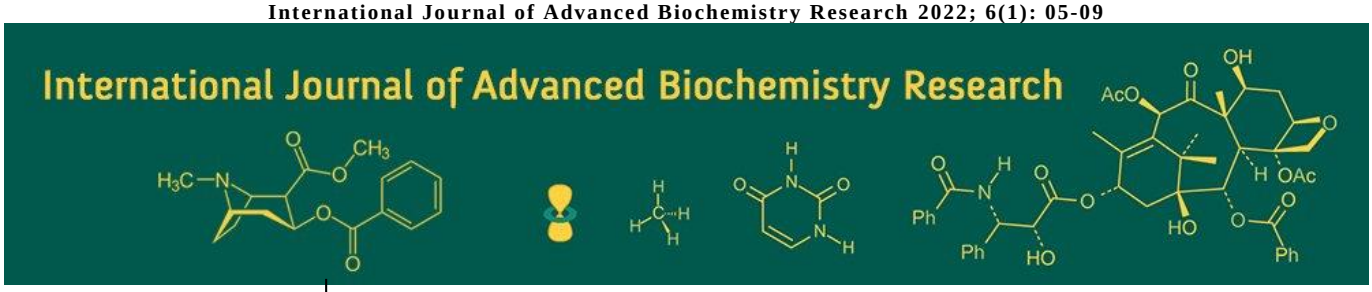

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Correlation between body surface area of newborns of different gestational ages with urine total proteins and urine microalbumin

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Abstract
Objective: To establish a correlation between body surface area of newborns at different gestational ages and urine total proteins and urine microalbumin.
Methods: Cross sectional study was conducted at a tertiary hospital in India. We randomly selected 175 normal newborns of different gestational ages. Systemic random spot second urine samples of normal newborns were selected (urine which baby had passed for the first time after birth was not used for sampling. Samples were used to estimate urinary proteins (total) (mg/dl), and urine albumin (mg/dl).
Results: Proteinuria is common in newborns at all gestational ages. Tubular proteins are major constituents of urine proteins in neonatal urine, but a small amount of albumin is also lost in urine and their amounts increase linearly and proportionately as body surface area of newborn increases. This is a clear reflection of renal immaturity in newborns.
Conclusion: All newborns have abnormally high proteinuria at all gestational ages, which increase with increase in gestational age. Urine microalbumin also showed a very mild increase with age, but it was very insignificant in comparison to UTP.

Keywords: Gestational ages, newborn, UTP

Introduction
Water and waste byproducts which are formed as a result of human body metabolism are the major components of normal human urine. But various other substances can also be excreted through the urine of which protein is the most relevant clinically [1]. Though some small molecular weight tubular proteins are excreted through the glomerular filtrate, but their size is normally less than that of albumin molecule.
Minimal amounts of albumin can be excreted normally in urine. There is no absolute value of urine albumin levels defined in human urine at any age, but normal urine microalbumin creatinine ratio has been defined for adults as <30 gm/mg [2].
Similarly, Abnormal Total Proteinuria is defined in a number of ways through dipstick test, from spot urine sample and timed urine sample. For example, urine protein excretion, greater than 100 mg/m^2 of body surface area/24 hrs. Is considered abnormal. But no such value has been defined in newborns.
The purpose of the present study is to assess the urinary protein and urinary albumin excretion in normal neonates as per their body surface area (BSA) at different gestational ages.

Materials and Methods
The present study was conducted as cross-sectional study at a tertiary hospital in Jaipur, India. 175 normal newborns of different gestational ages, delivered at the department of Obstetrics and Gynecology at a tertiary hospital in India were randomly selected. Urine sample of selected newborns was collected (urine which baby had passed for the first time after birth was not used for sampling) using the Pediatric urine collecting bag. The sample was taken at 24 hours of life by. Samples were used to estimate urinary proteins (total) (mg/dl) and urine albumin (mg/dl). Body surface area of all newborns was calculated using the following Haycocks *et al*. formula.

$$\text{Body Surface Area (BSA)} = \text{weight}^{0.5378}(\text{grams}) \text{ `length}^{0.3964}(\text{cm})\text{'} \ 0.024265$$

Inclusion Criteria

Baby

1. All babies of 28 to 42 weeks of gestation.
2. All babies with normal vaginal delivery and lower segment caesarean section (LSCS).

Mother

1. All mothers were selected irrespective of their gravid status
2. All mothers who were not suffering from any illness during antenatal periods like Pregnancy Induced Hypertension (PIH), Diabetes, Hypothyroidism or Hyperthyroidism.

Exclusion Criteria

Baby

1. All babies with Apgar score < 7
2. All large for date babies
3. All babies with cord blood serum creatinine >1 mg/dl
4. All babies suffering co-morbid illness

Mother

All mothers with serum creatinine >1mg

Tests used

1. Urine total proteins were estimated using the Pyrocatechol Violet method.
2. Urine albumin was estimated using Immunoturbidometric method
3. All tests were assayed on Vitreous 4600 analyser

Table 1: Gestational age bands of sample newborns and their urine total protein values

Gestational age (days)	N	MIN UTP	AVG UTP	MAX UTP	Pearson correlation and coefficient (r)
196 - 210	4	22	20.7	26	
210 - 224	3	18	21.6	28	
224 - 238	6	11	19.6	29	
238 - 252	13	19	23.4	30	0.237
252 - 266	39	5	23.7	30	
266 - 280	77	13	24.8	56	
> 280	33	19	26.7	50.3	

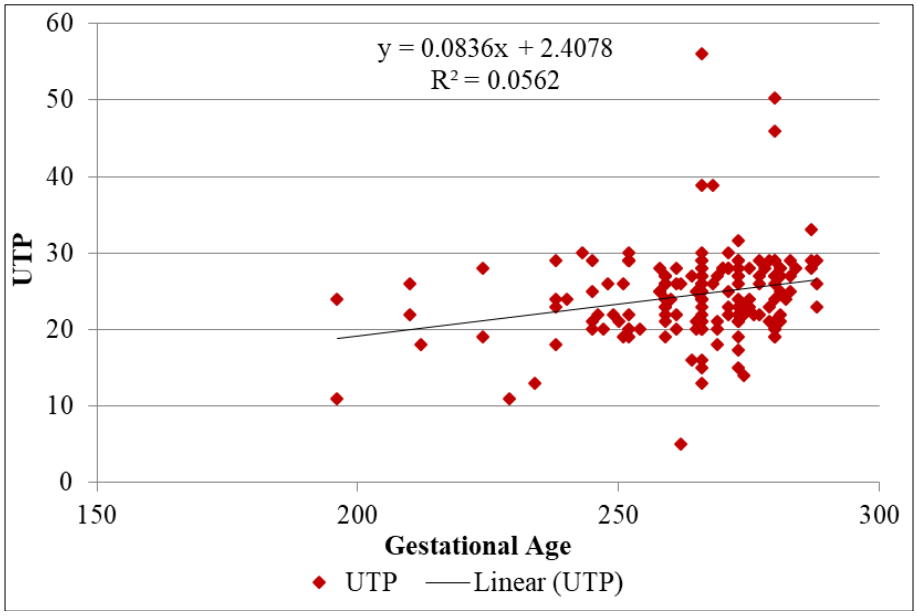

Fig 1: Relationship between urine total protein values of newborns with their gestational age at 24 hours of life

Table 1 depicts the gestational age bands of sample newborns and their urine total protein values distributed according to the gestational age bands.

It can be seen that the urine total protein was higher in >280 days of life with the average urine total protein value of 26.7 mg/dl with the minimum and maximum values being 19 mg/dl and 50 mg/dl respectively.

The minimum value of urine total protein was seen at 224-238 days of life with the urine total protein value being 19.6 mg/dl. The average urine total protein values at 196-210, 210-224, 238-252, 252-266, 266-280 days of life was 20.7 mg/dl, 21.6 mg/dl, 23.4 mg/dl, 23.7 mg/dl, 24.8 mg/dl respectively.

The figure 1 shows the relationship between urine total protein value of newborns with their gestational age at 24 hours of life. It was found that there is a positive correlation between the urine total proteins of newborns and their gestational age as the Pearson coefficient was 0.237.

Therefore, with an increase in the gestational age the urine total protein will increase by 0.237.

Table 2: Gestational age bands of sample newborns and their urine microalbumin values

Gestational age (days)	N	MIN UM	AVG UM	MAX UM	Pearson correlation and coefficient (r)
196 - 210	4	3.1	5.8	6.8	
210 - 224	3	1	1.7	2.1	
224 - 238	6	0.7	4.55	7.6	
238 - 252	13	1.4	5.2	7.9	0.040
252 - 266	39	0.7	4.5	8.9	
266 - 280	77	0.8	5.1	12.3	
> 280	33	0.9	4.8	12	

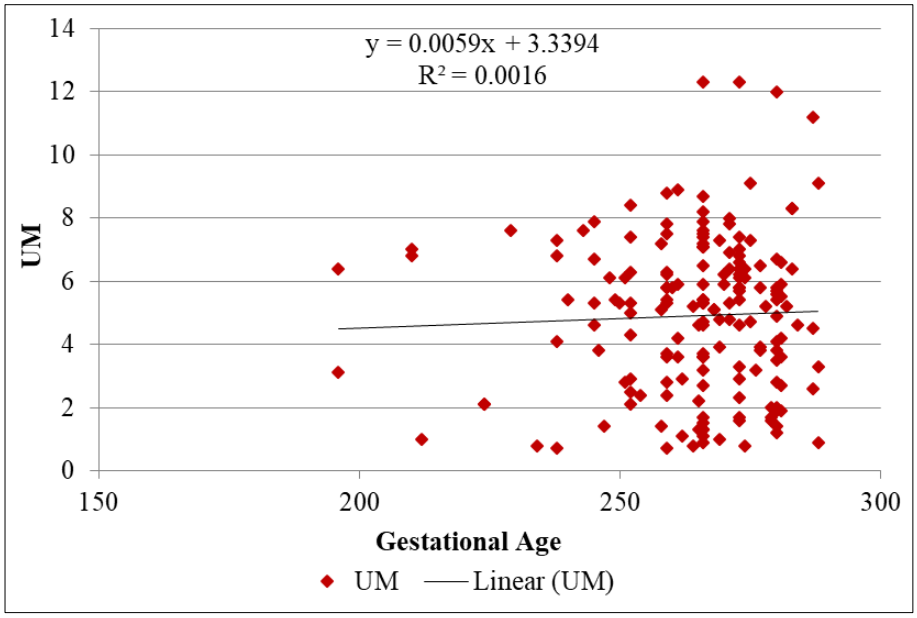

Fig 2: Relationship between urine microalbumin value of newborns with their gestational age at 24 hours of life

Table 2 depicts the gestational age bands of sample newborns and their urine microalbumin values distributed according to the gestational age bands.

It can be seen that the urine microalbumin was highest in 196-210 days of life with urine total protein value of 5.8 mg/dl with the minimum and maximum values being 3.1 mg/dl and 6.8 mg/dl respectively.

The minimum value of urine microalbumin was seen at 210-224 days of life with the urine microalbumin value being 1.7 mg/dl.

The average urine microalbumin at 224-238, 238-252, 252-266, 266-280 and at >280 days of life was 4.55 mg/dl, 5.2 mg/dl, 4.5 mg/dl, 5.1 mg/dl, 4.8 mg/dl respectively.

Figure 2 shows the relationship between the urine microalbumin value of newborns with their gestational age at 24 hours of life.

There is a positive correlation between urine microalbumin of newborns and the gestational age of newborns as the Pearson coefficient was 0.040.

It shows that to increase in the gestational age, there will be an increase in the urine microalbumin by 0.040.

Table 3: Bands of body surface area of sample newborns and their urine total protein values

BSA	N	MIN UTP	AVG UTP	MAX UTP	Pearson correlation and coefficient (r)
0.09-0.12	7	11	19	26	0.171
0.12-0.15	5	11	21.6	28	
0.15-0.18	29	18	24	30	
0.18-0.21	83	5	25	56	
0.21-0.24	41	15	25.1	50.3	
0.24-0.27	10	20	24.2	28	

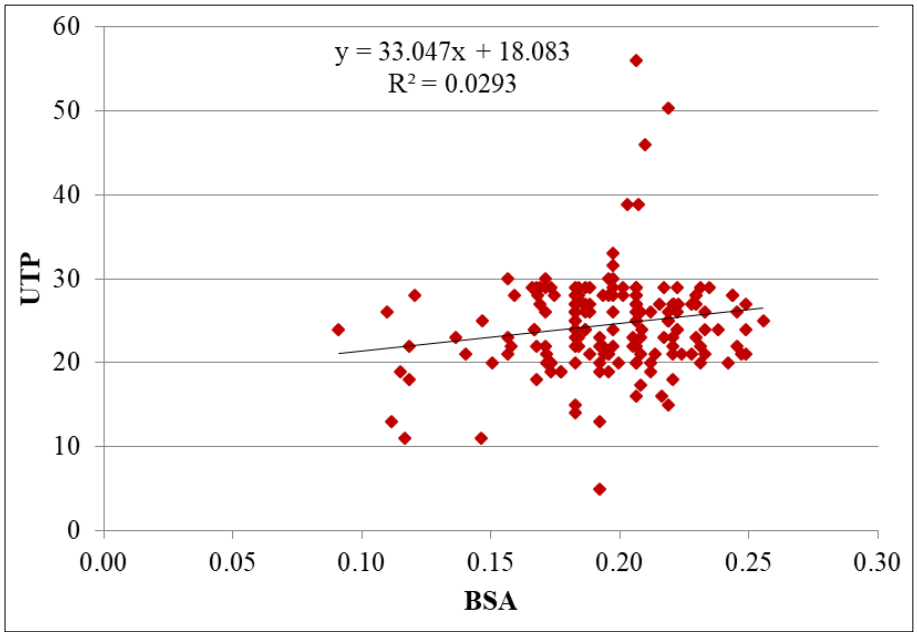

Fig 3: Relationship between urine total protein value of newborns with their body surface area at 24 hours of life

Table 3 shows the bands of body surface area of sample newborns and their urine total protein values distributed according to the body surface area bands.

It can be seen that the urine total protein was highest in the band group 0.21-0.24 with an average value of 25.1 mg/dl with the minimum and the maximum values in this band group being 15 mg/dl and 50.3 mg/dl and the number of samples taken in this group were 41.

The minimum value of urine total protein was seen in the other band group 0.09-0.12 with urine total protein value 19 mg/dl. The average value of urine total proteins at band groups 0.12-0.15, 0.15 -0.18, 0.18-0.21. 0.24-0.27 were 21.6 mg/dl, 24 mg/dl, 25 mg/dl, 24.2 mg/dl respectively.

Figure 3 shows the relationship between urine total protein value of newborns with their body surface area at 24 hours of life.

It was found that urine total protein has a positive correlation with the body surface area of the newborns as the Pearson coefficient for the same is 0.171.

Hence, with an increase in the body surface area, there will be an increase in the urine total proteins by 0.171.

Table 4: Bands of body surface area of sample newborns and their urine microalbumin values

BSA	N	MINUM	AVGUM	MAXUM	Pearson correlation and coefficient (r)
0.09-0.12	7	0.8	3.8	7	0.069
0.12-0.15	5	2.1	5.9	7.6	
0.15-0.18	29	0.7	4.7	8	
0.18-0.21	83	0.7	4.7	12.3	
0.21-0.24	41	0.8	5.2	12	
0.24-0.27	10	1.9	5	8.7	

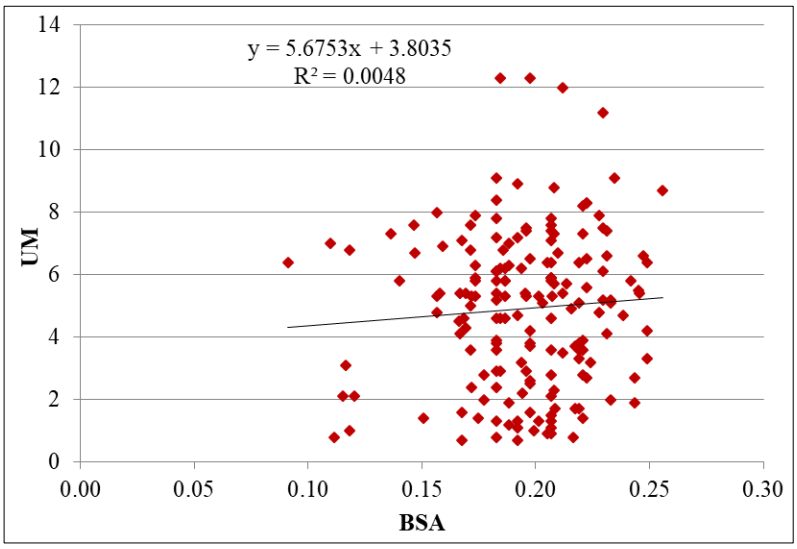

Fig 4: Relationship between urine microalbumin of newborns with their body surface area at 24 hours of life

Table 4 shows the bands of body surface area of sample newborns and their urine microalbumin values distributed according to the body surface area bands.

It can be seen that the urine microalbumin was highest in the band group 0.12-0.15 with the average value of 5.9 mg/dl and the minimum and the maximum values in this group being 2.1 mg/dl and 7.6 mg/dl respectively, the number of samples taken in this group was 5.

The minimum value of urine microalbumin was seen in the other band group 0.09-0.12 with urine total protein value 3.8 mg/dl. The average values of urine microalbumin at band groups 0.15 -0.18, 0.18-0.21, 0.21-0.24, 0.24-0.27 were 4.7 mg/dl, 4.7 mg/dl, 5.2 mg/dl, 5 mg/dl respectively. Figure 4 shows the relationship between the urine microalbumin value of newborns with their body surface area at 24 hours of life.

It was found that urine microalbumin has a positive correlation with the body surface area of the newborns as the Pearson coefficient for the same is 0.069. Therefore, with the increase in the body surface area, there will be an increase in the urine microalbumin by 0.069.

Table 6: Pearson Correlation Coefficient table

		UTP	UM
Gestation	Pearson Correlation	.237**	.040
BSA	Pearson Correlation	.171*	.069

**. Correlation is significant at the 0.01 level (2-tailed)

*. Correlation is significant at the 0.05 level (2-tailed)

Discussion

The presence of pathological proteinuria and albuminuria raises high suspicion of renal parenchyma involvement like glomerulopathy and/or renal failure [2]. Renal pathologies leading to proteinuria and albuminuria are quite rare in neonates which gives a false impression that neonatal urine did not contain any protein or albumin.

On the contrary, there are various studies such as in 2015 Chahrazed E.H, Theirry. C, Severine. T *et al* [3]. conducted a study in France to update the normal upper values of the urinary total protein-to-creatinine and albumin-to-creatinine ratios in term newborns. They concluded that the upper-limit values for the total protein-to-creatinine ratio were 1431 on day 0-1 and 1205 mg/g (162 and 136 g/mol) on days 3-4 and those for the albumin-to-creatinine ratio were 746 and 301 mg/g (84 and 34 g/mol), respectively, which indicate that neonatal urine contains higher amounts of protein than expected due to immaturity of nephrons in neonatal kidneys.

Classically, values of urine protein are determined in a timed urine sample, but more recently, urine total protein or albumin to creatinine ratios have been developed for this purpose.

In adults and children, normal values of urine protein, urine albumin and their ratios to creatinine are very well established [4, 5], but these values cannot be applied to the neonatal population due to various differentiating features of this group like physiological immaturity of renal tubules [6, 7].

In the present study, we observed that there was a linear and directly proportional relationship gestational age and urine total protein in spot sample as can be seen from Fig 1. Similarly, the rise in absolute value of urine microalbumin in spot urine sample was also linear and directly proportional to the gestational age, but the proportional rise in urine microalbumin was less as compared to urine total proteins which can be seen through their correlation coefficient (r) values which were 0.237 and 0.040 for urine total proteins and urine microalbumin respectively.

This means that rise in spot sample of urine total protein will be 0.237 times in comparison to 0.040 times in urine microalbumin along with the increase in the gestational age. Similarly, urine total protein and urine microalbumin also had a linear relationship with the body surface area of newborns as seen in the above results. When we consider absolute values of urine total protein or urine microalbumin, the urine microalbumin values are on an average 25% of the urine total protein content of urine at all gestational ages and body surface are bands of newborns. Thus, the majority of proteins in neonatal urine is tubular protein.

Conclusion

We conclude that all newborns have abnormally high proteinuria at all gestational ages, which increases with an increase in gestational age. Urine microalbumin also showed a very mild increase with age, but it was very insignificant in comparison to UTP. This indicates, renal tubular immaturity is much more significant than glomerular immaturity and is predominantly at all gestational ages.

We further tried to find the relationship between BSA and UTP, UM and evaluated their correlations. We found that all forms of proteinuria (UTP, UM) had a linear relationship with BSA and there was a positive correlation with all of them with a Pearson correlation coefficient (r) being between 0.171 and 0.069 respectively. This finding is in line with that of our correlation analysis of these variables with gestational age.

Thus, though tubular proteins are major constituents of urine proteins in neonatal urine, but a small amount of albumin is also lost in the urine and their amounts increase linearly and proportionately as gestational age and body surface area of newborn increases.

Further large studies are needed to establish the normal range of acceptable proteinuria and albuminuria in neonates so that these reference values can be used for assessing the onset of kidney injury in the neonatal period.

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