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# Estimation of the normal values of renal parameters for adults in Antananarivo Madagascar

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## Abstract

**Objective**: This study is aimed at estimating the normal values of the plasma creatinine and urea of adults in Antananarivo.
**Methodology:** It was a transverse and descriptive study covering the period from September 20th to November 09th, 2017 at the National Center for Blood Transfusion and the laboratory of Joseph Ravoahangy Andrianavalona Antananarivo.
We measured the plasma creatinine and urea of all the blood donors who accepted to take part in this study and who met the inclusion and exclusion criteria. Normal values were defined by values between 2.5 and 97.5 percentiles.
**Results:** Among the 256 blood donors selected, 128 were men and 128 women. The average age was of 35.41 ± 11.37 years old. The references values of plasma creatinine range between 76-120 µmol/l for men and between 56-101 µmol/l for women. The average value is significantly higher for men than for women. There is a significant change depending on the weight. For urea, the reference values range between 2.43 – 6.22 mmol/l for men and between 2.29-5.87 mmol/l for women.
**Conclusion:** The reference values of our study have shown differences compared to those of other countries. Thus, each country, each region has to set its own reference values in order to ensure a good health management of their population.
**Keywords:** Normal values, urea, creatinine, blood donors, Antananarivo.

## 1. Introduction

The reference values are used to interpret the results of the laboratory tests. The reference values are the different values that the results of biological tests may take from healthy people. They are usually shown as an interval with a low and high limit which is set in compliance with the international recommendations [1]. A reference interval is very important for the physicians for clinic decision-making [2]. It is important for the screening, diagnosis, monitoring, development and therapeutic efficacy [3]. The normal values used in laboratories in Sub-Saharan Africa are mainly those from European or North American populations [4]. However, there are main differences for biochemical parameters according to age, sex, lifestyle, environment and genetic factors [5]. The significant difference of the reference intervals of biochemical parameters between different countries and different groups of population within the same country can be misleading and can lead to the wrong treatment of the patient as the physician misses the diagnosis [6-8]. Even if the exploration of renal function is usually done in each patient lab analysis prescription, Madagascar does not have yet normal values of renal biochemical parameters of the Malagasy population. The results are usually compared

with the reference values provided by the reagent kits manufacturers. This study is aimed at estimating the normal values of the plasma creatinine and urea of adults in Antananarivo.

## 2. Materials and methods

It was a transverse and descriptive study from September 20$^{th}$to November 09$^{th}$, 2017 at the National Center for Blood Transfusion and the laboratory of Biochemistry of Joseph Ravoahangy Andrianavalona Antananarivo. We conducted a study among volunteer and replacement blood donors at the National Center for Blood Transfusion. They have experienced predonation selection which was the inclusion criteria of this study (eligible blood donor or donor eligible to donate) [9-10]. Thereafter, creatinine and urea were assessed of the blood of the donors who fulfilled all inclusion criteria, except those who had some conditions which may change the creatinine and urea values, these conditions are described in table 1.

**Table 1: Inclusion and exclusion criteria**

| Inclusion criteria (eligible blood donor or donor eligible to donate) | Exclusion criteria |
|---|---|
| • Volunteer or replacement blood donation<br>• Age > 18 years and < 60 years<br>• Weight> 45kg<br>• Sleep duration more than 6 hours the night before<br>• Women who are neither pregnant, nor breastfeeding, nor being menstruated<br>• Absence of blood transfusion during the last 2 years<br>• Absence of risky sexual behaviour<br>• Absence of behavioral risks for transfusion transmitted infection: Human Immunodeficiency Virus (HIV), syphilis, hepatitis B virus, hepatitis C virus<br>• No tattoo, no piercing<br>• No notion of acupuncture treatment<br>• No recent accidental blood exposure<br>• Absence of recent blood donation (less than 8 weeks with a maximum of four donations per year for men and three donations for women).<br>• Absence of infectious disease of the near neighborhood k (jaundice, hepatitis, skin rash …)<br>• No fever within the last 15 days<br>• Absence of personal background of jaundice, dermatologic diseases, heart disease, prolonged fever, diabetes, high blood pressure, respiratory diseases, lymphadenopathies, joint pain, allergies, sexually transmitted infections<br>• No recent trip outside Madagascar<br>• Within the 6 last months: no malaria, no dental extraction or care, no injection or vaccination<br>• Does not follow any anti-diabetic or antihypertensive treatment. | • Notion of medicine intake within 4 weeks before the current blood donation in order to exclude nephrotoxic drugs which may result in transient change in the biochemical parameters such as the antibiotics (aminoglycosides, fluoro-quinolones, vancomycin, rifampicin), anti-cancer (5FU, Methotrexate), Antifungal (Amphotericin B ...)<br>• Personal and family background of kidney diseases<br>• Toxic habits (alcohol, tobacco, drugs)<br>• Severe underweight case or obesity (BMI<16.5 or BMI > 30) [11].<br>• Some abnormalities in the blood sample such as haemolysed, coagulated blood, icteric blood or with insufficient quantity. |

The study parameters were age, sex, weight, height, BMI, systolic and diastolic blood pressure, ethnic group and profession.

Blood was obtained by venipuncture and 3 to 4ml of venous blood has been taken in heparinized tube after getting informed consent. Biochemical parameters have been analyzed on BS 300 automated spectrophotometer (Mindray Co. Ltd, China). The creatinine was assessed by Jaffe technic (CREATININE Cromatest® REF1123010) and urea was assessed by enzymatic method (UREA/BUN BR Cromatest®REF 1158010). We have done control prior to each measurement series of analysis. The data entry and data processing were carried out on Epi-info 3.5.2 software. The comparison of the percentages used Chi square tests.

The variables studied have been described by the central tendency parameters and with their dispersion index. The 2.5$^{th}$ and 97.5$^{th}$ percentiles have been used to limit the normal values. We determined normal values for both male

and female. The significance threshold of p was set to be 0.05. The free and informed consent was required before each inclusion. This study has respected the concept of volunteering, anonymity and confidentiality. We obtained the agreement of the ethical committee of the National Institute of Community and Public Health under the decision n°002/2017-CEER/INSPC.

## 3. Results

We included 256 volunteer or replacement blood donors, with 128 men and 128 women. The average age was of 35.41 ± 11.37 years old (range of 18-64 years old). The ethnic group of Merina was the main ethnic group in our study (79%).

The socio-demographic characteristics of the population involved in this study are presented in Table 2.

**Table 2: Sociodemographic characteristics of the study population**

| Socio-demographic Characteristics | | n | % |
|---|---|---|---|
| Age range | < 24 | 58 | 22.7 |
| | 25-34 | 70 | 27.3 |
| | 35-44 | 62 | 24.2 |
| | 45-54 | 55 | 21.5 |
| | > 55 | 11 | 4.3 |
| Marital status | Married | 165 | 64.5 |
| | Widowed | 7 | 2.7 |
| | Divorced | 8 | 3.1 |
| | Single | 76 | 29.7 |
| Education level | Primary | 45 | 17.6 |
| | Secondary | 110 | 42.9 |
| | University | 97 | 39.0 |
| | Uneducated | 4 | 1.6 |
| Ethnic group | Merina | 203 | 79.3 |
| | Betsileo | 24 | 9.4 |
| | Betsimisaraka | 4 | 1.6 |
| | Bezanozano | 4 | 1.6 |
| | Otherethnic groups | 21 | 6.6 |
| Weight | 45-54 | 44 | 17.2 |
| | 55-64 | 82 | 32.0 |
| | 65-74 | 82 | 32.0 |
| | 75-84 | 35 | 13.7 |
| | 85-94 | 13 | 5.1 |

The results of the normal values of the creatinine as per the age and sex defined by the values between 2.5 and 97.5 percentiles are shown in table 3.

**Table 3: Normal values of the plasma creatinine as per the age and sex**

| Parameters | Age (years) | Men | Women |
|---|---|---|---|
| | | min-max | min-max |
| Plasma creatinine (µmol/l) | All age | 76-120 | 56-101 |
| | >24 | 74-107 | 53-92 |
| | 25-34 | 67-125 | 54-81 |
| | 35-44 | 76-114 | 56-94 |
| | 45-54 | 66-114 | 64-101 |
| | >55 | 88-114 | 69-94 |

**Table 4: Gender-based breakdown of the plasma creatinine value**

| Average Standard Deviation (SD) | | | |
|---|---|---|---|
| | Men (n=128) | Women (n=128) | p |
| Plasma creatinine (µmol/l) | 97 ± 11.54 | 77 ± 11.22 | 0.000* |

As far as the plasma creatinine is concerned, the average value is significantly higher for men than for women.

**Table 5: Age-based breakdown of the plasma creatinine value**

| Age (Years) | Average± SD* | P value |
|---|---|---|
| <24 | 84.86±13.79 | NS |
| 25-34 | 88.74 ±18.42 | |
| 35-44 | 88.11±13.84 | |
| 45-54 | 88.61±13.46 | |
| > 55 | 93.09 ±15.32 | |

*Standard deviation

There is no significant change of the average values of the plasma creatinine depending on the age.

**Table 6: Weight-based breakdown of the plasma creatinine value**

| Weight (kg) | Average±SD | p value |
|---|---|---|
| 45-54 | 83.52±12.74 | 0.014* |
| 55-64 | 85.64±13.11 | |
| 65-74 | 89.20±16.81 | |
| 75-84 | 93.00±16.39 | |
| >85 | 94.38±16.34 | |

A significant change depending on the weight was found as far as plasma creatinine is concerned. (Table 6).

**Table 7: Normal values of the plasma creatinine without considering the age and sex**

| Parameters | Value |
|---|---|
| Plasma Creatinine (µmol/l) | Of all age and sex |
| | 56-120 |

Table 7 shows a breakdown of the plasma creatinine value without considering the age and sex (of all age and sex).

Table 8 shows the results of the plasma urea normal values as per the age and sex of adults in Antananarivo defined by the values between 2.5 and 97.5 percentiles.

**Table 8: Normal values of the plasma urea as per the age and sex**

| Parameters | Age (Years) | Men | Women |
|---|---|---|---|
| | | min-max | min-max |
| Plasma urea (mmol/l) | Of all age | 2.43-6.22 | 2.29-5.87 |
| | <24 | 2.30-5.97 | 2.17-4.73 |
| | 25-34 | 2.37-6.69 | 2.85-5.07 |
| | 35-44 | 2.38-5.97 | 2.29-5.02 |
| | 45-54 | 2.43-6.04 | 2.16-6.71 |
| | > 55 | 3.73-4.41 | 2.86-5.21 |

**Table 9: Gender-based breakdown of the plasma urea value**

| Average±SD | | | |
|---|---|---|---|
| Plasma urea (mmol/l) | **Men (n=128)** | **Women (n=128)** | **P value** |
| | 4.31±0.99 | 3.89 ±0.97 | 0.0009* |

As far as plasma urea is concerned, the average value is significantly higher for men than for women (table 9)

**Table 10: Age-based breakdown of plasma urea value**

| Age (Years) | Average±SD | p value |
|---|---|---|
| < 24 | 4.6±1.01 | NS |
| 25-34 | 4.16±0.94 | |
| 35-44 | 3.87±0.96 | |
| 45-54 | 4.28±1.13 | |
| >55 | 4.29±0.85 | |

There is no significant change of the average values of plasma urea as per the age and weight (table 10)

**Table 11: Weight-based breakdown of plasma urea value**

| Weight (kg) | Average±SD | p value |
|---|---|---|
| 45-54 | 3.81±0.82 | NS |
| 55-64 | 4.14±1.10 | |
| 65-74 | 4.09±0.95 | |
| 75-84 | 4.37±1.10 | |
| >85 | 4.23±0.87 | |

**Table 12: Breakdown of plasma urea without considering the age and sex**

| Parameters | Value |
|---|---|
| Plasma urea (mmol/l) | Of all age and sex |
| | 2.37-6.22 |

## 4. Discussion

The reference values give some information about everybody's health status [12]. The size of our population study agrees with the current recommendation of the Clinical and Laboratory Standards Institute (CLSI) and the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC-LM) which give a sufficient number of reference individuals ≥120 [13].

There is a predominance of the Merina ethnic group in this study (79%). Indeed, this is normal because the population of Antananarivo is represented by the Merina ethnic group even if there are people from other ethnic groups who have migrated to Antananarivo.

Our study has shown a significant difference between men and women for the plasma creatinine and urea, as in some Africans [3,12]. The difference between the muscle mass of a woman and a man may explain the significant difference of the plasma creatinine [14]. The important difference regarding weight may have the same explanation**.** The main source of creatinine in the body is the skeletal muscle mass as it is [15] the final product of the muscle energy metabolism. Creatinine is remarkably constant in each individual. If there is some doubt about kidney function, it is important to evaluate the clearance of the creatinine which does not consider the variation of the body weight and muscle mass [16].

The men plasma creatinine values in our study are somewhat higher those find in Ouganda [17], in Mbeya [3], Nigeria [18] and Kenya [19]. The same case was found in women except for Nigeria. As far as the plasma creatinine values are concerned, without considering the gender and age, our results have shown much higher values than those published in Ouganda but lower than those found in the USA [3, 17, 20].

It should be noted that the reference values measured are influenced not only by the population and environmental parameters but also by the technique of dosage and the inter-laboratories variation. It may explain some differences between our values and those of other countries [3]. Our results for the plasma urea values found in men are much higher than those found in Ouganda, Nigeria and Kenya [17-19]. The same case was found in these African countries except for Nigeria (our study: 2.29-5.87 mmol/l, Oungada: 1.57-5.03 mmol/l). Without considering the gender and age, our results have shown higher values than those published in Ouganda [17] but lower than those published in the USA [3, 20]

Our study has not shown any significant change of the plasma urea average values depending on the age and weight. Indeed, the plasma urea value is depending on the catabolism of endogenous proteins, hydration status, hepatic synthesis of urea and renal excretion in urea [14].

## 5. Conclusion

This study has allowed setting the normal values of plasma creatinine and urea of the population in Antananarivo. The reference values of our study have shown differences compared to those of other countries. Thus, each country, each region shall set its own reference values in order to follow the health status of their population.

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