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Original Article

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Sonographic Evaluation of Normal Fetal Adrenal Gland Size in Second and Third Trimester

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ABSTRACT

Background: This study was conducted to delineate a standard nomogram for fetal adrenal gland dimensions in an Indian cohort and to examine the relationship between fetal adrenal gland and kidney lengths.
Methods: Prior to the commencement of the study, approval was sought from the ethical committee, and informed consent was acquired from 123 expectant mothers attending the VIMS & RC's Radio-diagnosis department between 18 and 37 weeks of gestation. These participants underwent ultrasonography using a curvilinear transducer 2-6 MHz on a Philips Affiniti 50G machine. Sagittal and coronal views were used to record the maximum dimensions of both adrenal glands. Thereby, a reference range for the adrenal gland size during the second and third trimesters was deduced.
Results: During 18-24 weeks, measurements for the right adrenal gland were: medial limb (1.01 * 0.51), body (0.16 * 0.35), lateral limb (1.02 * 0.51), with a concurrent kidney size of 19.16± 1.95 mm. For the left adrenal gland: medial limb (1.01 * 0.49), body (0.16 * 0.34), lateral limb (1.01 * 0.5), and kidney size 19.8± 1.52 mm.For 25-30 weeks, right adrenal gland measurements were: medial limb (1.08 * 0.5cm), body (1.34 * 0.65cm), lateral limb (1.79 * 0.8cm), with kidney size being 25.83± 1.64 mm. The left adrenal gland revealed medial limb (1.08 * 0.81cm), body (1.34 * 0.65cm), lateral limb (1.8 * 0.8cm), and kidney size at 26.07± 1.46 mm.From 31-35 weeks, the right adrenal gland dimensions were: medial limb (2.34 * 1.13cm), body (1.75 * 0.85cm), lateral limb (2.29 * 1.1cm), and kidney size at 31.57± 0.67 mm. The left adrenal gland showed medial limb (2.3 * 1.04cm), body (1.8 * 0.86cm), lateral limb (2.34 * 1.19cm), and kidney size at 32.03± 2.45 mm. Lastly, between 36-40 weeks, the right adrenal gland measurements were: medial limb (2.61 * 1.31cm), body (2.32 * 1.06cm), lateral limb (2.58 * 1.27cm), and kidney size was 35.36± 1.61 mm. The left adrenal gland had medial limb (2.6 * 1.3cm), body (2.33 * 1.07cm), lateral limb (2.6 * 1.32cm), with a kidney size of 35.33± 1.51 mm.
Conclusion: he study, a cross-sectional analysis conducted in the Radio-diagnosis department at Vydehi Institute of Medical Sciences and Research Centre, Bangalore, successfully established a standard nomogram for fetal adrenal gland dimensions in an Indian cohort during the second and third trimesters. Additionally, the established fetal renal to adrenal ratio validated and enriched the derived data.

Key Words: *Sonographic Assessment, Fetal Adrenal Gland Size, Nomogram, Indian Population, Fetal Renal to Adrenal Ratio*

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INTRODUCTION

Adrenal glands are paired glands located in the suprarenal region which perform a vital role in the body metabolism by secreting various steroid hormones and neurotransmitters.[1] The adrenal gland development is interesting and peculiar. Studies on foetal supra renal glands help in understanding the embryology of Suprarenal glands and are also useful in obstetrics, perinatology and foetopathology.[1]

The two main parts of the adrenal gland have different roles. The outside adrenal cortex, the definitive zone, produces multiple glucocorticoid hormones including cortisol that regulates the blood glucose and plays a role in foetal metabolism. The inside core, known as the fetal zone, produces dehydroepiandrosterone sulphate (DHEAS) which stimulates maternal parturition.[2]

Normal development of the fetal kidneys is also crucial to neonatal outcome and knowledge of the normal range of dimensions of the fetal kidney and adrenal gland is important for identification of abnormalities. Many causes have found to result in variation of size of adrenal gland and consequent change in renal: adrenal gland ratio. Thus, imaging plays a critical role in determining the normal baseline reference range of adrenal gland and to differentiate normal from abnormal pathologies.[2]

Risk factors in pregnancy like maternal diabetes and hypertension impair the growth of adrenal glands3. The nomograms of adrenal glands observed by ultrasonography are of clinical importance and facilitates in planning prevention and management of a foetus in high-risk pregnancies. This requires a feasible and repeatable screening.[3]

Imaging of adrenal glands help in evaluating common abnormal conditions like adrenal hemorrhage/calcification and adrenal gland hyperplasia which is seen as glandular enlargement with maintained cortico-medullary zone differentiation.[4,5]

Foetal adrenal gland size has a positive correlation with gestational age and estimated body weight .[6] Only limited data on reference values for fetal adrenal gland measurements have been published. Not many studies covered the entire second and third trimesters and some used only postmortem specimens.[7] There still seems a lacuna in literature, hence this study was undertaken.

AIMS & OBJECTIVES

1. To establish a nomogram for normal fetal adrenal gland size in Indian population
2. To correlate the foetal adrenal gland length with foetal kidney length.

METHODOLOGY

* **Study setting** : The present study was carried out in Vydehi Institute of Medical Sciences and Research Centre in Bengaluru.
* **Study population**:
  Pregnant women in their second and third trimester referred to the Department of Radio-diagnosis from the department of Obstretics and Gynaecology at Vydehi Institute of Medical Sciences and Research Centre were included in the study
* **Study design:**
  Thepresent study was carried out asacross sectional prospective study**.**
* **Duration of study:**
  Overaperiod of18months between March 2021-July2022.
* **Inclusion criteria:**

1. Patients >18 years
2. Gestational age between 18 and 37 weeks confirmed by ultrasound

* **Exclusion criteria:**

1. <18 years
2. Changes in fetal growth (estimated fetal weight below the 10th percentile or above the 90th percentile)
3. Chronic disease in the mother (arterial hypertension, pregestational diabetes mellitus, gestational diabetes mellitus, gestational hypertension).
4. K/c/o Congenital adrenal hyperplasia previously treated with glucocorticoids.
5. Fetal adrenal anomalies (adrenal masses/ haemorrhage/ hyperplasia).
6. Patients on corticosteroids
7. K/c/o fetal ectopic kidney, unilateral renal agenesis and large renal cysts

Study methods

* Patients admitted during study period were screened for eligibility to be included in the study based on the study inclusion and exclusion criteria. Eligible patients were informed and explained about the study and were also provided with a patient information form of the study. An informed consent was taken from the patients willing for participating in the study.
* Institutional Ethical Committee clearance was obtained prior.
* The data was collected using a pre-tested proforma (attached) which included details like demographic data, clinical symptoms, clinical profile along with history, examination and investigations.
* They were subjected to ultrasound using a curvilinear transducer 2-6 MHz of Philips Affiniti 50G machine.
* Foetal adrenal gland size was estimated on ultrasound and a reference range was established.
* Maximum thickness of the body, the medial and the lateral limbs were measured in sagittal and coronal planes.

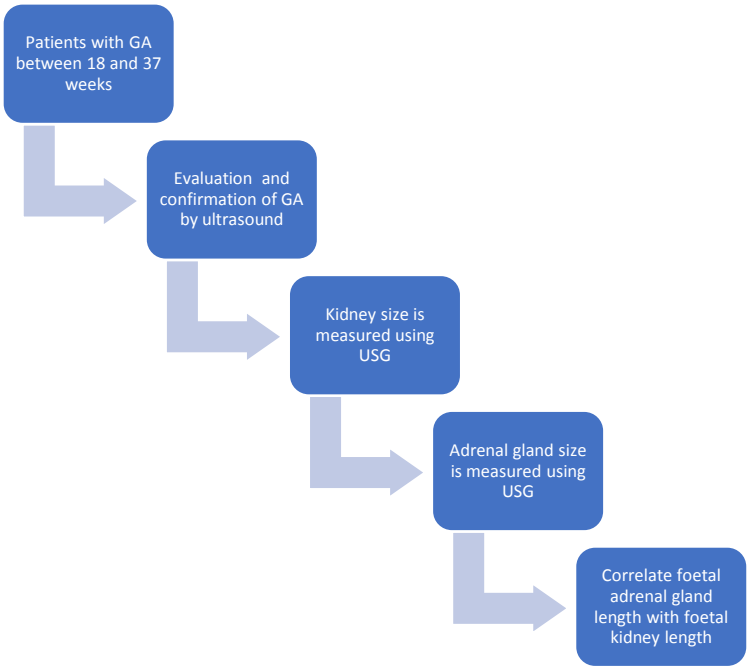

Figure 4:Data collection methodology

SAMPLE SIZE OF ESTIMATION

N = [z 1-α/2 + z1-β/ c]2

Where

N = required sample size

Z1-α/2 = 2.58 at 99 percent confidence interval.

Z1-β = 0.84 at 80 percent power.

C= 0.5 X ln [1+ r /1-r]

r = correlation coefficient (0.3)

C=0.5 X ln [1+ 0.3 /1-0.3]

C= 0.3049

N= [2.58 +0.84/0.3094]2

A sample size of 123 for the study to have a power of 80% and 95% confidence levels.

TECHNIQUE:

Axial and sagittal images of adrenal glands are taken. Images are well analyzed to visualize both adrenal glands separately and in relation to other structures. Maximum length of the adrenalglandis measured involving the body, medial limb and lateral limb. Maximum width of the body is taken at the level of junction of body and both limbs . Maximum width of the limbs are measured perpendicular to the longaxis of gland in axial images.

STATISTICAL ANALYSIS

The collected data was coded, entered into Microsoft excel work sheet and exported to SPSS. Data was analysed using statistical package for social sciences (SPSS) version 21.Data collected was presented in the form of tables, means, percentages and diagrams.

RESULTS

Table 1: Distribution according to gestational age

Gestational age	Frequency	Percent
18- 24 weeks	25	20.3%
25- 30 weeks	30	24.4%
31- 35 weeks	35	28.4%
36- 40 weeks	33	26.9%
Total	123	100%

Table 1 :shows the gestational age distribution , 20.3% were between 18- 24 weeks, 24.4% were between 25- 30 weeks, 28.4% were between 31- 35 weeks and 26.9% were between 36- 40 weeks.

Table 2: 18- 24 weeks

Adrenal gland	Right (L*W)(cm)	Left (L* W)(cm)
Medial limb	1.01* 0.51	1.01* 0.49

Body	0.16* 0.35	0.16* 0.34
Lateral limb	1.02* 0.51	1.01* 0.5
Kidney (mm)	19.16± 1.95	19.8± 1.52
Ratio between kidney & adrenal gland (L)	9.4: 1	9.8: 1

L: length W: width mm: Millimetercm: Centimeter

Table 2 shows the adrenal gland measurements during the 18- 24th week were, in the right adrenal gland the medial limb was 1.01* 0.51, body was 0.16* 0.35, lateral limb was 1.02* 0.51 and the kidney size was 19.16± 1.95 mm.
In the left adrenal gland, the medial limb was 1.01* 0.49, body was 0.16* 0.34, lateral limb was 1.01* 0.5 and the kidney size was 19.8± 1.52 mm.

Table 3: 25- 30 weeks

Adrenal gland	Right (L*W) (cm)	Left (L* W) (cm)
Medial limb	1.08* 0.5	1.08* 0.81
Body	1.34* 0.65	1.34* 0.65
Lateral limb	1.79* 0.8	1.8* 0.8
Kidney (mm)	25.83± 1.64	26.07± 1.46
Ratio between kidney & adrenal gland (L)	9: 1	9.05: 1

L: length W: width mm: Millimeter cm: Centimeter

Table 3 shows the adrenal gland measurements during the 25- 30th week were, in the right adrenal gland the medial limb was 1.08* 0.5cm, body was 1.34* 0.65cm, lateral limb was 1.79* 0.8cm and the kidney size was 25.83± 1.64 mm. In the left adrenal gland, the medial limb was 1.08* 0.81cm , body was 1.34* 0.65cm, lateral limb was 1.8* 0.8cm and the kidney size was 26.07± 1.46 mm.

Table 4: 31- 35 weeks

Adrenal gland	Right (L*W) (cm)	Left (L* W) (cm)
Medial limb	2.34* 1.13	2.3* 1.04
Body	1.75* 0.85	1.8* 0.86
Lateral limb	2.29* 1.1	2.34* 1.19
Kidney (mm)	31.57± 0.67	32.03± 2.45
Ratio between kidney & adrenal gland (L)	6.8: 1	6.9: 1

L: length W: width mm: Millimeter cm: Centimeter

Table 4 shows the adrenal gland measurements during the 31st- 35th week were, in the right adrenal gland the medial limb was 2.34* 1.13cm, body was 1.75* 0.85cm, lateral limb was 2.29* 1.1cm and the kidney size was 31.57± 0.67 mm.
In the left adrenal gland, the medial limb was 2.3* 1.04cm, body was 1.8* 0.86cm, lateral limb was 2.34* 1.19cm and the kidney size was 32.03± 2.45 mm.

Table 5: 36- 40 weeks

Adrenal gland	Right (L*W)(cm)	Left (L* W)(cm)
Medial limb	2.61* 1.31	2.6* 1.3
Body	2.32* 1.06	2.33* 1.07
Lateral limb	2.58* 1.27	2.6* 1.32
Kidney (mm)	35.36± 1.61	35.33± 1.51
Ratio between kidney & adrenal gland (L)	7.2: 1	6.7: 1

L: length W: width mm: Millimeter cm: Centimeter

Table 5 shows the adrenal gland measurements during the 36th- 40th week were, in the right adrenal gland the medial limb was 2.61* 1.31cm , body was 2.32* 1.06cm , lateral limb was 2.58* 1.27cm and the kidney size was 35.36± 1.61 mm.

In the left adrenal gland, the medial limb was 2.6* 1.3cm , body was 2.33* 1.07cm, lateral limb was 2.6* 1.32cm and the kidney size was 35.33± 1.51

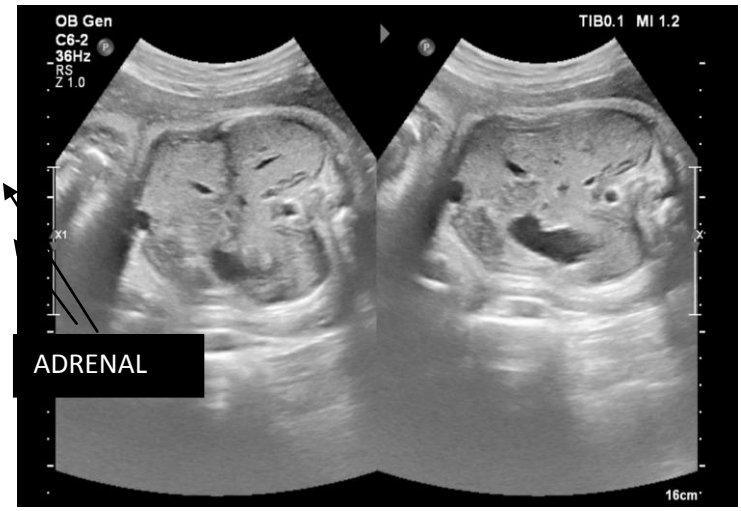

Fig 1 : In a 34 weeks POG with no known comorbidities ,axial USG images of abdomen shows bilateral adrenal glands.

DISCUSSION

The present study was carried out as a cross sectional study among pregnant women in their second and third trimester who underwent antenatal USG In the current practice, assessing the adrenal gland size is mostly a subjective attempt due to lack of sufficient data in the Indian population. Development of normometry of fetal adrenal gland width and length in Indian population with the help of USG will be beneficial for the identification of abnormal adrenal size in borderline cases and management of pregnancy outcome.

During the intrauterine life of a foetus, the size and shape of the normal adrenal gland seems to be dynamic . Gestational age plays a pivotal role in the same. It is important to know the normal range of adrenal gland thickness to distinguish between the normal and abnormal adrenal gland thickness. Hence the above study was conducted to establish fetal adrenal gland size in normal Indian population.

In the current study, 20.3% were between the GA of 18 - 24 weeks, 24.4% were between GA of 25 - 30 weeks, 28.4% were between GA of 31 - 35 weeks and 26.9% were between GA of 36 - 40 weeks

Our study reported that according the adrenal gland measurements during the 18- 24th week, in the right adrenal gland the medial limb was 1.01 * 0.51, body was 0.16 * 0.35, lateral limb was 1.02 * 0.51 and the kidney size was 19.16± 1.95 mm. In the left adrenal gland, the medial limb was 1.01 * 0.49, body was 0.16 * 0.34, lateral limb was 1.01 * 0.5 and the kidney size was 19.8 ± 1.52 mm.

The adrenal gland measurements during the 25 - 30th week were, in the right adrenal gland the medial limb was 1.08 * 0.5, body was 1.34 * 0.65, lateral limb was 1.79 * 0.8 and the kidney size was 25.83 ± 1.64 mm. In the left adrenal gland, the medial limb was 1.08 * 0.81, body was 1.34 * 0.65, lateral limb was 1.8 * 0.8 and the kidney size was 26.07 ± 1.46 mm.

The adrenal gland measurements during the 31st - 35th week were, in the right adrenal gland the medial limb was 2.34 * 1.13, body was 1.75 * 0.85, lateral limb was 2.29 * 1.1 and the kidney size was 31.57 ± 0.67 mm. In the left adrenal gland, the medial limb was 2.3 * 1.04, body was 1.8 * 0.86, lateral limb was 2.34 * 1.19 and the kidney size was 32.03 ± 2.45 mm.

The adrenal gland measurements during the 36th - 40th week were, in the right adrenal gland the medial limb was 2.61 * 1.31, body was 2.32 * 1.06, lateral limb was 2.58 * 1.27 and the kidney size was 35.36 ± 1.61 mm. In the left adrenal gland, the medial limb was 2.6 * 1.3, body was 2.33 * 1.07, lateral limb was 2.6 * 1.32 and the kidney size was 35.33 ± 1.51 mm.

Here we have systematically compared our study results with similar studies done.

The study by Eric R. Rosenberg, et al.,[4] was a prospective study done in 75 consecutive pregnant women at 15-40 weeks of gestation referred for obstetric sonography with an aim to determine the morphology of the fetal adrenal at different stages of pregnancy. Results showed that the patients were in the GA range of 15 to 40 weeks with a mean GA of 28.6 weeks 52. Earlier in gestation, the adrenal gland was less distinctly visualized .But beyond 32 weeks, the pattern of an anechoic limb with a distinct echogenic core was seen. Consistently identical planes of section from patient to patient were impossible to attain due to fetal motion and limb positions; therefore, precise measurements of the length of

the gland could not be obtained. However, the average thickness was 4.5 mm. The gland was found in 12% of fetuses of less than 26 weeks gestation and 90% of fetuses of more than 26 weeks. The gland characteristically has two long limbs that are relatively anechoic (thought to be the fetal zone of the cortex) and a central echogenic line in each limb (presumed medulla). The changes seen in the adrenal gland as pregnancy progresses are reviewed and correlated with the adrenal glands in infants 52. These characteristics of the participants of this study were similar to those of the current study participants.

The study by Mattawan Jamigorn, et al.,[5] was aimed to create nomograms of the whole foetal adrenal gland and the foetal zone at 16 – 24 weeks of gestation in the Thai population, and to evaluate the relationships between the gestational age and the whole foetal adrenal gland and the foetal zone. Study showed a linear correlation between gestational age and the length, width and depth of the whole foetal adrenal gland at 16–24 weeks of gestation. A linear correlation was also found between gestational age and the length, width and depth of the foetal zone at 16 – 24 weeks of gestation.

This study shows the linear growth of the foetal adrenal gland and foetal zone from 16 – 24 weeks of gestation. These characteristics of the participants and results of this study were similar to those of the current study.

The prospective cohort study conducted by Noochanart Pattanapanyasat, et al.,[6] at the antenatal care unit of Rajavithi hospital from October 2018 to August 2019 among 286 singleton pregnant women at the gestational age of 25 to 37 weeks was aimed to identify the average measurements for the fetal adrenal gland and examine the relationship between the fetal adrenal gland sizes at different gestational ages between 25 and 37 weeks of gestation. Findings showed that the mean maternal age was 27.62 ± 5.50 years, mean pre-pregnancy BMI was 21.57 ± 3.00 kg/m2 , mean GA at delivery was 38.5 ± 1.00 weeks and mean birth weight was 2982.08 ± 355.09 grams 51. These characteristics of the participants of this study were not similar to those of the current study participants due to variation in the sample size and inclusion criteria. However, the study concluded that whole fetal adrenal gland and the fetal zone were enlarged correspondingly with GA and was visible and measurable in all planes during the prenatal period between 25 and 37 weeks of gestation when using a two-dimensional ultrasound. The results of this study was seen to be in concordance with our study.

The prospective cross-sectional study by Talita Micheletti Helfer, et al.[7] on 204 normal singleton pregnancies between 24 and 37 + 6 weeks of gestation was aimed to establish reference ranges of the fetal adrenal gland (AG) and fetal zone (FZ) volumes using three-dimensional ultrasound [54]. This study concluded that mean results of fetal AG and FZ values were 0.42 cm3 (0.04-1.22) and 0.10 cm3 (0.02-0.47) respectively. The best-fit quantile regression models for fetal AG and FZ volumes as the function of GA were in first-degree models: AG = -0.937 + 0.041 × GA (R2 = 0.124) and FZ = -0.201 + 0.009 × GA (R2 = 0.127), respectively. The reference ranges of AG and FZ volumes using 3DUS between 24 and 37 + 6 weeks of gestation were established and exhibited good repeatability . These characteristics of the participants of this study were similar to those of the current study participants.

In our study we included 123 patients between 18 and 37 weeks of gestation and attempt was made to set a baseline reference range for the normal fetal adrenal gland in Indian population. Hence total of 246 adrenal glands were studied in our study.

One drawback in our study was the non-inclusion of fetal adrenal volume. But as various studies have already established that parameter, we sought to include fetal adrenal to renal ratio as a variable parameter for assessment which was not done in Indian population or in prior studies.

Due to limited literature found in regards to this topic, we have contributed to the future research.

CONCLUSION

The present study is a prospective cross- sectional study conducted in the department of Radio- diagnosis at Vydehi Institute of Medical Sciences and Research Centre, Bangalore. with a purpose to establish a nomogram of normal fetal adrenal gland size in Indian population.

The study was done from March 2021 to July 2022. A total of 123 subjects were included in the study. After obtaining consent from all the subjects' detailed history and clinical examination was done and noted using a pre tested questionnaire.

During the second and trimester subject's ultrasound was done using curvilinear transducer 2-6 MHz of Philips Affiniti 50G machine to measure the maximum thickness of the body, the medial and the lateral limbs in sagittal and coronal planes as well as calculating the kidney to adrenal ratio.

We have established the normogram of fetal adrenal size for 2nd and 3rd trimester gestational age as well as provided a comprehensive analysis regarding the same.

In addition, fetal renal to adrenal ratio was given to further demonstrate and validate the above.

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