International Journal of Advances in Scientific Research
ISSN: 2395-3616 (Online)
Journal DOI: 10.7439/ijasr

Research Article

Reference Interval for Certain Renal Profile parameters in North Indian Population from Rajasthan

Dharmveer Yadav[*1], Monika Gupta[2], Sandhya Mishra[1] and Praveen Sharma[3]

[1]*Department of Biochemistry, SMS Medical College, Jaipur, India*
[2]*Department of Biochemistry, SN Medical College, Jodhpur, India*
[3]*Department of Biochemistry, AIIMS, Jodhpur, Rajasthan, India*

***Correspondence Info:**
Dr. Dharmveer Yadav
Department of Biochemistry,
SMS Medical College, Jaipur, India
E-mail: dharam143s@gmail.com

Abstract

Objective: Reference intervals are an essential part of laboratory medicine. Current study was planned to evaluate renal parameters in the healthy defined group of individuals which would serve as reference values of renal parameters for the North Indian population from Rajasthan.

Design & Methods: Present study was conducted on 2021 apparently healthy individuals of North Indian origin ranging in age from 15-60 years, were selected randomly using defined criteria. Fasting samples were analyzed for Urea, Creatinine, Uric Acid, Sodium, Potassium and Chloride. Data were analyzed for middle 95 percentile (2.5th-97.5th percentile), median and 95% confidence interval using SPSS software package version 10.0.

Result: RI for Urea, Creatinine and uric acid were lower in female (16-42mg/dl, 0.6-1.2mg/dl, 2.4-6.8mg/dl) as compared to male (17.00-44.35mg/dl, 0.7-1.5mg/dl, 2.8-7.2mg/dl). There was a progressive increase in urea, uric acid and Creatinine with increase in age. Though no appreciable differences could be observed in respect to most of renal parameters in rural versus urban, a wider range for uric acid was observed in urban population (2.50-7.20mg/dl). Except for Na^+, K^+ and Cl^-, rest of parameters i.e. urea, creatinine, uric acid were higher range in obese as compared to non obese (17-45 Vs 17-44, 0.66-1.5 Vs 0.60-1.40, 2.5-7.4 Vs 2.5-7.0). Uric acid level was also found to be higher in non vegetarian population (2.6-7.5mg/dl).

Conclusion: Findings of this study provide sex, age, BMI, habitat and diet specific renal function reference values to be used for North Indian population.

Keywords: Reference Interval, Renal Profile Parameters, North Indian Population.

1. Introduction

Reference intervals serve as the basis of laboratory testing and aid the physician in differentiating between the healthy and diseased patient. The population-based reference interval is the most widely used tool for interpretation of individual patient laboratory test results [1]. Reference values are used in interpreting results of laboratory measurements, clinical trials screening and as the basis of safety monitoring for trial participants [2].

These reference values are used to assess health in humans and are based on the effective performance of the major body organs such as the liver, pancreas, heart and kidney. Kidney function tests comprise a variety of individual tests and procedures that can be used to evaluate how well the kidney functions. These tests help to determine if the kidneys are performing their tasks adequately [3]. Measured laboratory parameters are influenced not only by individual factors such as age, sex, and lifestyle, but also by population and ecological factors such as ethnicity, climate, and altitude; they vary not only between individuals but also populations [4]. The reference intervals in use are usually referred from text books or article or values provided by the kit manufacturers. Moreover India is country with extreme seasonal variations, extreme variations in temperature, different dietary habits, life style and physical activity which could affect blood levels of several parameters. There is a need to realize, whether, there is a requirement for restructuring the reference interval for an Indian population [5].

To our knowledge, there is no population-based study so far on reference intervals of renal profile parameters in North India. Hence the standard reference interval, particularly of international origin, needs to be validated in our population. The aim of this study was to establish reference values for renal function test parameters and to determine possible differences between published and local reference ranges.

2. Materials and Methods

2.1 Study Population

In this study, the reference population had been selected randomly using defined criteria from the different areas of Jaipur. The present study was conducted in the Department of Biochemistry at S.M.S. Medical College and Associated Group Hospitals, Jaipur on 2021 apparently healthy individuals of north Indian origin. Out of 2021 individuals 494 were excluded using appropriate exclusion criteria defined by IFCC and NCCLS [6]. Finally 1527 individuals were included in our study. Information regarding age, sex, disease if any, dietary habits, physical activity, smoking or alcoholic habit, anthropometric parameters were obtained in respect to each subject. All the individuals were called personally in the laboratory. They originated from diverse socio-economic backgrounds with variable dietary habits. The institutional ethics committee approved the study and informed consent was obtained from the study population. This was a minimal risk study and was conducted in accordance with the protocol and Good Clinical Practices to ensure protection of all aspects of the ethical rights and welfare of research participants.

2.2 Exclusion Criteria

a) Pathophysiological States - Renal failure, cardiac diseases, chronic respiratory diseases, liver diseases, malabsorption syndromes, malignancies and haematological disorders which included anaemias; b) Systemic Diseases – Hypertension and Diabetes mellitus; c) The chronic intake of pharmacologically active agents like alcohol, tobacco or oral contraceptives, (for more than six months during the time of the health checkup); d) Replacement or Supplementation Therapy e.g. Thyroxine, Insulin; e) Modified Physiological States - Pregnancy, psychological and mental disorders - exercise/physical training /food intake prior to blood collection; f) Other Factors - Obesity (BMI >30 kg/m^2).

2.3 Sampling

After overnight fasting, venous blood was drawn from anticubital vein using asceptic technique. Analysis of samples was done after proper standardization of the instruments with the help of calibrators and controls. Samples which were lipemic, hemolytic or icteric were not considered in the study. To minimize pre-analytical variation, the same phlebotomist collected the blood specimens.

2.4 Methods of Estimation

All specimens from each individual were assayed in a single batch, using the same lots of reagents to minimize the analytical variation. Fasting samples were analyzed for renal profile parameters using IFCC approved method. Serum Urea, Creatinine and Uric Acid were analyzed by Urease Method [7], Mod. Jaffe's Kinetic Method [8] and Uricase Method [9] respectively. Sodium, Potassium and Chloride were estimated by ISE Method of Fully Auto Analyzer AU400 [10]. All tests were performed on fully autoanalyzer AU–400 by Olympus.

2.5 Quality Control

To ensure the reproducibility and repeatability of the test results, the laboratory participated in established external quality assessment programs by CMC, Vellore & BIORAD and a comprehensive internal quality control program and the results were accordingly released after calibrating the values between mean$\pm$1SD. The quality control check was done every day and standard Deviation (SD) and coefficient of variance (CV) were calculated.

2.6 Statistical Analysis

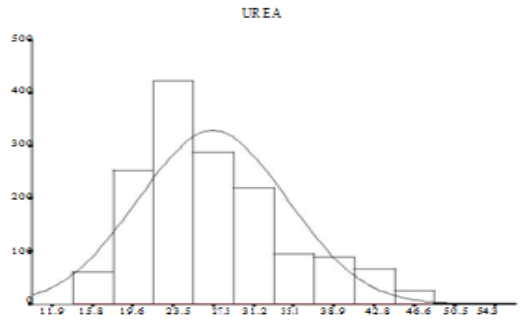
In present study, non parametric methodology for determination of reference interval has been adopted as recommended by IFCC [11] and NCCLS [12] and most of the biochemical parameters included revealed non Gaussian distribution [Figure 1-6]. Median, central 95 percentile and 90% confidence interval (CI) were calculated. The 97.5 percentile and 2.5 percentile formed the upper and lower reference limits of the population. Statistical analysis was done using SPSS version 10.0 package[13].

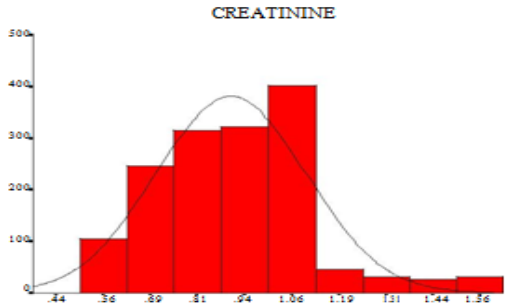
3. Results and Discussion

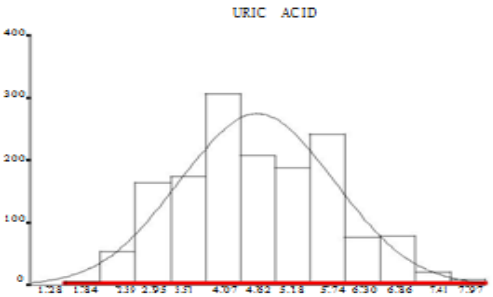
Table 1: Reference Interval of Renal Function Test Parameters in North Indian Population

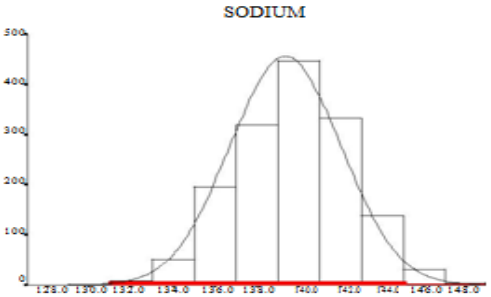
			Urea (mg/dl)	Creatinine (mg/dl)	Uric Acid (mg/dl)	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)
Total (n=1527)	Mean±SD		27.6±7.03	0.91±0.19	4.70±1.23	139.40±2.68	4.40±0.45	104.54±3.74
	Median		26.00	0.90	4.50	140.0	4.40	105.00
	95 Percentile	2.5	17.00	0.60	2.50	134.00	3.60	95.00
		97.5	44.00	1.50	7.00	144.00	5.40	110.00
	90% CI	Lower	16.64-7.36	0.50-0.70	2.44-2.56	133.88-134.12	3.58-3.62	94.82-95.18
		Upper	43.64-44.36	1.48-1.52	6.94-7.06	143.88-144.12	5.38-5.42	109.82-110.18
Male (n=865)	Mean±SD		28.20±6.7	0.96±0.16	5.03±1.12	139.67±2.70	4.38±0.43	104.63±2.74
	Median		28.00	0.90	5.00	140.00	4.30	105.00
	95 Percentile	2.5	17.00	0.70	2.80	134.00	3.60	95.00
		97.5	44.35	1.50	7.24	145.00	5.40	110.00
	90% CI	Lower	16.51-17.49	0.58-0.82	2.72 -2.88	133.82-134.18	3.58-3.62	94.71-95.29
		Upper	43.86-44.84	1.38-1.62	7.16-7.32	144.82-145.18	5.38-5.42	109.71-110.29
Female (n=662)	Mean±SD		25.23±5.97	0.80±0.16	4.15±1.14	138.96±2.49	4.42±0.45	104.81±2.71
	Median		24.00	0.80	4.00	139.00	4.40	105.00
	95 Percentile	2.5	16.00	0.60	2.40	134.00	3.60	95.00
		97.5	42.00	1.20	6.80	144.00	5.50	110.00
	90% CI	Lower	15.53-16.47	0.46-0.74	4.66-4.74	133.82-134.18	3.56-3.64	94.76-95.24
		Upper	41.53-42.47	1.06-1.34	2.10-11.50	143.82-144.18	5.46-5.54	109.76-110.24
Age <20 years (n=119)	Mean±SD		24.06±6.01	0.83±0.18	4.57±1.17	139.79±1.86	4.52±0.49	104.49±2.08
	Median		22.00	0.80	4.30	140.00	4.40	104.50
	95 Percentile	2.5	16.00	0.60	2.40	136.00	3.70	101.00
		97.5	42.00	1.30	6.90	143.00	5.50	108.00
	90% CI	Lower	14.80-17.20	0.56-0.64	2.18-2.62	135.67-136.33	3.60-3.80	100.65-101.35
		Upper	40.80-43.20	1.26-1.34	6.68-7.12	142.67-143.33	5.40-5.60	107.65-108.35
Age 20-40 years (n=841)	Mean±SD		26.80±7.03	0.89±0.19	4.55±1.23	139.56±2.68	4.38±0.45	104.45±3.74
	Median		25.00	0.90	4.40	140.00	4.40	105.00
	95 Percentile	2.5	17.00	0.60	2.50	134.00	3.60	95.00
		97.5	42.00	1.30	6.80	145.00	5.40	110.00
	90% CI	Lower	16.57-17.43	0.48-0.72	2.42-2.58	133.82-134.18	3.56-3.64	94.69-95.31
		Upper	41.57-42.43	1.18-1.42	6.72-6.88	144.82-145.18	5.36-5.44	109.69-110.31
Age 41-60 years (n=567)	Mean±SD		27.96±7.03	0.92±0.19	4.74±1.23	139.11±2.68	4.41±0.45	104.66±3.74
	Median		28.00	0.90	4.80	139.00	4.30	105.00
	95 Percentile	2.5	17.00	0.60	2.50	134.00	3.60	95.00
		97.5	45.00	1.50	7.40	144.00	5.30	110.00
	90% CI	Lower	16.35-17.65	0.42-0.78	2.38-2.62	133.76-134.24	3.56-3.64	94.73-95.27
		Upper	44.35-45.65	1.32-1.68	7.28-7.52	143.76-144.24	5.26-5.34	109.73-110.27
Rural (n=566)	Mean±SD		26.30±6.14	0.84±0.18	4.40±1.13	139.14±2.46	4.37±0.46	104.58±2.66
	Median		25.00	0.80	4.30	139.00	4.30	105.00
	95 Percentile	2.5	17.00	0.60	2.40	134.84	3.60	95.00
		97.5	42.83	1.38	6.80	144.83	5.40	109.00
	90% CI	Lower	16.47-17.53	0.44-0.76	2.30-2.50	134.64-135.04	3.56-3.64	94.76-95.24
		Upper	42.30-43.36	1.22-1.54	6.70-6.90	144.63-145.03	5.36-5.44	108.76-109.24
Urban (n=961)	Mean±SD		25.65±6.82	0.83±0.17	4.31±1.23	139.11±2.72	4.44±0.43	104.78±2.76
	Median		26.00	0.90	4.60	140.00	4.40	105.00
	95 Percentile	2.5	17.00	0.60	2.50	134.00	3.60	96.00
		97.5	44.00	1.40	7.20	144.00	5.50	110.00
	90% CI	Lower	16.53-17.47	0.48-0.72	2.42-2.58	132.24-135.76	3.58-3.62	95.73-96.27
		Upper	43.53-44.47	1.28-1.52	7.12-7.28	143.82-144.18	5.48-5.52	109.73-110.27
BMI <25 (n=1224)	Mean±SD		25.15±6.41	0.79±0.18	4.04±1.19	138.94±2.60	4.42±0.44	104.71±2.71
	Median		26.00	0.90	4.50	140.00	4.40	105.00
	95 Percentile	2.5	17.00	0.60	2.50	134.00	3.60	95.00
		97.5	44.00	1.40	7.00	144.00	5.50	110.00
	90% CI	Lower	16.61-17.39	0.48-0.72	2.42-2.58	133.86-134.14	3.58-3.62	94.76-95.24
		Upper	43.61-44.39	1.28-1.52	6.92-7.08	143.86-144.14	5.48-5.52	109.76-110.24
BMI ≥ 25 (n=303)	Mean±SD		25.46±7.11	0.84±0.17	4.47±1.23	138.99±2.74	4.41±0.43	105.0±2.75
	Median		26.00	0.90	4.50	140.00	4.40	105.00
	95 Percentile	2.5	17.00	0.66	2.50	134.00	3.60	95.60
		97.5	45.00	1.50	7.40	144.40	5.40	110.00
	90% CI	Lower	16.12-17.88	0.64-0.68	2.36-2.64	133.69-134.31	3.54-3.66	95.25-95.95
		Upper	44.12-45.88	1.38-1.62	7.32-7.48	144.09-144.71	5.34-5.46	09.65-110.351
Vegetarian (n=1096)	Mean±SD		26.94±6.71	0.88±0.19	4.57±1.21	139.29±2.63	4.39±0.44	104.75±2.70
	Median		26.00	0.90	4.40	140.00	4.30	105.00
	95 Percentile	2.5	17.00	0.60	2.50	134.00	3.60	95.00
		97.5	44.00	1.40	7.00	144.58	5.40	110.00
	90% CI	Lower	16.57-17.43	0.48-0.72	2.44-2.56	133.84-134.16	3.58-3.62	94.75-95.25
		Upper	43.57-44.43	1.28-1.52	6.94-7.06	144.42-144.74	5.38-5.42	109.75-110.25
Non Vegetarian (n=431)	Mean±SD		26.82±6.31	0.91±0.16	4.84±1.18	139.54±2.65	4.42±0.44	104.60±2.79
	Median		26.00	0.90	4.80	140.00	4.40	105.00
	95 Percentile	2.5	17.00	0.60	2.60	134.00	3.60	95.00
		97.5	45.00	1.50	7.50	144.00	5.50	110.00
	90% CI	Lower	16.35-17.65	0.44-0.76	2.48-2.72	133.75-134.25	3.56-3.64	94.73-95.27
		Upper	44.35-45.65	1.32-1.68	7.38 -7.62	143.75-144.25	5.46-5.54	109.73-110.27

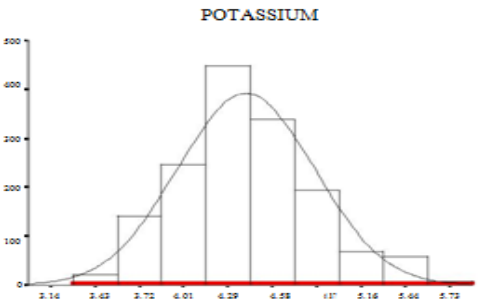
Figure 1 – 6: Distribution Curves of Renal Function Test Parameters

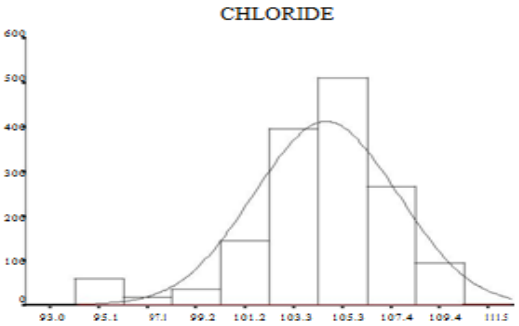


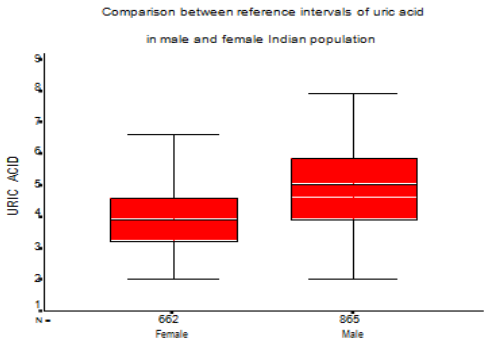












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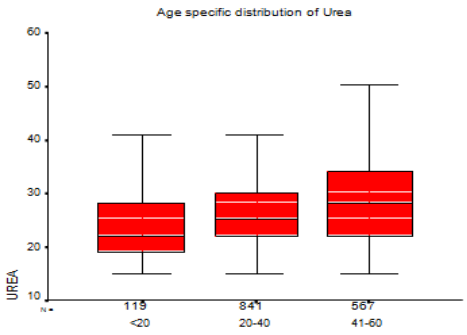

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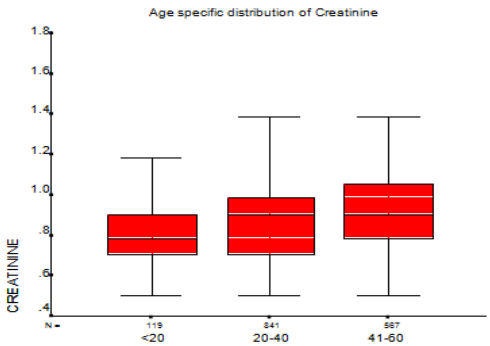

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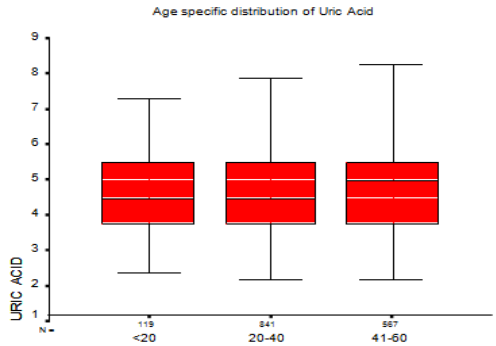

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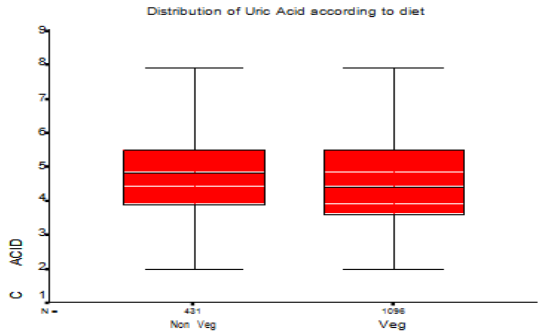

Fig No. 11

The results obtained for the parameters of renal function test are tabulated in the Table 1 which depicts mean±SD, median, 95 percentile and 90% confidence interval (CI) of renal function test parameters in north Indian population according to various partitioning criteria.

Renal function tests have significance in both health and disease and play important role in diagnosis and prognosis as well. Since the Reference Interval (RI) of most of the biochemical parameters test performed to assess renal functions has shorter internal hence mild to moderate changes in biochemical parameters are of diagnostic value, to differentiate pre renal, renal and post renal conditions.

Since no systematic study has been attempted to establish RI for these biochemical parameters in Indian population, the present is a novel attempt to establish RI for various biochemical parameters such as urea, Creatinine, Uric acid and electrolytes (Na^+, K^+ and Cl^-). The normal standard RI reported for urea (mg/dl), creatinine (mg/dl), uric acid (mg/dl), sodium (mEq/L), potassium (mEq/L) and chloride (mEq/L) was 15-45; 0.6-1.6; 2.6-6.0; 135-145; 3.5-5.5 and 95-105 respectively as reported in various books of clinical biochemistry [14].

The mean ±SD, median and reference interval for urea was 27.6±7.03 mg/dl, 26.0 mg/dl and 17.0-44.0 mg/dl, for creatinine 0.91±0.19 mg/dl, 0.90 mg/dl and 0.6-1.5 mg/dl, for uric acid 4.70±1.23 mg/dl, 4.5 mg/dl and 2.5-7.0 mg/dl, for sodium 139.4±2.68 mEq/L, 140.0 mEq/L and 134.0-144.0 mEq/L, for potassium 4.4±0.45 mEq/L, 4.4 mEq/L, 3.6-5.4 mEq/L and for chloride was 104.54±3.74 mEq/L, 105.0 mEq/L and 95.0-110.0 mEq/L respectively.

In the present study, RI for these biochemical parameters observed coincided with the reported RI [Table 1]. In an another study conducted by Ashavaid et al reported lower RI for urea and Creatinine ranging from 4-35mg% and 0.7-1.3mg% respectively in individuals of Mumbai opted for BUPA Health Screening Programme [5]. The lower RI indicates preponderance of vegetarian and young individuals participating in the study. Despite different methodology adopted and different racial population RI observed for these biochemical parameters are almost similar to studies conducted in different countries [15-19].

As far as gender difference is concerned except Urea, Creatinine and uric acid rest of the parameters were in similar reference interval. RI for Urea, Creatinine and uric acid were lower in female (16-42mg/dl, 0.6-1.2mg/dl, 2.4-6.8mg/dl) as compared to male (17.00-44.35mg/dl, 0.7-1.5mg/dl, 2.8-7.2mg/dl) with lower cutoff of lower and upper limits [Figure 7].

The significantly higher values of the reference ranges for urea, creatinine and uric acid in males compared to females indicates sex differences in these kidney function test parameters. Similar findings have been reported in populations of Mbeya, Tanzania; Kampala, Uganda and Kericho, Kenya [20-22]. The finding of significant sex differences for creatinine agrees with the well established fact that males have higher reference range values for creatinine than females due to the higher muscle and bone mass. Similar results have been reported from China and Asia [23-24].

Among various biochemical parameters examined in relation to renal functions except urea, uric acid and Creatinine rest all parameters remained unchanged with advancing age. There was a progressive increase in urea, uric acid and Creatinine with increase in age. Age specific distribution of Urea, Creatinine and Uric Acid has shown in Figure 8, 9 and 10.

Though no appreciable differences could be observed in respect to most of renal parameters in rural versus urban, a wider range for uric acid was observed in urban population (2.50-7.20mg/dl). As per BMI concerned no marked difference was observed in reference interval of renal parameters. Except for Na^+, K^+ and Cl^-, rest of parameters i.e. urea, creatinine, uric acid were higher range in obese as compared to non obese (17-45 Vs 17-44, 0.66-1.5 Vs 0.60-1.40, 2.5-7.4 Vs 2.5-7.0) [Figure 11].

Uric acid level was also found to be higher in non vegetarian population (2.6-7.5mg/dl) which can be related to nucleoprotein rich in non vegetarian diet (Non vegetarian Vs Vegetarian – 2.6-7.5mg/dl Vs 2.5-7.0mg/dl).

4. Conclusion

Every laboratory may establish reference ranges for their population for a “reality check” of the internationally referred values. The findings of this study provide sex, age, BMI, habitat and diet specific renal function reference values to be used in North India and opens an avenue for similar studies to be

carried out in other geographical regions for various other parameters. This will ensure better evaluation and interpretation of renal function results, leading to good clinical practice and proper research thus improving quality of healthcare in this region.

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