

SOME BIOCHEMICAL INDICATORS OF THE AMNIOTIC FLUID – POSSIBLE WAY FOR EVALUATION OF THE RENAL DEVELOPMENT

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Abstract : The scope of our research resided in the investigation of the creatinine, urea, uric acid and glucose levels in the amniotic fluid from 19 pregnant women. The subjects were chosen based on pathological results at the double test, respectively triple test, to which amniocentesis was suggested for the FISH (Fluorescent In Situ Hybridization) analysis at the “Cuza Vodă” Obstetric and Gynecology Hospital from Iași. Screening of the above mentioned markers was made in order to evaluate the maturation and functioning of the fetal kidney. The obtained values for creatinine, urea, uric acid and glucose were correlated with the maternal age. The pregnant women included in this study were in the second pregnancy trimester. Following the biochemical analysis we calculated a median creatinine value in the amniotic fluid which is correlated with the median values from the literature (within the specific reference interval), which demonstrate a normal development for the fetal kidneys.

INTRODUCTION

Amniotic fluid is considered an important indicator of the fetal development and therefore of the fetal kidneys. A first method of diagnostic is sonography, which helps the evaluation of the fetal anatomy, maturity, comfort status and detection of the fetal abnormalities, including those of the urinary system. Lettgen et al.[3] reported that almost 50% of the sonographic abnormalities in fetuses were malformations of the renal and urinary system. According to Shackelford et al. [8], the sonographic discoveries were not enough for the renal function evaluation. The biochemical analysis of the amniotic fluid, as a new diagnosis method, comes in the aid of sonography, through the confirmation or infirmation of the distinguished suspicion. Dosing of the creatinine and urea in the amniotic fluid allows the renal maturity evaluation. [5]. The developmental study of the fetal kidney in the time of the embryogenesis as well as the knowledge about the functioning of various cellular transporters during pregnancy can give important information about the physiology and pathophysiology of the majority of the syndromes that appear within this time frame, only depending of the fetal age [6, 9, 10].

In the present study, we focused on the investigation the creatinine, urea, uric acid and glucose levels in the amniotic fluid from 19 pregnant women with normal pregnancies from the “Cuza Vodă” Obstetric and Gynecology Hospital from Iași. The results were correlated with maternal age and fetal kidney maturation and function, as a method for prenatal diagnostic.

MATERIALS AND METHODS

The investigated subjects were 19 pregnant women with normal pregnancies in “Cuza Vodă” Obstetric and Gynecology Hospital from Iași. The patients were separated in three age groups : 23-29 years, 30-35 years and 36-43 years. The gestational age was established according to the last period of the menstruation and after sonographic measurements. We mention that all of the patients were in the second pregnancy trimester, the optimal period for amniocentesis.

Amniocentesis is definitely the most known and practical method of invasive fetal diagnostic [2]. Samples of amniotic liquid that contained blood were eliminated from the study. The amniotic fluid was stored at a temperature of -20°C, until the time of the analysis. Creatinine, urea, uric acid and glucose values in the amniotic fluid were determined on the automatic analyzer Hitachi 917, through colorimetric – enzymatic methods and UV test optimized according with the IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) and DGKC (Deutsche Gesellschaft für Klinische Chemie). The concentrations of the four biochemical indicators investigated in the amniotic fluid were expressed in mg/dl.

The obtained data were statistically analyzed, with the help of the Student test [1, 11], reporting the values gathered for the pregnant women from the second (30-35 years) and third age group (36-43 years) to the values obtained from the pregnant women in the first age group (23-29 years).

RESULTS AND DISCUSSIONS

From the total of 19 patients, 5 were included in the first age group 23-29 years, 6 in the second age group 30-35 years and 8 in the third age group 36-43 years.

The pregnant women from the first age group (23-29 years) had a median creatinine concentration in the amniotic fluid of 0.7 mg/dl (fig. 1a). In the case of the patients from the second age group 30-35 years, respective the third age group 36-43 years, the creatinine levels in the amniotic fluid records a median value of 0.616 and respectively 0.625 mg/dl (fig. 1a). As we can see, the values of creatinine in the amniotic fluid at the second and third age group are practically identical. We can see a small difference between the creatinine values from the first pregnant women in the first age group and the values of this indicator at the pregnant women from the second and third age group; this difference being meaningful from the statistical point of view.

In the literature no reference interval for creatinine in the amniotic fluid from the second pregnancy trimester could be found, only the median of 0.9 mg/dl as mentioned by Wallach [12].

Considering that the creatinine values obtained by us are close to the median value in the literature [12], we can consider that the fetal kidney development takes place in normal conditions.

The median concentration of urea in the amniotic fluid sampled from pregnant women from the first age group is 23.980 mg/dl (fig.1b). The urea value in the amniotic fluid at pregnant women from the second age group is 19.866 mg/dl, and at the third age group is 25.662 mg/dl (fig. 1b). Practically, the urea values in pregnant women from the first and third age group are close and insignificant from the statistical point of view. In the amniotic fluid from the pregnant women in the second age group (30-35 years) a small urea quantity is obtained that differs meaningful then the level of this indicator at pregnant women from the first and third age group.

According to the specialty literature [12], in the gestational time the urea content in the amniotic fluid rises constantly, reaching the median value of 33.9 mg/dl at the pregnant women with over 38 weeks of pregnancy. No values regarding the urea level in the amniotic fluid at the pregnant women in the second gestational trimester could be found in the literature.

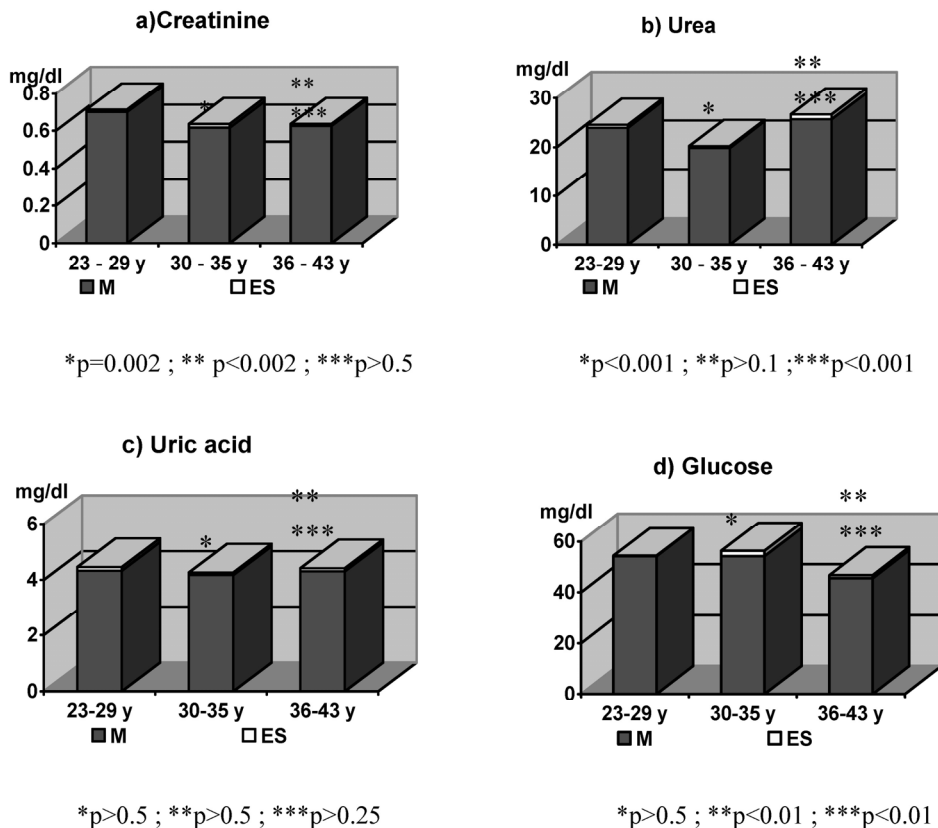


Figure 1. Creatinine (a), urea (b), uric acid (c) and glucose (d) concentrations, expressed in mg/dl, in the amniotic fluid sampled from pregnant women in the second gestational trimester.

At the pregnant women in the first age group, the median concentration of the uric acid in the amniotic fluid is 4.32 mg/dl (fig. 1c). A value in the same range for the uric acid in the amniotic fluid (4.166 mg/dl) was found in pregnant women from the second age group, as well as those in the third age group (4.30 mg/dl uric acid). Median values of the uric acid in the amniotic fluid, obtained through this study are close to the value of 3.7 mg/dl as indicated for the second gestational trimester by Wallach [12]. According to this author [12], uric acid concentration in the amniotic fluid rises along side the pregnancy age, reaching 7.5 mg/dl after 38 pregnancy weeks.

Median concentration for glucose obtained by us in the amniotic fluid is 54.20 mg/dl for pregnant women from the first age group, 54.183 mg/dl for the pregnant women from the second age group, but for the pregnant women with the age over 35 years, the smallest value was recorded, namely 45.62 mg/dl. This last value differs meaningful from the values found in pregnant women from the first two age groups.

According to Oliveira [5], glucose concentration from the amniotic fluid lowers gradually during the pregnancy period. In the same way, Wallach [12] mentions that the glucose level in the

amniotic fluid in the last pregnancy trimester is diminished at 10.7 mg/dl. According to Wallach [12], the values for glucose in the amniotic fluid can be correlated with those in the blood from the navel cord because the substance present in the amniotic fluid are excreted by the fetus and implicated in its metabolism.

At non-pregnant women, creatinine, urea and glucose are used to the evaluation of the complex functioning of the human kidneys. In the first half of the pregnancy, creatinine concentrations are similar in the maternal serum and amniotic fluid. Fetal kidneys begin to develop in the time of the fourth and fifth gestational week and excrete urine in the amniotic fluid between the eighth and eleventh week. Hence, important modifications are expected in the amniotic fluid composition as the gestation progresses and fetal maturation takes place.

Pregnant women included in the study had a median creatinine concentration in the amniotic fluid of 0.7; 0.616 and respectively 0.625 mg/dl, similar to the median normal serum value. Generally, values under 1.6 mg/dl indicate a small weight of 2500 grams and a pregnancy smaller than 37 weeks. The literature describes a creatinine median value for the second gestational trimester of 0.9 mg/dl. Our results are very close, demonstrating the normal kidney development in the studied subjects. According to Wallach [12] and Oliveira [5] median creatinine value, rises along with the pregnancy, reaching at delivery 2.0 mg/dl due to the development of the muscular mass. The increase in the creatinine and urea profile during the normal pregnancy is due to the glomerular maturation and maturation of the tubular function.

We observed correlations between the values of the first and second lot, with different ages, namely $*p=0.02$, respectively $**p<0.02$, thus demonstrating the fact that maternal age does not implies modifications.

The median urea values recorded at patients from this study are closer, 23.980, 19.860 respectively 25.662 mg/dl. Urea being one of the most stable markers can be considered a basal indicator of the maturation of fetal kidneys. There is a correlation to be seen between the values of the first batch and the third ($*p<0.001$ and $***p<0.001$), which means that, in the present study, there is no influence of the maternal age on the fetal kidney maturation.

The median values for uric acid levels recorded in the literature are equal to 3.7 mg/dl. In the present study, the median values for pregnant women from the three age groups were close, namely 4.32 ; 4.166 and respectively 4.30 mg/dl. Uric acid levels are not significantly changed, but in correlation with creatinine, urea and glucose levels in the fetal kidney development, this indicator represents a basic parameter for the evaluation of the renal maturity.

Uric acid and glucose levels sustain the fact that the maternal age does not conditions the renal markers concentration (creatinine, urea, uric acid and glucose) analyzed in this study.

Creatinine, urea and uric acid values correlated to those in the amniotic fluid found in the literature are similar and reveal the maturity of the renal glomerulus.

The heterogeneity of the patients is a limitation of our study, but from ethical reasons we considered that in order to obtain amniotic fluid samples a medical indication for amniocentesis was necessary. Also to this patients amniocentesis was recommended because they had a triple test with pathological values. The levels of the biochemical parameters are not outside the reference intervals found in the literature and are correlated to the normal cyto-genetic results.

We can say that the values obtained in the present study, do not present any pathological increases or decreases with significant importance for the fetus or for the mother. Values under the reference interval for amniotic fluid can be due to the fetal necessities. Creatinine and urea analysis from the amniotic fluid allow the evaluation of the renal maturity and function during the pregnancy. Maternal age does not influence the amniotic fluid biochemistry.

CONCLUSIONS

The measured amniotic fluid creatinine levels for the pregnant women in the second trimester are in correlation with the literature data, which demonstrates the maturity of the fetal renal glomerulus. In this way, the creatinine can be considered the main marker in the evaluation of the renal maturity and function.

Urea, according to the literature data, is the most stable marker, and has its origin in the filtering function of the fetal kidney and, correlated with creatinine levels suggests its importance as a renal marker.

Uric acid does not present significant modifications in the amniotic fluid as it was described in the literature. It is thereby a not so specific marker for the maturation of the fetal kidney, but the modifications (where they are found) correlated with the creatinine and urea values are important in the differentiate diagnostic.

As the uric acid, glucose levels do not change significant during pregnancy, these indicators being of importance only in the correlation with creatinine.

Creatinine and glucose levels in the amniotic fluid allow the evaluation of the renal maturity and function during pregnancy.

Maternal age does not significantly influence the aforementioned biochemical indicators in the amniotic fluid.

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