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Original Research Paper

Medicine

# "FETAL ADRENAL GLAND VOLUME IN PREDICTING PRETERM LABOUR"

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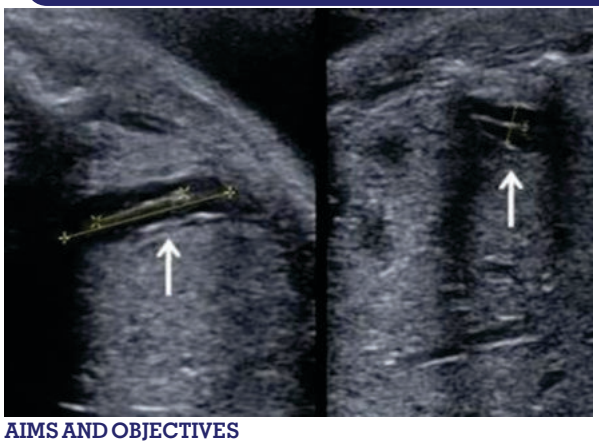
**KEYWORDS :**



## AIMS AND OBJECTIVES

To determine the role of fetal adrenal gland measurements as a marker for onset of labour.

## INTRODUCTION

Placental clock' plays a pivotal role in interrupting theuterine quiescence and thus initiating a cascade of eventsleading to onset of labor [1, 21.The placental clock worksthrough its mediator placental corticotrophin-releasinghormone (CRH), which in turn causes activation (andenlargement) of the fetal adrenal gland.This knowledgeimparts a clue that fetal adrenal gland measurement inpregnancy can be used as a noninvasive marker for onset oflabor.This concept has been investigated and found usefulin prediction of preterm labor [3, 4].As the psychosocial structure of the society is changing.we find increasing number of women who are interested inprediction of spontaneous onset of labor, even at term. Inthe present scenario, a clinical cervical asses sment or anultasonographic cervical length measurement is used forthe same.We hypothesize that a measurement of adrenalgland volume can predict a preterm as well as a term laborwith same efficacy as the final mechanism and "placentalclock' theory holds good for both.

## MATERIALS AND METHODS

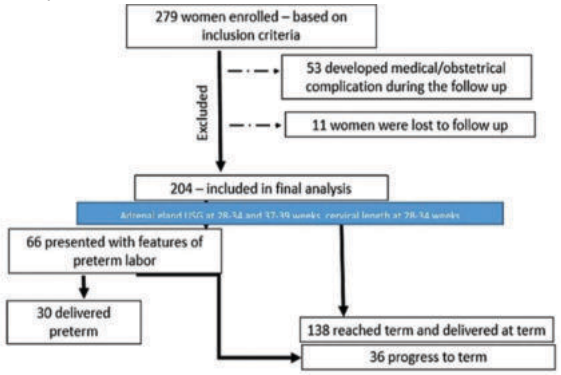
This prospective observational study was conducted at atertiary care center affiliated to a medical university, overaperiod of 2 years (September 2020 - August 2022).Theproject followed ethical guidelines of the institutionalreview board and was approved by Ethics Committee, NSCB Medical College,Jabalpur, India.Women with uncomplicated singleton pregnancy whopresented in our antenatal clinic between 28 and 34 weeksof gestation and were planning to come for follow-up anddelivery were recruited. Cases with any medical or obstetric complication were excluded. All participants wereprovided with a study information sheet, and they wereallowed to ask questions regarding the study and theirparticipation. A written informed consent was thenobtained.Demographic details, obstetric history, examinationfindings, and investigation results of women enrolled wereof recorded in a standard pro forma. Gestational age wasdetermined according to the last menstrual period, when itagreed with first trimester ultrasound examination. Otherwise, only the later was considered for the same.All women, who consented to participate in the study.were subjected to 2D ultrasonographic measurement of thecorrected fetal adrenal gland volume (cFAGV) and fetaladrenal zone parameters including the width ratio anddepth ratio at 28-34 weeks. Additionally. these womenalso underwent a transvaginal ultrasonographic cervicallength (CL) measurement.The cohort was followed up toterm, and a reassessment of cFAGV and fetal adrenal zoneparameters was repeated between 37 and 39 weeks.Women who presented with features of preterm labor(before 37 completed weeks) underwent a scan at the timeof presentation to record cFAGV and fetal adrenal zoneparameters.Details of ultrasonographic imaging used for all caseswere: Philips HD 11 XE, 2 D Ultrasound Machine (manof ufactured in USA), model number 989605325 131.


To avoid the bias, all patients were imaged by a singlesonographer.To obtain measurements, the right fetal adrenal glandwas imaged, as it is better visualized, compared to leftadrenal gland which is usually obscured by the rib shadow.The fetal adrenal gland is visualized as a hypoechoic,for inverted V'-shaped structure/cap-like structure abovekidney. Both transverse and sagittal planes were obtained.laborThe length of the gland was measured in the sagittal plane,whereas the width and depth of the adrenal gland weremeasured in the transverse plane (Fig. la, b).The fetal adrenal zone is visualized as hyperechoiccenter in the fetal adrenal gland.The width and depth of thefetal adrenal zone were noted in the transverse plane(Fig. ).The fetal adrenal gland volume was calculated using theovera ellipsoid formula (0.523 x length x width x depth).Corrected fetal adrenal glaGV) wasvolumeobtained from dividing fetal

adrenal gland volume by theestimated fetal weight, so as to make it a gestational-age-independent factor.To measure the cervical length, standard criteria werefollowed. A transvaginal probe (5-9 MHz) was used, andclosed portion of the cervix from the internal to external oswas measured.or

### Statistical Analysis

Data collection, computation, and analysis were done usingSPSS 16 software. Demographic details were expressed asmeans. cFAGV, fetal adrenal zone parameters, and thecervical length were expressed as medians. Mann-WhitneyU test and Wilcoxon signed-rank test were used to comparethe medians. Significance was assumed at ap value of lessthan 0.05. Receiver operated curve (ROC) was plotted todetermine the cutoff values, and the sensitivity and specificity were noted and area under the curve of 0,9-l:excellent predictor, 0.8-0.9: good predictor, 0.7-0.8: fairpredictor, 0.6-0.7: poor predictor, 0.5-0.6 fails to predict,were assumed.




## RESULTS

Two hundred and sixty-eight pregnant women wereenrolled in the study at 28-34 weeks' antenatal visit.During the follow-up period, 53 women had to be excludedas they developed gestational hypertension or preeclampsia(28), gestational diabetes (13). intrauterine growth restric-tion (5), preterm pre-labor rupture of membranes (3), pla-centa praevia (2), and severe upper respiratory tractinfection (2). Eleven women were lost to follow-up.Thus,a total of 204 women were included in the final analysisstudy. Out of these, 138 women reached term without anycomplication, whereas 66 (32.35%) presented with featuresof preterm labor. Among those who presented with pretermlabor, only 30 women (14.7% of total cohort studied)delivered preterm, while 36 women among this group alsoprogressed to term.Thus a total of 174 women progressedtill term (Fig. 2). Among 66 of the study population waspresented with features of preterm labor, 20 were in active

**Table 1** Comparison of fetal adrenal gland parameters and cervical length measurements during the first scan done between 28 and 34 weeks, among women who continued till term versus women who eventually presented with features of preterm labor

| Variable | Women who continued till term ($N$ = 138) | Women who eventually presented with features of preterm labor ($N$ = 66) | $p$ value |
|---|---|---|---|
| cFAGV (mm³/kg body weight) | 241.35 | 404.70 | 0.00 |
| FAZ/FAG width ratio | 0.48 | 0.55 | 0.06 |
| FAZ/FAG depth ratio | 0.46 | 0.49 | 0.53 |
| Cervical length (cms) | 3.4 | 3.1 | 0.6 |

*cFAGV* corrected fetal adrenal gland volume, *FAZ* fetal adrenal zone, *FAG* fetal adrenal gland)

labor who delivered before any intervention. Rest 46received tocolytics with tablet nifedipine 20 mg stat followed by 10 mg TDS for average duration of 2 days.Mean age of the study population was27.20 + 3.72 years.Most of them were primigravidas(749%). Eight women among the study population had aprevious history of preterm delivery with a mean gesta- tional age at preterm delivery in the previ0us pregnancybeing 31.52 +141 weeks. Seven of these had a pretermdelivery even in the present pregnancy.Women who were enrolled for the study underwent theirfirst scan at a mean gestational age of 32.27 t 1.25 weeks.Women presented with features of preterm labor within amean duration of 8.16 + 1.30 days from the time of firstscan at a mean period of gestation of 33.35 t 1.32 weeks.The mean period of gestation of preterm delivery in thestudy population was 34.30 + 1.01 weeks. Mean period ofgestation at the follow-up Scan of at term was38.30 + 1.01 weeks.There was an interval of5.21 0.67 days between this scan and delivery with amean gestational age at delivery of 39.10 t 1.05 weeks.We compared the adrenal gland parameters and cervicallength during the first scan (28-34 weeks) among thosewho progressed uneventfully to term with those who presented with features suggestive of preterm labor (Table 1).Women, who developed features of preterm labor eventu-ally, had a significantly high cFAGV (404.70 mm/kg bodyweight) during the first scan compared to those whoreached term asymptomatically (241.35 mm/kg bodyweight).The difference in the fetal adrenal zone ratios andthe cervical length were not statistically significant todetermine those at risk of developing features of pretermlabor.On plotting a ROC to determine the cutoff value ofcFAGV, during the first scan, area under the curve was

**Table 2** Comparison of fetal adrenal gland parameters and cervical length measurements during the first scan done between 28 and 34 weeks, among women who continued till term versus women who eventually delivered preterm

| Variable | Women who continued till term ($N$ = 138) | Women who delivered preterm ($N$ = 30) | $p$ value |
|---|---|---|---|
| cFAGV (mm³/kg body weight) | 241.35 | 422.34 | 0.00 |
| FAZ/FAG width ratio | 0.48 | 0.62 | 0.00 |
| FAZ/FAG depth ratio | 0.46 | 0.55 | 0.02 |
| Cervical length (cm) | 3.4 | 2.5 | 0.02 |

*cFAGV* corrected fetal adrenal gland volume, *FAZ* fetal adrenal zone, *FAG* fetal adrenal gland)

0.90 with 95% confidence interval of lower limit of 0.83and upper limit of 0.97.A cutoff value of 271.16 mm'/kgbody weight showed 90% sensitivity and 81.9% specificityin predicting women who are at risk of developing featuresof preterm labor based on the first scan done between 28and 34 weeks (Fig. 2).On comparing fetal adrenal gland parameters, we founda statistically significant difference between women whohad a preterm delivery and those who progressed till termin the study population. Cervical length also was signifi-cantly less among those who eventually delivered preterm.(Table 2) ROC was hence plotted to determine the cutoff values.

**Table 3** Comparison of the efficacy of various parameters (with the ROC determined cutoff values) and cervical length (≤ 2.5 cm) during first scan in prediction of preterm delivery

| Statistical Characteristics | c FAGV (%) | Fetal adrenal gland width ratio (%) | Fetal adrenal gland depth ratio (%) | Cervical length (%) |
|---|---|---|---|---|
| Sensitivity | 96.67 | 96.67 | 80 | 56.67 |
| Specificity | 83 | 86.2 | 54 | 90.8 |
| Positive predictive value | 49.50 | 54.69 | 23.05 | 51.52 |
| Negative predictive value | 99.31 | 99.33 | 94.00 | 92.40 |

*cFAGV* corrected fetal adrenal gland volume, *FAZ* fetal adrenal zone, *FAG* fetal adrenal gland)

Based on these cutoff values determined by theROC for cFAGV (cutoff 348.78 mm°/kg body weight),fetal adrenal gland width ratio (cutoff 0.71) and fetaladrenal gland depth ratio (cutoff 0.59) and efficacy in termsof sensitivity, specificity, positive and negative predictivevalues were calculated.This was compared with the efficacy of cervical length (with a standard cutoff of 2.5 cm)for prediction of preterm delivery. Fetal adrenal glandwidth ratio had the best efficacy (sensitivity 96.67%,specificity 86.2%) followed by cFAGV (sensitivity96.6796, specificity 83%6) (Table 3).

**Table 4** Distribution of the fetal adrenal gland parameters estimated during the second scan of women who went into spontaneous labor at term and those who had to be induced ($N$ = 174)

| Variable | Women who went into spontaneous labor ($N$ = 117) | Women who had to be induced ($N$ = 57) | $p$ value |
|---|---|---|---|
| Corrected fetal adrenal gland volume (mm³/kg body weight) | 393.05 | 290.92 | 0.01 |
| FAZ/FAG width ratio | 0.70 | 0.67 | 0.52 |
| FAZ/FAG depth ratio | 0.65 | 0.61 | 0.5 |

*cFAGV* corrected fetal adrenal gland volume, *FAZ* fetal adrenal zone, *FAG* fetal adrenal gland)

In this study, we went one step further ahead to studyadrenal parameters among the two groups of the womenwho reached term (those who delivered spontaneouslyversus those who had to be induced in view of past dates)(Table 4).We found a statistically significant difference inthe cFAGV among these two group at the scan which wasdone at term (spontaneous labor 393.05 mm /kg versusinduced labor 290.92 mm/kg: p value 0.01).

## DISCUSSION

The idea of using fetal adrenal gland parameters to predictthe onset of labor is based on the concept of *placentalclock. There have been some studies in the past to validatethis idea for prediction of preterm delivery [3, 4].

Identi-fication of the process of parturition that occurs over weeksto months prior to delivery timeline may provide anopportunity to clinical intervention [5, 6].We found a cFAGV cutoff value of 271.16 mm /kgbody weight and 90% sensitivity and 81.9% specificity inpredicting women who are at risk of developing features ofpreterm labor based on the scan done between 28 and34 weeks. However, for preterm delivery, a cutoff value of348.78 mm/kg body weight had a 96.7% sensitivity and83% specificity in our study population.Turan et al. weremore specific and concluded that a cFAGV of greater than422 mm/kg was best in predicting preterm birth within5 days, with a sensitivity and specificity of 92% and 99%, respectively.

Multiple logistic regression analysis showedthat cAFGV was the only significant independent predictorfactor of preterm birth within 5 days of measurement[3, 4]. Reference range of fetal adrenal gland measurements using 2D ultrasound have been developed, startingfrom as early as 15th week of pregnancy, which might helpto corelate findings as per the period of gestation. [7] It isvery obvious that the cFAGV increases with the risk ofpreterm delivery and can be relied upon to predict andfollow-up women for assessing the risk of preterm deliv-ery.Till now only the cFAGV has been emphasized uponin the literature; however, we found that fetal adrenal glandwidth ratio had the best efficacy (sensitivity 96.67%,specificity 86.2%) in prediction of preterm delivery.Studies comparing 2D and 3D ultrasounds have concluded that estimation of fetal adrenal gland volume ismore accurate for prediction of preterm labor with 3Dultrasound. [4] Same investigators have also demonstratedthat enlargement in depth of fetal zone by 2D ultrasound iseven better predictor of preterm labor than 3D volumecalculation. [3].Additionally, we also observed an association of fetaladrenal gland parameters with the probability of sponta-neous onset of labor at term. Our findings are in agreementwith the results of other studies, which showed that, inprimates and humans, activation of the fetal hypothalamic-pituitary-adrenal axis results in increased output of dehy-droepiandrosterone, dehydroepiandrosterone sulfate,androstenedione, and cortisol, both at term or preterm [8).

Specific measurements and cutoff values can be ana-lyzed in future to make it more applicable for prediction ononset of labor even at term. In the literature, not only forprediction of labor but fetal adrenal gland measurementshave also been used to evaluate successful outcome ofinduction of labor [9].The results will be more beneficial if studied in a largerpopulation and with variables. Establishment of day-wisepredictable cutoffs will definitely give fetal adrenal glandsa new position in the prediction of labor (term or preterm)in modern obstetrics.This kind of predictability not onlywill give the obstetrician time to optimally utilize resourcesbut also will give the parturient and her family a clarity of plan.

## CONCLUSION

2D ultrasound measurement of fetal adrenal gland parameters (fetal adrenal gland width ratio and cFAGV) can beused as a marker for prediction of preterm delivery.cFAGV at term can also be used to predict the possibilityof spontaneous onset of labor.

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