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ORIGINAL RESEARCH

# Establishment of Reference Intervals for Common Renal and Liver Function Parameters in Healthy Adults in Mogadishu, Somalia: A Cross-Sectional Study

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**Introduction:** Reference intervals (RIs) are crucial for the accurate interpretating of laboratory test results in clinical settings, serving as benchmarks for evaluating individual health status. This study investigates the influence of sex and age on common liver function tests (LFTs) and renal function tests (RFTs) in healthy adults in Mogadishu, Somalia.

**Methods:** A community-based cross-sectional study was carried out from October 2022 to January 2023 on a randomly selected sample of 255 healthy participants from Mogadishu, Somalia. Approximately 5 mL of whole blood was collected from each participant and processed screening of hepatitis B and C, and human immunodeficiency virus, and then biochemical analyses were conducted for common liver and kidney parameters.

**Results:** The study found significant sex and age-related differences in the measured LFTs and RFTs parameters. For LFTs, males had higher levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) compared to females (ALT: 11.5 vs 7.5 U/L; AST: 25.5 vs 19.1 U/L; both $p < 0.001$). Age-related differences were also observed, with individuals aged 30 and above had higher levels of ALT and AST compared to those aged 18–29 (ALT: 10.9 vs 8.5 U/L; AST: 24.3 U/L vs 21.0 U/L, both $p < 0.001$). For RFTs, males had higher levels of creatinine (0.9 vs 0.7 mg/dL), urea (23.1 vs 16.1 mg/dL), and uric acid (5.2 vs 4.2 mg/dL) than females, all with $p < 0.001$.

**Conclusion:** The study established population specific RIs for common liver and renal function parameters and revealed significant variations across sex and age groups. These findings underscore the importance of developing and using local RIs to ensure accurate clinical interpretation and effective patient management. Further research with larger sample sizes and in diverse regions of Somalia is highly recommended.

**Keywords:** reference intervals, liver function tests, renal function tests, Mogadishu, Somalia

## Introduction

Reference intervals (RIs) are fundamental in laboratory testing, helping physicians differentiate between healthy individuals and those with medical conditions.[1,2] Typically derived from a reference distribution that captures 95% of a population's values,[3,4] these intervals are crucial benchmarks for the accurate interpretation of individual test results in clinical settings, aiding in the diagnosis, monitoring, and treatment of health disorders.[5,6] Given the significant variability in RIs across different populations, it is recommended that each country establishes its own RIs tailored to its specific demographic as per the guidelines of Clinical and Laboratory Standard Institute (CLSI) and International Federation of Clinical Chemistry.[7–9] This practice ensures that the reference values accurately reflect the local population's unique

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genetic, diet, and environmental characteristics, thereby enhancing the precision and reliability of diagnostic interpretations and improving patient care.

The liver and kidneys are essential organs with critical physiological functions. The kidneys are responsible for maintaining blood volume, regulating mineral concentrations in the bloodstream, and excreting metabolic waste products.[10] Conversely, the liver is involved in multiple processes, including metabolism, digestion, detoxification, and carbohydrate storage.[11] Renal Function Tests (RFTs) and Liver Function Tests (LFTs) are the primary diagnostic assays utilized for the evaluation of renal and hepartic disorders, respectively. RFT, which assess kidney function through markers such as creatinine, urea, and uric acid, are crucial for diagnosing renal impairment and guiding treatment.[10] Similarly, LFTs which include measurements of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are key components of routine clinical assessments used to evaluate liver health, diagnose liver diseases, and monitor treatment efficacy.[11]

In Somalia, there is a notable gap in locally derived RIs for clinical chemistry parameters. Existing reference intervals used in Somali healthcare settings are often based on data from foreign populations, which may not accurately represent the unique genetic, dietary, and environmental conditions of the local population. Recent studies in other African countries have shown that reference intervals for LFTs and RFTs can vary significantly from those established in Caucasian populations, highlighting the potential for misdiagnosis and suboptimal patient management when non-local reference values are used.[10]

Establishing population-specific reference intervals for LFTs and RFTs in Somalia is therefore crucial. Given the financial constraints and the critical role of liver and kidney function in overall human health, our study focused on establishing RIs for the most common LFTs and RFTs parameters. Thus, this study aims to develop and validate reference intervals for common LFTs and RFTs for adults in Mogadishu, providing a more accurate basis for diagnosing and managing liver and kidney conditions in the Somali population. By aligning the reference intervals with local demographic characteristics, this research seeks to enhance the precision of clinical assessments and improve patient outcomes.

# Methods

## Study Design and Site

A community based cross-sectional study was conducted from October 2022 to January 2023 in Mogadishu, the capital city of Somalia. Mogadishu is situated along the coast of the Indian Ocean, approximately at sea level, and serves as the country's largest city and main port. The city is located in the southeastern region of Somalia and plays a central role in the nation's economy, politics, and culture.

## Study Population and Participant Selection

Participants were selected using random sampling method from within the community. A list of eligible participants based on pre-defined criteria (healthy volunteers, aged 18–49 years, residing in Mogadishu, Somalia) after providing written consent were invited to participate health-check up at Somali Sudanese Specialized Hospital including; Medical history, physical examination, and serological screening.

## Ethical Approval

The study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki of 1964.[12]

It obtained an ethical approval from the Jamhuriya University of Science Research Ethics Committee (Ref: VPR&D/1016/EC/052023). Written informed consent was taken from all participants before their involvement in the study.

## Inclusion and Exclusion Criteria

All participants were required to meet the pre-established clinical history, physical examination, and CLSI inclusion and exclusion criteria. The exclusion criteria included various medical conditions that affect liver and kidney, such as anemia, cardiovascular disease including high blood pressure and diabetes. Furthermore, participants were excluded if they were

undergoing drug therapy, engaging in heavy smoking, suffering from chronic conditions like diabetes, had donated blood within the last three months, or had undergone recent surgery.

## Sample Size Determination

The sample size was determined based on CLSI guidelines, aiming for 242 individuals (121 males and 121 females) to ensure adequate representation for sex-based RIs. Additionally, a 5% non-response rate was included, bringing the final sample size to 255 participants.[13]

## Sample Collection

After cleaning the skin with 70% alcohol on anterior view of the elbow, a needle with a holder was inserted into the antecubital fossa, and up to 5 mL of whole blood was drawn via venepuncture using BD Vacutainer test tubes (Shandong Chengwu Medical Products Factory, Shandong, China). The blood was then allowed to clot for 20 minutes and centrifuged at 3000 RPM for 10 minutes to separate the serum from the cellular components and then processed for serological and biochemical tests. Samples could not process within 2 hours were stored at 2–8 °C and analyzed within 3 days.

## Serological Tests

Prior to serological screenings, participants underwent a health check-up by a licensed physician at Somali Sudanese Specialized Hospital, Mogadishu, Somalia. Subsequently, standard test kits (inTec Products, Inc., China) were utilized to conduct serological tests for the detection of hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus 1 and 2 (HIV-1 and HIV-2).

## Biochemical Analysis

Every sample underwent biochemical testing including AST, ALT, creatinine, urea, uric acid, albumin (ALB), and total protein (TP) using the Beckman Coulter: *AU 480 Chemistry System*, following the manufacturer's instructions and standard operating procedures (SOP). The measured parameters and methods are as follows: ALT (kinetic UV-LDH method), AST (kinetic UV-MDH method), TP (Biuret reaction), ALB (Bromocresol green method), creatinine (Jaffe method), urea (Berthelot method), and uric acid (uricase method).

## Quality Control

The biochemical analyzer was calibrated according to the manufacturer's recommendations. To ensure the accuracy of the analyzer, normal and abnormal control samples were run daily as an internal quality control. Most of the quality control results revolved around the target values of the analytes and quite often-registered values similar to the target value of the analyte under study. Additionally, the laboratory that performed all testing is enrolled in external quality assurance testing program One World Accuracy, Canada.

## Statistical Analysis

Statistical analyses were conducted using SPSS (version 21). RIs were established in accordance with CLSI C28-A3 guidelines. The data were analyzed for normality by employing the Kolmogorov–Smirnov and Shapiro–Wilk tests. Descriptive statistics including the $2.5^{th}$ and $97.5^{th}$ percentile, mean, median, and range were calculated. Differences between males and females were evaluated using the Student's *t*-test or the Mann–Whitney *U*-test, depending on the data's distribution. A statistical significance was set less than at 0.05.

# Results

## LFTs

The reference interval, defined from the $2.5^{th}$ to the $97.5^{th}$ percentile, revealed significant sex-related differences in the LFTs. Specifically, males exhibited significantly higher ALT levels compared to females (4.0–27.3 U/L vs 2.0–23.6 U/L, p-value

<0.001). Similarly, AST levels were higher in males than in females (16.0–39.9 U/L vs 6.5–33.6 U/L, p-value <0.001); while ALB and TP levels showed slight differences in the lower and upper limit of reference intervals between males and females (3.9–5.5 g/dL vs 3.5–5.5 g/dL, p= 0.001; and 5.6–8.0 g/dL vs 5.6–8.5 g/dL, p= 0.005) respectively (Table 1).

Significant age-related differences were observed. Participants aged 30 years and older exhibited significantly higher ALT levels compared to those aged 18–29 years (2.0–27.0 U/L vs 2.0–25.0 U/L, p < 0.001). Similarly, AST levels demonstrated a comparable trend, with individuals aged 30 and older displaying elevated levels compared to those aged 18–29 years (12.6–40.0 U/L vs 6.8–39.2 U/L, p < 0.001). However, no significant age-related differences were noted in ALB and TP levels, indicating comparable levels between the older and younger age groups (Table 1).

**Table 1** Biochemical Reference Values for Liver Function Tests (LFTs) Based on Participants on Sex and Age

| Analyte (unit) | All | N | Mean | 95% CI for mean | Median | Range | $2.5^{th}$- $97.5^{th}$ percentile | *P* value |
|---|---|---|---|---|---|---|---|---|
| **Sex** | | | | | | | | |
| Alanine aminotransferase (ALT), U/L | Combined | 252 | 9.8 | 9.0–10.5 | 8.0 | 1–42 | 2.0–24.7 | < 0.001 |
| | Male | 141 | 11.5 | 10.6–12.5 | 10.0 | 3–34 | 4.0 −27.3 | |
| | Female | 111 | 7.5 | 6.4–8.6 | 6.0 | 1–42 | 2.0 −23.6 | |
| Aspartate aminotransferase (AST), U/L | Combined | 252 | 22.7 | 21.9–23.6 | 22.1 | 2.4–41.4 | 9.6–39.6 | < 0.001 |
| | Male | 141 | 25.5 | 24.5–26.5 | 24.9 | 13.3–41.4 | 16.0–39.9 | |
| | Female | 111 | 19.1 | 18.0–20.3 | 18.9 | 2.4–41.0 | 6.5–33.6 | |
| Albumin, g/dL | Combined | 252 | 4.6 | 4.6–4.7 | 4.7 | 3.2–5.7 | 3.6–5.5 | 0.001 |
| | Male | 141 | 4.7 | 4.7–4.8 | 4.7 | 3.8–5.7 | 3.9–5.5 | |
| | Female | 111 | 4.5 | 4.4–4.6 | 4.6 | 3.2–5.6 | 3.5–5.5 | |
| Total protein, g/dL | Combined | 252 | 6.7 | 6.6–6.8 | 6.6 | 5.6–8.7 | 5.6–8.3 | 0.005 |
| | Male | 141 | 6.6 | 6.5–6.7 | 6.6 | 5.6–8.7 | 5.6–8.0 | |
| | Female | 111 | 6.8 | 6.7–7.0 | 6.8 | 5.6–8.7 | 5.6–8.5 | |
| **Age** | | | | | | | | |
| Alanine aminotransferase (ALT), U/L | Combined | 252 | 9.8 | 9.0–10.5 | 8.0 | 1–42 | 2.0–24.7 | < 0.001 |
| | 18–29 | 119 | 8.5 | 7.4–9.5 | 7.0 | 1–42 | 2.0–25.0 | |
| | ≥ 30 | 133 | 10.9 | 9.9–12.0 | 10.0 | 2–34 | 2.0–27.0 | |
| Aspartate aminotransferase (AST), U/L | Combined | 252 | 22.7 | 21.8–23.6 | 22.0 | 2.4–41.4 | 9.6–39.6 | < 0.001 |
| | 18–29 | 119 | 21.0 | 19.7–22.2 | 20.6 | 2.4–41 | 6.8–39.2 | |
| | ≥ 30 | 133 | 24.3 | 23.1–25.4 | 23.4 | 11.3–41.4 | 12.6–40.0 | |
| Albumin, g/dL | Combined | 252 | 4.6 | 4.6–4.7 | 4.7 | 3.2–5.7 | 3.6–5.5 | 0.019 |
| | 18–29 | 119 | 4.7 | 4.6–4.8 | 4.7 | 3.5–5.6 | 3.6–5.6 | |
| | ≥ 30 | 133 | 4.6 | 4.5–4.7 | 4.6 | 3.2–5.7 | 3.6–5.4 | |
| Total protein, g/dL | Combined | 252 | 6.7 | 6.6–6.8 | 6.6 | 5.6–8.7 | 5.6–8.3 | 0.001 |
| | 18–29 | 119 | 6.8 | 6.7–7.0 | 6.8 | 5.6–8.7 | 5.6–8.6 | |
| | ≥ 30 | 133 | 6.5 | 6.5–6.6 | 6.5 | 5.6–8.5 | 5.6–8.0 | |

**Abbreviations**: U/L, units per liter; mg/dl, milligram per deciliter; g/dL, gram per deciliter, CI, confidence interval.

## RFTs

According to the sex-related differences, the results revealed significant differences in creatinine, urea, and uric acid levels between males and females. Males recorded a higher creatinine level than females (0.7–1.5 mg/dl vs 0.5–1.1 mg/dl, p= <0.001); For urea, males also showed higher levels than females (11.6–54.7 mg/dl vs 7.8–29.6 mg/dl, p= <0.001); uric acid levels were also higher in males than females (3.2–7.4 mg/dl vs 2.3–6.7 mg/dl, p= <0.001), as data is shown in Table 2.

Regarding age-related differences in RFTs, significant variations were observed in creatinine, urea, and uric acid levels among different age groups. Comparing the ≥30 age group to individuals aged 18–29 years, the older group exhibited slightly higher creatinine levels (0.5–1.5 mg/dL vs 0.5–1.2 mg/dL, p < 0.001). Urea levels also demonstrated a significant variation with a similar trend, as the older age group (≥30 vs 18–29 years) recorded significantly higher levels compared to the younger groups (8.3–52.7 mg/dL vs 8.5–29.4 mg/dL, p < 0.001). Similarly, uric acid levels were lower in the younger age group compared to the older age group (3.0–7.5 mg/dL for the older group vs 2.3–6.6 mg/dL for the younger cohort, p < 0.001) (Table 2).

**Table 2** Biochemical Reference Values for Renal Function Tests (RFT) Based on Participants Sex and Age

| Analyte (unit) | All | N | Mean | 95% CI for mean | Median | Range | 2.5th- 97.5th percentile | *P* value |
|---|---|---|---|---|---|---|---|---|
| **Sex** | | | | | | | | |
| Creatinine, mg/dL | Combined | 252 | 0.9 | 0.8–0.9 | 0.9 | 0.5–1.6 | 0.5–1.3 | < 0.001 |
| | Male | 141 | 1 | 0.9–1.0 | 1.0 | 0.5–1.6 | 0.7–1.5 | |
| | Female | 111 | 0.7 | 0.7–0.8 | 0.7 | 0.5–1.3 | 0.5–1.1 | |
| Urea, mg/dl | Combined | 252 | 20.0 | 19.0–21.1 | 18.2 | 7.3–59.4 | 8.6–52.7 | < 0.001 |
| | Male | 141 | 23.1 | 21.6–24.7 | 20.3 | 8.1–59.4 | 11.6–54.7 | |
| | Female | 111 | 16.1 | 15.2–17.0 | 15.5 | 7.3–32.8 | 7.8–29.6 | |
| Urate, mg/dl | Combined | 252 | 4.7 | 4.5–5.0 | 4.5 | 1.6–34.0 | 2.5–7.3 | < 0.001 |
| | Male | 141 | 5.2 | 5.0–5.3 | 5.1 | 1.9–8.9 | 3.2–7.4 | |
| | Female | 111 | 4.2 | 3.7–4.8 | 3.8 | 1.6–34.0 | 2.3–6.7 | |
| **Age** | | | | | | | | |
| Creatinine, mg/dL | Combined | 252 | 0.9 | 0.9–1.0 | 0.9 | 0.5–1.6 | 0.5–1.3 | < 0.001 |
| | 18–29 | 119 | 0.8 | 0.8–0.9 | 0.8 | 0.5–1.4 | 0.5–1.2 | |
| | ≥ 30 | 133 | 0.9 | 0.9–1.0 | 0.9 | 0.5–1.6 | 0.5–1.5 | |
| Urea. mg/dl | Combined | 252 | 20.0 | 19.0–21.1 | 18.2 | 7.3–59.4 | 8.6–42.7 | < 0.001 |
| | 18–29 | 119 | 17.7 | 16.6–18.7 | 16.9 | 7.6–52.5 | 8.5–29.4 | |
| | ≥ 30 | 133 | 22.2 | 20.5–23.9 | 19.8 | 7.3–59.4 | 8.3–52.7 | |
| Urate, mg/dl | Combined | 252 | 4.7 | 4.5–4.8 | 4.5 | 1.6–34.0 | 2.5–7.3 | < 0.001 |
| | 18–29 | 119 | 4.5 | 4.0–4.4 | 4.1 | 1.9–34.0 | 2.3–6.6 | |
| | ≥ 30 | 133 | 5.0 | 4.9–5.3 | 5.0 | 1.6–8.90 | 3.0–7.5 | |

**Abbreviations**: RFTs, renal function tests; U/L, units per liter; mg/dl, milligram per deciliter; g/dL, gram per deciliter, CI, confidence interval.

## Discussion

Accurate interpretation of laboratory test results is crucial for correctly diagnosing various diseases. LFTs and RFTs are crucial for diagnosing and monitoring various health conditions.[14] However, the RIs commonly used for these tests in Somalia are often based on data from foreign populations. This may not accurately represent Somali ethnics due to variations in factors such as diet, genetics, and environment.[15] The aim of this study was to establish population-specific ranges for liver and renal parameters in a healthy Somali adult population (aged 18 to 49 years) in Mogadishu, Somalia. By comparing these local values to established foreign ranges and examining variations related to sex and age, our study highlights the critical need for tailored clinical biochemistry RIs to enhance the healthcare delivery system in Somalia.

The studied RFTs revealed significant sex-based differences in creatinine, urea, and uric acid levels, along with age-related variations in these biochemical parameters. These findings are consistent with a prior study indicating that renal parameters vary by sex and age.[3] In this study, the creatinine and urea levels observed for males and females were higher than those reported in Northeast Ethiopia,[16] the United States,[17] Uganda,[18] Ghana,[19] Tanzania,[20] and Kenya.[21] However, Northwest Ethiopia reported similar findings,[22] with creatinine levels closely matching our findings. These differences may be attributed to variations in ethnicity, demographics, body fat distributions, and hormonal levels within the population.[23]

The study also revealed significant differences in various liver parameters based on sex and age.[3] For instance, the median ALT and AST levels showed significant differences between males and females. The higher AST and ALT levels in males compared to females in this study align with prior studies from Ethiopia,[6,24] Tanzania,[20] and Uganda.[18] These sex-specific variations in liver enzymes may be partially attributed to variations in fat distribution and muscle mass, which are influenced by sex hormones.[25,26] Moreover, our reference intervals for AST and ALT values are lower than those reported in Kenya,[27] the Amhara Regional State of Ethiopia,[24] and the United States.[28] The reference values of AST and ALT varied between studies, primarily due to differences in ethnicity, dietary habits, gender, age, and body fat distributions.[25,29] The liver enzyme levels can also vary depending on lifestyle and other environmental factors.[30,31]

No reference interval differences for sex and age were observed in the studied group for total protein and albumin levels. The total protein and albumin levels were the same for both genders, which is consistent with most studies of African adults.[19,20,22] In this study, the lower limit of the reference interval for total protein is comparable to reports from Northeast Ethiopia[6] and the United States,[28] but lower than those from Uganda,[18] and Tanzania.[5,20,32] This study provides valuable insights into the sex- and age-related differences in liver (AST, ALT) and renal (creatinine, urea, uric acid) function parameters within Somali population, contributing to the growing body of knowledge in this area. In contrast, no significant sex- or age-related differences were found for TP and ALB levels.

## Conclusion

The findings of this study demonstrate differences between our RIs and the foreign reference ranges currently used in local hospitals in Somalia. The results of our study reveal that LFTs (AST and ALT) and RFTs (creatinine, urea, and uric acid) exhibit elevated levels in males in comparison to females. In addition, elders exhibit a similar pattern of LFTs and RFTs compared to younger age groups. However, it's important to note that while AST and ALT levels showed significant differences, no significant sex or age-related differences were observed for other LFT parameters including total protein and albumin. These findings show the limitations of using reference intervals that do not apply to a specific population. This underscores the critical need to develop reference ranges tailored to the Somali population to ensure accurate clinical interpretation, improve diagnostic accuracy, and enhance treatment effectiveness. Despite budgetary constraints restricting this study to specific parameters, it serves as crucial initial step towards creating comprehensive RIs specifically tailored for the Somali population. We plan to include a broader range of biochemical parameters and cover diverse regions of Somalia in future studies.

## Strengths and Limitations

This study presents a significant strength by addressing the limitations of using reference ranges derived from foreign populations for Somali patients. Additionally, it analyses sex- and age-related differences in the studied parameters,

contributing to a more nuanced understanding of how reference ranges may vary within the Somali population. However, the study has some limitations, namely that it was conducted solely in Mogadishu, Somalia, and it is findings may not be broadly applicable to the entire Somali population across various regions. Furthermore, the lack of detailed exploration into dietary habits, which can significantly impact liver and kidney function, represents another limitation.

## Abbreviations

LFTs, Liver function tests; RFTs, Renal function tests; RIs, Reference intervals; CLSI, Clinical and laboratory standard institute; BD, Becton Dickinson; HBV, hepatitis B virus; HCV, hepatitis C virus; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; TP, Total protein; Albumin, ALB; SOP, standard operating procedures; U/L, Units per liter; mg/dl, milligram per deciliter; g/dL, gram per deciliter, CI, confidence interval.

## Data Sharing Statement

The data analyzed in this study are available from the manuscript.

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## Disclosure

The authors report no conflict of interest in this work.

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