

# Reference intervals for serum creatinine and urea in the adult western Sudanese population

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Submitted: June 2023

Accepted: December 2023

Published: February 2024

**Citation:** Mohammed et al. Reference intervals for serum creatinine and urea in the adult western Sudanese population, South Sudan Medical Journal, 2024;17(1):6-10 © 2024 The Author (s) **License:** This is an open access article under [CC BY-NC](https://creativecommons.org/licenses/by-nc/4.0/) DOI: <https://dx.doi.org/10.4314/ssmj.v17i1.2>

## ABSTRACT

**Introduction:** Serum creatinine and urea levels are affected by numerous factors such as ethnicity, environment, age, sex, and anthropometric measurements. The Clinical and Laboratory Standards Institute (CLSI) recommends that each laboratory should establish its own reference intervals for biochemistry and haematology. There are no local reference intervals for serum creatinine and blood urea in Sudan; instead, intervals derived from worldwide research are used. The purpose of this study was to determine the blood urea and serum creatinine reference intervals for healthy adults in the Western Sudanese population.

**Method:** Randomly selected adult Sudanese residents of Al Fashir City who were from the Western Sudan states of Kordofan and Darfur were the subjects of a cross-sectional study conducted in September and October 2018. We recruited 153 participants. After giving their consent, they were evaluated using a questionnaire that collected medical history and demographic information. We used standard techniques to measure blood pressure, body mass index, urea, and creatinine. Kolmogorov-Smirnov tests were used to assess the distributions of the creatinine and urea values, and reference intervals calculated. T-tests were used to investigate differences of mean creatinine and urea levels by sex and age. IBM SPSS Statistics version 25 was used to analyse the data and  $p \leq 0.05$  was considered significant.

**Results:** Overall, the reference intervals (Mean $\pm$ 1.96\*SD) for serum creatinine and urea levels were 0.45-0.92 mg/dL and 7.6-27.9 mg/dL respectively, compared to international reference intervals adopted from the American Board of Internal Medicine (ABIM) serum creatinine (males 0.7-1.3, females 0.5-1.1 mg/dL) and blood urea (17.12-42.8 mg/dL for both sexes) and The Western Sudanese population's mean serum creatinine and urea levels were, respectively, 0.69 mg/dL and 17.8 mg/dL. Male sex was associated with higher levels of both creatinine and urea ( $p < 0.001$ ).

**Conclusion:** This study documented lower reference intervals for creatinine and urea in the Western Sudanese population.

**Key words:** creatinine, urea, reference, intervals, renal, function, test, Sudan

## Introduction

Serum creatinine, urea, cystatin and beta-2 microglobulin are endogenous markers of kidney function. Serum creatinine and urea are the cheapest of these to measure and easily accessible. Exogenous filtrated markers, like inulin, are accurate indicators but impractical. The management of chronic kidney disease greatly depends on the accurate measurement of both filtrated markers, which are acknowledged as the best overall indicator of kidney function.<sup>[1]</sup> While industrialized nations have thoroughly studied the levels of these markers, most African nations have not.<sup>[2]</sup>

Most laboratories in Sudan use reference intervals that are taken from developed country populations, which may not apply to the Sudanese population. In a study to ascertain the normal values of respiratory function for Sudanese, such a difference was observed.<sup>[3]</sup>

The aim of this research was to determine the reference intervals of serum creatinine and urea in healthy adults in the Western Sudanese population. Additionally, the data were analysed by age and sex, and compared with regional and international studies.

## Method

### Study design and setting

In September and October of 2018, adults from the Western Sudan states (Darfur and Kordofan) who resided in Al Fashir city participated in a cross-sectional study.

Three federal Kordofan states—the north, south, and west—and five federal Darfur states—the north, south, central, east, and west—combine to form the western Sudan region. With an estimated population of 5,207,900 in 2017, Kordofan spans an area of 376,145 km<sup>2</sup> (146,932 miles<sup>2</sup>), with the Nuba Mountains located in the southeast. The main town is El-Obeid. With the Marrah Mountains (Jebel Marra) in the middle of the region, Darfur occupies 493,180 km<sup>2</sup> (190,420 sq mi) and is home to 9,241,369 people according to estimates from 2017. The three largest towns in the area are Nyala, Geneina, and Al Fashir.<sup>[4, 5]</sup>

### Study population and eligibility criteria

College students voluntarily participated in the study, as did employees of both sexes working in factories, laboratories, and schools. The study included individuals who had no acute or chronic conditions at the time of enrolment, with ages ranging from 18 to 64, and originally from the western Sudan region.

### Sample size and technique

According to the International Federation of Clinical Chemistry (IFCC) and Clinical and Laboratory Standards Institute (CLSI) recommendations on the establishment of reference intervals, the sample size should include at least 40 participants for each analysis category if data values are normally distributed and a parametric method is used.<sup>[6]</sup> Originally, we had planned to gather at least 240 samples, or 120 samples for each sex. However, due to budgetary constraints, we were only able to gather 153 samples.

### Study procedure and data collection

After gaining informed consent, participants were evaluated using a questionnaire that asked about personal information and medical history. Standard methods (mercury sphygmomanometer and a stethoscope, weight (kg)/height (m)<sup>2</sup>, and Mindray B 300 chemistry auto analyzer), were used to measure blood pressure, body mass index, and serum creatinine and blood urea respectively.

### Quality control

All pre analytical and post-analytical precautions were followed in order to guarantee the precision and accuracy of the test results, as indicated by CLSI-IFCC. The manufacturer recommended using commercial standards for daily calibration of the analyzer. Every day, the analyzer's accuracy was checked using controls for normal, abnormal low, and abnormal high values. 10% of the sample was reanalyzed in the Blood Bank quality control laboratory, using the same kind of chemistry analyzer, as part of an external quality control procedure.

### Data analysis

IBM SPSS Statistics version 25 was used to conduct the statistical analysis. We used the Kolmogorov-Smirnov test to test whether values were normally distributed. The CLSI (C28-A3) guidelines suggest using mean $\pm$ (1.96 \* SD) to define the reference intervals (thus accounting for 95% of the data values) when the data have a normal distribution, and 2.5th and 97.5th percentile otherwise.<sup>[6]</sup> Means and standard deviations (SD) were calculated, both overall and for sub-groups by age and sex. T-tests were then used to compare sub-groups, using a significance level of  $p \leq 0.05$ .

## Results

A total of 153 individuals were studied: 56 (36.6%) males and 97 (63.4%) females. Ages ranged between 18- 64

years with a mean of 23.5 years. Table 1 shows means and SDs for blood pressure and BMI.

The means (SDs) of serum creatinine levels for females and males were 0.66 (0.11) and 0.75 (0.12) mg/dL

**Table 1. Blood pressure and BMI (n=153)**

Test	Mean	SD	Range	Minimum	Maximum
Systolic BP mmHg	113.9	11.2	55	80	135
Diastolic BP mmHg	73.7	6.8	40	50	90
Body mass index	22.6	3.3	16.6	18.0	34.6

**Table 2. Serum creatinine and blood urea (n=153)**

Test	Mean	SD	Range	Minimum	Maximum
Urea mg/dL	17.8	5.2	23	10	33
Creatinine mg/dL	0.69	0.12	0.6	0.4	1.0

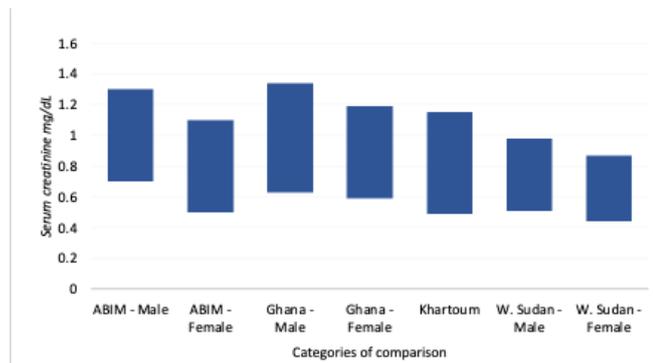


Figure 1. Comparison of serum creatinine mg/dL reference intervals (upper and lower values) between Sudanese (Khartoum/Western), African (Ghanaian) and international reference (ABIM)

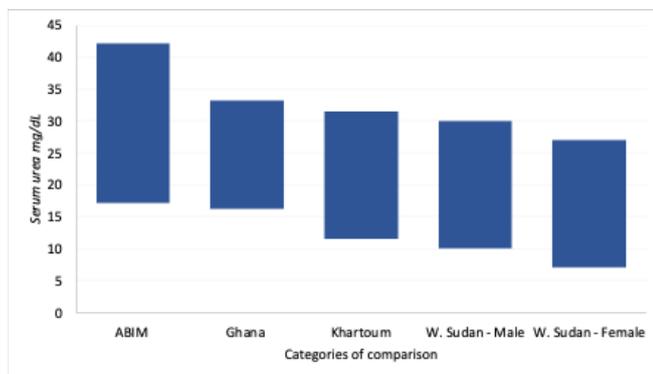


Figure 2. Comparison of serum urea mg/dL reference intervals (upper and lower values) between Sudanese (Khartoum/Western), African (Ghanaian) and international reference (ABIM)

respectively. For blood urea they were 17 (5) and 20 (5) mg/dL for females and males respectively. The reference intervals (mean±1.96\*SD) of serum creatinine for females and males were (0.44-0.87) and (0.51-0.98) mg/dL respectively. For blood urea they were (7-27) and (10-30) mg/dL levels for females and males respectively.

The mean of serum creatinine and urea levels for combined males and females are shown in Table 2.

For all participants the results showed lower reference intervals of serum creatinine and urea levels (0.45-0.92mg/dL and 7.6-27.9mg/dL respectively) compared to the regional (Ghanaian)<sup>[7]</sup> study reference intervals of serum creatinine and urea levels (0.55-1.3 mg/dL and 16.2-34.2 mg/dL respectively) and international reference intervals adopted from ABIM<sup>[8]</sup>, for serum creatinine (males 0.7-1.3, females 0.5-1.1 mg/dL) and for blood urea (17.12-42.8 mg/dL) (Figures 1 and 2).

T-tests showed that serum creatinine and urea correlate significantly with sex, with higher levels in males. Serum creatinine levels increased with age while urea level decreased with age, but the effect was not significant (Table 3).

## Discussion

In this study we set out to determine the local reference intervals of serum creatinine and blood urea as this is a recommendation from CLSI.

Our findings showed lower serum creatinine and urea levels when compared to ABIM<sup>[8]</sup> and to a Ghanaian study.<sup>[7]</sup> The study showed little difference when compared to another Sudanese study<sup>[9]</sup> (Figures 1 and 2). These international and regional variations in the results might be due to ethnic and geographic variations between the studies' populations. Furthermore, western countries' life style, especially a diet rich in protein, may have led to a higher production of endogenous substances; that is a main reason why CLSI recommend establishing local reference intervals.

The means of the serum creatinine and urea levels were slightly higher in males than females, consistent with other studies.<sup>[9, 10, 11]</sup>

Although the mean serum creatinine concentrations were slightly higher with advancing ages this did not reach significance. This is similar to the findings of others.<sup>[9, 12, 13]</sup> With advancing age the mean serum urea concentrations tended to be lower but not significantly so.<sup>[14]</sup>

**Table 3. T-tests of the means of serum creatinine and urea by sex and age**

Variables	Category	Creatinine mg/dL			Urea mg/dL		
		Mean	SD	p-value	Mean	SD	p-value
Sex	Male	0.75	0.13	<0.001	20	5	<0.001
	Female	0.66	0.11		17	5	
Age	18-40 years	0.69	0.13	0.779	18	5	0.846
	41-64 years	0.74	0.10		16	3	

## Conclusion

Both serum creatinine and blood urea concentrations reference intervals were lower than the ABIM reference intervals. Both serum creatinine and blood urea concentrations were higher in males than in females ( $p < 0.001$ ).

## Recommendation

A fully supported household survey project including all Sudan states is needed to establish biochemical and haematological reference intervals for the Sudanese population and to encourage young Sudanese researchers to collaborate with the Federal Ministry of Health to achieve this goal.

## Limitation

Because of the war in Sudan the authors no longer have access to the data and so have not been able to follow all of the recommendations from the reviewers but this did not affect the clarity of the paper.

## Acknowledgments

The authors thank all volunteers who participated in this study, and the SSMJ editorial team.

## Ethical consideration

Ethical approval of this study was obtained from the Sudanese Federal Ministry of Health and from The National Ribat University, Faculty of Medicine, Khartoum, Sudan.

**Conflict of interest:** None

**Funding:** None

**Author contributions:** Muaath Ahmed Mohammed comprehensively contributed to the data collection,

and study design, and wrote the manuscript. Ibrahim Abdelrahim Ali and Abdaraihem Alborai Abeadalla contributed to data collection, analysis, and interpretation, and edited the paper. Omer Abdelaziz Musa contributed to supervision of the project, study design and reviewing the scientific context. All authors approved the final manuscript.

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