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Analysis of kidney volume growth during the fetal period in humans*

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Summary. The growth of fetal kidney volume was studied in 290 specimens taken from 145 fresh human fetuses (85 males and 60 females) with gestational age ranging from 13 to 36 weeks postconception (WPC). Normative equations and curves of the growth of renal volume were obtained for male and female fetuses and for the whole sample in the second trimester (13–24 WPC) and in the third trimester (25–36 WPC) of gestation. There was no difference between the growth in volume of the right and left kidneys. Fetal kidney volume increases with a more intense rhythm in the early fetal period (13–24 WPC). During the second trimester, there was no difference between the values for renal volume of male and female fetuses. In the third trimester, male fetuses had renal volumes significantly greater than the female fetuses. The normative parameters of renal volume could have practical applications in detection and monitoring of renal anomalies in fetal and perinatal urology.

Key words: Kidney – Fetal kidney – Renal volume – Renal growth – Fetal urology – Renal anomalies

The widespread use of antenatal sonography has increased recognition of anomalies in the fetal urinary tract. Several fetal anomalies, including renal agenesis, obstructive lesions, cystic disease, hypotrophy and nephromegaly may be clinically silent but readily identified by sonography [12, 16]. In utero detection of these anomalies prevents delay in postnatal diagnosis and enables early surgical repair of significant lesions [23].

To aid early detection of renal anomalies, normal growth values must be established. Although some studies have been done on the quantitative development of fetal kidney [1, 3, 9, 17–20], we are not aware of any data on renal volume growth for male and female fetuses in the second and third trimesters of gestation.

The present work aims to provide new information and normative parameters of growth in renal volume during the fetal period.

Materials and methods

We studied 290 fresh kidneys taken from 145 human fetuses (85 male, 60 female) who had died because of premature birth or perinatal asphyxia. All were in an excellent condition of preservation (degree 1 of Steeter [22]), and none of them had any kind of congenital malformation.

The gestational age of the fetuses ranged between 13 and 36 weeks postconception (WPC) and was estimated according to the foot length criterion [1, 2, 6, 11, 14, 18–20] (Table 1).

After classification, the fetuses were perfused through the right common carotid artery with Larssen's preservative solution (formula used in the Cochin Hospital, Paris, France [19]). This solution preserves the main anatomical characteristics of the specimens in their non-fixed condition: color, consistency and dimensions. Moreover, the injection of Larssen's solution dissolves blood clots and restores the amount of fluid in the fetal vascular system.

After perfusion, the kidneys were removed, dissected and weighed in a digital balance (0.001 g precision).

Table 1. Distribution of the fetuses studied by gestational age (in weeks postconception, WPC)

Gestational age WPC	Female	Male	Total (%)
13–16	05	14	19 (13.1)
17–20	14	21	35 (24.1)
21–24	13	17	30 (20.7)
25–28	11	10	21 (14.5)
29–32	11	13	24 (16.6)
33–36	06	10	16 (11.0)
Total	60	85	145 (100.0)

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Table 2. Equations of median growth curves for RV correlated to gestational age (WPC)

Sample	Second trimester	Third trimester
Male	$RV = 1.05 \times 10^{-5} WPC^{4.04}$	$RV = 8.71 \times 10^{-5} WPC^{3.33}$
Female	$RV = 4.68 \times 10^{-2} WPC^{4.31}$	$RV = 4.37 \times 10^{-2} WPC^{1.48}$
Total	$RV = 8.51 \times 10^{-6} WPC^{4.11}$	$RV = 1.20 \times 10^{-3} WPC^{2.55}$

Equations are presented in the form $Y = b \cdot X^k$
$P < 0.001$ for all correlations

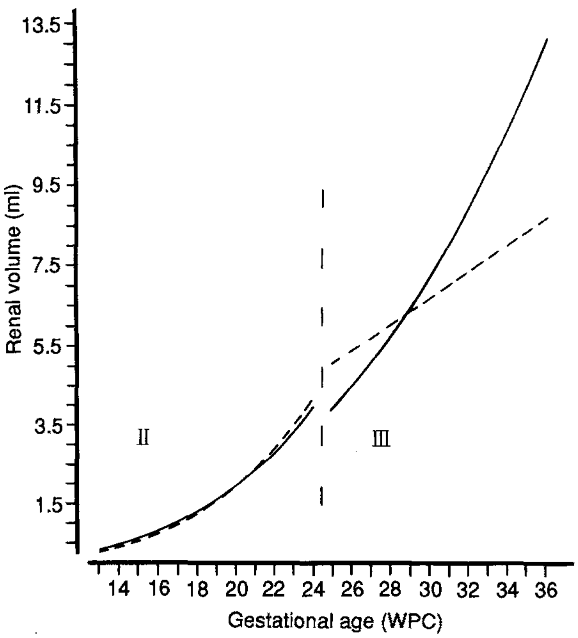

Fig. 1. Growth curves of renal volume (RV) correlated to gestational age in weeks postconception (WPC). This analysis considered males (——) and females (– – –) separately during the second trimester (*II*) and the third trimester (*III*)

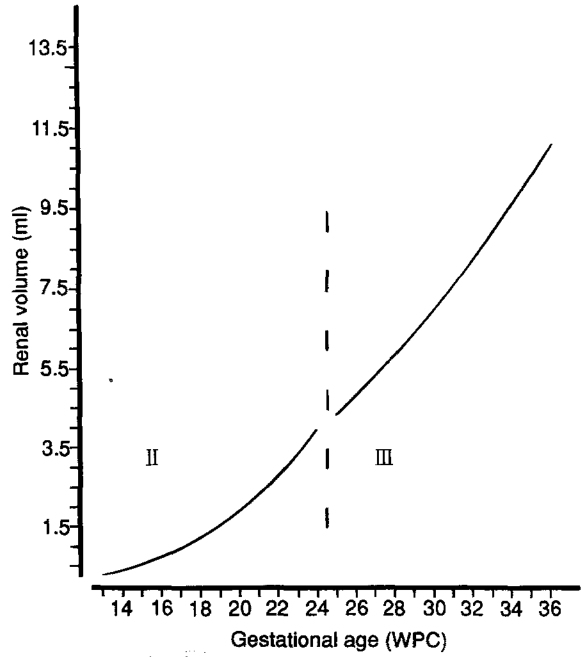

Fig. 2. Growth curves of RV correlated to gestational age (WPC). This analysis took account of the whole sample (male and female fetuses together) during the second trimester (*II*) and the third trimester (*III*)

Estimation of renal volume

The volume of an organ can be estimated by its immersion in water (measurement of water displacement). The volume was considered to be the same as the weight [5, 20], since the fetal kidney is composed of a considerable amount of liquid, its density being similar to the water density (weight = volume × density; water density = 1). When the kidney weight was compared with the volume estimated by means of water displacement, the results were similar. For this reason, the renal volume was estimated by weighing the kidney.

Statistical correlations

To determine the equations for curves of growth in kidney volume, a mathematical model was used which correlates the renal volume (RV) to the fetal gestational age in (WPC). The model is defined by the form: $Y = b \cdot X^k$, *where* Y is the dependent variable (RV) X is the independent variable (fetal gestational age in WPC) and b and k are the parameters to be estimated. These parameters can be interpreted as: b, the Y value when $X = 1$ (i.e. the value for kidney volume when the fetus is at 1 week of gestation); and K, the ratio of kidney growth to variation in gestational age (elasticity) [4, 15, 21, 24]. To estimate the parameters b and k, the data (X and Y) were transformed into logarithms ($\log Y = \log b + k \cdot \log X$), making use of the least-square method possible. To evaluate the statistical significance of this mode, Pearson's r correlation coefficient and Student's t test were used [15]. Statistical comparisons of the estimated equations were performed using Fisher's F test [15].

Results and discussion

The equations of the median growth curves for RV correlated to gestational age (WPC) are presented in Table 2.

Figures 1 and 2 show growth curves for RV correlated to gestational age (WPC) during the second trimester (13–24 WPC) and during the third trimester (25–36 WPC) of gestation. Figure 1 shows curves for male and female fetuses separately and Fig. 2 curves for the whole sample (male and female fetuses together).

Comparison of the volumes obtained for right and left kidneys confirmed that there was no statistically significant difference between the right and left sides during the second or the third trimester (Fischer's test [15]). Thus, the equations and the growth curves are presented considering right and left kidneys together.

Analysis of Figs. 1 and 2 shows that either in the second or in third trimesters, the growth curves have superior concavity. This can be deducted by observing that in the equations presented in Table 2, k is always greater than unity ($k > 1$). This has been termed positive allometric growth or positive allometry [4, 18, 19, 24]. When k coefficients are equal to or close to 1, the corresponding curves are linear, and this situation is termed isometric growth or isometry. When k is less than unity the corresponding curves have inferior concavity; this case is termed negative allometric growth or negative allometry.

The growth curves for the second trimester present greater concavity than those for the third trimester (Figs. 1 and 2), which indicates that the renal volume increases more intensely in the early fetal period (second trimester). This can also be evinced by comparing the values for k, which are greater for the second trimester than for the third trimester (Table 2).

Figure 1 presents growth curves for renal volume separately for male and female fetuses during the second and third trimesters. Analysis of the growth curves for the second trimester shows that they are almost superposed, which indicates that growth is similar in both sexes. Fisher's test [15] confirmed that this similarity was statistically significant. Thus, during the second trimester, growth of fetal renal volume may be evaluated and monitored without taking fetal sex into account (Fig. 2). Nevertheless, analysis of the third-trimester growth curves shows that male fetuses have greater values for renal volume than female fetuses, and this difference was also confirmed as statistically significant. In consequence, during the third trimester, if fetal sex determination is achieved (almost always possible), renal volume must be evaluated and monitored with reference to the specific curves and equations for male and female fetuses separately. The reason for this sex difference in renal development remains unknown. Pedersen [13] used ultrasonography to study the fetal development in utero and found that male fetuses were larger than female fetuses from 12 WPC. He proposed that these differences were probably due to a genetic rather than a hormonal mechanism. Jean-Faucher et al. [8] studied the influence of sex hormones in rat kidneys and concluded that the kidneys from male rats are larger than the kidneys from female rats because of both cellular hyperplasia and hypertrophy. These authors reported that sexual dimorphism in kidney size is not congenital but is programmed by neonatal endogenous androgens.

Gonzales et al. [3], studying the size and the weight as measures of renal growth in fixed fetuses during the third trimester of gestation, reported that left renal growth was more pronounced than right renal growth. This disagrees with our results. Those authors also stated that they did not find any difference between the sexes, which also disagrees with our findings; in fact, the third trimester is precisely the period in which sex differences in fetal kidney growth become apparent [18, 19]. Casey and Carr [1] studied the renal weight growth in 200 fetuses between 6 and 17 WPC and found a faster growth rate in the early fetal period; they also showed that there are no statistically significant differences between right and left kidneys. These findings agree with our results for the second trimester. Holloway et al. [7], studying the renal volume of neonates by ultrasound, reported no difference between the sexes. This finding disagrees with the present observations recorded at the end of the third trimester.

Since the fetal kidney volume can be ascertained by ultrasound in utero [9, 16, 17] by using the ellipsoid volume formula (volume = length $\times$ width $\times$ 0.5236) [7, 9, 10, 16, 17], normative equations and curves for growth of fetal kidney volume could have practical applications in the determination and monitoring of anomalies that alter renal size. These curves could also be used as an ancillary index for determination of gestational age.

In conclusion, during the second and third trimesters of gestation, there was no difference between the growth of right and left kidney volumes, for male or for female fetuses. Fetal kidney volume grows at a faster rate in the early fetal period (second trimester). In the second trimester, male and female fetuses had similar values for renal volume. In the third trimester, male fetuses had significantly greater values than female fetuses for renal volume.

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