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ORIGINAL ARTICLE

# Size and Volume Charts for Fetal Adrenal Gland: A Prospective Study in Indian Population

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**Abstract** The fetal adrenal gland plays a pivotal role in perinatal survival. Because imaging the fetal adrenal gland is not part of routine antenatal ultrasonography (US), there is a paucity of available data about imaging techniques. The purpose of this study was to construct gestational age-wise data for fetal adrenal gland size and volume (2D US measurements) for 20, 21, 22 and 32 weeks of gestation and define a technique to measure the gland ultrasonographically. One year prospective study, at a single centre. 87 consecutive pregnant women with uncomplicated singleton pregnancy were included. Exclusion criteria were multiple pregnancy, maternal complications, congenital anomalies or fetal growth abnormality and a previous child suffering with Congenital Adrenal Hyperplasia (CAH). All measurements were made in 2 dimensional ultrasonography. In coronal sections of the fetal abdomen, fetal adrenal glands were identified just above the upper pole of the kidney to measure length and breadth. With the fetal spine in an anterior position, fetal adrenals were identified on either side of the spine and the width was measured. The gestational age included was 20, 21, 22 and 32 weeks. Both fetal adrenal glands could be visualised and identified in all cases (100%). Length, breadth, width and volume of both the glands for the above gestational ages with 95% confidence limit have been calculated. Antenatal imaging of the fetal adrenal gland can be done by 2D US if indicated.

**Keywords** Fetal adrenal gland · Prenatal diagnosis of CAH · Size and volume charts

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## Introduction

The human fetal adrenal gland is structurally and functionally unique from other species. Through steroidogenesis, it plays a pivotal role in prenatal regulation of intrauterine homeostasis, in fetal development and maturation and also in initiation of parturition [1]. It has an essential role postnatally i.e. production of glucocorticoids, androgens and mineralocorticoids. Appropriate development and function of the fetal adrenal cortex is critical for perinatal survival.

Using various modalities, continuous efforts are being made to understand the biophysiology and pathology of fetal adrenal glands and ultrasonography is one such modality. Ultrasonography is a safe and non-invasive tool for assessment of fetal organs. With the advent of high resolution ultrasonography machines, fetal adrenal glands can be visualized in most of the cases during second and third trimester US examinations, when an attempt is made to do so [2]. However, imaging fetal adrenal glands is not a part of most of routine obstetric ultrasonographic examination guidelines. There is paucity of available data on prenatal imaging of normal and abnormal fetal adrenal gland and therefore, whenever fetal adrenal gland pathology is suspected during ultrasound examination, it often poses a confusing situation [3].

The fetal adrenal gland can be enlarged (adrenomegaly) in various conditions like congenital adrenal hyperplasia, fetal macrosomia due to maternal Diabetes Mellitus or large for dates fetus, overgrowth syndromes like Beckwith-Weidman syndrome and adrenal haemorrhage. Focal

enlargement can occur in conditions like adrenal gland cyst. In rare syndromes like Wolman's, there is bilateral enlargement and calcification of the fetal adrenal gland [4]. Fetal adrenal gland hypoplasia can be seen in anencephaly, Trisomy 18, and congenital X linked adrenal hypoplasia [5]. Knowledge of the normal range of dimensions of adrenal gland is important for suspecting and identification of abnormalities.

Due to ethnicity, racial, physiological, environmental differences amongst the population worldwide, regional Nomograms become necessary. The purpose of this study was to construct gestational age wise data for fetal adrenal gland dimensions and volume (2D US measurements) for an Indian population for 20, 21, 22 and 32 weeks. Obstetric US is performed most commonly during these gestational weeks and there are good chances of picking up adrenal abnormality at this period of time. We also aim at defining a technique to measure the gland when required.

## Material and Methods

This was a prospective study conducted at a single centre in South India which is a tertiary referral centre of ultrasound (mainly obstetric ultrasound). The study period was October 2016 to September 2017. During this study period, 87 consecutive women referred for routine obstetric ultrasound with uncomplicated singleton pregnancy with a gestational age of 20, 21, 22 and 32 weeks were included. Exclusion criteria for the study were women with significant medical history including hypertension, diabetes, hypothyroidism, known adrenal pathology or women on systemic corticosteroids for any conditions. Women with a history of congenital adrenal hyperplasia in previous offspring were also excluded from the study. Similarly, fetuses with major congenital abnormality of any system, suspected fetal growth restriction, large for gestational age fetuses, adrenal pathology and multiple gestations were excluded from the study. Approval for conducting this study was granted by the institutional ethical committee.

## Method

All adrenal measurements were taken by two expert sonologists with over 20 years of experience. All measurements were taken in 2D ultrasonography by a transabdominal method using a multifrequency curvilinear probe of 3.5–5 MHz on high resolution machines.

A coronal section of the fetal abdomen is imaged with the aorta in the midline and both kidneys identified on either side. Fetal adrenal glands were identified in this section as triangular hypoechoic structures just above the upper pole of the kidney. After freezing an optimized image, two measurements were made in this plane. Superoinferior distance (Length) and maximum side to side distance (Breadth). For the third measurement, with the fetal spine in an anterior position, first both fetal renal pelvises were identified, and then moving the probe cephalad, fetal adrenals were identified on either side of the spine as 'rice grain' or lentiform hypoechoic structures with a hyperechoic streak in the centre. The third transverse measurement was made at the thickest portion of the adrenal gland (Width) in this plane [2] Figs. 1, 2.

In all cases, maternal characteristics like height in centimetres and weight in kilograms were documented. Gestational age and fetal biometric parameters were also noted namely Biparietal diameter (BPD), Head circumference (HC), abdominal circumference (AC) and Femur length (FL). The gestational age was corrected as per CRLor HC

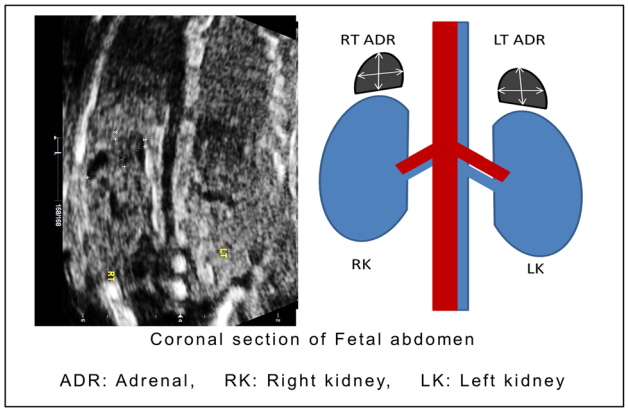


**Fig. 1** Coronal section of the fetal abdomen with aorta in the midline. Both the adrenals are seen on either side just above the kidneys as hypoechoic, triangular structures. The superior-inferior distance is the length and the maximum side to side distance is the breadth.

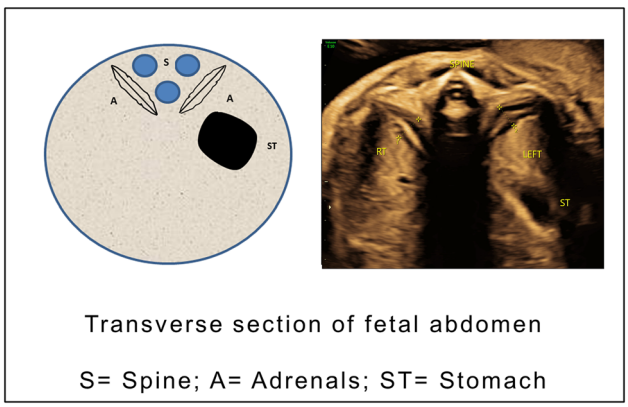


**Fig. 2** Transverse section of the fetal abdomen with spine anterior position. Both the adrenal glands are seen as 'rice grain' on either side of the spine. Width of the adrenal is measured in this plane

**Table 1** Number of cases in each gestational age group and also the mean of Biparietal Diameter (BPD), Head Circumference (HC) and Femur length (FL) for that particular age group

| GA in Weeks | Numbers | Mean biparietal diameter (mm) | Mean head circumference (mm) | Femur length (mm) |
|---|---|---|---|---|
| 20 | 20 | 47 | 174 | 33 |
| 21 | 27 | 51 | 185 | 36 |
| 22 | 16 | 53 | 195 | 38 |
| 32 | 24 | 78 | 274 | 59 |

whenever required, or was calculated by the first day of the last menstrual period where women had regular periods and were sure of dates.

## Results

The study period included 87 consecutive women with an uncomplicated singleton pregnancy.

The gestational ages included were 20, 21, 22 and 32 weeks. These particular gestational weeks were included as our centre is a referral centre for Level II and III obstetric ultrasonography. The expectant mothers are mostly referred between 20 and 22 weeks for targeted scan for fetal anomaly or at around 32 weeks for assessment of interval growth of the fetus.

Both fetal adrenal glands could be visualised and identified in all cases (100%).

More than 15 samples were included in each gestational age group (Tables 1, 2).

The length, breadth and Width were measured in millimetre (mm) for both adrenal glands in all fetuses.

The volume was calculated by the formula:

Mean volume = Mean length × Mean breadth × Mean width × 0.523.

The 95% confidence limit was calculated separately for all the parameters of right and left gland for each group.

**Table 2** Gestational age-wise length, breadth, width and volume of right and left adrenal gland with 95%confidence limit

| Weeks of GA | Right adrenal | Left adrenal |
|---|---|---|
| *Length (95% confidence interval) in Millimetre* | | |
| 20 | 11.2 ± 0.999 | 11.6 ± 0.907 |
| | (10.2 to 12.2) | (10.7 to 12.5) |
| 21 | 11.4 ± 0.871 | 11.5 ± 0.901 |
| | (10.5 to 12.3) | (10.6 to 12.4) |
| 22 | 11.8 ± 0.892 | 11.1 ± 0.823 |
| | (10.9 to 12.7) | (10.3 to 11.9) |
| 32 | 20 ± 1.21 | 19.7 ± 1.15 |
| | (18.8 to 21.2) | (18.5 to 20.8) |
| *Breadth (95% confidence interval) in Millimetre* | | |
| 20 | 5.42 ± 0.565 | 5.38 ± 0.478 |
| | (4.86 to 5.99) | (4.9 to 5.86) |
| 21 | 6.24 ± 0.404 | 6.52 ± 0.385 |
| | (5.84 to 6.64) | (6.14 to 6.91) |
| 22 | 6.97 ± 0.916 | 6.42 ± 0.671 |
| | (6.05 to 7.89) | (5.75 to 7.09) |
| 32 | 8.9 ± 0.896 | 8.77 ± 0.964 |
| | (8 to 9.8) | (7.81 to 9.73) |
| *Width (95% confidence interval) in Millimetre* | | |
| 20 | 4 ± 0.456 | 4.19 ± 0.535 |
| | (3.54 to 4.46) | (3.65 to 4.72) |
| 21 | 4.23 ± 0.438 | 4.5 ± 0.468 |
| | (3.79 to 4.67) | (4.03 to 4.97) |
| 22 | 5.19 ± 0.622 | 5.2 ± 0.681 |
| | (4.57 to 5.81) | (4.52 to 5.88) |
| 32 | 6.16 ± 0.604 | 5.99 ± 0.68 |
| | (5.56 to 6.76) | (5.31 to 6.67) |
| *Volume (95% confidence interval) in Cubic Millimetre* | | |
| 20 | 1.33 ± 0.258 | 1.34 ± 0.202 |
| | (1.07 to 1.59) | (1.14 to 1.54) |
| 21 | 1.67 ± 0.367 | 1.74 ± 0.205 |
| | (1.3 to 2.04) | (1.53 to 1.94) |
| 22 | 2.27 ± 0.51 | 1.94 ± 0.346 |
| | (1.76 to 2.78) | (1.59 to 2.29) |
| 32 | 5.92 ± 1.28 | 5.61 ± 1.65 |
| | (4.64 to 7.2) | (3.96 to 7.26) |

## Discussion

Adrenal glands are vital for human survival, mainly because of steroidogenesis. On ultrasonography, the appearance of the gland resembles a rice grain with hypoechoic surrounding and hyperechoic central line. The adrenal glands are relatively large in the fetus as compared to early postnatal life. After delivery, their size decreases rapidly and increases again at the end of first year of postnatal life, attending maximum size and weight of adulthood [3]. Congenital adrenal hyperplasia (CAH) is one of the common pathological conditions causing adrenomegaly in fetal life. Classic CAH can present with life threatening salt wasting and may prove fatal if undiagnosed and untreated. If diagnosed and treated early, the condition has favourable outcome and can prevent morbidity and mortality [6, 7]. During the prenatal period, bilaterally

enlarged fetal adrenal glands can be the only marker for CAH [8]. Fetal adrenomegaly can be seen in few other conditions as well, but all of them are not life threatening.

Fetal adrenal glands imaging has not gained much popularity even in the era of high resolution imaging, though, various efforts have been made to image the adrenal glands and have been subjected to few sonographic investigations.

In early 1980, Rosenberg et al. tried to image the glands but could identify than in only 12% cases before 26 weeks of gestation and 90% of cases beyond this age [9]. In 1983, Jeanty et al. established the size chart for fetal adrenal glands from 20 to 40 weeks of gestation but the sample size was only 46 patients out of which the gland could be identified in only 70% cases [2]. Bronstein et al. in 1993 imaged fetal adrenal between 12 and 17 weeks of gestation by transvaginal ultrasonography and stated that there is a linear progressive growth of fetal adrenal gland between 12 and 17 weeks of gestation. Establishing nomograms with post-mortem samples was not feasible after Naeye et al. found that in post-mortem examinations fetal adrenal glands were relatively reduced in weight. Also the specimens were of fetuses with some pathology or unexplained deaths and nomogramic data should be derived from healthy fetuses of uncomplicated pregnancies. Vuuren et al. in 2012 published size chart for fetal adrenal gland. In this study they followed up 100 pregnant women every 4 weeks and charts for length of adrenal gland were established. However, every woman had to undergo Sonography 6–7 times during pregnancy, which increases the cost of the study [3]. Recently, Jamigorn et al. in 2017 created nomograms for whole fetal adrenal gland and fetal zone but again included gestational age groups between 16 and 24 weeks only. [10].

Our study is the first of its type in South India. Due to high resolution imaging, we in our study could identify both adrenal glands in all the cases. We have got a reasonable sample size of 87 and we have tried establishing data for 20, 21, 22 and 32 weeks of gestation for fetal adrenal gland, which is the most common period during pregnancy to get an obstetric USG done. The appearance of the adrenal on ultrasonography and the technique of imaging have already been discussed. However, imaging fetal adrenal glands does need training, practice and patience. In our study it was done by sonologists having minimum 20 years of experience in fetal imaging.

There are other methods described in the literature for measurement of fetal adrenal gland. Van Vuuren measured the length of each adrenal gland by subtracting the length of the kidney from the total length of the kidney including the adrenal gland and plotted nomograms for fetal adrenal gland length [3]. However, owing to the pyramidal shape of the gland, Nomograms for volume of the gland should be more appropriate and hence, we have measured the gland in three dimensions by the technique described above. A similar technique has been mentioned by Jeanty et al. [2].

Unfortunately, we could not get a minimum of 15 cases for all gestational age groups. The uneven distribution of cases could have caused a minor error in the present result as well and more studies with more sample size and even distribution of cases are beneficially warranted. However, in a way this distribution could be useful because 20–22 weeks and 32 weeks are worldwide most accepted and common period of sonographic evaluation of the fetus and chances of picking up a pathology including adrenal pathology are high during this time. In our study we have got a reasonable sample size for the above mentioned gestational period and hence, these values could be reliable at least for these gestational periods.

## Limitation of Our Study and Future Scope

Unavailability of good sample size for gestational weeks other than those mentioned was a major limitation of our study. Nevertheless, this can be considered a pilot study and more comprehensive prospective studies with a larger sample size and equal distribution of cases can be considered.

Technical difficulties like maternal habitus, reduced liquor or fetal position may be encountered while imaging fetal adrenal glands.

Also with advent of 3 dimensional ultrasonography calculating volume of fetal adrenal gland using 3D technique could be a future prospect.

## Conclusions

Imaging fetal adrenal glands during prenatal obstetric ultrasonography is possible and easy when proper technique is followed. Adrenal gland measurement should be conducted when warranted as it may be the only pointer for adrenal pathology like CAH. The data of our study could be used as reference values. However, further trials with a larger sample size are warranted.

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**Compliance with Ethical Standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethics Approval** Approval for conducting this study was granted by Institutional ethical committee.

**Availability of Data and Material** Available on request.

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