Ultrasound Obstet Gynecol 2012; **40**: 659–664
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.11169

Size and volume charts of fetal kidney, renal pelvis and adrenal gland

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KEYWORDS: adrenal gland; fetal; kidney; prenatal diagnosis; renal pelvis; size; ultrasonography; volume

ABSTRACT

Objective *To establish reference curves for size and volume of the fetal kidney, renal pelvis and adrenal gland, as measured using ultrasound from the 15th week of gestation.*

Methods *This was a prospective, longitudinal study of 96 fetuses in low-risk singleton pregnancies, in which we performed serial ultrasound examinations at 4-week intervals. The length and anteroposterior and transverse diameters of both kidneys, the anteroposterior and transverse diameters of the renal pelvises and the length of the adrenal glands were measured three times at each examination, with the average being used for further analysis. Reference charts were constructed using multilevel statistical analysis and comparisons were made with previously published charts derived from cross-sectional data.*

Results *We present nomograms for fetal kidney dimensions and volume, renal pelvis dimensions and adrenal gland length. The new charts show differences in shape and have narrower percentile bands in comparison to previously published reference ranges.*

Conclusions *These new charts of measurements of the fetal kidney, renal pelvis and adrenal gland, from a prospective, longitudinal study, may be useful in the diagnosis and assessment of pathology of the kidney and adrenal gland. Copyright © 2012 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Normal development of the fetal kidneys is crucial to neonatal outcome and knowledge of the normal range of dimensions of the fetal kidney, renal pelvis and adrenal gland is important for the identification of abnormalities.

Various papers on intrauterine renal growth have been published, but many of these studies suffered from methodological issues, such as failing to validate gestational age by measuring crown–rump length[1–7], not covering the whole of the second and third trimesters of pregnancy[4,5,8–14], not measuring the kidney in three dimensions[1,2,4,5,8,14,15] or using preterm infants[16–18] or postmortem specimens[16,17,19,20]. Several studies used a mixture of cross-sectional and longitudinal data[1–3,5–8,10,14,15,18–21].

Only limited data on reference values for fetal adrenal gland measurements have been published[22–28]; no studies covered the entire second and third trimesters and some used only postmortem specimens[22,23]. Moreover, ultrasound-validated gestational age was not used in any of these studies.

The distinction between size and growth is frequently ignored in studies using a mixture of cross-sectional and longitudinal data. Cross-sectional data can only be used for size reference curves, while longitudinal data obtained by measurements of fetuses on a series of occasions may be used for size and growth reference curves[29–32]. There are inevitably some data missing in any longitudinal study, which can cause difficulties when constructing nomograms. This problem can be overcome by the use of multilevel analysis[33], which allows for the dependency of measurements in hierarchically structured data, whereas traditional regression analysis presupposes the independence of observations. Further advantages of multilevel analysis are that it can be used to examine separately the effects of variables relating to different levels (at the same time point) and it can also be used

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Accepted: 23 March 2012

when measurements have been made at different time points.

The aim of this study was to construct reference curves for the fetal kidney, renal pelvis and adrenal gland, based on prospective longitudinal data.

METHODS

One hundred and one women with consecutive low-risk singleton pregnancies were asked, during a dating ultrasound scan (using crown–rump length[34]), to participate in the study. After written informed consent had been obtained, the fetuses were divided into two groups, in order of registration. One half was examined at 16, 20, 24, 28, 32, 36 and 40 weeks of gestation and the other half at 18, 22, 26, 30, 34, 38 and 42 weeks of gestation. Exclusion criteria were: chromosomal or congenital anomalies of the fetus, small-for-gestational age (SGA) or large-for-gestational age at birth (birth weight < 2.3rd or >95th percentile, respectively, for gestational age[35]) and maternal disease that might affect fetal growth (diabetes mellitus or hypertension requiring treatment).

All examinations were performed by one operator (H.D.-E.), using a Toshiba Power Vision 6000, type SSA 370 A (Toshiba, Tokyo, Japan) ultrasound machine, equipped with the 2.8–6-MHz PVM 375 AT multifrequency transabdominal transducer. The length of both left and right kidneys was measured in a sagittal plane with the full length and the renal pelvis visible. The length of each adrenal gland was measured in the same plane by subtracting the length of the kidney from the total length of the kidney including the adrenal gland (Figure 1). Perpendicular to this, in the transverse plane, the largest anteroposterior (AP) and transverse diameters of each kidney were measured by placing the calipers from outer border to outer border. In the same plane, the maximal AP and transverse diameters of each renal pelvis were measured, placing the calipers on the inner borders of the renal tissue. All measurements were made in millimeters and repeated three times. To avoid possible bias, the operator was blinded to the display of previous measurements for each repeat. The three repeat measurements were averaged and stored in a database.

The kidney volume (V) was calculated using the formula for an ellipsoid: $V = (\pi/6) \times L \times D \times TD$, where L = kidney length, D = AP diameter and TD = transverse diameter. Measurements of the dimensions of the kidney and adrenal gland and the calculated kidney volumes from the left and right sides were compared and averaged prior to the construction of reference charts.

Multilevel statistical analysis was performed with the software program Mln (Multilevel Model Project, London, UK)[33] and SPSS, version 15 (IBM Corporation, New York, NY, USA) was used to construct nomograms. The serial measurements of the kidney and renal pelvis were modeled against the gestational age, nested within the dataset of each fetus, resulting in a two-level model. By fitting a model using serial measurements, the influence of random missing values is decreased. Reference charts were constructed and are reported using the mean and SD for the overall population derived from the multilevel modeling.

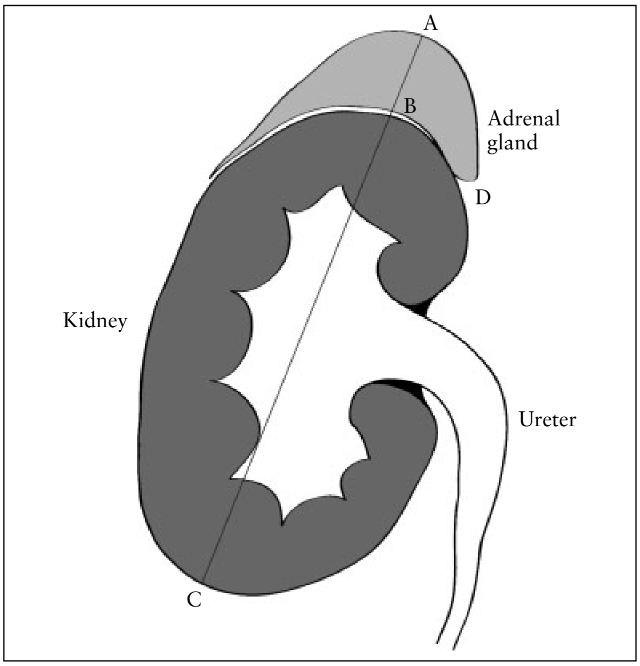

Figure 1 Diagram illustrating our method for measurement of fetal adrenal gland length (AB): kidney length (BC) was subtracted from total kidney length including adrenal gland (AC), i.e. AB = AC – BC. In studies by Hata *et al.*[24,25], fetal adrenal gland size was measured as distance AD.

Reproducibility of measurements

For analysis of intraobserver variation, a single observer (H.D.-E.) obtained two sets of measurements from an additional sample of 30 pregnancies (gestational age range, 17 + 0 to 38 + 4 weeks) and, for analysis of interobserver variation, measurements were obtained in another 20 pregnancies (gestational age range, 18 + 0 to 23 + 0 weeks) by two observers (Observer 1 (L.P.) and Observer 2 (H.D.-E.)). There were no exclusion criteria for this part of the study. Each observer repeated each measurement three times, with the average being used for analysis, as described above. For the evaluation of interobserver variation, the observers were blinded to each other's measurements.

Statistical analysis was performed using SPSS, version 15. Bland–Altman plots[36] were produced to examine bias and agreement in order to determine if there was good consistency between measurements. In addition, Cronbach's alpha (α) and the intraclass correlation coefficient (ICC) were calculated[37].

RESULTS

Five fetuses were excluded due to postnatal findings: two were SGA and three had congenital anomalies (one each of triploidy, club foot and hydronephrosis with AP diameter of the renal pelvis > 10 mm). In all other fetuses, no abnormalities were found on postnatal screening.

In the remaining 96 consecutive low-risk pregnancies, fetal measurements were obtained from both kidneys, both renal pelvises and both adrenal glands at a total of 596 separate examinations across gestation. The median number of scans per pregnancy was six (5.2% of the women had five scans, 68.8% had six scans and 26.0% had seven scans per pregnancy). In some cases the full set of examinations could not be performed because delivery occurred before the planned end of the study. Missing data occurred in some cases because we were not able to measure the renal pelvis in all dimensions ($n = 49$ missing measurements from 596 examinations).

Statistical analysis was first performed separately on measurements from right and left sides; in all cases measurements from each side were virtually identical (Figure S1 online). There was a high correlation between the left and right sides for the following variables: kidney length ($r = 0.985$), AP diameter ($r = 0.953$) and transverse diameter ($r = 0.932$), and adrenal gland length ($r = 0.959$). There was no asymmetry between right and left measurements of AP diameter of the renal pelvis: kappa = 0.642 (Table S1). In only 4/574 comparisons between right and left AP diameters of the renal pelvis was there a difference of > 4 mm between the measurements.

The data for all right and left kidney, renal pelvis and adrenal gland measurements were therefore averaged to obtain the reference charts. In most cases, a quadratic model with random intercept and random linear effect of gestational age gave the best fit (i.e. the intercept as well as the linear effect of gestational age differed between individuals). Details of the reference equations obtained for the mean and SD of each variable are given in Appendix S1 online. The size nomograms of the 5th, 50th and 95th fitted centiles for kidney length and AP and transverse diameters are shown in Table S2, with the corresponding charts in Figure 2a–c. The data for AP and transverse diameters of the renal pelvis are given in Table S3 and Figures 2d and S2, those for the length of the adrenal gland are given in Table S4 and Figure 2e and data for kidney volume are given in Table S5 and Figure 2f.

There was a strong linear correlation between kidney length and adrenal gland length ($r = 0.870$) (Figure S3). The length of the adrenal gland was on average 27% (range, 25–29%) of that of the kidney (ratio 2 : 7) and this relationship did not change with gestational age or kidney size.

Our new size and volume centile charts were compared with charts previously published by Chitty and Altman[38] for kidney length, AP diameter, transverse diameter, AP renal pelvis measurements and kidney volume (Figures S4–S8). Chitty and Altman published the 3rd, 10th, 50th, 90th and 97th centiles for each measurement, and so comparison was made by plotting equivalent centiles derived from our study against their charts. Our charts showed differences in shape and narrower percentile bands in comparison to the previously published reference ranges.

Reproducibility of measurements

All kidney dimensions and adrenal gland length could be measured at all examinations in the pregnancies recruited for the evaluation of measurement reproducibility. A summary of the analysis of intraobserver variation is shown in Table S6. High values were observed for alpha and ICC, with both > 0.9 for all measurements. A summary of the interobserver analysis is given in Table S7. High values were observed for alpha and ICC, > 0.9 and > 0.8, respectively, for all measurements.

DISCUSSION

Longitudinal data obtained by measurements of fetuses on a series of occasions may be used to derive reference curves for size and growth[29–32]. Our charts of the fetal kidney and fetal renal pelvis were derived from longitudinal data obtained from prospective investigations that were carried out specifically for the development of centile charts for assessing renal size at a known gestational age between 16 and 42 weeks of gestation. Several charts of fetal kidney size have been published, but a number of the previous studies had shortcomings in their data collection or suffered from methodological pitfalls and used incorrect methods in their design[1–7,13–15,20,21]. Moreover, our study has the added advantage that the statistical analysis used is able to correct for missing data.

Chitty and Altman[38] obtained their data on fetal kidney size from a cross-sectional study, including approximately 15–20 cases per week, with measurements performed only once for each fetus. The most obvious difference between our kidney size charts and those of Chitty and Altman[38] is the generally narrower ranges that we found. The fact that we repeated each measurement three times at each examination may have resulted in the narrower ranges observed. We found that the increase in renal volume during pregnancy is exponential until birth, while the charts provided by Chitty and Altman[38] suggest that the increase in renal volume tends to slow down at the end of pregnancy. With regards to the dimensions of the fetal renal pelvis, Chitty and Altman[38] published a chart based on cross-sectional data from fetuses measured once for the purpose of the study, but examined only a low number of fetuses at each week of gestation (mean, 7; range, 3–11). Their chart suggests linear growth of renal pelvis size, with a wide range, whereas we found a curvilinear relationship, with no increase in size from 32 weeks onwards and a considerably narrower range (Figure S7).

The adrenal glands are relatively large in the fetus in comparison to early in postnatal life. After delivery, their size decreases rapidly and increases again at the end of the first year of postnatal life, attaining maximum weight and size at adulthood[39]. The fetal adrenal gland has been the subject of only a few previous sonographic investigations[22–28,40], with the latest study published in the early 1990s. Insufficient resolution of equipment at that time resulted in an inability to obtain accurate

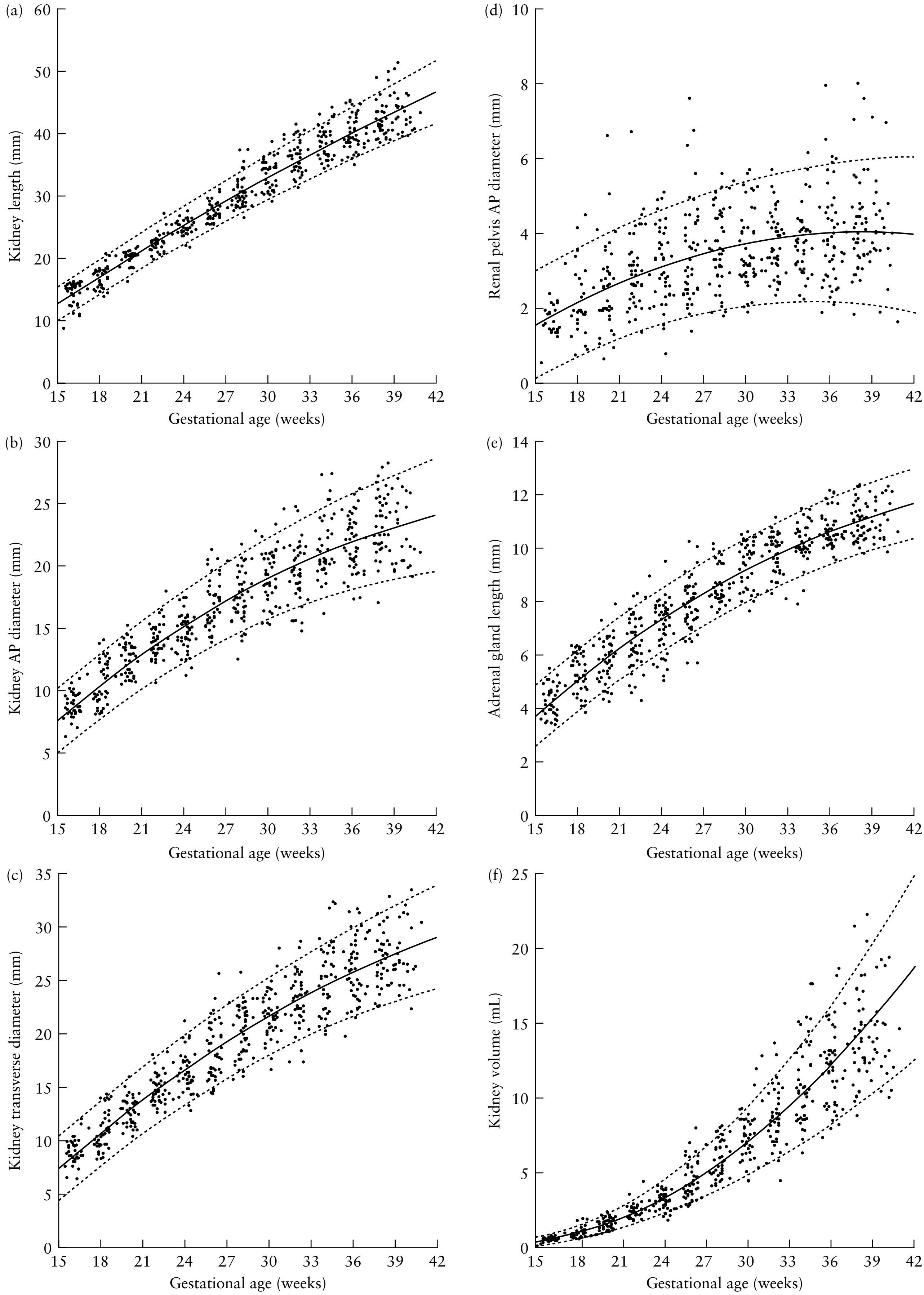

Figure 2 Reference charts of kidney length (a), kidney anteroposterior (AP) diameter (b), kidney transverse diameter (c), renal pelvis AP diameter (d), adrenal gland length (e) and kidney volume (f), showing raw data (•) and fitted 5^{th}, 50^{th} and 95^{th} centiles.

data, especially during the second trimester[24–27,41]. In the early 1980s, Rosenberg *et al.*[28] were able to identify the adrenal glands in only 12% of cases before 26 weeks' gestation and in 90% beyond that age. Around the same period, Jeanty *et al.*[26] were unable to detect the adrenal gland in 30% of cases before 25 weeks' gestation and in 6.5% of cases at term. All previous reference charts were constructed using cross-sectional data, and several charts showed evidence of methodological weaknesses such as the use of postmortem specimens[22,23] or the measurement of only one adrenal gland[27].

We assessed the correlation between adrenal and kidney lengths since this may be of significance in high-risk pregnancies. Naeye[42] found in postmortem examinations that the fetal adrenal glands were relatively more reduced in weight than was body weight in cases of intrauterine growth restriction. Hata *et al.*[24,25] found a decrease in the calculated adrenal gland surface area in growth-restricted fetuses and others have found small fetal adrenal glands when the mother was using glucocorticosteroids because of congenital adrenal hyperplasia[40]. There have been two case reports on the ultrasound diagnosis of congenital adrenal hyperplasia[43,44].

Direct comparison of previously published size charts for the adrenal gland with our own was not possible. Hata *et al.*[24,25] published two studies on this topic, but in one they gave no raw data and in the other we could not use the data because they measured the length of the adrenal gland in a different way from that used in our current study (Figure 1). We chose to measure the size of the adrenal gland in line with the length of the kidney since this measurement can be standardized more easily, with the borders of the adrenal gland being more easily visualized at these points. Jeanty *et al.*[26] gave averaged data with a range for every 5 weeks from 20 weeks' gestation onwards and Lewis *et al.*[27] published data between 30 and 39 weeks' gestation but only provided information on the adrenal gland length in comparison with kidney length and biparietal diameter.

In conclusion, given that renal pathology often presents late in pregnancy, our reference charts for size and volume of the fetal kidney may be useful in cases of diagnostic problems. The same holds for cases of dilatation of the renal pelvis, which is a common sonographic finding in pregnancy. We observed that the ratio of 2 : 7 between the adrenal gland length and kidney length does not change with gestational age, and this finding may also be useful for the detection and evaluation of abnormal growth.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Appendix S1 Multilevel analysis models for calculations for kidney, renal pelvis and adrenal gland size charts

Figure S1 Correlations of left and right kidney length measurements with gestational age and with each other

Figure S2 Size chart of fetal renal pelvis transverse diameter with fitted 5th, 50th and 95th centiles

Figure S3 Scatterplot of data of fetal kidney and adrenal gland length with fitted correlation line

Figures S4–S8 Comparison of centiles obtained in this study and those obtained by Chitty and Altman[38] for fetal kidney length (Figure S4), kidney anteroposterior diameter (Figure S5), kidney transverse diameter (Figure S6), renal pelvis anteroposterior diameter (Figure S7) and kidney volume estimation (Figure S8)

Table S1 Comparison of measurements between right and left renal pelvis anteroposterior diameters

Tables S2–S5 Fitted centiles for fetal kidney length, anteroposterior diameter and transverse diameter (Table S2), renal pelvis anteroposterior and transverse diameters (Table S3), adrenal gland length (Table S4) and kidney volume (Table S5), showing number of fetuses for each week between 16 and 42 weeks of gestation

Tables S6 and S7 Intraobserver (Table S6) and interobserver (Table S7) variation in length and anteroposterior and transverse diameter measurements of kidney and in length of adrenal gland

