

***Sonographic Assessment of the Types of
Yolk Sac Abnormalities in First
Trimester Missed Miscarriage***

THESIS

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BY

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Abbreviations

AP	Anteroposterior
AGM	Aorta/Gonad/Mesonephros
BPM	Beats per minute
CRL	Crown rump length
DIC	Disseminated intravascular coagulopathy
ECC	Extracoelomic cavity
EPL	Early pregnancy loss
FSH	Follicle stimulating hormone
GA	Gestational age
GD	Growth-disorganized
hCG	Human chorionic gonadotropin
IUP	Intrauterine pregnancy
IVF	Invitro fertilization
IUGR	Intrauterine growth restriction
IGF2	Insulin-like growth factor 2
Ig	Immunoglobulin
L	Longitudinal
LMP	Last menstrual period
MD	Mean diameter
MSD	Mean sac diameter
NK	Natural killer
PCOS	Polycystic ovary disease
SD	Standard deviation
SONAR	Sound Navigation and Ranging
SYS	Secondary yolk sac

T	Transverse
TVS	Transvaginalsonography
US	Ultrasound
VTE	Venous thromboembolism
YS	Yolk sac
3D	Three dimensional ultrasound
mIU/ml	Milli–international units per milliliter

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INTRODUCTION

Missed miscarriage refers to a pregnancy in which there is a fetal demise, before 20 weeks of gestation, without outside intervention together with absent uterine activity to expel the products of conception (**Griebel et al., 2005**). The criteria for the first trimester missed miscarriage are a gestational sac with a mean diameter of more than 12 mm without a yolk sac, or a mean gestational sac diameter exceeding 16 mm without an embryo; or a yolk sac of more than 6 mm mean diameter (with or without abnormal morphology) that ultimately fails to develop an embryonic structure; or an embryo with a crown-rump length (CRL) of more than 5 mm without cardiac activity, or the loss of previously identified cardiac activity (**Salamanca et al., 2013**).

Multiple etiologic factors, including parental chromosomal abnormalities, immunological factors, endocrinological disorders, congenital uterine anomalies, polycystic ovarian syndrome, hereditary thrombophilia, infections and environmental factors, have been identified for missed miscarriage, and these conditions may occur in ~50% of all women with miscarriages (**Hatasaka, 1994**). Apart from the above etiologic factors, gene polymorphisms have been proposed as a risk factor that increases the chance of miscarriage in otherwise healthy women (**Pietrowski et al., 2005**).

Since 1980, improvements in the resolution of vaginal transducers have led to the study of the conceptus at increasingly early stages of gestation. **Lindsay et al., (1992)** reported that the yolk sac appears at the 5th week of gestation and its diameter increases steadily (≈ 0.1 mm/d) until the end of the 10th week. In the same study, the upper limit of a normal yolk sac diameter in pregnancies with a gestational age of 5 to 10 weeks was defined as 5.6 mm.

Normally, the yolk sac is a round structure with an anechoic center that is surrounded by a uniformly thick and well-defined echogenic wall (**Levi et al., 1997**). Typically, when the 10th or

11th week of gestation is completed, the yolk sac starts to degenerate and rapidly shrinks(*Gulbis et al., 1998*).

Assessment of the yolk sac should be part of a complete first-trimester sonographic examination. An abnormality in the sonographic appearance of a yolk sac can predict subsequent embryonic death or abnormalities. Therefore, accurate recognition of the normal and abnormal sonographic findings related to the yolk sac can be used to anticipate the course of pregnancy (*Tan et al., 2012*). It seems that changes in yolk sac appearance (size, shape and echogenicity) are probably a consequence of poor embryonic development or even embryonic death, rather than being a primary cause of an early pregnancy failure (*Kupesic and Kurjak, 2001*).

There are two types of miscarriage: sporadic and recurrent. Unlike sporadic miscarriage, recurrent miscarriage tends to occur even if the fetus has a normal chromosome complement (*Sullivan et al., 2004*). Recurrent miscarriage tends to affect women with specific reproductive characteristics (*Jivraj et al., 2001*). About 25%-50% of pregnancies end in sporadic miscarriage, usually due to random fetal chromosomal abnormalities (*Greenwold and Jauniaux, 2002*). The risk of which rises with increasing maternal age (*Regan and Rai , 2000*).

In a recent study, *Salamanca et al., (2013)* found a correlation between morphology of conceptuses and yolk sac appearance in cases of missed miscarriage. This study classified yolk sac abnormalities into size and shape.

Accordingly, knowledge of the sonographic appearances of yolk sac abnormalities in cases of missed miscarriage may be important for the diagnosis and management of early pregnancy failure.

AIM OF THE STUDY

The aims of our study are to measure and describe the patterns of yolk sac abnormalities and to identify the relation between these abnormalities and other early embryonic morphologic abnormalities detected by transvaginal sonography (TVS) in cases of first trimester missed miscarriage.

Research question:

In cases of missed miscarriage, is there any relation between the patterns of yolk sac abnormalities and early embryonic morphologic abnormalities detected by TVS?

Research hypothesis:

There is a relation between the patterns of yolk sac abnormalities and early embryonic morphologic abnormalities detected by TVS in first trimester missed miscarriage.

Patients and methods

Study design:

This study will be a cross sectional study.

Population:

The study will be carried out on 204 women (ages, 18-45 years); who have missed miscarriage with gestational age ≤ 11 weeks which will be diagnosed by TVS. Missed miscarriage pregnant females will be recruited from Obstetric Ultrasound Clinic, Demerdash Hospital, Ain Shams University. Written informed consent will be obtained for all the participants after explaining the details of the study for them, as agreed upon by the ethical committee.

Sample size:

The sample size of our study will be 204 patients. This was estimated based on the study titled Early Embryonic Morphology Sonographically Assessed and its Correlation with Yolk Sac in Missed Abortion by *Salamanca et al., (2013)* in the Department of Obstetrics and Gynecology, faculty of medicine, Granada, Spain. In the above study it was revealed that out of 200 patients 15 (7.5%) range; 3.5%-10.5% had echogenic yolk sac (least prevalent abnormality). A sample size of 204 patients of our study will be sufficient (confidence interval 95%). The sample size our study was calculated using Epi-info 2002. Qualitative data will be analyzed using chi-squared tests.

Inclusion criteria:

Pregnant women (ages, 18-45 years) with gestational age ≤ 11 weeks coming for first trimester sonographic evaluation who will be diagnosed as missed miscarriage.