

Yolk sac diameter as a prognostic factor for first trimester pregnancy outcome

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ABSTRACT

Aims: To evaluate yolk sac diameter as a predictor of first trimester pregnancy outcome.

Methods: This was a prospective observational study conducted at Paropakar Maternity and Women's Hospital from October 2017 to October 2018. Pregnant women in between seven and ten weeks of gestation were enrolled. Transabdominal sonography was performed to measure yolk sac diameter and followed up till 12 weeks of gestation to see the outcome. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for yolk sac diameter with regards to abnormal pregnancy outcome.

Results: There were 80 cases enrolled and a significant positive correlation was found between yolk sac diameter and gestational age. Abnormal yolk sac diameter, irrespective of gestational age, had sensitivity of 92.95%, specificity 66.66%, positive predictive value 95.6% and negative predictive value of 54.54% in predicting abnormal pregnancy outcome.

Conclusions: The measurement of yolk sac diameter between seventh and tenth weeks of gestation can predict first trimester pregnancy outcome. This is useful while counseling pregnant women regarding risk of abnormal outcome and need for follow up ultrasonography.

Keywords: first trimester; pregnancy outcome; prognostic factor; yolk sac diameter

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INTRODUCTION

First trimester is crucial, since 80% of pregnancy losses occur spontaneously during this period.¹ Contributing factors are diverse, so there is difficulty in reliably predicting the outcome of pregnancy. There is a need for accurate method to assess the early pregnancies that allows early indication of unwanted outcomes. This can guide a tailored and pre-emptive management strategy, and aids in a much needed psychologic preparation of the expecting mother.

Numerous ultrasound signs have been proposed as predictive of poor pregnancy outcome, including an excessively large, excessively small, or irregular gestational sac, a large or irregular yolk sac, weak decidual reaction and a slow embryonic heart rate.²⁻⁶ Yolk sac plays a pivotal role in exchange of essential substrates between mother and embryo before the placental circulation establishes. It reaches the

highest level of functional activity during the fourth to seventh week and undergoes degeneration after the twelfth week.^{7,8} With transabdominal sonography (TAS), the yolk sac is mostly evident by seven weeks of gestational age, when its diameter reaches a mean of 20 mm.¹

TAS is the routine practice at our set up, whereas transvaginal sonography (TVS) is preferred when difficulty in visualization and assessment of early pregnancies. This study was aimed to evaluate the usefulness of TAS-determined yolk sac diameter measured between seven and ten weeks of gestation in predicting the outcome of the first trimester pregnancy.

METHODS

This was a prospective observational study conducted at the outpatient setting of Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu from

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October 2017 to October 2018. A written informed consent was obtained from all participants after institutional approval.

Intrauterine singleton pregnancy of seven to ten weeks of gestation (WOG) and who wished to continue pregnancy were included. The diagnosed molar pregnancy, structural abnormalities of uterus and cervix, fetal congenital anomaly and a history of radiation or chemotherapeutic exposure were excluded. Sample size was calculated by prevalence method for the outcome.

Besides sonographic records participants' age, gravida, menstrual regularity, last menstrual period, previous abortions, medical co-morbidity and personal history such as smoking and alcohol intake, and hemoglobin, platelets, urine microscopy were also recorded.

In cases where the yolk sac was not visualized on the first ultrasound, the participants were asked to repeat TAS in a two week time. They were reminded via the hospital telephone one day before completion of two weeks. Next follow up was at the end of 12 weeks. The participants that failed to show up for the repeat scan were excluded from the study. Self reporting of any complication was insured and final telephone call was made at the end of 12 weeks. Any form of pregnancy failure was taken as abnormal outcome.

More than two standard deviation of yolk sac diameter, crown rump length or gestational sac was considered abnormal. Sensitivity, specificity, positive predictive value and negative predictive value of abnormal YSD in predicting the abnormal pregnancy outcome are calculated. McNemar test was applied in predicting abnormal pregnancy outcome. The analysis was performed using SPSS 20. Two-tailed *p*-value less than 0.05 was considered significant.

RESULTS

Eighty pregnant women between seven to ten weeks of gestation completed the study. Embryo was visualized in all participants with presence of heart rate. And, no obvious congenital anomalies were identified during the ultrasound examination. Two cases needed a repeat ultrasound done two weeks later for yolk sac to be visualized. Nine had abnormal pregnancy outcome (six missed abortions and three spontaneous abortions).

The mean age of participants was 24.01±4.76 years (range: 17-36). Mean BMI was 22.14±2.87 kg/m² (range: 15.62-28.93). Three women studied had hypothyroidism and six had anemia. Five abnormal pregnancy outcomes observed in women between 26 to 30 years age. Four abnormal pregnancy outcomes occurred in primigravida, two in second gravida, two in third gravida and one in fourth gravid; three had previous one abortion and one had two abortions.

In participants with normal first trimester outcome, the mean yolk sac diameter increased with increasing gestational age. Mean YSD was 5.88 mm (range: 3.7-6.4) in abnormal pregnancy outcome [Table-1].

Table-1: YSD at a particular gestational age in normal pregnancy outcome (N=71)

GA (Week)	N	Minimum (mm)	Maximum (mm)	Mean (mm)	SD	± 2 SD
7 th	25	4	5.5	4.933	0.4373	4.05-5.807
8 th	17	3.8	5.6	5.147	0.5088	4.12-6.16
9 th	21	4	5.8	5.319	0.4697	4.37-6.25
10 th	8	4.7	6	5.575	0.4062	4.76-6.38
Cumulative	71	3.8	6	5.171	0.4999	4.17-6.17

YSD: yolk sac diameter; GA: gestational age; SD: standard deviation

Abnormal pregnancy outcome in relation to mean YSD irrespective of the gestational age groups was found to be statistically significant but it was not significant for each week from 7th through 10th week [Table-2]. The calculated sensitivity, specificity, positive predictive value and negative predictive value were 92.95%, 66.6%, 95.6% and 54.54 % respectively.

Table-2: Yolk Sac diameter in relation to pregnancy outcome

YSD	Outcome		Total	McNemar	p-value
	Normal	Abnormal			
Normal	66	3	69	0.727	0.000
Abnormal	5	6	11		
Total	71	9	80		

YSD: Yolk sac diameter

Sensitivity and PPV of YSD when was used as a predictor to determine the first trimester pregnancy outcome were both above 90% [Table-3].

Table-3: YSD in predicting pregnancy outcome by gestational age

GA	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
7 th week	96	50	96	50
8 th week	88.2	66.6	93.7	66.6
9 th week	95.2	50	95.2	50
10 th week	87.5	50	87.5	50
Average	91.7	54.1	93.1	54.1

GA: Gestational Age; PPV: Positive Predictive Value; NPV: Negative Predictive value

There was a significant positive correlation of the mean YSD when analyzed with CRL, GSD and gestational age respectively. The mean GSD was 33.37±9.34, and the mean CRL was 19.2±7.66. Pearson's correlation coefficient of YSD calculated for CRL, GSD and GA were 0.433, 0.299 and 0.329 respectively.

DISCUSSION

The major findings of our study highlight that YSD in all participants ranged between 3.7-6.4 mm with mean of 5.25 (SD 0.59) whereas the mean YSD in women who had a normal pregnancy outcome was 5.17 mm. The largest YSD with a normal outcome was 6 mm. The sensitivity and PPV for YSD were both considered good in predicting first trimester pregnancy outcome.

In concordance with our study, the study by Manchanda et al⁹ showed that pregnancies with YSD more than six mm could predict abnormal outcome with a very high sensitivity and specificity of 100 and 96% respectively. In a separate retrospective study,¹⁰ the ongoing pregnancy rates for YSD of <2 mm, 2-6 mm and >6 mm were 20%, 89.2% and 20% respectively showing that continuation of pregnancy is most compatible when the YSD is between 2-6 mm. However, in the study by Moradan et al¹¹ the largest YSD with a normal outcome was found to be 6.6 mm.

Chama et al¹² found YSD as the predictor of abnormal pregnancy in 105 women with a sensitivity of 91.4%, specificity of 66% and a PPV of 88.8%. These values are comparable with that of ours. Likewise,

the study done in 117 women by Stampone¹³ also showed almost similar value except a higher negative predictive value of 95%.

In the study by Kucuk et al, abnormal YSD allowed the prediction of abnormal pregnancy outcome with a sensitivity of 65%, specificity of 97%, PPV of 71% and NPV of 95%.¹⁴ In another study the upper limit of normal YSD between five to 10 WOG was 5.6 mm and the sensitivity of predicting an abnormal outcome was 61.29%, specificity was 96.48% and PPV was 79.17%.⁴ Cut-off value of mean ±SD is taken in most of the studies like this study.^{4,12,14} But Berdahl et al¹⁵ applied a specific cut off value for the YSD at 5 mm to allow an easier patient counseling; and Cepni et al¹⁶ defined normal YSD as that falling between the 5-95% confidence interval.

The crucial role of yolk sac in a normal morphologic development of the embryo is well established. However, there appears to be no absolute highest value for YSD that can accurately predict an abnormal outcome. And, normality of the YSD has been defined in several ways and not by its biometry alone. Shape, quality of the yolk sac, its rim and central characteristics and the design of the study, characteristics of study population and period of follow up may attribute to the differences in the results obtained.^{11,14,17}

The YSD value was shown to be increasing from the seventh to tenth WOG, being positively correlated with CRL, GSD and GA. Similar findings were observed in several other studies too.^{13,18,19} Significant linear correlation between YSD and gestational age was also observed among the patients who had normal pregnancy outcome in the study by Cepni et al.¹⁶

Abnormal pregnancy outcome was observed in 11.25% of cases in our study. This rate varies on study design and demographic factors like 8-20% in some studies^{20,21}, 24% by Nawal et al¹⁸ and 32.7% by Lindsay et al.⁴

Advanced maternal age is associated with increasing anomaly but 61.6 % of our study population belonged to the 21 to 30 years age group and a smaller sample size could not correlate the general understanding.²²⁻²⁴ Four out of nine had past pregnancy loss and this seems to be a risk factor as described by other studies.^{25,26}

CONCLUSIONS

Yolk sac diameter, crown rump length and gestational sac diameter determined by transabdominal ultrasound between seven to ten weeks of gestation were positively correlated with the gestational age but with minimal variation in Yolk sac diameter.

Abnormal yolk sac diameter identified at seven to ten weeks, irrespective of gestational age group can predict an abnormal outcome of pregnancy at the end of the twelve weeks with a sensitivity of 92.9% and positive predictive value of 95.6%.

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