Evaluation of Reference Interval of Serum Uric Acid Level During Pregnancy in Tertiary Care Hospital of Rawalpindi

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ABSTRACT

Objective: To determine the reference interval of uric acid in uncomplicated pregnancies.
Study Design: Cross-sectional study.
Place and Duration of Study: Pathology Department, Armed Forces Institute of Pathology, Rawalpindi Pakistan.
Methodology: Data was collected from 807 pregnant females after informed consent. Healthy females of first and second-trimester gestational amenorrhea with no previous significant surgical, medical and gynecological/obstetric history were included. In contrast, patients on drugs like anti-epileptics, anti-hypertensives, steroids, and poor obstetric history were excluded. Information regarding dietary, medical and family history and the use of tobacco, beverages, and current physical activity was collected using a standard questionnaire. Reference Interval was computed by using the 3rd and 97th percentile systems.
Results: Mean age of study participants in the first trimester of pregnancy was 22.37 ± 2.54 years, while in the second trimester was 27.14 ± 3.62 years. Data was segregated into three age groups: 18-29 years (186, 23%), 30-35 years (452, 56%) and 36-43 years (169, 21%). Uric acid levels observed in the first and second trimesters were 95.8-260.14 umol/l and 96-268 umol/ respectively.
Conclusion: Serum Uric Acid levels differed in normal pregnancy compared to the non-pregnant state. Moreover, this study also provides optimal reference intervals of uric acid levels for pregnancy's first and second trimesters.

Keywords: Pregnancy, Reference interval, Uric acid.

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INTRODUCTION

Serum uric acid (SUA) is the major end product of purine metabolism in humans, and the level of uric acid is controlled by the balance between uric acid production and excretion.[1] Hyper uricemia is consi-dered a marker for eclampsia, pre-eclampsia and pregnancy-induced hypertension (PIH).[2] As clinicians use reference values for interpretation of the results of measurements, it needs to correctly represent a defined group of the population that should have close similarity with the patients under treatment coming for investigation.[3] Many studies have noted that increased uric acid levels during pregnancy correlate with both maternal and fetal mortality and morbidity.[4,5] Despite well-recognised development of pregnancy induced physiological changes and their potential for neutering traditional laboratory values, only a few laboratories give clinicians traditional reference ranges throughout gestation. Moreover, many laboratories fail to report traditional values for females versus males. Most laboratories have reference intervals for healthy men and women, but lack reference intervals for pregnant women.[6]

The same reference intervals should be used, independent of which laboratory performs that measurement. There is, however, a trend to establish standard reference intervals. There are international calibrators for many of our most frequently used tests to reduce differences in assay results between manufacturers.[7] External quality assurance programs also aim to reduce inter-laboratory differences. Thus, test results for high volume assays performed at different laboratories in most cases are pretty similar.[8]

Physiological and biochemical changes in pregnancy influence many of our laboratory tests. There is an increased risk of missing significant changes due to pathological conditions and erron-eously interpreting regular changes as pathological events without adequate reference intervals.[9,10] Pre-pregnancy uric acid levels are achieved after 24 weeks of gestation. However, before that, it is below the uric acid level of the pre-pregnancy state in the early gestational period because many biochemical changes influence the uric

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acid level, and hyperuricemia during pregnancy is considered a marker of pre-eclampsia and eclampsia. Therefore, it is essential to develop reference intervals for the different periods during uncomplicated pregnancies. This study was planned to evaluate the reference interval of serum uric acid levels of pregnant females reporting to a tertiary care hospital for prenatal evaluation in Rawalpindi. Besides the need for baseline reference laboratory ranges that will be used to monitor physiological or pathological changes during pregnancy.

METHODOLOGY

It was cross sectional study. Eight hundred and seven participants of different socioeconomic statuses were screened for the study keeping in mind clinical laboratory improvement amendment (CLIA) recommendations of taking at least 120 samples for determination of reference interval and then including some extra to cater for the outliers. Sampling technique was non-probability convenient sampling. Study was carried out after approval from Institutional Ethical Review Board of AFIP Rawalpindi (vide IRB approval certificate no: FC-CHP16-1/READ-IRB/18/735).

Inclusion Criteria: Healthy females of first and second trimester gestational amenorrhea with no previous significant medical or surgical history were included in this study.

Exclusion Criteria: Patients who used drugs like anti-epileptics, anti-hypertensives, steroids and patients who had poor obstetric history were not included.

Baseline information, including detailed dietary, medical and family history and the information on lifetime use of tobacco, beverages, and current physical activity, was collected using a standard questionnaire. To ensure the accuracy and precision of the test results, all the pre-analytical, analytical and post-analytical precautions were considered.

Instruments, personnel, and procedure validation were carried out through an internal quality control (IQC) program with the calculation of standard deviations (SD) and coefficients of variation (CV). Three millilitres of blood was collec-ted in a yellow top gel tube after taking informed consent from each participant to use their body fluids for research purposes. Serum was prepared by centrifugation at 3500 rpm for three minutes, and analysis was done within 4 hours of collecting samples. Serum uric acid levels were estimated using a spectrophotometric technique using the uricase enzymatic principle on Siemens's random access discrete chemistry auto analyser ADVIA 1800. All the results were analysed on a routine chemistry auto analyser, and external quality control and internal quality control confirmed validation of accuracy.

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Percentiles were computed in first and second-trimester reference interval values for serum uric acid levels. Normally distributed continuous variables were presented as mean ± SD while non-parametric continuous variable was calculated as the median and interquartile range (IQR). For reference ranges in each trimester, percentiles were computed in each gestation in an uncomplicated pregnancy. The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 807 healthy pregnant females were recruited following the inclusion criteria. The participants were segregated into three age groups: 18-29 years 186 (23%), 30-35 years; 452 (56%) and 36-43 years; 169 (21%). Participants of the study belonged to different areas. 541 (67%) participants had come from urban areas, while 266 (33%) came from rural areas of District Rawalpindi.

The mean age for females reported in the first trimester was 22.37 ± 2.54 years, and that in the second trimester was 27.14 ± 3.62 years. Pregnant females in the first and second trimesters were 273 (33.8%) and 181 (22.4%), respectively. Whereas 195 (24%) and 158 (19%) multigravidas were included in the first and second, respectively (Table-I).

Table-I: Baseline characteristics of study population.

Attributes of Participants	Healthy Pregnant Females (n)	First Trimester n (%)	Second Trimester n (%)
No. of Patients	807	392 (48.57)	415 (51.40)
Primigravida	454	273 (60.13)	181 (39.86)
Multigravida	353	195 (55.24)	158 (44.76)
Age (Mean ± SD) Years	807	22.37 ± 2.54	27.14 ± 3.62

Table-II: Uric Acid levels during different trimesters of pregnancy.

	Mean ± SD	3rd Percentile	50th Percentile	97th Percentile	Reference Interval	Non-Pregnant Reference Interval
1st Trimester						95- 370
Uric Acid (umol/l)	166 ± 42	96	161	260	96-260	
2nd Trimester						
Uric Acid (umol/l)	172 ± 38	96	171	268	96-268	

Reference intervals for serum uric acid levels determined in the 1st and 2nd trimester by 3rd to 97th percentiles were shown in Table–II.

DISCUSSION

Our study showed that uric acid levels were different for different trimesters of normal pregnancy compared to the non-pregnant state. In the first-trimester uric acid level computed is 96-260 umol/l, while in the second trimester, 96-268 (umol/l) uric acid level is computed. This study provides a reference interval for serum uric acid levels for pregnant females' first and second trimesters in and around the Rawalpindi area.

Hyperuricemia is considered a marker for eclampsia, pre-eclampsia and pregnancy-induced hypertension (PIH).[11] This study was conducted to explore the reference interval of serum uric acid levels in average pregnant women in the first and second trimester of pregnancy. Some studies have reported that increased serum uric acid levels during pregnancy correlated with maternal and fetal mortality and fetal and maternal morbidity.[12,13]

Powers *et al,*[14] in the US, showed that uncomplicated serum uric acid levels were decreased by 25-35% in early pregnancy but remained elevated throughout pregnancy until parturition; after that, they reached non-pregnant female levels. These findings correlated with the current study results, which showed lower concentration of serum uric acid levels in pregnant women in the first trimester during the same increase in the second trimester. Fang *et al,*[15] mentioned that increased serum uric acid levels in normal pregnancy could be a sign of renal failure and a marker of pre-eclampsia. The mean age of that study population was 48 ± 2.5 years which was different from the current study, where mean age in the first trimester was 22.37 ± 2.54years, and in the second trimester it was 27 ± 3.54 years. Increased maternal age is also essential for maternal and fetal complications during pregnancy. In a study by Fisher *et al,*[16] a comparison of serum uric acid levels between non-pregnant and pregnant women was studied, and it was observed that serum uric acid cutoff level in early pregnancy was 267 ± 1.3 umol/land in pre-eclampsia patients the cut off level of serum uric acid was 386.62 umol/with a sensitivity of 94% and specificity of 78%which correlated with the results of our study.

Wagner *et al,*[17] documented that a lower level of serum uric acid levels during normal pregnancy was a sign of both maternal and fetal wellbeing, while a higher level could point towards PIH and renal diseases. It was also shown that the reference interval of uric acid for normal pregnancy needs to be <250 umol/l, which is less than the reference interval of non-pregnant women of reproductive age. This cut off is close to the reference interval found in our study.

Koike *et al,*[18] studied that serum uric acid levels >390 umol/was considered an early marker for pre-eclampsia and renal disease during pregnancy. Moreover, the results of our study also revealed that the reference interval of serum uric acid levels should be 95-268 umol/l in normal pregnancy.

This study was conducted to explore the reference intervals of uric acid during different trimesters of normal pregnancy. However, a multi-centric approach is needed for evaluating high serum uric acid levels as an early marker for renal disease and pregnancy-induced hypertension.

CONCLUSION

Serum Uric Acid levels differed in normal pregnancy compared to the non-pregnant state. Moreover, this study also provides optimal reference intervals of uric acid levels for pregnancy's first and second trimesters.

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RECOMMENDATIONS

Based on the current study's findings, we strongly recommend that each laboratory have its set standardised reference intervals for analytes that should be different from the non-pregnant values owing to the numerous physiological changes that occur throughout pregnancy.

Conflict of Interest: None.

Authors' Contribution

QUA: Manuscript writing, editing, data analysis, MG: Sample/Data collection, manuscript writing, NA: Study design, manuscript editing, AA: Sample collection, data interpretation, KMU: Sample collection, AS: Manuscript writing.

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