PLASMA AND AMNIOTIC FLUID URIC ACID IN PREECLAMPSIA

by

M. K. VISHVANATHAN

and

LEELA RAMAN

SUMMARY

Amniotic fluid uric acid in pre-eclampsia is elevated mainly due to hyperuricemia, irrespective of whether the mother received diuretic treatment. It also reflects impending fetal morbidity, especially above the levels of 10 mg/dl. Thus the measurement of uric acid in amniotic fluid may have a prognostic significance in pre-eclamptic toxemia.

Amniotic fluid creatinine and uric acid have been shown to increase in pre-eclampsia (Singh, 1973; Corswell and Semple, 1974). It is suggested that increase in these two components in pre-eclampsia is due to diuretic therapy (Mcallister *et al* 1973; Corswell Semple 1974; Votta *et al* 1975). However, no reports have appeared to indicate as to whether maternal hypercreatininemia or hyperuricamia seen in pre-eclampsia is reflected in the amniotic fluid levels in the absence of diuretic therapy.

The present study was undertaken to measure levels of amniotic fluid uric acid and creatinine in pre-eclamptics.

Material and Methods

Twenty-two normal women and 23 women suffering from mild and severe pre-eclampsia between 32-40 weeks of gestation were admitted to toxaemia ward of ICMR unit at Vani Vilas Hospital, Bangalore. Severe pre-eclamptic women had B.P. above 150/100 mm of Hg and positive proteinuria as tested by sulphosalicylic acid. Except bed rest in lateral position and sedatives, none of the women were given diuretics. Amniotic fluid samples were obtained by trans-abdominal amniocentesis under aseptic conditions, after 48 hours of admission. Simultaneous blood samples were drawn from these subjects.

Amniotic fluid was centrifuged and the supernatant fluid analysed for uric acid and creatinine. Serum was separated and analysed for uric acid and creatinine. True creatinine in these samples was measured by Folin method (1956) after treating the samples with Lloyds reagent. Uric acid was measured by Folin and Denis Method (1916). Values obtained were expressed as mg/dl.

Both normal and pre-eclamptic women were divided into preterm (less than 37 weeks) and term groups and data analysed. Maturity of the fetus was assessed after delivery by neurological and clinical examination.

From: National Institute of Nutrition Indian Council of Medical Research Jamai-Osmania, P.O., Hyderabad-500 007, A.P. India.

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Results

(1) *Creatinine:* (Table 1)

Since no difference was seen in serum creatinine between preterm and term levels, data was pooled and analysed. serum creatinine in pre-eclamptic women (both preterm and term) was significantly higher (1.28 ± 0.08 mg/dl) as compared to the mean level seen in the normals (0.88 ± 0.32 mg/dl; P < 0.001).

Amniotic fluid creatinine was significantly higher in preterm (2.19 ± 0.13 mg/dl) and term (2.75 ± 0.11 mg/dl) pre-eclamptics as compared to the levels seen in normal preterm (1.85 ± 0.15 mg/dl) and term (2.28 ± 0.05 mg/dl) women. In both normals and toxemic pregnants, term amniotic fluid creatinine was higher (P < 0.001) than in preterm samples. A close correlation was seen between the amniotic fluid creatinine and serum creatinine in the preterm pre-eclamptics (r = 0.8255; P <0.001). However, no correlation was observed at term between plasma and amniotic creatinine level. Similarly, no correlation was seen between amniotic fluid creatinine and uric acid.

Uric acid: (Table II)

Since no differences were seen in the preterm and term values, the data was pooled and analysed for both serum and amniotic fluid uric acid.

TABLE I

Plasma and Amniotic Fluid Creatinine Mg/Dl in Normal and Pre-eclamptic Women

	Plasma creatinine mg/dl (Pooled)	Amniotic fluid creatinine mg/dl	
		Preterm	Term
Normals	0.88 ± 0.32 (22)	1.85 ± 0.10 (7)	2.29 ± 0.05* (15)
Pre-eclamptics	1.28 ± 0.08*** (23)	2.19 ± 0.13* (7)	2.76 ± 0.11*** (16)

Values are Means ± SEMs ( ) sample size
* P <0.05, *** P <0.001 as compared to normals
P < 0.001 + as compared to preterm levels.

TABLE II

Plasma and Amniotic Fluid Uric Acid Mg/Dl in Normal and Pre-eclamptic Women

	Plasma uric acid mg/dl	Amniotic fluid uric acid mg/dl
Normals	4.68 ± 0.36 (18)	6.45 ± 0.35 (18)
Mild pre-eclamptics	5.23 ± 0.52 (9)	7.80 ± 0.55* (9)
Severe Severe pre-eclamptics	6.57 ± 0.43*** (14)	10.67 ± 0.50*** (14)

Values are Means ± SEMs ( ) sample size.
* P <0.05, *** P <0.001 as compared to normals.

Mean serum uric acid level was significantly higher (6.57 ± 0.43 mg/dl) in severe pre-eclamptics than in normals (4.68 ± 0.35 mg/dl; P < 0.001). In mild pre-eclamptics the values were in between normals and severe pre-eclamptics (5.23 ± 0.52 mg/dl).

Amniotic fluid uric acid were also significantly higher ($P < 0.001$) in severe pre-eclamptics (10.67 ± 0.49 mg/dl) as compared to normals (6.45 ± 0.35 mg/dl) and mild pre-eclamptics (7.80 ± 0.55 mg/dl).

A highly significant correlation ($r = 0.7173$; $P < 0.001$) was seen between serum and amniotic fluid uric acid when data was pooled for normals and pre-eclamptics (Fig. 1).

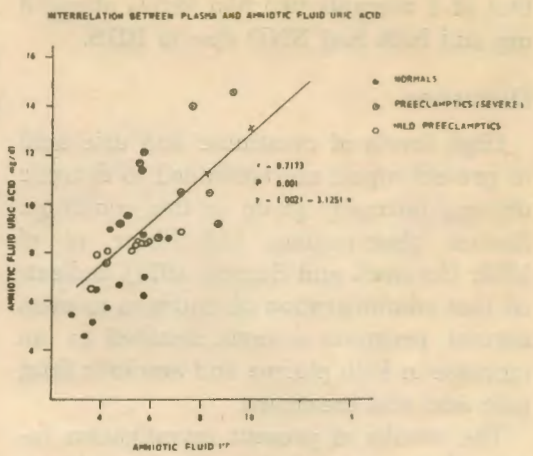

Fig. 1.

Fetal Outcome

Fetal outcome was analysed in relation to both amniotic fluid creatinine and uric acid. No relation could be found between amniotic fluid creatinine on one hand and fetal death on the other. With respect to uric acid, it proved to be a very good predictor of impending fetal death in pre-eclamptics, especially when the values were above 10 mg/dl. The amniotic fluid uric acid was above 10 mg/dl in 10 subjects of whom 5 had still-births and 4 had premature live births. Only 1 mother with premature still-birth had uric acid level within normal range (Table III).

TABLE III

Outcome of Pregnancy in Relation to Amniotic Fluid Uric Acid

No.	Duration of gestation	SB/LB	AMF uric acid mg/dl	Maternal condition
1.	Premature	S.B.	10.92	Severe PET
2.	Premature	S.B.	8.6	Severe PET
3.	Premature	L.B. and Cong. Malform	17.00	Chronic pyelonephritis
4.	Full term	S.B. 3.5 Kg.	12.50	Severe PET
5.	Full term	S.B. 2.5 Kg.	14.00	Severe PET
6.	Premature	S.B. 1.6 Kg.	11.40	Severe PET
7.	Premature	L.B. 2.25 Kg.	14.67	Severe PET
8.	Premature	L.B. 2.00 Kg.	11.71	Severe PET
9.	Twins—Premature	2.5 Kg. 2.2 Kg.	10.54	Severe PET
10.	Premature	L.B. 2.3 Kg.	10.54	Severe anemia and PET
	Normals			
1.	Premature	N.N.D. 1.75 Kg. R.D.S.	8.05	Normal
2.	Full term	N.N.D. 3.2 Kg. R.D.S.	10.50	Normal
3.	Premature	L.B. 1.5 Kg.	5.7	Normal
4.	Premature	L.B. 1.5 Kg.	7.6	Normal

N.N.D. — Neonatal Death.

Out of 4 normals two had levels above 8 mg and both had NND due to RDS.

Discussion

High levels of creatinine and uric acid in pre-eclampsia are attributed to diuretic therapy normally given in this condition. Earlier observations (Mcallister *et al* 1973; Corswell and Semple 1974) indicated that administration of diuretics to even normal pregnant women, resulted in an increase in both plasma and amniotic fluid uric acid and creatinine.

The results of present investigation indicated that even in the absence of diuretic therapy, levels of amniotic fluid creatinine and uric acid were significantly higher. These correlated well with maternal serum levels which also were raised in this condition. While in normal pregnancy, amniotic fluid creatinine above 2 mg. proved to be a good index of fetal maturity, the same criteria could not be applied in pre-eclamptic toxaemia. Thus its usefulness as index of fetal maturity loses significance in pre-eclampsia.

Bagneaud *et al* (1969) suggested that variation in amniotic fluid creatinine in pre-eclamptics did not depend on maternal serum levels. While this was true in case of term pre-eclamptics and normals, the close correlation seen between amniotic fluid creatinine and maternal serum creatinine in preterm pregnancy indicated that hypercreatininemic state of the mother resulted in greater secretion of the compound in amniotic fluid. However, at term, due to major contribution by the fetal urine, correlations are not observed between serum and amniotic fluid.

Attempts to correlate amniotic fluid uric acid with gestational maturity, were not successful in this study unlike the observations made earlier (Wolf *et al* 1970; Harrison, 1972; Teoh *et al* 1973; Doran *et al* 1970). Extensive scatter of values encountered in the earlier and present studies at all gestational ages thus limits its usefulness as an indicator of fetal maturity. Also no differences were found between term and preterm levels of uric acid in the present study. It is felt that source of amniotic fluid uric acid is mainly from fetal urine (Harrison, 1973). However, a high degree of correlation between plasma and amniotic fluid levels seen in the present study indicated that the major source of amniotic fluid uric acid is secretion from maternal plasma and that the fetal urine contributed only to a small extent. This was also confirmed by the observation that a poor degree of correlation existed between amniotic fluid uric acid and creatinine, since latter was mainly derived from fetal urine.

The results also suggest that amniotic fluid uric acid may be a better predictor of fetal outcome in pre-eclampsia. While normal levels do exist with poor fetal outcome, it would appear that high levels in amniotic fluid above 10 mg/dl invariably precede fetal death or premature delivery in majority of pre-eclamptics. This observation is similar to earlier observation (Widholm and Kuhlback, 1965), where high plasma levels of uric acid were associated with increased fetal deaths in pre-eclampsia.

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