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RESEARCH PAPER

Smaller than expected crown-rump length ultrasound measurements in 1st-trimester pregnancy: does it have any risk of subsequent pregnancies?

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Background and aims: Crown-rump length (CRL) measurement is usually used to predict threatened abortion or spontaneous miscarriage in early pregnancy. The present study aimed to examine whether there is any association between smaller-than-expected CRL and subsequent adverse pregnancy outcomes in the population under study. Materials and methods: This prospective study included 256 pregnant women with intrauterine, viable singleton spontaneous pregnancies with 6-13 weeks of gestation attending the Obstetrics and Gynaecology department, Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta. The expected CRL was determined based on a recognized growth curve of gestational age and CRL. The observed and expected CRL deviations were expressed as a z-score and evaluated between the miscarried and viable pregnancy groups. Results: The average maternal age at enrolment was 26.2±5.9 years. The majority (52.7%) of women were nulliparous. Most of the participants (62.9%) women had completed education up to the secondary level and had an average body mass index (60.5%). The mean gestational age was 9.4±1.5 weeks. Among 256 pregnant women, 26(10.1%) resulted in spontaneous miscarriages. The mean z score of CRL was significantly lower among the miscarried group than the continued pregnancy group (-1.91 vs -0.86, p-value 0.03). Also, the mean maternal age was considerably higher (30.50 vs 25.74, p-value< 0.01) in the miscarried group than in the continued pregnancy group. Conclusion: Smaller than expected crown rump length is a potential contributing factor for subsequent pregnancy loss. Ultrasound biometry evaluation may offer important information regarding fetal growth and threatened miscarriage.

Keywords: Crown-rump length; gestational age; maternal age; body-mass index.

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INTRODUCTION

Early pregnancy loss or spontaneous miscarriage is a common complication that may affect almost 10% of spontaneous pregnancies. While in assisted pregnancies, the incidence of miscarriage is almost 30%.[1] Various serologic and ultrasound markers are developed to identify the pregnancies at risk of miscarriage.[2,3] However, the major drawback of serologic markers is that they can help only in already-diagnosed miscarriages.

Transvaginal ultrasound provides highly reliable, high-resolution images for diagnosing early intrauterine pregnancies and the subsequent development of the fetus.[4] Ultrasound measurements like Gestational and yolk sac, fetal heart rate, and CRL are the ultrasound parameters used to evaluate viability and development of early pregnancy. CRL measurement is usually used to predict threatened abortion or spontaneous miscarriage in early pregnancy.[5-7] Various studies have reported an association between smaller-than-expected CRL and increased probability of miscarriage.[7-9]

Most studies regarding adverse pregnancy outcomes and their association with CRL in early pregnancy are conducted in developed countries. Literature on the topic

is very limited in the context of the Indian population, specifically in the underdeveloped region of North-east India. The present study is undertaken amongst pregnant women with single viable intrauterine pregnancies of 6-13 weeks gestation attending the Obstetrics and Gynaecology department of Fakhruddin Ali Ahmed Medical College and Hospital (FAAMC & H), Barpeta, Assam. The present study aimed to examine whether there is any association between smaller-than-expected CRL and subsequent adverse pregnancy outcomes in the population under study.

MATERIALS AND METHODS

This current study was carried outat the Radiology Department of FAAMC & H, Barpeta, Assam,from May 2017 to December 2018. The study included pregnant women of 6-13 weeks gestation attending the Obstetrics and Gynaecology department of FAAMC & H, Barpeta, Assam. The prospective study included 256 pregnant women having intrauterine, viable singleton spontaneous pregnancies. The ethics committee of FAAMC & H approved the study. Before data collection, informed consent was obtained from each participant after explaining the study's objectives.

Pregnant women with regular menstrual cycles having ultrasonographically confirmed 6-13 weeks gestation with viable singleton intrauterine pregnancy were included. Multiple pregnancies, pregnancies with assisted conception, and pregnancies of more than 13 weeks of gestation were excluded.

An ultrasound machine (SIEMENS ACUSON X 300, Germany) with a 2-5 MHz transducer (SECTOPROBE CH 2-5 MHz) was used to determine pregnancy viability and fetal biometry measurements. Three values of embryonic CRL were measured, and the expected CRL was determined following international references.[10] The pregnancy outcomes were recorded as subsequently miscarried and continued pregnancies as perhospital records or directly contacting the participant. The deviations of each observed and expected CRL value were expressed as z-scores and compared between the two outcome groups

RESULTS

The age of the participants ranged from 15-42 years. The average maternal age was 26.2±5.9 years. Almost 40% of the participants were more than 30 years of age. At the same time, only 12.9% of the participant were below the age of 20 years. Most women (52.7%) were nulliparous, and most participants (62.9%) had completed education up to the secondary level. Almost 60.5% of the studied women had anormal body mass index. The average gestational age was 9.4 ± 1.5 weeks at the time of CRL measurement (**Table 1**).

Table 1 Demographic features of the participants

Characteristics	Categories	Frequency	Percent
Age	< 20 years	33	12.9
	20-24 years	78	30.5
	25-29 years	43	16.8
	30-34 years	31	12.1
	>= 35 years	71	27.7
Parity	Nulliparous	135	52.7
	Multiparous	121	42.3
Educational status	Illiterate	26	10.2
	Primary	33	12.9
	Secondary	161	62.9
	Graduate	28	10.9
	Postgraduate	8	3.1
BMI	Normal	155	60.5
	Underweight	79	39.9
	Overweight	22	8.6
Socio-economic status	Lower	54	21.1
	Lower middle	46	18.0
	Middle	51	19.9
	Upper middle	52	20.3
	Upper	53	20.7

A total of 356 pregnant women were recruited for the study, out of which 26(10.1%) resulted in spontaneous miscarriages. The mean z score of CRL was significantly lower among the miscarried groupthan the group that continued pregnancy (-1.91 vs -0.86, p-value 0.03). Also, the average maternal age was significantly higher (30.50 vs 25.74, p-value< 0.01) in the miscarried group than in the continued pregnancy group. The chi-square test showed significant deviations in the maternal age group (p-value<0.01) and BMI (p-value 0.01) between the two groups. Categorizing the z score of CRL into two groups with the cut-off of -1, it has been found majority (65.4%) of miscarried pregnancies had a CRL z score below -1. However, the association was not significant (**Table 2**).

Table 2 Comparison between miscarried and continued pregnancy group

Variables	Continued pregnancy	Miscarried	p-value t-test
Maternal Age			
<=20 years	32 (13.9%)	1 (3.8%)	0.001
21 -25 years	75 (32.6%)	3 (11.5%)	
26-30 years	39 (17.0%)	4 (15.4%)	
31-35 years	22 (9.6%)	9 (34.6%)	
> 35 years	62 (27.0%)	9 (34.6%)	
Parity			
Nulliparous	123 (53.5%)	12 (46.2%)	0.53
Multiparous	107 (46.5%)	14 (53.8%)	
BMI			
Normal (18.5-24.9)	144 (62.6%)	11 (42.3%)	0.01
Underweight (<18.5)	70 (30.4%)	9 (34.6%)	
Overweight (≥25.0)	16 (7.0%)	6 (23.1%)	
Socio-economic status			
Lower	47 (20.4%	7 (26.9%)	0.92
Lower middle	41 (17.8%)	5 (19.2%)	
Middle	46 (20.0%)	5 (19.2%)	
Upper middle	47 (20.4%)	5 (19.2%)	
Upper	49 (21.3%)	4 (15.4%)	
CRL z score			
-1 or more	120 (52.2%)	9 (34.6%)	0.1
Below -1	110 (47.8%)	17 (65.4%)	

According to the univariate logistic regression results, women over 35 years old at the time of conception were about three times more likely to miscarry (Crude or 3.15; 95% C.I.-0.95-10.44). Also, overweight women had a significantly almost five times higher risk of miscarriage than women with normal BMI. The occurrence of miscarriages was marginally higher among the lower CRL group, as those with a CRL z score below -1 are almost at twice the risk of miscarrying. After controlling for maternal age group, parity, BMI, and socioeconomic status, the multivariate logistic regression with the backward wald technique found that pregnancies smaller than predicted CRL (CRL z score blow -1) had an approximately three times greater risk of miscarriage (Table 3).

Table 3 Multivariate analysis for predicting miscarriage

Variables		Crude OR (95% CI)	p- value	Adjusted OR (95% CI)	P-value
Age- group	26-30 years	ref			
	<=20 years	.34 (0.07-1.69)	.19	.34 (0.07-1.68)	.184
	21 -25 years	.41 (0.12 -1.44)	.17	.39 (0.11-1.36)	.138
	31-35 years	1.57 (0.50-4.95)	.44	1.40 (0.44-4.49)	.567
	> 35 years	3.15 (0.95-10.44)	.06	4.28 (1.20-15.24	.025
Parity	Nulliparous	ref			
	Multiparous	1.34 (0.59-3.02)	0.48		
BMI	Normal (18.5-24.9)				
	Underweight (<18.5)	1.68 (0.68-4.25)	0.27		
	Overweight (≥ 25.0)	4.91 (1.60-15.06)	0.005		
Socio-economic status	Upper	ref			
	Upper middle	1.30 (0.33-5.15)	.71		
	Middle	1.33 (0.34-5.27)	.68		
	Lower middle	1.49 (0.38-5.93)	.57		
	Lower	1.82 (0.50-6.64)	.36		
CRL z score	-1 or more	ref		ref	
	Below -1	2.06 (0.88-4.81)	.09	2.76 (1.08-7.03)	0.03

DISCUSSION

Ultrasound measurement of CRL is a common approach to assessing gestational age and is avaluable indicator of fetal growth in early pregnancy. The current research aims to measure whether smaller than expected CRL in the 1st-trimester pregnancy has any risk for subsequent pregnancy outcomes among participants attending the obstetrics and gynaecology department of a tertiary care hospital in Northeast India.

The study included 356 pregnant women, among whom 26(10.1%) resulted in spontaneous miscarriages. The mean CRL z score was significantly lower among the miscarried group than the group that continued pregnancy (-1.91 vs -0.86, p-value 0.03). Various other studies in a hospital setting also reported smaller-than-expected CRL in early pregnancy as a significant predictor of subsequent miscarriage.[7-9,11] It was also found that the majority (65.4%) of miscarried pregnancies had a CRL z score below -1. A recent study from Bangladesh also reported a vital relationship between negative CRL z-score categories and the probability of miscarriage.[12]

The mean maternal age was also significantly higher (30.50 vs 25.74, p-value< 0.01) in the miscarried group than in the continued pregnancy group. Significant differences were found between the maternal age groups (p-value<0.01). Various studies have documented increasing maternal age as a potential factor for fetal trisomy and chromosomal abnormalities responsible for early fetal demise.[13] The current results suggest that women with maternal age above 35 years have almost three times more risk of miscarriage (Crude OR 3.15; 95% C.I.-0.95-10.44). Various studies also reported maternal age as a significant predictor of miscarriage.[12,14]

Overweight women were also found to beat almost five times more risk of miscarriage than those with normal BMI in the present study. Various studies have reported an association between BMI and subsequent pregnancy results.[15,16] Literature suggests that whether they used assisted

reproductive techniques or natural conception, overweight or obese women are at a considerably higher risk of miscarriage.[17-21]

CRL is a significant indicator of early fetal growth and neonatal outcome. The latest study has reported various maternal characteristics such as maternal age, parity, BMI, and folic acid supplementation as independently associated factors of CRL in the first trimester. The same study findings suggested that CRL is negatively associated with adverse pregnancy outcomes like SGA, preterm birth, and admission rate to the NICU.[22] The CRL smaller to gestational age is found to be a significant risk factor for early pregnancy loss in the present study.

Limitations: The study is based on a single tertiary care hospital and conducted on a small sample size, so the findings could not be generalized to the whole population. Secondly, various influencing factors of early miscarriage, like vaginal bleeding, prior history of miscarriage, hypertension, and gestational diabetes, were not included in the study.

CONCLUSION

The findings suggest that smaller-than-expected crown rump length is a significant risk factor for subsequent pregnancy loss. Fetal biometry evaluation through ultrasound may provide helpful information regarding fetal growth and threatened miscarriage. Careful clinical assessment and systematic ultrasound monitoring may help provide much-needed help and support to the pregnant woman.

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