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Prospective Study in Predicting Pregnancy Outcome Using Yolk Sac Parameters in First Trimester

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Abstract: Objective: ***Yolk sac is the first ultrasonographically visible extra embryonic structure within the gestational sac. In Early pregnancy, threatened and spontaneous abortions is the most common complication. As per some studies, enlarged or small yolk sac predicts poor pregnancy outcome. Whereas other studies, they conclude normal outcome. Thus, the purpose of this study is to study and evaluate the inner diameter and the shape of yolk sac in first trimester using transabdminal ultrasonography and to correlate it with pregnancy outcome. Materials and Methods: A prospective study conducted in Institute of Obstetrics and Gynecology, Egmore, Chennai. Total of hundred pregnant antenatal mothers were chosen between the study period November 2017 to Octoberr 2018. Once selected, they were divided into two groups of 8 to 10 weeks and 10 to 12 weeks. They underwent transabdominal ultrasound to see the size and characteristics of yolk sac, results were recorded and patients are followed up till 20 weeks to see for pregnancy outcome like abortion or normal course. Results: In patients with normal outcome the mean diameter of yolk sac has been 4.35 mm. In patients with abortion as outcome, the mean yolk sac diameter has been ranging from 5.5 mm. Any deviation of more than 2 SD met with increased rates of spontaneous abortion. In this current study, about 88% of cases had abortion which were found to have abnormal size of the yolk sac Conclusion: Yolk sac size and characteristics are important determinants of outcome of pregnancy. This should be monitored in early pregnancy to assess the outcome of pregnancy.***

Keywords: ***Yolk sac size, First trimester ultrasound, Pregnancy outcome, Abortion***

1. Introduction

Yolk sac is the first ultrasonographically visible extra embryonic structure within the gestational sac. Between Human embryo and mother, yolk sac is the primary route of exchange before circulation of placenta is established. Yolk sac reaches its highest level of functional activity in 4th to 7th week of embryonic development. It serves as a hematopoietic, secretory, metabolic, immunogenic, excretory function.

Primary Yolk sac forms at approximately twenty four days of menstrual age. When the extraembryonic coelom forms, primary yolk sac is pinched off and the secondary yolk sac is formed at 27 to 28 days of menstrual age. This as mentioned above becomes the first embryonic structure to be visualized in gestational sac sonographically.

Gross changes in its morphology, indicate significant dysfunction of this transport system between maternal and fetal parts. This also may indicate impending embryonic demise. In the early stage of pregnancy, evaluation of embryo and gestational sac by ultrasound is very important.

Accurate differentiation between normal pregnancy and loss of pregnancy in early gestation is the most important clinical challenge.

The estimated implanted pregnancies resulting in spontaneous abortion during 1st trimester is around thirty to forty percent. Critical landmark to identify a true gestational sac is the Yolk sac. Ultrasound shows Yolk sac as a round structure with anechoic center bordered by a regular well defined echogenic rim.

In Early pregnancy, threatened and spontaneous abortions is the most common complication. As per some studies, enlarged or small yolk sac predicts poor pregnancy outcome. Whereas other studies, they conclude normal outcome. Thus, the purpose of this study is to evaluate the yolk sac size and correlate with outcome of pregnancy.

2. Aims And Objectives

To study and evaluate the inner diameter and the shape of yolk sac in first trimester using transabdominal ultrasonography and to correlate it with pregnancy outcome.

3. Materials and Methods

This study is a prospective one. The study is conducted in Institute of Obstetrics and Gynecology, Egmore, Chennai. Pregnant patients attending the antenatal outpatient clinic are chosen for study including women with uncomplicated singleton pregnancy between 8 to 12 weeks and excluding patients with medical comorbidities like anemia, diabetes mellitus, hypothyroidism and chronic hypertension which may cause abnormal pregnancy outcomes. Patients with structural anomalies of uterus and cervix are also excluded from the study. Total of hundred patients are chosen between the study period November 2017 to October 2018.

Gravida	1	14(41.2%)	20(35.7%)	4(40.0%)
	2	10(29.4%)	22(39.3%)	4(40.0%)
	3	6(17.6%)	8(14.3%)	0
	4	4(11.8%)	4(7.1%)	2(20.0%)
	5	0	2(3.6%)	0
Para	0	20(58.8%)	26(46.4%)	4(40%)
	1	8(23.5%)	22(39.9%)	4(40%)
	2	4(11.8%)	8(14.3%)	0
	3	2(5.9%)	0	2(20%)

Consanguinity of marriage	No	20(58.8%)	36(64.3%)	6(60%)
	Yes	14(41.2%)	20(35.7%)	4(40%)
Socioeconomic class	Class 3	2(5.9%)	2(3.6%)	0
	Class 4	16(47.1%)	14(25%)	2(20%)
	Class 5	16(47.1%)	40(71.4%)	8(80%)
Previous abortions	0	28(82.4%)	42(75%)	10(100%)
	1	2(5.9%)	10(17.9%)	0
	2	2(5.9%)	2(3.6%)	0
	3	2(5.9%)	2(3.6%)	0
()* - % within count				

The selected patients are divided into two groups. One group with patients with gestational age between 8-10 weeks and the other group includes patients with gestational age between 10-12 weeks. They shall undergo Trans abdominal Ultrasound by the same sonographer to find out the;

- Yolk sac size(inner diameter)
- Yolk sac shape
- Rim and center echogenicity
- Number of sacs
- If calcification is present/ absent

Patients are followed up till 20 weeks. If the pregnancy continued beyond 20 weeks, then it is considered as normal pregnancy outcome. If it ended with abortion, then it is considered as an abnormal pregnancy outcome. Observation and statistical analysis will be made comparing yolk sac diameter with the outcome of pregnancy at 20 weeks for each group separately.

4. Observation

In this study, totally 100 patients were taken. In the first group, that is the 8- 10 weeks group, totally 52 patients were studied. In this group, the normal outcome was seen in 18 patients, missed abortion was seen in 28 patients and Blighted ovum in 6 patients. In the second group, 48 patients were studied. The gross outcome in this group was, normal outcome in 16 patients, 28 patients had missed abortion, blighted ovum was noted in 4 patients.

So, overall in this study 34 patients had normal outcome of pregnancy, 56 patients had missed abortion, blighted ovum was noted in 10 patients. The data was distributed as follows.

Table 1: Data distribution

Parameter		Normal outcome()*	Missed abortion	Blighted ovum
Total		34	56	10
Gestational age	8-10 weeks	18(52.9%)	28(50.0%)	6(60.0%)
	10-12 weeks	16(47.1%)	28(50.0%)	4(40.0%)
Age of the patient	<20 years	2(5.9%)	8(12.1%)	10(10.0%)
	21-30 years	26(76.5%)	48(72.7%)	74(74.0%)
	>31 years	6(17.6%)	10(15.2%)	16(16.0%)

In patients with normal outcome the mean diameter of yolk sac has been 4.35 mm. In this normal outcome group, the lower bound diameter that has been recorded ranges from 3.87mm and the upper bound diameter recorded was 4.84mm. The abnormal outcome may be missed abortion or blighted ovum. In patients with abortion as outcome, the mean yolk sac diameter was 5.5 mm. In this group the lowest diameter recorded has been around 4.9mm and upper bound diameter recorded has been 6.10mm.

In the blighted ovum group the mean diameter that has been recorded was around 7.6mm. So when compared to other groups of both normal and abortion as outcome, the diameter is more. The lowest value that was recorded was around 7.23mm and the highest value was around 7.97mm. This clearly shows that in both 8-10 weeks and 10-12 weeks group studied the mean yolk sac diameter in groups of abnormal outcomes has been on the higher side than normal outcome patients. The mean standard deviation in abortion group has been 2.248, whereas the standard deviation in normal outcome group is in the range of 1.390.

Table 2: Yolk sac size in different pregnancy outcomes

Pregnancy Outcome	N	Mean yolk sac size mm)	SD	SE	95% CI for Mean	
					Lower bound	Upper bound
Normal	34	4.35	1.39	0.238	3.87	4.84
Missed abortion	56	5.5	2.248	0.3	4.9	6.1
Blighted ovum	10	7.6	0.516	0.163	7.23	7.97
Total	100	5.32	2.084	0.208	4.91	5.73

SD Standard deviation, SE Standard Error

In the bar diagram depicted below, if the yolk sac lies within normal range then there is a increase in normal outcome when we follow up the patient. But when there is more than 2 standard deviation in the diameter of yolk sac, the incidence of abortion is greater. Similarly, when the yolk sac diameter falls less than two standard deviation, missed abortion is greater.

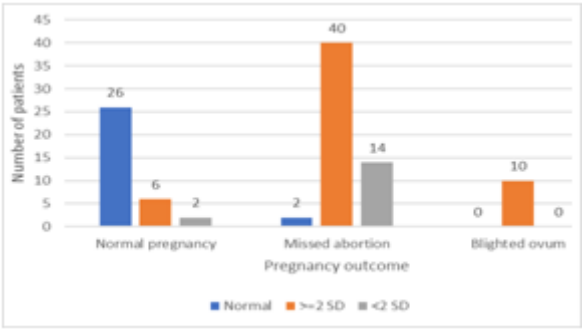

Figure 1: Pregnancy outcome in different SD(Standard Deviation) of yolk sac size

The reverse correlation also suggests that normal diameter and characteristics of yolk sac correlates well with normal outcome of pregnancy. When there is a deviation of size which was on the higher side of diameter of yolk sac then the abortion rates increase drastically.

When we take into account the data of patients who were found to have normal characteristics of yolk sac in ultrasound, there has been 76.5% normal progression pregnancy. But in a small percentage of patients, namely 3.6 %, with normal characteristics of yolk sac, there has been abortion noted. Similarly, in case of abnormal yolk sac characteristics, normal progression is noted only in small percentage of patients. But most of the patients, that is around 54 patients had abortion.

Table 3: Pregnancy outcome with respect to Yolk Sac Size

Parameter		Normal outcome()*	Missed abortion	Blighted ovum
Yolk sac size	Normal[a]	26(76.5%)	2(3.6%)	0
	Abnormal[b]	8(23.5%)	54(96.4%)	10(100%)
Total		34(100%)	56(100%)	10(100%)
()* - % within count				

[a]Anormal yolk sac has a diameter of two to five millimeter and a circular shape with no degenerations.
[b]Abnormal yolk sac has diameter less than two mm or bigger than five millimeter and does not have circular shape and with degenerations.

The data is comparable by chi- square test and the p value is 0.000 hence there is a statistical significance with yolk sac diameter and the final outcome as the P value is less than 0.05. This suggests that the yolk sac diameter has been a crucial factor in finding out the outcome of pregnancy in this first table noted.

Table 3: Diagnostic or screening test evaluation

	Normal	Abnormal	Total
Abnormal	64	8	72
Normal	2	26	28
	66	34	100
Parameter		95% CI	Method
Sensitivity	96.97%	(89.61, 99.17)	Wilson Score
Specificity	76.47%	(60, 87.56)	Wilson Score
Positive Predictive Value	88.89%	(79.58, 94.26)	Wilson Score
Negative Predictive Value	92.86%	(77.35, 98.02)	Wilson Score
Diagnostic Accuracy	90%	(82.56, 94.48)	Wilson Score

The above analysis helps us to come to a conclusion that the measurement of yolk sac diameter has a diagnostic accuracy of 90% in predicting the pregnancy outcome.

5. Discussion

We have undertaken two groups for study. In the 8- 10 weeks group, totally 52patients were studied. In this group, the normal outcome was seen in 18 patients, Missed abortion was seen in twenty eight patients, Blighted ovum was seen in 6 patients.

In the next group, which ranged from patients in 10 – 12 weeks, forty eight patients were studied. The gross outcome in this group was, normal outcome in sixteen patients, 28 patients had missed abortion, blighted ovum was noted in four patients. So, overall in this study 34 patients had normal outcome, 56 patients had missed abortion, blighted ovum was noted in ten patients.

In this study, less than 20 years of age is 10 patients. 74 patients were between 21- 30 years, which is about 74. Above 31 years of age, 16 patients were studied. Below 20 years of age, 2 had normal outcome, 6 had missed abortion, 2 patients had blighted ovum. In the age 21 to 30 years, 26 had normal outcome, 42 had missed abortion, 6 patients had blighted ovum. Above 31 years, 6 patients had normal outcome, 8 had missed abortion, 2 patients had blighted ovum.

In consanguineous marriage, the yolk sac diameter was slightly higher and it has resulted in increased rates of abortion in this present study. This finding could not be correlated with other studies.

Normal outcome patients had a mean diameter of yolk sac has been 4.35 mm. In patients with abnormal outcome, the mean yolk sac diameter has been ranging from 5.5 mm. In blighted ovum group, the mean diameter that has been recorded was around 7.6. This clearly shows that in both 8-10 weeks and 10-12 weeks group studied the mean yolk sac diameter in groups of abnormal outcome has been on the higher side than normal outcome patients.

The present prospective observational study clearly demonstrates the fact that visualization of yolk sac and its measurement and morphology is very important for assessing the normal pregnancy outcome.

In previous studies which were carried by Xie YJ et al, non visualization of yolk sac in ultrasound was reported in 0.6% cases. But in this study we were able to record yolk sac diameter and morphology in all the cases studied. In the studies done by Heller R et al, Moradan S et al, Jose L et al, and Shetty AS et al different percentages of non-visualization of the yolk sac were found as 11%, 4.54% , 20.3%, and 4.3%respectively which were much higher than other studies.[1]

Similar findings were reported by Heller R et al, Jose L et al and Sanam Moradan et al. So based on these above mentioned studies, they strongly support the findings of this observational study, that a yolk sac should always be present in case of normal pregnancies.[2]

In Contrast to the present study, Kurtz AB et al and Shetty AS et al depicted the fact that detection of the yolk sac was not an early predictor of pregnancy outcome and they concluded that the absence of the yolk sac was not consistently predictive of a spontaneous abortion. In the study done by Shetty AS et al, only 75%of the cases with absent yolk sac ended in spontaneous abortions.[3]

72% of the cases in this present study showed abnormalities in yolk sac size. Data that was reported by Adija P et al and Küçük T et al, showed that according to them 10% cases and 11.2%cases had abnormal size of the yolk sac. In the same way, in the study by Jose L et al, 5.6% of cases had abnormal size of the yolk sac.[3]

In this current study, about 96% of cases had abortion which were found to have abnormal size of the yolk sac, while in the study that was carried out by Küçük T et al and Adija P et al, abortions due to abnormal yolk sac size occurred in 64.5% and35.71% respectively.[4] These percentages shown above in other studies were much lower than the findings noted in this study. The reason that could be behind these differences in percentages and findings could be the smaller sample size of this present study.

Coming to the dimension of the yolk sac, enlarged yolk sac or larger in size yolk sac (about 2 SD more than normal) was responsible for 71.4% of the abortions in the present study.[5] When compared to other studies, the study which was carried out by Tan S et al and Adija P. et al, abortion

occurred in 37.5%and 80% of the cases respectively in which there was enlarged yolk sac was noted.[6]

In the present study, about six cases, even though they had enlarged yolk sac diameter, they progressed beyond 20 weeks of gestation. So around 17% cases may still progress based on this study. This brings none of the cases having enlarged yolk sac size continued beyond 20weeks.

This finding is somewhat in accordance with the findings of Küçük T et al who had reported that 28.5% of cases of enlarged yolk sac progressed to have a normal outcome.

While in the study that was done by Berdahl DM et al, he reported that 66.25% of the cases, which had enlarged yolk sac still progressed into normal outcome. So the percentage is slightly higher with this study.[7]

According to the study that was done by Malinowski W et al, if we visualize a bigger sized yolk sac, then it is a indicator of poor pregnancy outcome. With concordance with the studies mentioned above, the study conducted by Moradan S et al also showed that yolk sac size was an important factor for prediction of spontaneous abortion. So, these findings are in accordance with the findings of present study.[8]

Cho FN et al has documented the existence of a very large yolk sac, as large with a diameter of 8.1 mm in a normal live pregnancy.[9]So, this finding is also not in accordance with the previous studies. In this study, less than two standard deviations in size of yolk sac is noted in 16 cases. The percentage was around 16 %.In the present study, small size yolk sac was found in 1.4% of cases.

The data given by of Jose L et al was lower, that is about 3.7%.11.11% of the cases of the present study aborted because of small yolk sac size. In the study done by AdijaP et al 1.4% had smaller yolk sac.

In the study by Adija P et al, a smaller yolk sac was related with a high percentage that is about 40% of abortions. In this study, the result showed 14 % of cases had abortion.

6. Conclusion

The findings of the present study showed that the yolk sac size can be an important predictor for the progression of pregnancy till term and is also useful in predicting the predicting the successful outcome. It has been observed that a larger or a smaller size of the yolk sac reduced the success of pregnancy and may lead to fetal loss in the form of abortion.

So we can see that assessing the yolk sac parameters by an early ultrasonogram, can be useful in predicting the pregnancy which may end up in fetal loss. So that these pregnancies can be followed up at closer intervals by ultrasonogram to detect the fetal loss at the earliest.

However, further research with a well designed study group with a bigger population is necessary to study the role of yolk sac diameter in predicting the pregnancy outcome in first trimester and it helps in detecting the at risk pregnancies and may avoid unnecessary delay in detecting early pregnancy loss.

Thus by assessing the yolk sac parameters helps in predicting the pregnancy loss at the earliest and thus the patients may be in close follow up and may prevent inadvertent bleeding episodes which may be detrimental to the mother.

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