THE STUDY OF AMNIOTIC FLUID URIC ACID AND CREATININE AS AN INDEX OF FOETAL MATURITY IN NORMAL PREGNANCIES

by

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With a considerable reduction in maternal mortality, the attention is now directed towards reducing perinatal deaths. The commonest cause predominently responsible for neonatal deaths is prematurity. A high rate of induction in PET, diabetes and placental insufficiency makes it very important to ascertain that the foetus is sufficiently mature. Various techniques have been tried to assess the foetal age.

The present study was undertaken to find out the normal creatinine and uric acid levels in amniotic fluid at different periods of gestation. From these values obtained, the foetal age was deduced in normal pregnancies with unknown gestational period.

Material

Fifty-eight samples were studied at gestational periods as shown in Table I.

Group I—32 samples of amniotic fluid were obtained from normal pregnant women with known gestational period.

Group II—Comprised of 25 specimens from 23 patients who did not know their expected date of delivery. Their pregnancies were otherwise uncomplicated.

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TABLE I
Gestational Period

Pregnancy in weeks	Normal	Unknown L.M.P.	Total
20	4	-	4
24	2	-	2
34	1	4	5
36	-	2	2
37	2	-	2
38	2	5	7
39	9	5	14
40	13	9	22
41	-	-	-
42	-	-	-
43	-	-	-
Total	33	25	58

Creatinine was estimated by FOLIN WU method, using Jaffe picric acid reaction. When amniotic fluid is treated with picric acid, and sodium hydroxide, the creatinine present combines with picric acid to give an orange coloured compound, creatinine picrate. The intensity of the colour is proportional to the concentration of creatinine present. A standard solution of creatinine is similarly treated and final colours compared in a photoelectric calorimeter.

Uric acid: Protein in amniotic fluid is precipitated by sodium tungstate and sulphuric acid. The protein free supernatent is treated with phosphotungstic acid, when a blue colour is produced due to reduc-

tion of alkaline phosphotungstate by uric acid. The colour is compared in a photo-electric calorimeter with that of a standard uric acid solution similarly treated.

Observations

Group I—Creatinine.

Six samples studied between 20-24 weeks showed creatinine concentration varying between 0.5 mg-0.9 mg% with a mean level of 0.71 mg%.

The only patient studied at 34 weeks gave creatinine reading of 1.5 mg% and a repeat study at 39 weeks gave a value of 2 mg%. There was no false positive reading in these cases.

Between 37-40 weeks, 26 samples were studied. The creatinine level ranged between 1.9 mg%-3.2 mg% with a mean value of 2.5 mg%. Except for one specimen which gave a reading of 1.9 mg%, all readings were above 2 mg% (correct assessment in 96.15% cases). Although a rise in the level was noted after 34 weeks, no linear rise was seen. All 26 women delivered within a week of this study, and babies weighed between 1900 gms-3800 gms. Four babies weighed less than 2500 gms., but creatinine level was more than 2 mg%. Thus it was possible to identify "small for date babies."

Uric Acid: Uric acid level ranged from 2.5 mg- 3.5 mg with a mean value of 3 mg% in 6 samples studied between 20-24 weeks gestation.

One sample at 34 weeks showed uric acid level of 6 mg%. The subsequent analysis in the same patient at 39 weeks gave a reading of 8 mg%. There was no false positive reading in any of these cases.

Between 37-40 weeks, uric acid level varied between 6.80 and 13.50 mg%, with a mean value of 9.0 mg%.

In 20 out of 26 samples studied after 37 weeks, the uric acid, level was 8 mg% or more. If 8 mg was considered as index of 37 weeks maturity, correct assessment was obtained in 76.92% cases. However, accepting 7.5 mg% as suggesting 37 weeks maturity, accurate reading was noted in 96.15% cases. One faise negative reading of 6.8 mg% at 39 weeks also had a low creatinine level of 1.9 mg%, but the baby weighed 2800 gm at birth. Four small for date babies weighing less than 2500 gms had normal uric acid levels. This shows that neither uric acid nor creatinine had any positive bearing on foetal weight.

Uric acid too showed scatter values after 37 weeks gestation, and failed to show a linear rise.

Group II—Creatinine.

The 6 samples taken at clinically estimated 34-36 weeks showed the levels varying from 1.50 to 1.70 mg%, with a mean level of 1.61 mg%. Two of these cases who had a repeat estimation at 38 weeks and 40 weeks showed a rise in creatinine level above the maturation index.

In 19 samples, between 37-40 weeks, creatinine values ranged between 1.7 mg and 3.2 mg%, with a mean value of 2.5 mg%. Only 1 case showed a level of 1.7 mg% at presumably 38 weeks. Uric acid was also low and the baby weighed only 2200 gms. This suggests that clinical estimation was most probably inaccurate and pregnancy was below 37 weeks. Two cases suspected of placental insufficiency had normal creatinine values, but babies weighed less than 2400 gms each. These findings prove that creatinine level is related only to gestational period and is useful in detecting "small for date" babies.

Uric acid: In 6 samples studied at 34-36 weeks, uric acid values ranged between 5 and 10.5 mg%, with a mean value of

7.8 mg%. The repeat amniocentesis in 2 cases showed a rise from 6.7 to 8.8 mg% at 38 weeks, and from 5 mg% to 10 mg% at 40 weeks respectively.

In 19 samples studied after 37 weeks, uric acid levels were between 7.5 and 13 mg%, with a mean level of 9.7 mg%. One specimen which had the level of 7.5 mg at 38 weeks also showed a low creatinine level of 1.7 mg and babies weighed 2200 gms. This case has been discussed earlier.

Uric acid values were very much scattered and positive correlation was not seen with the foetal weight.

Like creatinine, uric acid levels were also above the maturation index in 2 cases of placental insufficiency.

Discussion

Amberg and Rowntree were the first to discover creatinine in human amniotic fluid in 1905, and Jeffcoate and Scott in 1959 suggested that amniotic fluid creatinine was a product of foetal kidney.

In the last trimester, the number of functional glomeruli increases and creatinine which is completely filtered by the glomeruli and not reabsorbed by the tubules is therefore expected to be present in increasing concentration in foetal urine which is excreted into amniotic fluid.

Pitkin and Zwirek (1967) were the first to utilize this knowledge in predicting foetal maturity. They observed that the level remained constant or increased only slightly upto 34 weeks, after which there was a steep rise. After 37 weeks, creatinine level was 2 mg% or more in 94% cases. Doran *et al* (1970) and Enlander (1972) demonstrated creatinine level below 1 mg% below 28 weeks.

Teoh *et al* (1973) found the level of 0.3 mg% at 10 weeks and 1 mg at 30 weeks. The level rose steeply to reach 1.8 mg% at 35 weeks. At term, the mean level was 2 mg%. There was no false positive reading in this series, but one low reading of 1.9 mg% was obtained at 39 weeks. The correct prediction was thus possible in 96.15% cases (25 samples).

Our prediction on assessment of foetal age tallies with those of Pitkin and Zwirek (1967), Horger and Hutchison (1969) and Andrews (1970), who predicted foetal age in 94% cases, using 2 mg% as maturation index. Roopnarine Singh (1970) observed that 95% cases had creatinine level of 1.72 ± 0.56 mg% at 37 weeks and 2.74 ± 0.55 mg% at 41 weeks. Chandriok, *et al* (1971) observed creatinine level of 2 mg% or more beyond 37 weeks in 80% of their 115 cases. Similar observations have been reported by Thatte and Phadnis (1973) and Sinha (1975).

Although Roopnarine Singh (1970), Mukherjee (1975) and Doran *et al* (1974) noted a positive correlation between creatinine level and foetal weight, our own observation and that of Droegmuller *et al* (1969) Begneaud *et al* (1969) and Mendelbaum *et al* (1969) failed to show such a correlation. If this is true, it is possible to identify "small for date babies" by this study.

Uric acid: Uric acid also exiginates from foetal kidneys, and its level would be expected to rise with advancing pregnancy. Windle in 1940 first observed a rise in the level with increased gestation.

Our findings are similar to those described by Wolf (1970) and Enlander (1972).

Taking 7.5 mg% as indicating at least 37 weeks maturity accurate assessment was made in 96.15% cases. Only 1 specimen which gave a low reading of 6.8 mg% at 39 weeks also showed a low creatinine level, but baby weighed 2800 gms.

Harrison (1972) predicted foetal maturity in 79% of his cases, using 8.5 mg% as index of at least 38 weeks maturity. Before 38 weeks, none of his cases showed this level.

Our study showed scattered values after 36 weeks, and failed to show a linear rise, as suggested by other workers.

In group II, there were two false positive findings at 36 weeks as assessed clinically. The creatinine level gave correct findings.

Beyond 36 weeks, uric acid estimation was helpful in gauzing the foetal age. The only reading which was below 7.5 mg% also showed a lower reading of creatinine, and the baby proved to be immature at birth.

There was no positive correlation between uric acid levels and the birth weight. Similarly, the levels were normal in cases of small for date babies.

Conclusion

Creatinine appears to give more accurate estimation of foetal age than uric acid near term, but the use of 2 or more parameters improve the assessment.

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