholesterol levels is small [27, 28]. Another limitation is that we did not screen for other infections like malaria and helminths which could impact hematological indices such as hemoglobin levels and eosinophil counts respectively.
Conclusions

We conclude that these reference values are contemporary and represent an improvement on how the previous values were obtained. We suggest that these reference ranges can be immediately adopted for use in the clinical care of patients in our institutions including use in research.

Acknowledgments

The authors would like to thank all the study participants, staff of the UZ-UCSF central laboratory, the research staff who collected all the data and the field coordinators who assisted in the coordination of the study. Joelle Brown, PhD, and Amy J. Markowitz, JD provided editorial comments.

Author Contributions

Conceptualization: JGH ZMC ZARG WPS.

Formal analysis: JGH GM WT WPS.

Investigation: MWM WPS GM WT.

Methodology: GM WT.

Software: GM WT.

Supervision: JGH ZMC.

Writing – original draft: WPS JGH ZMC ZARG MM GM WT MFB NMN NN.

Writing – review & editing: WPS JGH ZMC MWM NN NMM GM WT MFB ZARG.

References

1. Bain BJ. Ethnic and sex differences in the total and differential white cell count and platelet count. J Clin Pathol 1996; 49:664–6 PMID: 8881919

2. Ezeilo GC. Non-genetic neutropenia in Africans. Lancet 1972; 2:1003–4. PMID: 4116936

3. Lugada ES, Mermin J, Kaharuza F, Ulvestad E, Were W, Langeland N, et al. Population based hematologic and immunologic reference values for a healthy Ugandan population. Clin Diagn Lab Immunol. 2004; 11:29–34 doi: 10.1128/CDLI.11.1.29-34.2004 PMID: 14715541

4. Aina O, Dadik J, Charurat M, Amangaman P, Gurumdi S, Mang E, et al. Institute of Human Virology/Plateau State Specialist Hospital AIDS Prevention in Nigeria Study Team. Reference values of CD4 T lymphocytes in human immunodeficiency virus-negative adult Nigerians. Clin Diagn Lab Immunol. 2005 Apr; 12(4):525–30. doi: 10.1128/CDLI.12.4.525-530.2005 PMID: 15817761

5. Emmanuel JC, French TJ. Normal hematological values in male Rhodesians. Cent Afr J Med. 1977; 23:4–7. PMID: 844094

6. Marima-Matariara HT. Reference values of liver function analytes in Zimbabwean women. Cent Afr J Med. 1985; 31:98–100 PMID: 4005951

7. Gomo ZA. Concentration of lipids, lipoproteins and apolipoproteins in Serum of Zimbabwean Africans. Clin Chem. 1985; 31:1390–2. PMID: 3926349

8. Mukiibi JM, West JG. Platelet counts in normal Zimbabweans: Preliminary observations. Cent Afr J Med. 1987; 33:99–102. PMID: 3440291

9. Musabayane CT, Ndlovu CE, Bwitty P, Msamati BC. Serum albumin concentrations in rural Zimbabweans. Cent Afr J Med. 1995; 41:204–8. PMID: 7553792

10. Scott MG, Le Grys VA, Klutts JS. Electrolytes and blood gases. In: Burtis CA, Ashwood ER Bruns DE, editors. Tietz textbook of clinical chemistry and molecular diagnostics. 4th Ed. St Louis: Elsevier Saunders 2006. P984–91
11. Clinical and Laboratory Standards Institute (CLSI). Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory-Approved Guideline, vol. 28. 3rd ed. Wayne, PA: CLSI document C28-A3;2008
12. 2012 Census-ZIMSTAT. Available from: http://www.zimstat.co.zw/dmdocuments/Census/CensusResults2012/National_Report.pdf. Accessed 1 April 2015
13. Gomani P, Matubu AT, Mujuru HA, Munjoma MW, Tinago W, Mandozana G et al. Hematological and biochemical laboratory reference intervals for Zimbabwean adolescents. Clin Lab. 2015; 61(1–2):101–11. PMID: 25807644
14. Karita E, Ketter N, Price MA, Kayitkenkore K, Kaleebu P, Nnunvuba A et al. CLSI derived hematological and biochemical reference intervals for healthy adults in eastern and southern Africa. PLoS One 2009; 4:e4401. doi: 10.1371/journal.pone.000440120 PMID: 19197365
15. Lawrie D, Coetzee LM, Becker P, Mahlangu J, Stevens W, Glencross DK. Local reference ranges for full blood count and CD4 lymphocyte count testing. S Afr Med J. 2009; 99:243–8. PMID: 19588777
16. Saathoff E, Schneider P, Kleinfeldt V, Geis S, Haule D, Maboko L et al. Laboratory reference values for healthy adults from southern Tanzania. Trop Med Int Health. 2008; 13:612–25. doi: 10.1111/j.1365-3156.2008.02047.x PMID: 18331386
17. Segodoli TM, Henderson FL, Rose CE, Turner KT, Zeh C, Fonjungo PN, et al. Normal laboratory reference intervals among healthy adults screened for a HIV pre-exposure prophylaxis clinical trial in Botswana. PLoS One. 2014 Apr 8; 9(4):e93034. doi: 10.1371/journal.pone.0093034. eCollection 2014 PMID: 24714095
18. Eller LA, Eller MA, Ouma B, Kataaah P, Kyabaggu D, Tumusime R, et al. Reference intervals in healthy adult Ugandan blood donors and their impact on conducting international vaccine trials. PLoS One. 2008; 3:e3919. doi: 10.1371/journal.pone.0003919 PMID: 19079547
19. Ezeilo GC. The aetiology of neutropenia in healthy Africans. East Afr Med J. 1974 Dec; 51(12):936–42. PMID: 4455493
20. Tikly M, Blumsohn D, Solomons HD, Govender Y, Atkinson PM. Normal haematological reference values in the adult black population of the Witwatersrand. S Afr Med J. 1987 Jul 18; 72(2):135–6 PMID: 3616787
21. Cross JP, Heyns AD. Haematological references values for the Basotho. S Afr Med J. 1983; 63:480–3. PMID: 6836426
22. Kibaya RS, Bautista CT, Sawe FK, Shaffer DN, Satteren WB, Scott PT, et al. Reference ranges for the clinical laboratory derived from a rural population in Kericho, Kenya. PLoS One 2008; 3:e3327. doi: 10.1371/journal.pone.0003327 PMID: 18833329
23. Taylor EH, Fink LM, Pappas AA. Reproducibility of creatinine kinase isoenzymes electrophoresis. Clin Chem. 1989; 35:710. [22]
24. Woldeemichael K, Haileamlak A, Muluneh AT, Alemeseged F, Tessema F, Asefa M, et al. Biochemical profile at Gilgel Gibe field research center, southwest Ethiopia Ethiop J Health Sci. 2012; 22(Spec Iss):51–60. [23]
25. Maphephu SM, Kasvosve I. Reference intervals for serum total cholesterol, HDL cholesterol and non-HDL cholesterol in Baswana adults. S Afr Med J. 2011; 101:546–7 PMID: 21920130
26. National Institutes of Health (2004) NIH Division of AIDS Table for Grading the Severity of Adults and Pediatric Adverse Events, Clarification August 2009. Available from: http://rsc.tech-res.com/safetyandpharmacovigilance/gradingtables.aspx. Accessed September 28 2014.
27. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002; 106:3143–3421. PMID: 12485966
28. Doran B, Yu G, Xu J, Weintraub H, Mora S, Maron DJ, et al. Prognostic value of fasting vs non-fasting low density lipoprotein cholesterol on long term mortality: Insight from the National Health and Nutrition Survey III (NHANES-III). Circulation 2014; 130(7):54653. doi: 10.1161/CIRCULATIONAHA.114.010001