Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 20 (4), pp. 291–296 (1979)

Amniotic fluid creatinine and uric acid levels in high risk pregnancy

By

Adrienne STUBER and Clara MÉSZÁROS

Schöpf-Merei Hospital, Budapest

Received March 21, 1979

Comparison of two methods of creatinine and uric acid assay in amniotic fluid showed that the two-point-reaction rate measurement of creatinine and the enzymatic assay of uric acid give more reliable results than the methods used previously. At the end of pregnancy, increased creatinine and uric acid levels were found. In cases of blood group incompatibility the values were mostly in the normal range, while in diabetic or toxaemic mothers higher, normal and lower values were equally found. It has been concluded that a single investigation does not suffice for the estimation of fetal maturity. Only repeated tests showing an increase in the creatinine and uric acid levels offer reliable information.

Estimation of fetal maturity in high risk pregnancy is an important test. Among others, biochemical analysis of amniotic fluid obtained by amniocentesis has been recommended for the purpose [10, 15, 17, 18, 19, 22, 23]. The commonly investigated constituents are creatinine, uric acid and phospholipids as their levels were found to increase with gestational age. The values obtained were, however, found to have too great a scatter in both normal and complicated pregnancies [3, 4, 8, 16, 21]. Therefore, selection of the most reliable methods of assay has a great importance.

This papers deals with the comparison of two different methods of creatinine and of two different methods of uric acid estimation in amniotic fluid and with their values in high risk pregnancies.

METHODS

For the estimation of creatinine, the well-known Jaffe method [7] and the two-point-reaction rate modification of the same reaction [2] were compared. For the estimation of uric acid, the photometric method [13] and the enzymatic determination with uricase [12] were compared, using the Boehringer Test-Combination Creatinine and the Urica-quant kit, respectively, in mixed pools of immature and mature amniotic fluids.

On the basis of these results, single specimens of amniotic fluid were investigated by the Boehringer tests.

MATERIAL

Amniotic fluids were obtained by abdominal amniocentesis. After centrifugation for 10 minutes they were analysed immediately or stored at −20 °C until analysed.

Mixed pools of amniotic fluids obtained from patients with blood group incompati-

bility were prepared in the following manner. After centrifugation, 5 ml volumes of amniotic fluid were poured together from 10 samples obtained at 30—32 gestational weeks and from other 10 samples obtained at 38—42 gestational weeks. Gestational age was calculated from the date of the last normal menstruation period.

The 75 patients investigated individually were grouped according to gestational age and diagnosis.

The distribution of the diagnoses is seen in Table I. The first group contained 37 patients with Rh and 2 patients with ABO incompatibility. The next group includes patients with diabetes and/or toxaemia, since these two diagnoses were found frequently in association.

Results and Discussion

Methodological studies

First, pure commercial standard solutions of creatinine and uric acid were measured with both methods. The results for creatinine are shown in Table II, and those for uric acid in Table III.

The data revealed clearly that the Boehringer methods allowed a much more exact determination of the two components that the classical ones, as regards both sensitivity and the biometrical parameters.

Table I

Distribution of diagnoses

	Patients	Samples
Blood group incompatibility	39	56
Diabetes and/or toxaemia	26	31
Previous stillbirth	4	4
Intrauterine atrophy	2	2
Placenta praevia	2	2
Hydramnios	1	1
Myoma	1	1
Total	75	97

Table II

Comparison of traditional Jaffe reaction and its 2-point reaction rate modification (concentration range 0.5—3.0 mg/dl)

Method	2-point reaction rate	Traditional
Sensitivity, mg/dl	0.12	0.34
Distorsion, per cent	0.61	2.6
r	0.998	0.990
S_{II}	± 0.061	± 0.17
V_k, per cent	3.6	10.0
Regression coefficient	$y = 0.10 + 0.941x$	$y = 0.12 + 0.937x$

TABLE III

Comparison of photometric and enzymatic uric acid estimation (concentration range 1.0—12.0 mg/dl)

Method	Enzymatic	Photometric
Sensitivity, mg/dl	0.24	1.62
Distorsion, per cent	0.9	2.7
r	0.987	0.940
S_H	±0.12	±0.81
V_k, per cent	1.9	12.3
Regression coefficient	$y = 0.30 + 0.782x$	$y = 1.23 + 0.830x$

Amniotic fluid investigations

Next, the creatinine and uric acid levels were analysed by both methods in mixed pools of immature and mature amniotic fluids. Results are shown in Table IV. It has been concluded that they demonstrate the higher accuracy of the two-point-reaction rate measurement of creatinine. The same Table IV shows the creatinine values in the pooled immature and mature amniotic fluids. the data are in agreement with the observation of an increase with gestational age of the amniotic fluid creatinine level.

Table V gives the values of uric acid in the same mixed pools: the level of this component, too, was in-

TABLE IV

Creatinine values estimated with two methods in mixed pools of immature and mature amniotic fluids

	Immature		Mature	
	2-p.r.r.	traditional	2-p.r.r.	traditional
Mean, mg/dl	1.14	1.43	1.96	2.41
Range, mg/dl	1.09—1.19	1.26—1.60	1.91—2.01	2.28—2.54
S.D. ±	0.05	0.17	0.05	0.13
V_k per cent	4.4	11.8	2.6	5.0

TABLE V

Uric acid levels estimated with Urica-quant in mixed pools of immature and mature amniotic fluids

	Immature	Mature
Mean, mg/dl	5.2	8.8
Range, mg/dl	5.1—5.3	8.6—9.0
S.D. ±	0.15	0.15
V_k, per cent	2.1	2.1

creasing with the progress of pregnancy.

The individual values for creatinine and uric acid in the amniotic fluids of high risk pregnancies are given in Figs 1 and 2 according to diagnosis and gestational age.

Both scattergrams show a wide range. For example, the values for creatinine at 33 weeks gestation ranged from 0.9 to 2.0 mg/dl, and at 38 weeks from 1.2 to 2.4 mg/dl; the corresponding uric acid values were at 33 weeks 5.0—13.0 and at 38

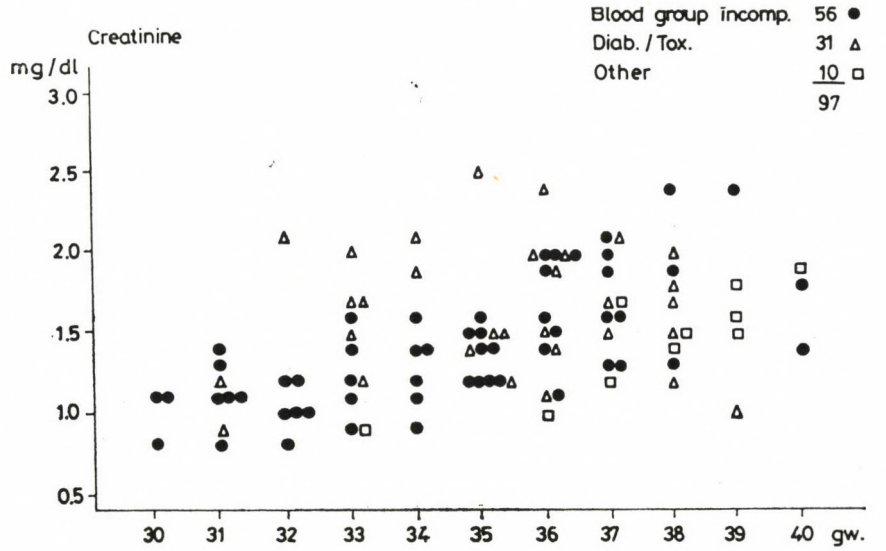

FIG. 1

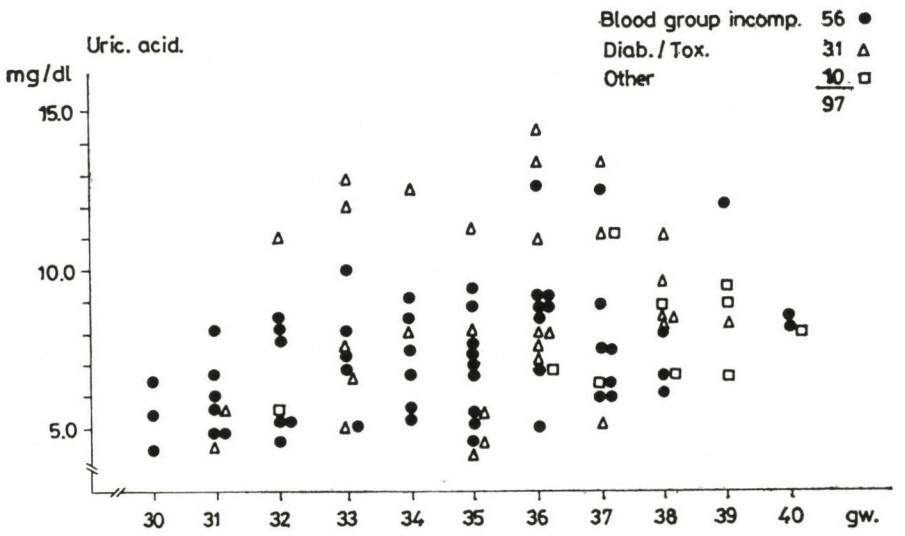

FIG. 2

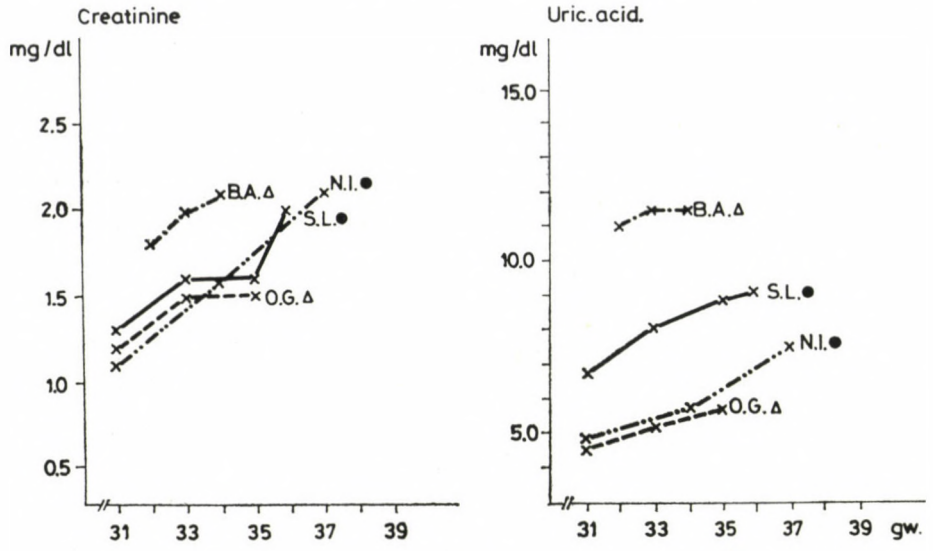

FIG. 3

weeks 6.2—11.0 mg/dl. In the cases of blood group incompatibility the values for both components were mainly in the central zone, and in the diabetic and/or toxaemic pregnants they were partly in the higher and partly in the normal or lower ranges. Since a group of authors observed a high amniotic fluid creatinine level in toxaemia and diabetes [1, 11, 14], and another group found normal or low values in similar pregnants [5, 6, 9], this only seems to mean that gestational age in high risk pregnancy cannot be estimated on the basis of a single investigation. Repeated analysis of the amniotic fluid must be done to obtain reliable information. This is demonstrated in Fig. 3, where only the values of the two patients with blood group incompatibility are in the normal range, but all the four show increasing levels.

Finally, the amniotic fluid and uric acid investigation must be completed with other tests, among others with the determination of the L/S ratio, this being the most reliable test for predicting fetal pulmonary maturity and the possible risk of respiratory distress syndrome [20].

ACKNOWLEDGEMENT

The skilful technical assistance of Mrs. Ildikó Kohányi is gratefully acknowledged.

REFERENCES

1. ANTON W., MENDE, H. E., BÖHM, K.: Biochemische Fruchtwasseruntersuchungen bei Übertragung und pathologischen Schwangerschaftsverlaufen. Zbl. Gynäk. **96**, 664 (1974).
2. BARTELS H., BÖHMER M.: Eine Mikromethode zur Kreatininbestimmung. Clin. chim. Acta **32**, 81, (1971).
3. DORAN, T. A., BJERRE, S., PORTER, C. J.: Creatinine, uric acid and electrolyte

in amniotic fluid. Amer. J. Obstet. Gynec. **106,** 325 (1970)
4. Doran, T. A., Benzie, R., Harkins, J., Jones, O. V., Porter, G. J., Thompson, D. W., Liedgren, S. I.: Amniotic fluid tests for fetal maturity. Amer. J. Obstet. Gynec. **119,** 829 (1974).
5. Doran, T. A., Malone, R. M., Benzie, R. J., Jones, O. V., Thompson, D. W., New, M. L.: Amniotic fluid tests for fetal maturity in normal and abnormal pregnancies. Amer. J. Obstet. Gynec. **125,** 586 (1976).
6. Emara, S. H., Hawary, E. M. F., Abdel-Karim, H. A.: Amniotic fluid total proteins, electrophoretic patterns, total amino acids and creatinine in diabetic women. Z. Geburtsh. **181,** 432 (1977).
7. Emmerich, R.: Arbeitsmethoden der inneren Medizin. Band V/1. G. Fischer Verlag, Jena 1969.
8. Foulds, J. W., Pennock, G. A.: Amniotic fluid creatinine: an unreliable index of fetal maturity. J. Obstet. Gynec. Brit. Cwlth **79,** 911 (1972).
9. Harrison, R. F.: Amniotic fluid creatinine levels in the normotensive and preeclamptic patient. J. Obstet. Gynec. **80,** 338 (1973).
10. Harrison, R. F., Henry, G. R.: Amniotic fluid polytest for estimation of fetal maturity in late pregnancy. Irish J. med. Sci. **143, 296** (1974).
11. Isaac, V., Lillie, E. W.: Amniotic fluid creatinine and birth weight in normal and toxaemic patients. J. Irish med. Ass. **65,** 9 (1972).
12. Kageyama, N.: A direct colorimetric determination of uric acid in serum and urine with uricase-catalase system. Clin. chim. Acta **31,** 421 (1971).
13. Lavery, J.: A simplified method for estimating plasma uric acid. Clin. chim. Acta **21,** 415 (1968).
14. Löfstrand, T., Fen, G., Holmberg, N.: Phospholipids and creatinine in amniotic fluid in relation to gestational age. Acta obstet. gynec. scand. **55,** 145 (1976).
15. MacVicar, J., Logan, R. W., Barnard, W. P.: Fetal maturity assessed from biochemical analysis of the liquor amnii. Scot. med. J. **18,** 84 (1973).
16. Myers, J. L., Harrel, M. J. P., Hill, F.: Fetal maturity: biochemical analysis of amniotic fluid Amer. J. Obstet. Gynec. **121,** 61 (1975).
17. Pitkin, R. M., Zwirek, S. D.: Amniotic fluid creatinine. Amer. J. Obstet. Gynec. **98,** 1135, (1967).
18. Quinlivan, W. G., Leslie, G., Reynold, W. F.: An evaluation of multiple tests and the lecithin/sphingomyelin ratio for determining gestational age. Amer. J. Obstet. Gynec. **116,** 1147 (1973).
19. Roux, J. F., Nakamura, J., Brown, E. G.: Further observations on the determination of gestational age by amniotic fluid analysis. Amer. J. Obstet. Gynec. **116,** 633 (1973).
20. Stuber, A., Ádám, J., Szőnyi, Gy.: A simple and rapid determination of the lecithin/sphingomyelin ratio in amniotic fluids and in pharingeal aspirates of newborn infants. Clin. chim. Acta **70,** 221 (1976).
21. Teoh, E. S., Lau, Y. K., Ambrose, A., Ratnam, S. S.: Amniotic fluid creatinine, uric acid and urea as indices of gestational age. Acta obstet. gynaec. scand. **52,** 323 (1973).
22. Wolf, P. L., Bloch, D., Tsudaka, T.: Biochemical profiles of amniotic fluid to assess fetal maturity. Clin. Chem. **16,** 843 (1970).
23. Woyton, J., Sward, J., Dzioba, A., Gajewska, A., Szacki, J.: Behaviour of total oestrogen, pregnandiol and creatinine levels in the amniotic fluid in the last weeks of pregnancy. J. Obstet. Gynaec. Brit. Cwlth **80,** 909 (1973).

A. Stuber, M. D.
Knézits u. 14.
H-1092 Budapest, Hungary