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A study of urinary uric acid level in preterm neonates

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Abstract
Aim: done to find out the reference range of urinary uric acid in term and preterm neonates appropriate for their gestational age.
Material and method: Male infants predominated because of the difficulty of collecting urinary specimens in the females. In females urine samples often get lost or were inaccurate with respect to volume and timing. Disposable urine collectors were used. Gestation was assessed by maternal menstrual history and ultrasound scan. The newborn was under constant supervision. Three spot samples were collected from each newborn (i.e. total of 120 samples) few hrs apart (on the basis of as and when urine passed) within 24 hrs of delivery and analyzed in the biochemistry laboratory in the hospital immediately. After collection, urine sample were frozen at -20C until further analysis. Spot single urine samples were considered. Urinary uric acid was estimated in auto-analyzer (model ERBA XL600) by spectrophotometric uricase method. Preparation of reagent by pouring the content of bottle of L2 (enzyme reagent) into bottle of L1 (buffer reagent).this working reagent is stable for at least 4 weeks when stored at 2-8ºC upon storage the working reagent may develop a slight pink colour however this does not affect the performance of the reagent.
Result: Statistical analysis was carried out by using unpaired sample `t" test and p value of <0.001 was taken significant, n is sample size. The most significant difference found in this study, is mean urinary uric acid level was found significantly higher in normal appropriate for gestational age preterm infants than term babies on day one of their life.
Conclusion: there was hardly any variation in the uric acid levels in three different urine samples collected several hours apart. This shows that only spot sample was taken as a reference value and can be compared with that of the patients.

Keywords: Preterm Neonates Urinary Uric Acid

Introduction
In humans, uric acid is derived from the ingestion of foods containing purine as well as endogenous synthesis of purine nucleotides, which are building blocks in the synthesis of nucleic acids. Compounds derived from the purine nitrogenous bases; adenine and guanine are essential to cellular metabolism and function. Whereas most mammals catabolize purine to uric acid, which is oxidized by uricase to urea and allantoin. Humans and primates produce uric acid as the end product of purine catabolism due to the absence of uricase [1, 2].
Uric acid as a poor soluble acid that requires continuous excretion by the kidneys to avoid toxic accumulation. As its poor solubility and its alteration in its production or excretion can produce high serum levels of uric acid. 3 Preterm infants born before 34–36 weeks of gestational age (GA) have not completed formation of the structural units of the kidney, the nephrons; a process that continues after birth, up to the 36th week. Preterm kidneys must adapt post-natally in order to cope with the increased metabolic demands of the rapid growth in this period [3]. Renal tubular function and glomerular function are immature at birth. This maturation is achieved by functional and structural renal changes. Urinary uric acid is associated with birth weight of neonate and several additional factor including fluid intake and diet are important in determining the rate of maturation of tubular function [4, 5].
This parameter which is related with gestational age and weight of the neonate which is early, cost effective, simple, quick and non invasive and painless parameter in tiny babies [6].
At present there is no reference range of urinary uric acid for term and preterms appropriate for their gestational age. This study has been done to find out the reference range of urinary uric acid in term and preterm neonates appropriate for their gestational age.

Material and Method

The present study was carried out on preterm appropriate gestational age (AGA) and term normal neonates without complication in the department of pediatrics, KIMS university from May 2009-May 2011 Karad. In this study 120 neonates were included who were born in this institute. Out of which 60 were preterm AGA and 60 were terms from May 2009 to May 2011 were taken.

Informed consent was taken from the patient for inclusion in the study. Polythene bags fixed around the perineum were used in female babies. Male infants predominated because of the difficulty of collecting urinary specimens in the females. In females urine samples often get lost or were inaccurate with respect to volume and timing. Disposable urine collectors were used. Gestation was assessed by maternal menstrual history and ultrasound scan. The newborn was under constant supervision. Three spot samples were collected from each newborn (i.e. total of 120 samples) few hrs apart (on the basis of as and when urine passed) within 24 hrs of delivery and analyzed in the biochemistry laboratory in the hospital immediately. After collection, urine sample were frozen at -20C until further analysis. Spot single urine samples were considered. Urinary uric acid was estimated in auto-analyzer (model ERBA XL600) by spectrophotometric uricase method. Preparation of reagent by pouring the content of bottle of L2 (enzyme reagent) into bottle of L1 (buffer reagent).this working reagent is stable for at least 4 weeks when stored at 2-8ºC upon storage the working reagent may develop a slight pink colour however this does not affect the performance of the reagent.

Alternatively for flexibility as much of working reagent may be made as and when desired by mixing together 4 parts of L 1(buffer reagent) and 1 part of L2 (enzyme reagent). Then put this solution run into auto-analyzer (model ERBA XL600). The value is multiply by 10 and gives the value of urinary uric acid. This indicates the value of urinary uric acid in the urine sample.

Result

In this study of 120neonates were studied out of which 60 neonates were preterms and 60 neonates were terms. Parameters studied included gestational age, weight and urinary uric acid. Statistical analysis was carried out by using unpaired sample `t‟ test and p value of <0.001 was taken significant, n is sample size. The most significant difference found in this study, is mean urinary uric acid level was found significantly higher in normal appropriate for gestational age preterm infants than term babies on day one of their life.

In this study ,the difference in mean uric acid values of the three different urine samples in babies in the 2.49-2 kg body weight range ,were not statically significance (p>0.3). In the 1.99-1.5 kg group the differences in all three mean uric acid values of three different urine samples were insignificant too.(p>0.2) too.

Table 1: Three spot urine samples within 24 hrs after delivery in preterms

Samples	Mean ±S.D.(mg/dl)
First	41.25±4.05
Second	41.05±3.96
Third	41.21±4.04
Final mean of all three mean values	41.17±4.06

Discussion

The study which was carried out in department of pediatrics between periods of May 2009 to May 2011. In present study showed that urinary uric acid is higher in preterm neonate AGA than term neonates. In 1996, Tsukahara H. *et al.*, did similar study in preterm neonates and term neonates and showed that urinary uric acid levels were significantly higher in preterm neonates as compared to terms [7]. The mean urinary uric acid is higher in preterm neonates.

In present study, the mean urinary uric acid level was 41.1±4.06 mg/dl. In 2009, Basu P, *et al*. did similar study which showed that urinary uric acid was increased in normal preterm neonates AGA. In their study mean urinary uric acid level was 6.50±5.99mg/dl in normal preterm AGA neonates [8]. The probable cause for is that the decline in FEUA with advancing gestational age appears to represent alteration in net renal tubular transport of uric acid, because the filtered load of uric acid increased with gestational age. In present study the birth weight 1.5-1.99(kg) and mean urinary uric acid was 42.19±3.2 (mg/dl) and birth weight 2-2.49(kg) and mean urinary uric acid as34.48±1.61 (mg/dl) which also showed that birth weight was inversely proportional to urinary uric acid. In present study the mean gestational age 32.49±0.09 and the mean urinary uric acid was 42.19±3.2 and the mean gestational age was 34.38±0.12weeks and mean urinary uric acid was 34.48±1.61mg/dl also showed that urinary uric acid is inversely correlated with gestational age. In 2009, P. Basu also showed that gestational age was inversely correlated with urinary uric acid. [9] In their study the mean gestational age was 33.52±1.25 weeks and mean urinary uric acid was 41.78±3.66mg/dl and gestational age 35.33±0.85 weeks and mean urinary uric acid was 31.87±3.12 (mg/dl) which showed that urinary uric acid was inversely related to their gestational age [10].

The probably the cause for this may be Appearance of uric acid in urine through nephrons follows four different steps-glomerular filtration, tubular reabsorpton, tubular secretion and tubular reabsorption distal to the secretory site. As all four steps are less well established in relatively premature kidneys and renal tubules of preterms AGA babies. Also due to filtered uric acid and net reabsorption of uric acid increases with post natal development. It is also facilitated by the deficiency of acidification and concentration of urine. This indicates that FEUA with postnatal age was unrelated to binding of uric acid to plasma protein or to urine flow [11].

Urinary uric acid excretion by preterm infants is influenced directly by immature renal function or subclinical kidney damage, indicating that urinary uric acid may act as an indicator of in vivo purine turnover in newborn infants. There was hardly any variation in the uric acid levels in three different urine samples collected several hours apart [12]. This shows that only spot sample was taken as a reference value and can be compared with that of the patients data. In the present study, the mean urinary uric acid was 18.6mg/dl and the final mean urinary uric acid was 18.6mg/dl. In 2009 Basu P. *et al*, in their study, showed that urinary uric acid level in term neonates in spot urine sample can help in estimating the value instead of 24 hours sampling [13]. The mean urinary uric acid of first sample was 19mg/dl and the final mean of urinary uric acid was 18.4mg/dl.

It is an easy, non-invasive, painless and cheap means of uric acid estimation in tiny babies. As this study is limited to day one only so further study is done to see the level on 2nd and 3rd day. Also studies can be undertaken to see spot urinary

uric acid level in asphyxiated babies of different gestational age. As the data is so short, further study has been done to assess the confirmation of our reference data.

Conclusion

In conclude, there was hardly any variation in the uric acid levels in three different urine samples collected several hours apart. This shows that only spot sample was taken as a reference value and can be compared with that of the patients‟ data. As per P.Basu studied that only one sample is sufficient for urinary uric acid which is well correlated with present study. The present study is not enough to prove that urinary uric acid is the only parameter for detecting the maturation of renal tubules and birth weight in terms and preterms appropriate for gestational age. So present study has some limitations as it is not correlated with serum creatinine, serum uric acid and urinary uric acid to creatinine ratio.

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