"EVALUATION OF YOLKSAC ABNORMALITIES IN PREDICTING ABORTIONS- A PROSPECTIVE STUDY"

By

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Dissertation submitted to BLDE University, Bijapur

In partial fulfillment of the requirements for the degree of

MS

IN

OBSTETRICS AND GYNAECOLOGY

Under the guidance of

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2014-15

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ACKNOWLEDGEMENTS

Firstly, I pray to the almighty god, thanking him for the bounty of life. I thank my parents who have nurtured me and supported me in all my endeavors, without their love and innumerable sacrifices; I would not be the person I am today.

I would like to express my deep gratitude to my guide, **Dr. P.B.JAJU** **M.D, Professor and H.O.D**, Department of Obstetrics an gynaecology, BLDEU'S Shri B. M. Patil Medical College; who was ever encouraging in his approach while helping me through my postgraduate course. He was always supportive and allowed me to work and develop at my own pace, guiding wherever necessary. His meticulous approach and quick attention along with giving equal value to time was inspiring. Without his guidance and support, it would have been impossible to complete this dissertation.

I am highly indebted to **Dr.S. R. MUDANUR, DR V.R.GOBBUR, DR MANPREET KAUR ,DR S.R BIDRI** Professor's, Department of Obstetrics and gynaecology, Shri B. M. Patil Medical College Bijapur, for their invaluable guidance, constant encouragement and support in any endeavor which I undertook. He was an example to everyone and inculcated a work ethic which will go a long way in developing my career.

I express my sincere gratitude to **Dr.NEELAMMA PATIL,** **M.S.** Associate Professor, Department of Obstetrices and gynaecology, Shri B.M. Patil Medical College Bijapur whose inspiration and guidance have helped me in preparing this dissertation.

It gives me pleasure to express my gratitude to **Dr. Shoba** Senior Resident Assistant Professor, **Dr. Aruna** **M.S**, Assistant Professor Department of Obstetrics and gynaecology, Shri B. M. Patil Medical College Bijapur, for their constant advice and encouragement.

I wish to express my thanks to **Dr. M. S. BIRADAR**, Principal, B.L.D.E.U'S Shri B. M. Patil Medical College Bijapur, for allowing me do this work, to access medical records, utilize clinical material and facilities in this institution.

I thank my husband **Dr Uday Bhanu**, my son **Aarov**, my brother and my father an mother in law for their continuous support and love.

I thank my friends and my colleagues **Dr. Deepa, Dr.Pooja, Dr. Shilpy Kumari, Dr. Keval, Dr. Lubna, Dr Monika**, PGs in the Department of Obstetrics and gynaecology who rendered immense help and support during my postgraduate course. I thank them from my heart.

I thank he statistician **Mr .Shankar** for his guidance in statistics and **Mr .Babu Patil** of Om Sai Internet centre for helping me inprinting the thesis.

I express my indebtedness to all patients who contributed in no small way to this dissertation, but, for whom this entire exercise would have been unimaginable. This study is dedicated to them.

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ABSTRACT

INTRODUCTION: The secondary yolk sac is the first extraembryonic structure that can be detected with ultrasonography in the chorionic cavity and can be seen from the 5th to the 12th week menstrual age, at the latest.

During organogenesis and before placental circulation is established, yolk sac is the primary source of exchange between the embryo and the mother.

Many studies on the prognostic significance of the yolk sac for the prediction of abortions have been performed with conventional sonography and more recently with TVS. The results are conflicting.

Thus aim of our study is to find the correlation of the morphology of yolk sac and its association with normal outcome and abortion and how it can be signified as an early predictor of pregnancy outcome.

MATERIALS AND METHODS:

A total of 150 Pregnant women,(asymptomatic and threatened abortion cases) attending obstetric OPD between 5-12 weeks of gestational age at BLDE University's Shri. B. M. Patil Medical College, Hospital and Research Center, Bijapur from Oct 2013 to June 2014.

RESULTS:

In this study 150 women who presented to the antenatal OPD of B.L.D.E Hospital, between 5 and 12 weeks of gestation were evaluated with transvaginal or transabdominal sonography. 16.7% incidence of abnormal pregnancy outcome. The probability of abnormal pregnancy outcome increased with maternal age. (P = 0.012.). The probability of abnormal outcome increased with the increase in gravidity of the

patient, with significant increase in the risk of abortion with Gravida 3 and more (0.0001).

Mean age of the study population was 25 years and 56% of the study population belonged to the age group of 21- 30 years. 49.3% of the study population were primigravidae.

The sensitivity of predicting an abnormal outcome was 61.29 %, specificity was 96.48 % and PPV was 79.17% (P<0.001) .The sensitivity and negative predictive value were highest when the scan was performed at 7th week of gestation and specificity and positive predictive value was highest at 6th week of gestation.

CONCLUSION:

We can conclude from the present study that measurement of the secondary yolk sac characteristics can be used as a valuable tool to predict abortions. Based on the results of this study and data available from the literature, it is certain that abnormal yolk sac diameter, shape and echogenicity is associated with poor pregnancy outcome.

LIST OF ABBREVIATIONS

AFP	-	Alpha-Fetoprotein
CRL	-	Crown Rump Length
DES	-	Diethylstilbestrol
FSH	-	Follicle Stimulating Hormone
GA	-	Gestational Age
GS	-	Gestational Sac
LH	-	Luteinizing Hormone
MSD	-	Mean Sac Diameter
NPV	-	Negative Predictive Value
NK	-	Natural killer
OPD	-	Out Patient Department
PI	-	Pulsatality Index
PPV	-	Positive Predictive Value
PSV	-	Peak Systolic Velocity
RPL	-	Recurrent Pregnancy Loss
SD	-	Standard Deviation
TAS	-	Trans Abdominal sonography
TVS	-	Trans Vaginal sonography
USG	-	Ultra Songraphy
WHO	-	World Health Organization
YS	-	Yolk Sac
YSD	-	Yolk Sac Diameter

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

INTRODUCTION

The word abortion derived from the Latin word aboriri-to miscarry. Abortion is defined by the World Health Organisation and Centres of disease control and prevention as pregnancy termination prior to 20 weeks of gestation or with a fetus weighing born weighing less than 500 gms. Despite this the definitions vary according to state laws.

Spontaneous abortions or early pregnancy failure is one of the most frequent complications of pregnancy, but great difficulty is still experienced in, reliably anticipating which pregnancies will terminate in abortion. This situation is particularly distressing to those patients with history of threatened or recurrent abortion who abort despite resting in the hospital for many weeks. Therefore there is a need for techniques which will allow early diagnosis to be made in these patients, preferably with such certainty that a more active line of management can be pursued if so desired.

The primary yolksac is a structure seen by the 22^{nd} to 28 th postmenstrual days and from which the secondary yolksac evolves.

The secondary yolk sac is the first extraembryonic structure that can be detected wit transvaginal sonography (TVS) in the chorionic cavity and can be seen from the 5th to the 12th week menstrual age, at the latest.

During organogenesis and before placental circulation is established, yolk sac is the primary source of exchange between the embryo and the mother. Yolk sac has nutritive, endocrine, metabolic, immunologic, secretory, excretory and hematopoietic functions.

Many studies on the prognostic significance of the yolk sac for the prediction of abortions have been performed with conventional sonography and more recently with TVS. The results are conflicting.

Thus further studies on the morphology of yolk sac and its association with normal outcome and abortion could help, as an early predictor of pregnancy outcome. More than 80% of the spontaneous abortions are in the first 12 weeks. Half of these result from chromosomal anomalies.

Hence the patients with abnormal yolksac morphological characteristics can be followed up with biochemical markers and invasive techniques in certain cases to confirm the etiology and for management in future pregnancies.

Biochemical markers used for screening are free beta-hcg, unconjugated estriol, inhibin A. The tests are mainly classified into triple test, quad test. Triple test are MSAFP, beta-hcg, serum estriol and in quad test inhibin A is also done along with the above markers.

Yolksac secretes some amount of AFP and other types of serum albumin mainly used for detection of anomalies and syndromes and chromosomal abnormalities. Some studies have been carried out for detection of anomalies by the conjunct use of biochemical markers and YSD.

These non invasive techniques help in diagnosis of most of the abnormal outcome and as a last resort certain invasive techniques like CVS, amniocentesis and cord sampling have been carried out as they themselves can cause abortions.

OBJECTIVES

To study the abnormalities of yolksac in first trimester and to assess its value in predicting abortions.

REVIEW OF LITERATURE

During the first trimester of pregnancy, a unique and dramatic sequence of events occurs, defining the most critical and tenuous period of human development: the remarkable transformation of a single cell into a recognisable human being.

The time span for the first trimester is based on menstrual dates; in a patient with a 28 day cycle it begins 2 weeks before fertilization (on the day of last menstrual period) and concludes 12 weeks later. In contrast embryonic dating begins with fertilization and hence, 2 weeks later than the first day of last menstrual period.[1]

Ultrasound scanning has become an integral part of antenatal care. Sir Ian Donald was the first to demonstrate and document the applications of ultrasound in the field of medical diagnosis. This pioneering work was published in The Lancet in June 1958.[2]

First trimester ultrasound scan was initially used to date pregnancy. In the past 15 years technological progress and in particular the introduction of transvaginal approach made possible the detailed examination of fetal anatomy in the first trimester.[3]

Transvaginal sonography allows the use of higher frequency transducers than the traditional abdominal ultrasound, thus providing superior resolution with earlier and more accurate identification of fetal structures. In view of these advantages transvaginal sonography is now used in obstetrics for an increasing number of indications.[4]

Indications for first trimester ultrasound include:[1]

- To identify the location and the number of gestational sacs
- To assign a gestational age to the pregnancy
- To determine whether an early pregnancy has a normal appearance or whether sonographic indicators are present that predict failure
- To evaluate maternal symptoms such as pain or bleeding per vagina
- To evaluate uterine contents before terminating pregnancy
- To guide diagnostic or therapeutic procedures that require visual guidance(i.e., chorionic villus sampling, amniocentesis)

Early screening of fetal complications. For example early detection of Down‘s syndrome and other chromosomal abnormalities can now be achieved by measuring early sonographic measurements and following up with fetal nuchal translucency between 11 and 14 weeks of gestation, and combining this information with maternal age and serum biochemical markers.

To comprehend the normal and abnormal sonographic findings in early pregnancy, it is important to understand normal development and the sequence of events during the first trimester.

MATERNAL PHYSIOLOGY AND EMBRYOLOGY

The endometrium-decidua is the anatomical site of blastocyst apposition, implantation, and placental development. From an evolutionary perspective, the human endometrium is highly developed to accommodate endometrial implantation and a hemochorial type of placentation.

There seems to be a narrow window of endometrial receptivity to blastocyst implantation that corresponds approximately to menstrual cycle days 20 to 24.[5]

During the first 2 weeks of pre – and periovulation, cyclic changes occur within both the ovaries and the endometrium as a result of influence of pituitary gonadotropic follicle stimulating hormone (FSH) and luteinizing hormone (LH).[6]

Initially under the influence of FSH, a mature ovarian follicle develops. Estrogen elaborated by the follicle causes the functional layer of endometrium to proliferate and become thicker, as the spiral arteries elongate and uterine glands increase in number and length as a result of an abrupt surge in LH, ovulation occurs, and an oocyte is extruded, typically on day 14 of the cycle. After ovulation the follicle collapses and transforms into the glandular corpus luteum, which produces progesterone and small amounts of estrogen. This hormonal activity is responsible for additional histological changes of endometrium as it enters the secretory phase, so named because the uterine glands now secrete material rich in glycogen.

The glands become increasingly wide, tortuous, and saccular and the uterine spiral arteries become increasingly coiled as they invade the superficial compact layer of endometrium. The endometrium continuous to thicken as a result of glandular and vascular growth and increased stromal fluid.

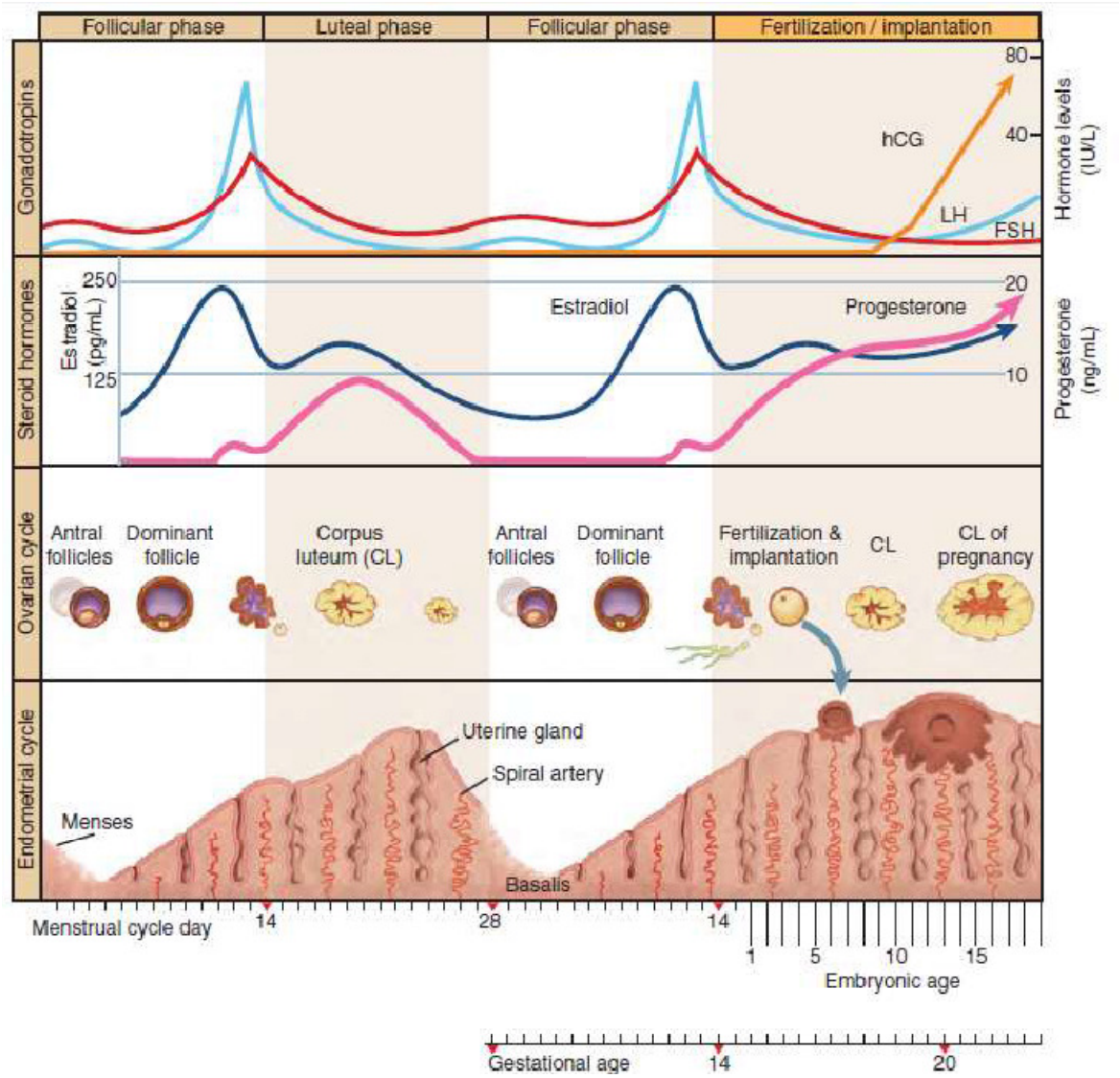


FIG 1: Ovarian and Endometrial Cycle

THE DECIDUA:

The decidua is a specialized, highly modified endometrium of pregnancy and is a function of hemochorial placentation. **Decidualization** – transformation of secretory endometrium to decidua—is dependent on estrogen and progesterone and factors secreted by the implanting blastocyst.[5]

Decidual structure:

The first scientific description of the **membrana decidua** was in the 18th century by William Hunter. The decidua is classified into three parts based on anatomical location. Decidua directly beneath blastocyst implantation is modified by trophoblast invasion and becomes the **decidua basalis**. The **decidua capsularis** overlies the enlarging blastocyst, and initially separates it from the rest of the uterine cavity. The remainder of the uterus is lined by **deciduas parietalis**—sometimes called **deciduas vera** when decidua capsularis and parietalis are joined.

The decidua parietalis and basalis, like the secretory endometrium, are composed of three layers. There is a surface, or compact zone—**zona compacta**; a middle portion,or spongy zone—**zona spongiosa**—with remnants of glands and numerous small blood vessels; and a basal zone—**zona basalis**. The zona compacta and spongiosa together form the **zona functionalis**. The basal zone remains after delivery and gives rise to new endometrium.[5]

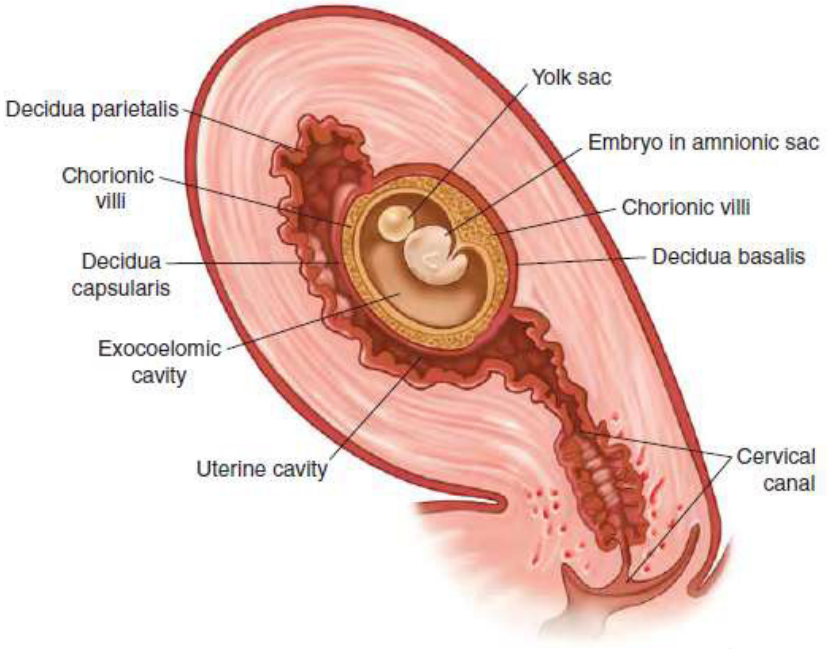


FIG 2: Decidual structure

Decidual Reaction:

In human pregnancy, the decidual reaction is completed only with blastocyst implantation. Predecidual changes, however, commence first during the midluteal phase in endometrial stromal cells adjacent to the spiral arteries and arterioles. Thereafter, they spread in waves throughout the uterine endometrium and then from the site of implantation. The endometrial stromal cells enlarge to form polygonal or round decidual cells. The nuclei become round and vesicular, and the cytoplasm becomes clear, slightly basophilic, and surrounded by a translucent membrane.Each mature decidual cell becomes surrounded by a pericellular membrane. The pericellular matrix surrounding the decidual cells may allow attachment of cytotrophoblasts through cellular adhesion molecules.[5]

Decidual Blood Supply:

As a consequence of implantation, the blood supply to the decidua capsularis is lost as the embryo-fetus grows. Blood supply to the decidua parietalis through spiral arteries persists, as in the endometrium during the luteal phase of the cycle. The spiral arteries in the decidua parietalis retain a smooth muscle wall and endothelium and thereby remain responsive to vasoactive agents that act on their smooth muscle or endothelial cells.

The spiral arterial system supplying the decidua basalis directly beneath the implanting blastocyst, and ultimately the intervillous space, is altered remarkably. These spiral arterioles and arteries are invaded by cytotrophoblasts. During this process, the walls of vessels in the basalis are destroyed. Only a shell without smooth muscle or endothelial cells remains. Importantly, as a consequence, these vascular

conduits of maternal blood—which become the uteroplacental vessels—are not responsive to vasoactive agents.[5]

Decidual histology:

The primary cellular components are the **true decidual cells**, which differentiated from the endometrial stromal cells, and numerous maternal bone marrow–derived cells. A striking abundance of large, granular lymphocytes termed **decidual natural killer cells (NK)** are present in the decidua early in pregnancy. In peripheral blood, there are two subsets of NK cells. About 90 percent are highly cytolytic and 10 percent show less cytolytic ability but increased secretion of cytokines.

In contrast to peripheral blood, 95 percent of NK cells in decidua secrete cytokines. About half of these unique cells also express angiogenic factors. These decidua NK cells likely play an important role in trophoblast invasion and vasculogenesis.[5]

The decidua basalis contributes to the formation of the basal plate of the placenta. The **Nitabuch layer** is a zone of fibrinoid degeneration in which invading trophoblasts meet the decidua. If the decidua is defective, as in placenta accreta, the Nitabuch layer is usually absent.

There is also a more superficial, but inconsistent, deposition offibrin—**Rohr stria**—at the bottom of the intervillous space and surrounding the anchoring villi.[5]

FERTILIZATION AND IMPLANTATION:

After fertilization in the fallopian tube, the mature ovum becomes a **zygote**—a diploid cell with 46 chromosomes—that then undergoes cleavage into blastomeres. In

the two-cell zygote, the blastomeres and polar body are free in the perivitelline fluid and are surrounded by a thick *zona pellucida*. The zygote undergoes slow cleavage for 3 days while still within the fallopian tube. As the blastomeres continue to divide, a solid mulberry-like ball of cells—the ***morula***—is produced.

The morula enters the uterine cavity about 3 days after fertilization.Gradual accumulation of fluid between the cells of the morula results in the formation of the early ***blastocyst.*** In the earliest stages of the human blastocyst, the wall of the primitive blastodermic vesicle consists of a single layer of ectoderm. As early as 4 to 5 days after fertilization, the 58-cell blastula differentiates into five embryo-producing cells—the ***inner cell mass*** and 53 cells destined to form ***trophoblasts***, which ultimately form chorionic membranes and fetal contribution to placenta. When blastocyst attains 107 cell stage the blastocyst is released from the zona pellucid as a result of secretion of specific proteases from the secretory-phase endometrial glands.[5]

Implantation of the embryo into the uterine wall takes place 6 or 7 days after fertilization. This process can be divided into three phases:

1. Apposition: initial adhesion of the blastocyst to the uterine wall
2. Adhesion: increased physical contact between the blastocyst and uterine epithelium
3. Invasion: penetration and invasion of syncytiotrophoblast and cytotrophoblast into the endometrium, inner third of the myometrium, and uterine vasculature

Successful implantation requires receptive endometrium appropriately primed with estrogen and progesterone. Uterine receptivity is limited to days 20 to 24 of the

cycle. Adherence to epithelium is mediated by cell-surface receptors at the implantation site that interact with receptors on the blastocyst.[5]

By the 4th menstrual week, the blastocyst, measuring only 1mm in diameter, becomes fully embedded into endometrial tissue.[1]

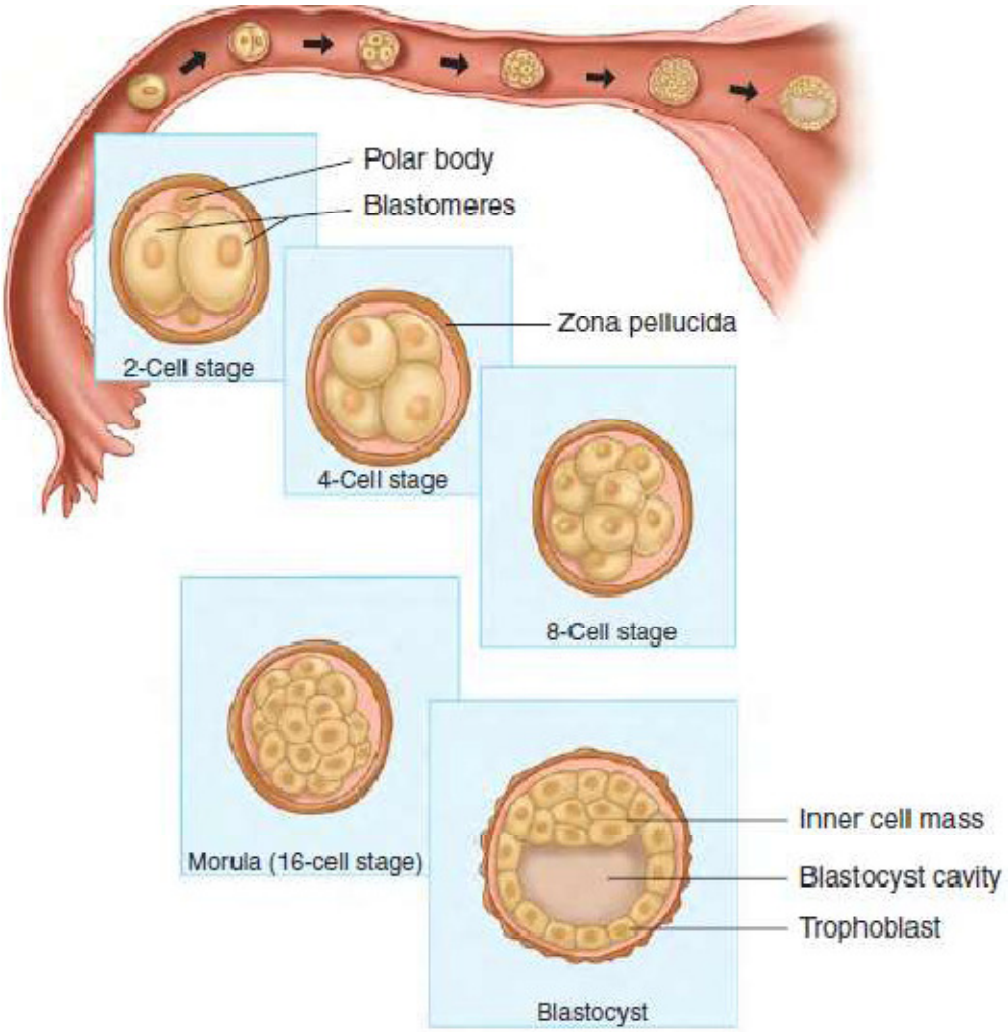


FIG 3: Cleavage and blastocyst formation

Second Week of Development (4th menstrual week):

Bilaminar Germ Disc DAY 8 (Day 22 menstrual age):

The blastocyst is partially embedded in the endometrial stroma. In the area over the embryoblast, the trophoblast has differentiated into two layers:

1. The cytotrophoblast: an inner layer of mononucleated cells.
2. The syncytiotrophoblast: an outer multinucleated zone without distinct cell boundaries.

Cells of the inner cell mass or embryoblast also differentiate into two layers:

1. Hypoblast layer: a layer of cuboidal cells adjacent to the blastocyst cavity.
2. Epiblast layer: a layer of high columnar cells adjacent to the amniotic cavity.

A cavity appears within the epiblast. This cavity enlarges to become the amniotic cavity. Epiblast cells adjacent to the cytotrophoblast are called amnioblasts; together with the rest of the epiblast, they line the amniotic cavity.[7]

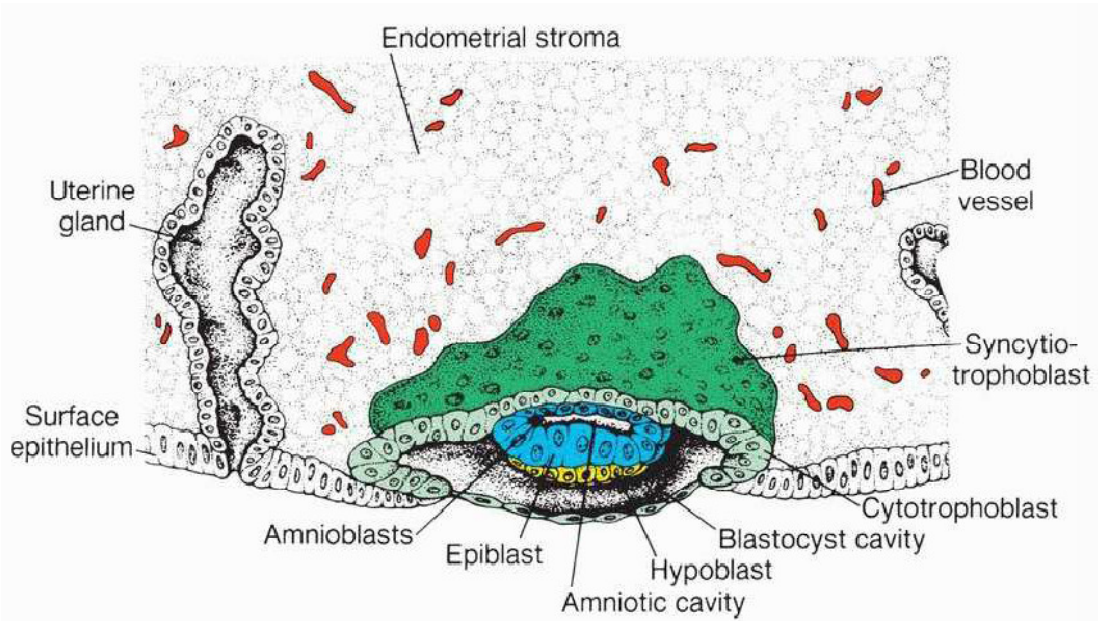


FIG 4: Day 8 human blastocyst

After implantation is complete, the trophoblast further differentiates along two main pathways, giving rise to villous and extravillous trophoblast. The **villous trophoblast** gives rise to the chorionic villi, which primarily transport oxygen and nutrients between the fetus and mother. The **extravillous trophoblast** migrates into

the deciduas and myometrium and also penetrates maternal vasculature, thus coming into contact with a variety of maternal cell types.

The extravillous trophoblast is thus further classified as **interstitial trophoblast** and **endovascular trophoblast.** The interstitial trophoblast invades the decidua and eventually penetrates the myometrium to form placental bed giant cells. These trophoblasts also surround spiral arteries. The endovascular trophoblast penetrates the lumen of the spiral arteries.[5]

DAY 9 (Day 23 menstrual age):

The blastocyst is more deeply embedded in the endometrium, and the penetration defect in the surface epithelium is closed by a fibrin coagulum. At the embryonic pole vacuoles appear in the syncytium.

When these vacuoles fuse, they form large lacunae, and this phase of development is thus known as the **lacunar stage.** At the abembryonic pole, meanwhile, flattened cells probably originating from the hypoblast form a thin membrane, the **exocoelomic (Heuser's) membrane** that lines the inner surface of the cytotrophoblast. This membrane, together with the hypoblast, forms the lining of the **exocoelomic cavity, or primitive yolk sac.**[7]

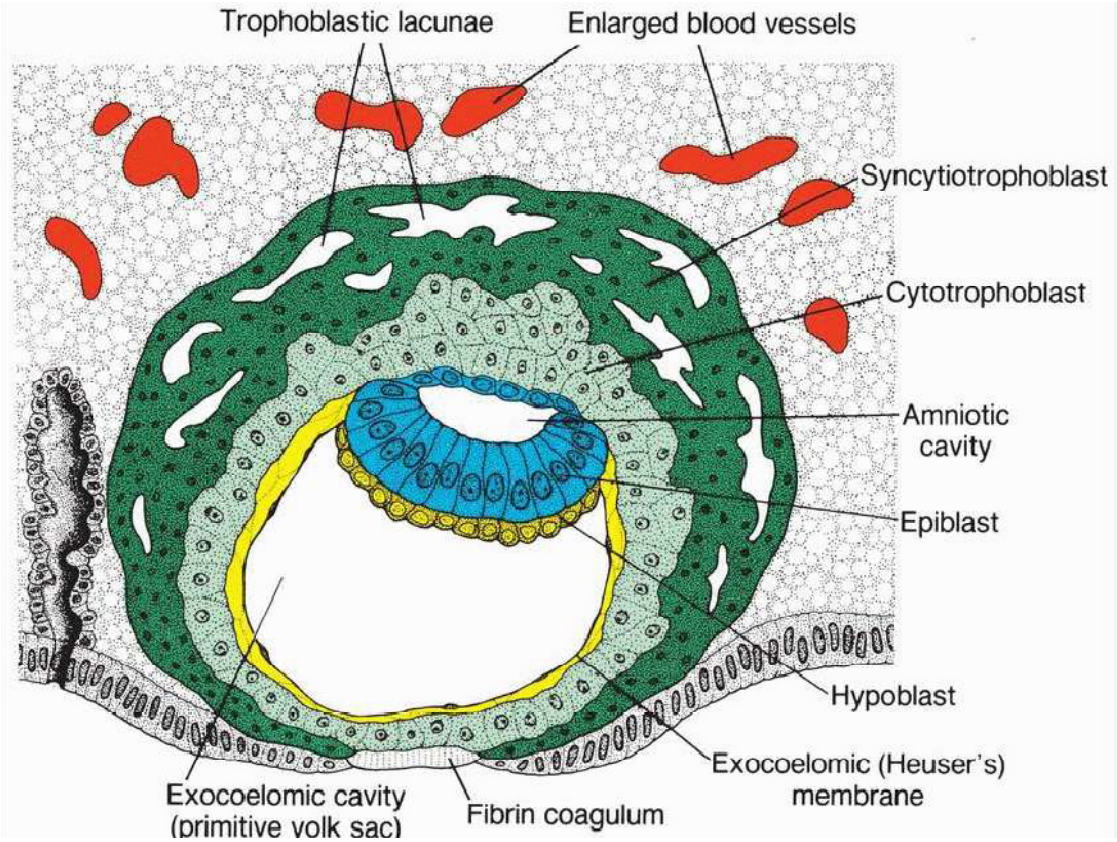


FIG 5: Day 9 human blastocyst

DAY 11 & 12 (Day 24 & 25 menstrual age):

By the 11th to 12th day of development, the blastocyst is completely embedded in the endometrial stroma. The trophoblast is characterized by lacunar spaces in the syncytium that form an intercommunicating network. This network is particularly evident at the embryonic pole; at the abembryonic pole, the trophoblast still consists mainly of cytotrophoblastic cells.

Concurrently, cells of the syncytiotrophoblast penetrate deeper into the stroma and erode the endothelial lining of the maternal capillaries. These capillaries, which are congested and dilated, are known as sinusoids. The syncytial lacunae become continuous with the sinusoids, and maternal blood enters the lacunar system. As the trophoblast continues to erode more and more sinusoids, maternal blood begins to flow through the trophoblastic system, establishing the **uteroplacental circulation**.

A new population of cells appears between the inner surface of the cytotrophoblast and the outer surface of the exocoelomic cavity. These cells, derived from yolk sac cells, form a fine, loose connective tissue, the **extraembryonic mesoderm**, which eventually fills all of the space between the trophoblast externally and the amnion and exocoelomic membrane internally. Soon, large cavities develop in the extraembryonic mesoderm, and when these become confluent, they form a new space known as the **extraembryonic coelom**, or **chorionic cavity.** This space surrounds the primitive yolk sac and amniotic cavity, except where the germ disc is connected to the trophoblast by the connecting stalk.

Growth of the bilaminar disc is relatively slow compared with that of the trophoblast; consequently, the disc remains very small (0.1 to 0.2 mm).[7]

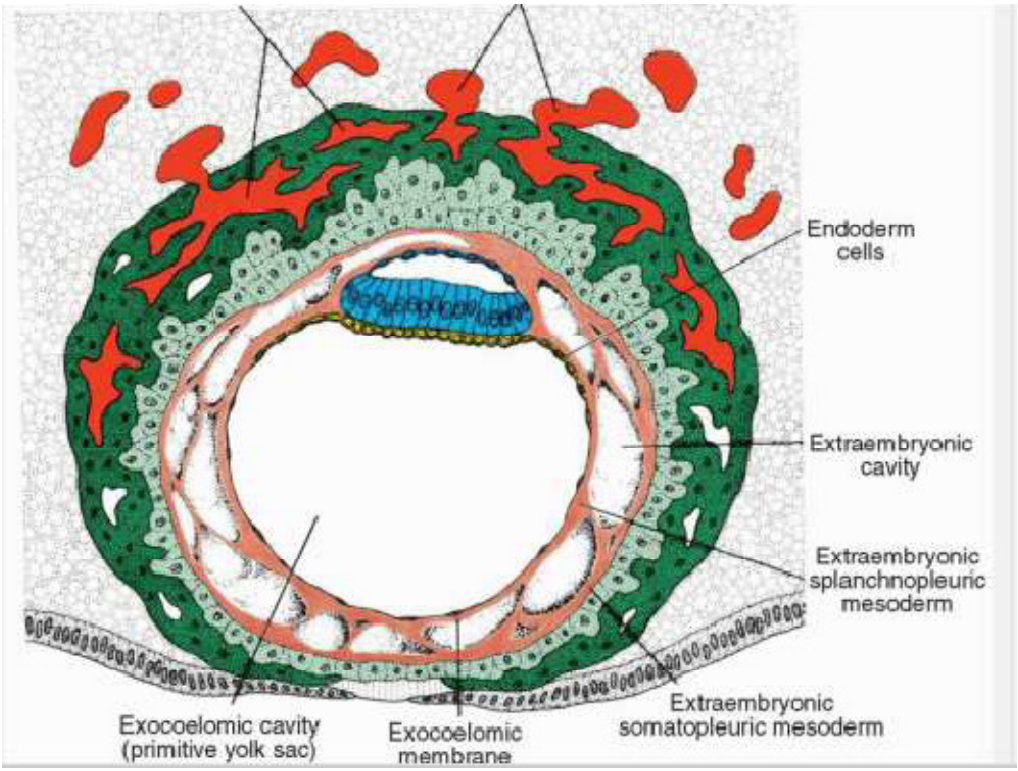


FIG 6: Day 12 human blastocyst

DAY 13 (Day 27 menstrual age):

The trophoblast is characterized by villous structures. Cells of the cytotrophoblast proliferate locally and penetrate into the syncytiotrophoblast, forming cellular columns surrounded by syncytium, known as **primary villi**.

In the meantime, the hypoblast produces additional cells that migrate along the inside of the exocoelomic membrane. These cells proliferate and gradually form a new cavity within the exocoelomic cavity. This new cavity is known as the **secondary yolk sac or definitive yolk sac**.

This yolk sac is much smaller than the original exocoelomic cavity, or primitive yolk sac. Meanwhile, the extraembryonic coelom expands and forms a large cavity, the **chorionic cavity**. The extraembryonic mesoderm lining the inside of the cytotrophoblast is then known as the **chorionic plate**. The only place where extraembryonic mesoderm traverses the chorionic cavity is in the **connecting stalk.** With development of blood vessels, the stalk becomes the umbilical cord.[7]

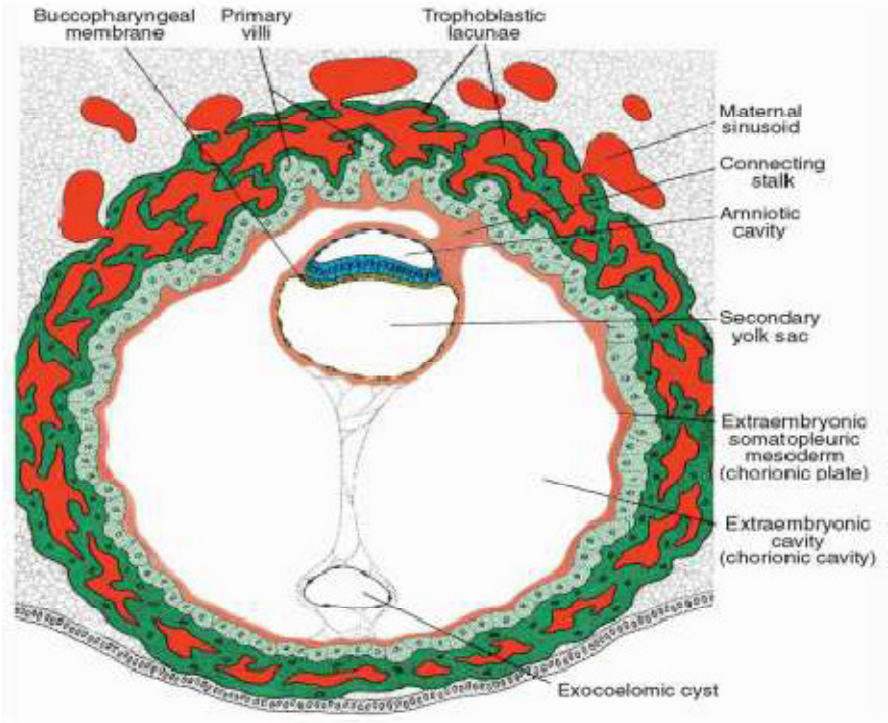


FIG 7: Day 13 human blastocyst

By the end of 4th week, the products of conception have attained a diameter of 2 to 3mm and are at the threshold of detection by transvaginal ultrasound.[1]

5TH MENSTRUAL WEEK:

The products of conception continue to enlarge primarily as a result of expansion of the chorionic cavity, which attains a diameter of 5 mm. This is identified by sonologists as gestational sac.

Secondary yolk sac is variably identified by scan and the developing embryo undergoes a process of gastrulation, which transforms it into a trilaminar disk with three germ layers (endoderm, mesoderm, and ectoderm). Despite these changes, embryo remains undetectable by scan.[1]

6TH TO 10TH MENSTRUAL WEEK:

This period constitutes the embryonic phase during which time all the major internal and external structures begin to form, The primordial heart begins to beat at the 6^{th} week.[6]

The appearance of the embryochanges dramatically as it is transformed from a flat disk like configuration to a c shaped structure, and it develops a human –like appearance. During embryogenesis, CRL grows rapidly, measuring 30mm by the end of 10th week.

NORMAL SONOGRAPHIC ANATOMY AND LANDMARKS IN EARLY PREGNANCY

At 4th week, despite complete implantation, the blastocyst remains undetectable to even high – resolution vaginal imaging because of its small size (1mm)

IDENTIFYING THE GESTATIONAL SAC:

The first definitive sonographic finding to suggest early pregnancy is visualization of the gestational sac. Using vaginal transducers with the frequencies of at least 5 MHz, the size threshold for sac detection is 2 to 3 mm, corresponding to between 4 weeks 1day GA to 4 weeks 3 days GA.[8]

Earliest appearance of a gestational sac is a small round fluid collection surrounded completely by a hyperechogenic rim of tissue. The central fluid collection is the chorionic cavity, and the surrounding echos are due to the developing chorionic villi and adjacent decidual tissue.

As the sac enlarges the hyperechogenic rim should be at least 2mm thick, and its echogenicity should exceed the level of myometrial echoes.[9]

It is typically located in the upper part of the decidualized endometrium in an eccentric position.

Intradecidual sac sign: As the sac implants into the decidualized endometrium, it should be adjacent to the linear central cavity echo complex, without initially displacing or deforming this hyperechogenic anatomic landmark.(FIG 8) Using this sign with transabdominal approach for diagnosing an early intrauterine pregnancy, sensitivity of 92%, specificity of 100% and accuracy of 93% was noted.[10]

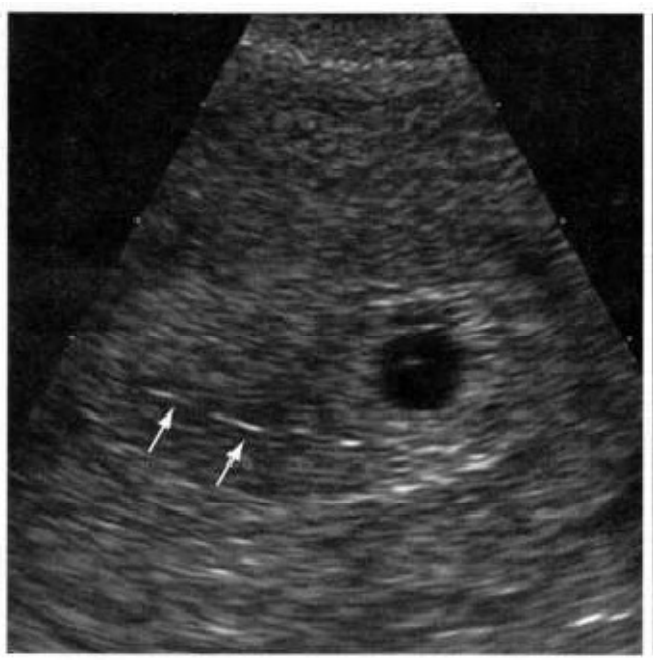


FIG 8: Intradecidual sac sign

Double decidual sac sign: It consists of two concentric echogenic lines surrounding a portion of the gestational sac. (FIG 9) The line closest to the sac represents the combines smooth chorion-decidua capsularis, whereas the adjacent, more peripherally located line represents the decidua parietalis. The uterine cavity is the potential space between the two lines and often contains a trace of fluid. This sign is universally present when the MSD is 10mm or greater. It is most effective with transabdominal sonography performed at 5 to 6 weeks GA because, using this approach, sonographers can confirm the presence of an intrauterine pregnancy before the yolk sc is visualized. With the advent of transvaginal sonography, this sign has a lesser role.[11]

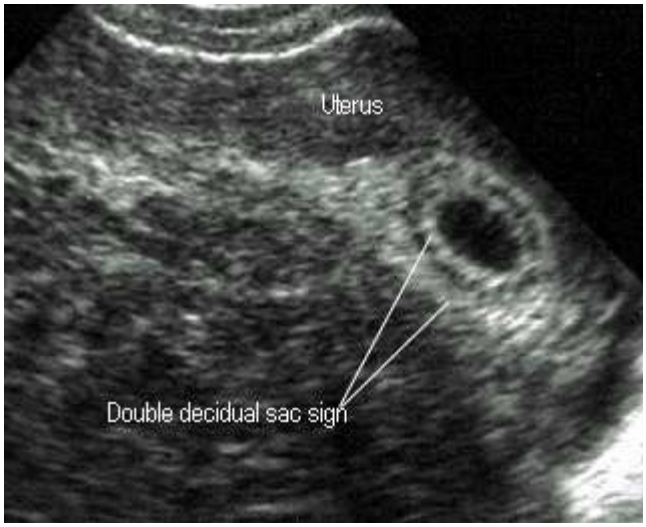


FIG 9: The double decidual sac sign

Table 1: Difference between the gestational sac and pseudo gestational sac of ectopic pregnancy[12]

	GESTATIONAL SAC	PSEUDOGESTATIONAL SAC
Localization	Eccentric	Central
Shape	Spheroid	Ovoid
Contour	Thick double layered wall	Thin mono-layered wall
Peritrophoblastic circulation	Exists	Non-existent

BLOOD FLOW IN EARLY PREGNANCY:

The characteristic first trimester main uterine artery waveform obtained at the uterocervical junction consists of high – resistance flow with a prominent diastolic notch, although the notch will occasionally be absent in a normal patient. The diastolic notch typically disappears during the second trimester and in some cases as early as 13 weeks gestation.[13]

Doppler signals can also be obtained from the spiral arteries or subchorionic vessels, located at the junction of the myometrium and hyperechogenic

choriodecidual tissues. Flow in these vessels is typically pulsatile, with a low resistance pattern.[1]

INDENTIFYING THE YOLK SAC

The yolk sac is the first anatomic structure identified within the gestational sac. Embryologically this is the secondary yolk sac. Using a transvaginal approach, it may be visible as early as the beginning of the 5th gestational week (MSD, 5 mm), and it is almost always seen by 5.5 weeks gestational age (MSD 8 mm).[14]

Using a transabdominal approach, the yolk sac should be evident by 7 Weeks gestational age, when the MSD is 20 mm.[15]

Because detecting a yolk sac unequivocally confirms that an intrauterine fluid collection represents an early intrauterine pregnancy as opposed to a pseudosac associated with an ectopic pregnancy, it is important to optimize scanning parameters to ensure its visualization.[16]

Yolk sac and its significance as a prognostic marker are described in later section.

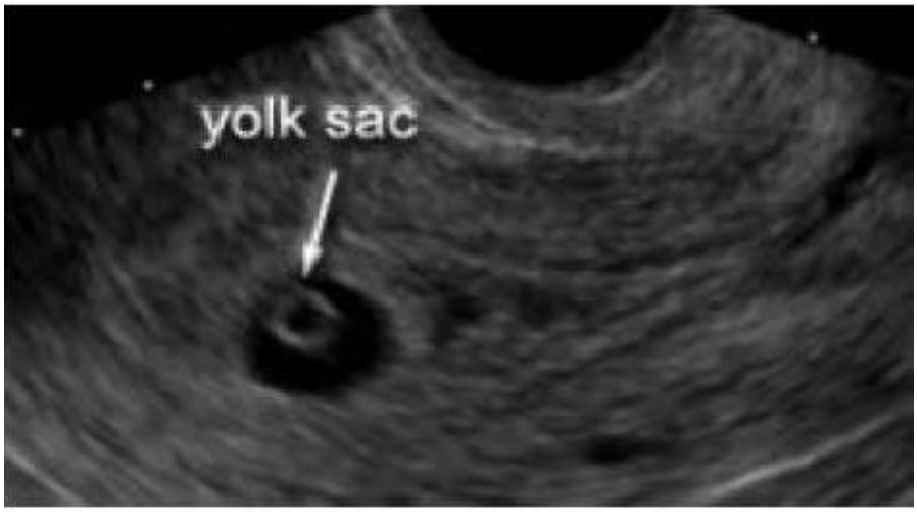


FIG 10: Yolk sac is the first structure to be seen by TVS even before fetal pole is seen. This patient had LMP 1 month 7days back and yolk sac is seen with mean YSD of 3.4 mm[17]

INDENTIFYING THE EMBRYO AND CARDIAC ACTIVITY:[1]

The threshold for embryo detection is when the disk measures 1 to 2 mm in length. Depending on the investigator, this corresponds to between 5 and 6 weeks gestational age and a MSD of between 5 and 12 mm.

Many sonologists consider the identification of cardiac activity in an embryo with a CRL of less than 5 mm as 6 weeks gestational age. Cardiac activity should be detected routinely when the embryo attains a length of 4 to 5 mm. This corresponds togestational of 6.0 to 6.5 weeks, at which time the MSD is 13 to 18 mm. Using a transabdominal approach cardiac activity should be evident by 8 weeks gestational age, when the MSD is 25 mm. When the cardiac activity is obtained before 6 weeks, the rate is relatively slow, typically between 100 and 115 bpm.

Thereafter, it increases rapidly, and by 8 weeks is between 144 and 170 bpm. After 9 weeks the rate plateaus at 137 to 144 bpm. Sonographic observations throughout the embryonic period from 6 to 10 weeks, reveals dramatic transformation of anatomic structures. CRL length increases by approximately 1 mm per day.

During the 6th week of development, with ventral folding of the cranial and caudal ends of the embryo, it changes rapidly from a flat disc into a 3D C- shaped structure. The rapidly developing brain and head become prominent as the rostral neuropore closes, and the caudal neuropore elongates and curves into a tail. Soon thereafter, as the amniotic sac surrounds the developing embryo, the yolk sac, and embryo diverge from one another.

Between 7 and 8 weeks, limb buds evolve into paddle- shaped upper and lower limbs, with early development of hands and feet.

By the 9th week, the extremities protrude ventrally, the trunk begins to elongate and straighten, and midgut herniation into the umbilical cord is prominent.

The 10th week (embryo length of 30 – 35 mm) reveals a distinctly human appearing embryo, with visible and relatively opposed hands and feet and the tail no longer present. Sonographic evidence suggests that, the return of the midgut to the abdominal cavity is completed by the end of the 11th week.[1]

INDENTIFYING FETAL MEMBRANES AND THE PLACENTA:

The amniotic membrane is not normally identified until 6.7 weeks at which time the CRL is 7 mm. Detection of an amniotic sac might be one of the useful signs indicating miscarriage when the CRL is less than 7 mm, at which point detection in normal cases is not yet possible.[18]

Rarely however it can be detected as a small membranous structure contiguous with the embryo but on the side opposite the yolksac, the term **double bleb sign** has been used to describe this anatomic relationship.[19]

Inability to visualize the amnion does not predict pregnancy failure. Detection of the amnion and its cavity confirms the presence of an intrauterine gestational sac. Because the amniotic cavity enlarges more rapidly than the chorionic cavity, the latter structure is obliterated as the amniotic membrane reaches the chorion. The process of apposition begins in the middle of the first trimester but is often incomplete until 12 to 16 weeks gestational age.

As placental development begins during the 8th gestational week, the hyperechoic ring surrounding the sac becomes asymmetric, with focal peripheral thickening of the most deeply imbedded portion of the sac.[1]

DETERMINING GESTIONAL AGE:

Between 5 and 11 weeks, gestational age (in days) can be calculated by a simple and convenient method by adding 30 to the MSD (in mm).[15,20] A yolk sac without an embryo or cardiac activity, detected by transvaginal scan, corresponds to 5.5 weeks GA.[21] With the normal development, in accordance with the formula noted previously, the MSD should be 8 mm. If the cardiac activity is detected but the CRL is too small to measure (< 5 mm), the GA is reported as 6 weeks.[21]

Between 6 and 12 weeks GA, determining CRL measurement is generally considered the most accurate method of dating a pregnancy.

ABNORMAL PREGNANCY OUTCOME AND ABORTION

WHO defines abortion as pregnancy termination prior to 20 weeks gestation or witha foetus born weighing less than 500 g.[22]

A spontaneous abortion, also called miscarriage. Is defined as the unintentional termination of pregnancy before 20 weeks of gestation or when the birth weight is less than 500 g. This is different from legal definition used for intentional abortion which is interruption of pregnancy before viability (the time when foetus is sufficiently developed to survive outside of the uterus).

The gestational age when foetal viability has been reached is legally defined as 24 weeks.

The prevalence of spontaneous abortion varies according to the diligence used in its identification. Wilcox and colleagues found that 31% of pregnancies were lost after implantation. Two thirds of these (22%) ended before pregnancy could be clinically detected.[23]

Spontaneous abortion is common complication of pregnancy in about 15% of recognizable pregnancies.[24] 80% of the spontaneous abortions are in the first 12 weeks and at least half result from chromosomal anomalies.[22]

A number of factors influence the spontaneous abortion rate. For example, clinically apparent miscarriage increases with parity as well as with maternal and paternal age. The frequency doubles from 12% in women younger than 20 years to 26% in those older than 40 years. For the same comparison of paternal ages, the frequency increases from 12 to 20%. It is not known if clinically silent miscarriages are similarly affected by age and parity.[22]

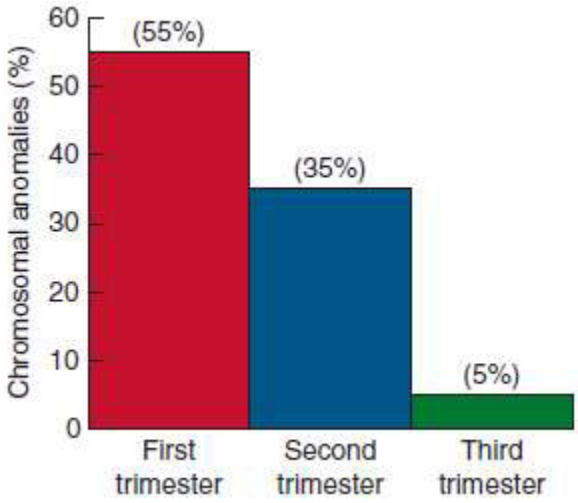


FIG 11: Frequency of chromosomal anomalies in abortus and still births during each trimester[22]

Foetal Factors:[22]

Early spontaneous abortions commonly display a developmental abnormality of the zygote, embryo, foetus, or at times, the placenta. In 50 to 60 % of spontaneously aborted embryos and foetuses, abnormalities in chromosomal numbers account for most wastage.

Aneuploid Abortion

Approximately 95 percent of chromosomal abnormalities are caused by maternal gametogenesis errors, whereas 5 percent are due to paternal errors.

TABLE 2: Chromosomal findings in abortus (incidence in percentage **Chromosomal Studies Kajii et al. (1980)[25] Eiben et al. (1990)[26] Simpson (1980)[27]**

Chromosomal Studies	**Kajii et al. (1980)[25]**	**Eiben et al. (1990)[26]**	**Simpson (1980)[27]**
NORMAL(euploid)			
46, XY and 46, XX	46	51	54
ABNORMAL(aneuploid)			
Monosomy X (45,X0)	10	**5**	**9**
Triploidy	**7**	**6**	**8**
Tetraploidy 2 4 3	**2**	**4**	**3**
Structural anomaly 2 2 2	**2**	**2**	**2**
Double or triple trisomy 2 0.9 0.7	**2**	**0.9**	**0.7**
Autosomal trisomy	**31**	**31**	**22**

Autosomal trisomy is the most frequently identified chromosomal anomaly with first-trimester miscarriages. Although most trisomies result from isolated nondisjunction, balanced structural chromosomal rearrangements are present in one partner in 2 to 4 percent of couples with recurrent miscarriage.

Autosomal trisomies for all except chromosome number 1 have been identified in abortuses, and those with autosomes 13, 16, 18, 21, and 22 are most common. Bianco and colleagues recently described that a previous miscarriage increased the risk of a

subsequent fetal aneuploidy from a baseline risk of 1.39 % to 1.67%. 2 or 3 previous miscarriages increased this to 1.84 and 2.18 percent, respectively.[28]

Monosomy X (45, X) is the single most common specific chromosomal abnormality.These cause Turner syndrome, which usually results in abortion and much less frequently in live-born females. Conversely, **autosomal monosomy** is rare and incompatible with life.

Triploidy is often associated with hydropic placental (molar) degeneration. Incomplete (partial) hydatidiform moles may be triploid or trisomic for only chromosome 16. Although these fetuses frequently abort early, the few carried longer are all grossly malformed. Advanced maternal and paternal age does not increase the incidence of triploidy.

Tetraploid abortuses are rarely live born and are most often aborted early in gestation.

Chromosomal structural abnormalities infrequently cause abortion. Some infants who are live born with a balanced translocation may appear normal.

Euploid Abortion: Chromosomally normal fetuses tend to abort later in gestation than those with aneuploidy. For example, although 75 percent of aneuploid abortions occurred before 8 weeks, euploid abortions peaked at approximately 13 weeks

Maternal Factors: [22]

Endocrine Abnormalities:

Hypothyroidism - Severe iodine deficiency may be associated with miscarriages. Thyroid autoantibodies alone have been associated with an increased incidence of miscarriage.

Diabetes Mellitus - Spontaneous abortion and major congenital malformation rates are both increased in women with insulin-dependent diabetes. The risk appears related to the degree of metabolic control in early pregnancy.

Drug Use and Environmental Factors:

Tobacco - Smoking has been linked with an increased risk for euploid abortion.

Alcohol - Both spontaneous abortion and fetal anomalies may result from frequent alcohol use during the first 8 weeks of pregnancy. The risk seems to be related to both frequency and dose.

Caffeine - Cnattingius and colleagues observed a significantly increased abortion risk only in women who consumed at least 500 mg of caffeine daily, roughly equivalent to five cups of coffee.

Radiation - In therapeutic doses given to treat malignancy, radiation is certainly an abortifacient. Although lower doses are less toxic, the human dose to effect abortion is not precisely known.

Environmental Toxins - An increased risk of miscarriage has been described for dental assistants exposed to 3 or more hours of nitrous oxide per day in offices without gas-scavenging equipment

Immunological Factors:[22]

A number of immune-mediated disorders are associated with early pregnancy loss. Many tend to cause recurrent miscarriage. Two primary pathophysiological models are the **autoimmune theory -** immunity against self, and the **alloimmune theory -**immunity against another person.

Autoimmune Factors:

Miscarriages are more common in women with systemic lupus erythematosus. Many of these women have antiphospholipid antibodies, which are a family of autoantibodies that bind to negatively charged phospholipids, phospholipids-binding proteins, or a combination of the two. They also are found in women without lupus. Indeed, in up to 5 percent of normal pregnant women, lupus anticoagulant (LAC) and anticardiolipin antibody have been linked with excessive pregnancy wastage. Women with both a history of early fetal loss and high antibody levels may have a 70-percent miscarriage recurrence rate. Antibodies to β2 glycoprotein may be especially problematic.

Alloimmune Factors:

It is suggested that normal pregnancy requires the formation of blocking factors that prevent maternal rejection of foreign fetal antigens that are paternally derived. A woman will not produce these serum blocking factors if she has human leukocyte antigens (HLAs) similar to those of her husband. Other alloimmune disorders have been posited to cause recurrent miscarriage, including altered natural killer (NK) cell activity and increased lymphocytotoxic antibodies

Inherited Thrombophilias: [22]

Some genetic disorders of blood coagulation may increase the risk of both arterial and venous thrombosis. The better studied thrombophilias are caused by mutations of the genes for factor V Leiden, prothrombin, antithrombin, proteins C and S, and methylene tetrahydrofolate reductase (hyperhomocysteinemia).

These are most commonly associated with recurrent miscarriage. As placental perfusion is minimal in very early pregnancy, thrombophilias may have greater clinical implications in later pregnancy.

Uterine Defects: [22]

Acquired Uterine Defects: Large and multiple uterine leiomyomas are common, and they may cause miscarriage. In most instances, their location is more important than their size. Uterine synechiae—Asherman syndrome - usually result from destruction of large areas of endometrium by curettage.

Developmental Uterine Defects: Abnormal mullerian duct formation or Fusion defects may develop spontaneously or may follow in utero exposure to diethylstilbestrol (DES). Although they can cause mid pregnancy loss and other preterm birth and pregnancy complications, it is controversial whether uterine defects cause early miscarriage.

Incompetent Cervix

This describes a discrete obstetrical entity characterized by painless cervical dilatation in the second trimester. It can be followed by prolapse and ballooning of membranes into the vagina, and ultimately, expulsion of an immature fetus. Unless effectively treated, this sequence may repeat in future pregnancies.

RECURRENT PREGNANCY LOSS:

It is classically defined as three or more consecutive pregnancy losses at 20 weeks or less or with fetal weights less than 500 grams. Most women with recurrent miscarriage have embryonic or early fetal loss, and the minority of losses are after 14 weeks. Although the definition includes three or more miscarriages, many agree that evaluation should at least be considered following two consecutive losses. This is because the risk of subsequent loss after two successive miscarriages is similar to thatfollowing three losses—approximately 30 percent. The causes of recurrent miscarriage parallel those of sporadic miscarriage, although the relative incidence differs between the two categories. For example, first-trimester losses with recurrent miscarriage have a significantly lower incidence of genetic anomalies.[29]

Vaginal bleeding is very common and is experienced by approximately 21% of pregnancies before the 20th week of pregnancy. 50% of these pregnancies eventually abort.[30]

The detection of embryonic activity is a good prognostic sign and most of these pregnancies will have favourable outcomes. Goldstein and colleagues examined the frequency of pregnancy loss following successful development of anatomical embryonic landmarks identified with endovaginal ultrasound:[31]

TABLE 3: Probability of spontaneous abortion with sonographic findings

STUCTURE VISUALIZED	PROBABILITY OF ABORTION
Gestational sac	11.5 %
Yolk sac	8.5 %
Embryo CRL < 5 mm	7.2 %
Embryo CRL 6 – 10 mm	3.3 %
Embryo CRL > 10 mm	0.5 %

Threatened abortion: It is a clinical term used to describe vaginal bleeding in early pregnancy and the cervix is long and closed. It occurs in approximately 21% of pregnancies before 20 weeks.

Blighted Ovum or Anembryonic pregnancy: This term is used to describe an abnormal pregnancy with a gestational sac but no visible embryo or yolk sac. Chromosomal abnormalities are common in blighted ova.

Missed abortion: If USG reveals an intrauterine sac with an embryo with no cardiac activity, the diagnosis of missed abortion is made.

Incomplete abortion: Diagnosis of incomplete abortion is made when bleeding and passage of tissue occurs through an open cervical canal and some products of conception still remain in the uterine cavity.

Complete abortion: If all the products of conception are expelled and the cervix found to be closed, the diagnosis is complete abortion.

Inevitable abortion: When bleeding occurs in association with lower abdominal pain and USG reveals an intact intrauterine pregnancy situated low in the uterus the diagnosis of inevitable abortion is made.

ULTROSONGRAPHIC SIGNS OF POOR PREGNANCY OUTCOME

Absent intrauterine sac:

If the uterus appears normal on sonographic examination, or if the endometrial echos appear prominent and no sac is visible, the differential diagnosis includes absence of pregnancy, a very early intrauterine pregnancy, or an ectopic pregnancy.

When the endometrium is abnormally thick or irregularly echogenic, the differential diagnosis includes intrauterine blood or retained products of conception after an incomplete spontaneous abortion, the decidual reaction associated with an ectopic pregnancy, or decidual changes resulting from an early but not yet visible intrauterine pregnancy.[1]

Patient history in conjunction with the quantitative level of hCG can often pinpoint the specific cause for the sonographic findings. Initially an hCG level of 6500 mIU/ml, calibrated to the first international reference preparation (first IRP), was the discriminatory level for identification of a gestational sac by transabdominal sonography [32-33]. Subsequent studies have established a lower discriminatory level corresponding to an HCG level of 3600 mIU/ml, by transabdominal sonography (first IRP) [20, 34]. By endovaginal USG, Nyberg et al. Established a discriminatory zone of 1000 mIU/ml (second IRP) corresponding to 2000 mIU/ml (first IRP), above which all patients had a gestational sac [35]. Goldstein et al. correlated sac diameters with HCG levels in 20 patients developing a discriminatory level of 1025 mIU/ml (first

IRP) with endovaginal USG [36]. Robert et al. established a discriminatory level of 1000mIU/ml (first IRP) corresponding to 32 days of gestation from LMP, for the presence of a gestational sac, using a 7 – MHz transvaginal probe.[37]

DETECTING A SAC WITHOUT AN EMBRYO

When the ultrasound examination reveals a sac without an embryo or yolk sac, the diagnosis is limited to one of the three entities

1. A normal early intrauterine pregnancy
2. An abnormal intrauterine pregnancy
3. A pseudogestational sac in an ectopic pregnancy

In theory an intrauterine sac can be distinguished from pseudogestational sac of ectopic pregnancy by using criteria mentioned previously in Table

1. In practice, this distinction is often difficult to make with certainty. Therefore, a follow up USG should be obtained to document subsequent appearance of yolk sac or embryo.

Abnormal sac criteria:

The threshold for detecting a normal intrauterine sac by transvaginal ultrasound is when the sac diameter is only 2 – 3 mm, this corresponds to a GA of slightly more than 4 weeks[8]. A sac should be detected consistently by both transabdominal and transvaginal sonography when its diameter is 5 mm, this corresponds to GA of 5weeks.[15]

Specific size criteria can be used to differentiate a normal from an abnormal intrauterine gestational sac. Using a transabdominal approach, discriminatory size criteria that suggest an abnormal sac include:[9,11]

1. Failure to detect a double dicidual sac when the MSD is 10 mm or greater
2. Failure to detect a yolk sac when the MSD is 20 mm or greater
3. Failure to detect an embryo with cardiac activity when the MSD is 25 mm or greater

Because of superior resolution, transvaginal approach should be used preferentially to evaluate any intrauterine fluid collection that lacks an embryo. Generally accepted transvaginal discriminatory criteria for determining an abnormal sac include:[14]

1. Failure to detect a yolk sac when MSD is 8 mm or greater
2. Failure to detect embryo and cardiac activity when MSD is 16 mm or greater.

Growth rate:

The terms blighted ovum and anembryonic pregnancy imply that developmental arrest occurred either before formation of the embryo or before it is detectable using the currently available equipment. Despite an anembryonic state, trophoblastic tissue often continues to function, resulting in continued gestational sac growth albeit at a diminished rate.[1]

Whereas the MSD increases by 1.13 mm/day in a normal gestation, the growth rate of an abnormal sac is only 0.7 mm/day. Based on these observations, Nyberg et al. suggest that gestational sac growth of less than or equal to 0.6 mm/day is evidence for abnormal development.[15]

Recommendations for theoptimal time of a follow-up sonogram are presented based on the initial sac size.

Ideally the repeat study should aim to identify both the yolk sac and the cardiac activity. For example if the initial MSD is 4 mm, a follow up scan should be done to detect cardiac activity when the sac achieves a diameter of 16 mm. Because normal sac diameter increases by approximately 1 mm/day, an appropriate time interval between the two sonographic examinations is at least 12 days. In contrast, if the initial sonographic examination reveals MSD of 12 mm (without cardiac activity), the follow up study should be done approximately 4 days later to determine whether the pregnancy is developing normally.

Trophoblastic appearance:

Initially described on the basis of transabdominal sonography, an abnormal appearing choriodecidual or trophoblastic reaction consists of a distorted sac shape, thin (<2mm) weekly echogenic, or irregular choridecidual reaction, and absence of double decidual sac when MSD exceeds 10 mm.[38]

Recently subtle trophoblastic abnormalities have been reported using a vaginal approach. Bajo we al[39] determined the significance of a difference in gestational age in weeks and a trophoblastic thickness of ≥ 3 mm in predicting poor prognosis in pregnancy outcome. The sensitivity of this sign in the prediction of spontaneousabortion was 82%, the specificity was 93%, the positive predictive value was 63% and the negative predictive value was 97.

Role of Doppler:

Flow around a pseudo gestational sac may be either absent or show only a minimal amount of low velocity flow (<8 cm/s PSV).[40]

In contrast, flow around an intrauterine gestational sac typically is high velocity with a low resistance pattern. This pattern can sometimes be seen with pseudogestational sac.[41]

This finding limits the usefulness of Doppler for making this important distinction. Also since Doppler sonography delivers more energy than gray scale ultrasound, its use should be minimized to prevent unnecessary and potentially harmful exposure of an earlyembryo.[42]

DETECTING A SAC WITH AN EMBRYO

Cardiac activity absent:

When the embryo is visible during a transabdominal ultrasound examination but cardiac activity is absent, the prognosis is usually poor. Occasionally however, cardiac activity is not detected in a very small embryo because of its size. On the basis of work by Pennell et al, the discriminatory embryo size for detecting cardiac motion transabdominally has been determined as being 9 mm. In their experience cardiac activity was absent in 21% of the normal pregnancies with a CRL of less than 9 mm.[43] Vaginal approach lowers the discriminatory CRL for detecting the cardiac activity.

Levi et al[44] suggested a 4 mm CRL cut-off because, in their experience, all the normal pregnancies had cardiac activity when the embryo achieved this length, whereas cardiac activity was absent in 18% of embryos with a CRL was less than 4 mm. In most cases, embryonic demise is due to a chromosome abnormality that leads to arrested embryonic development.[45]

Cardiac activity present:

Sonographic detection of cardiac activity not only confirms a living embryo but is also considered a favorable prognostic finding[44]. In general, if the cardiac activity is found in an aymptomatic women examined after 8 weeks' GA, the risk of loss is only 2 – 3 %.[46-47]

RISK FACTORS FOR EARLY PREGNANCY FAILURE:

Gestational age:

An inverse relationship exists between GA and an adverse outcome. Before 6.4 weeks GA, the incidence of subsequent demise ranges from 7% to 24%.[48-49] This loss rate declines to approximately 2% after 8 weeks. Increased early loss most likely reflects a well recognized high background rate of demise as a result of lethal chromosome mutations during this phase of pregnancy.[46-47]

Intrauterine blood:

Intrauterine collections of blood are found in many women with first trimester threatened abortion as well as some asymptomatic patients, During early pregnancy, as implantation occurs, the genesis for these collections most likely relates to the erosive effects of the chorion frondosum as it penetrates the decidua basalis. Later it is likely due to venous bleeding associated with separation or abruption of placental margin or marginal sinus. When this occurs blood dissects along the paths of least resistance and can be located in a variety of positions relative to the developing sac and placenta. As the blood tracks away and becomes remote from the placenta, it often elevates the attached chorionic membrane, dissecting it and the attached deciduas vera. In this manner it comes to surround the gestational sac.[1]

Acute hemorrhage is hyperechoic or isoechoic relative to placental tissue. With evolution liquefaction occurs, and the collection becomes more sonolucent but often contains residual low level echos.

Several studies suggested a 2 – 3 fold increased risk of spontaneous abortion[50] whereas others reported no increase in miscarriage rate despite a visible intrauterine hematoma.[51-52] One explanation for the varied opinions may relate to the location as opposed to the size of the hematoma. For example, a small retro placental hematoma may be associated with a relatively worse prognosis than a larger hematoma situated within the endometrial cavity and away from the placenta.[53]

Heart rate:

One report defines fetal bradycardia as less than 100 bpm before 6.2 weeks GA and less than 120 bpm between 6.3 and 7 weeks.[54] Multiple investigations document an adverse outcome with embryonic bradycardia.[55-56] Close and continued follow up of embryos with early bradycardia (at 6 to 7 weeks GA) is warranted, because even if the rate normalizes by 8 weeks GA, there is still a 25% demise rate by the end of first trimester.[57] Analyses of first trimester bradycardia also confirms an association with structural and chromosome abnormalities especially trisomy 18 and triploidy.[58-59] In contrast other chromosome defects, including trisomy 21, and especiallytrisomy 13 and turners syndrome, have an association with the first trimester tachycardia (determines at 10-14 weeks GA).[59]

Small sac – size growth delay:

In 2 reports evaluating pregnancy outcome in the presence of the first trimester oligohydramnios, the incidence of spontaneous abortion was between 80% and 94% despite normal cardiac activity.[60-61] In these studies, oligohydramnios was diagnosed

when the difference between the MSD and CRL was less than 5 mm. Even less severe discrepencies, in the range of 5 to 8 mm, are at increased risk for miscarriage, with a reported rate of approximately 25%.[60]

Amnion evaluation:

Abnormal amnion development is suggested when the membrane is easy to see or if its thickness and echogenicity approach that of the yolk sac.

Another abnormal finding is an enlarged amniotic cavity relative to the CRL.Because ultrasound imaging normally detects an embryo before the amnion, a finding that has been reported as highly suggestive of anabnormal pregnancy is visualization of this membrane without detection of an embryo.[62] In majority of the cases with an ―empty amnion‖ sign also have a MSD greater than 16 mm, which, in itself is consistent with a failed pregnancy.

YOLK SAC

Development of the Yolk sac:

Ultrsonographic visualization of yolk sac was first described by Mantoni and Pedersen(1979)[63]. Between the 22nd and 28th postmenstrualdays, the embryo contains only 2 layers – the embryonal ectoderm and the primary endoderm. The 2 layers form 2 cavities around the embryo –

The amniotic cavity (ectoderm) and theprimary yolk sac (endoderm). The secondary yolk sac evolves from the primary yolk sac by the 5th post menstrual week (29 to 36 days). By this time, the primary yolk sac is absorbed and the secondary yolk sac has completely developed.

The growth rate of the yolk sac is quicker than that of the amniotic cavity. At the beginning of the 5th week, it is the first visible structure in the chorionic cavity. It is round structure with an echogenic rim and a hypoechoic center. At this time it is 3 – 4mm. The secondary yolk sac is the unambiguous evidence of intrauterine gravidity. Until there is a detectable yolk sac inside the uterine cavity, we should always take ectopic pregnancy into account.

Around the 36 to 38 post menstrual days, the embryo becomes visible between the amniotic cavity and the yolk sac. It is only a 2 – 3 mm long, linear, hyperechoic structure. Even at this stage, we can detect the embryo‘s heart activity, although there is no detectable circulation in the yolk sac until the 6th week.

By the 9th week, the yolk sac grows to a diameter of 5 – 6 mm, but it begins to degenerate soon after, and disappears by the 12th week.[64]

Structure of the Yolk sac:[12]

The yolk sac is made up of 3 layers -

1. The inner endoderm
2. The middle mesenchyme
3. External mesothelial layer

Endodermal layer: It contains 10 – 20 μm wide columnar cells, with 0.5 – 1 μm long cilia on the surface. Inside the cells there are mitochondria, a highly developed Golgi apparatus, lysosomes, glycogen and intracellular vacuoles. These cells are very similar to liver cells due to their similar functions. The canalicular network of these cells also resembles that of the liver.

Mesenchymal layer: It contains blood vessels, red blood cells and macrophages. The vessels spring from the vitellointestinal duct. There is no basal membrane between the inner and middle layer.

Mesothelial layer: It contains 5 – 10 μm high cells with 2 – 5 μm microvilli on the surface. These cells are full of intracellular vacuoles. After the 9th week, the microvillus and the inner cells structures dissolve, and the yolk sac begins to degenerate.

Functions of the yolk sac:

Due to its structure and position, the yolk sac plays an important role in nutrition transport. The following facts support this role:

1. The wall and the cavity of the yolk sac are in direct contact with the primitive midgut.
2. Its histological structure is very similar to the liver
3. The composition of the coelomic fluid is significantly different from the amniotic fluid : it contains proteins, creatinine, and hCG in a higher concentration.[65]
4. The yolk sac synthesizes numerous proteins, which are later produced by the liver including AFP, alfa-1-antitrypsin, albumin, pre albumin and transferring.

Until the 10th post menstrual week, these factors are produced by the yolk sac and after that by the liver.[12]

Circulation of the Yolk sac:

About the end of 5th week, mesoderm cells located in the visceral mesoderm of the wall of the yolk sac differentiate into blood vessels and blood cells. Centrally located cells then give rise to primitive blood cells, while those on the periphery flatten and form endothelial cells lining blood islands. Blood islands approach each other rapidly by sprouting of endothelial cells and after fusion, give rise to small vessels. At the same time, blood vessels and capillaries develop in the extra embryonic mesoderm of the villous stems and the connecting stalk. By continuous budding, extraembryonic vessels establish contact with each other inside the embryo. Intraembryonic blood vessels, including the heart tube, are established in exactly the same manner as extraembryonic vessels.

The rhythmic contraction of the heart pumps the primitive blood from the connecting stalk towards the cranial portion of the embryo. Meanwhile, the intraembryonic blood vessels protrude into the chorion through the body stalk, and form capillary loops at the axis of the villi, giving rise to the placental circulation.

The intraembryonic circulation precedes blood flow in the intervillous space.Normal placental circulation starts only after the end of organogenesis around the 13th week, which confirms the significant role of the yolk sac in nutritive and transport functions.

Kupesic and Kurjek examined the circulation of the yolk sac and vitelline duct in early pregnancy. Before the 6th week, there is no detectable circulation in the body stalk or the yolk sac by ultrasound doppler examination. Between the 6 and 12 weeks, there is a non continuous, low velocity waveform with absence of diastolic flow.[66]

Overall visualization rate for the yolk sac vessels was 80%. The highest visualization rates were obtained in the 7th and 8th weeks of gestation reaching values of 90%. In the same period, the visualization of the vitelline duct arteries was 87% and 91%. A characteristic waveform profile included low velocity (5.8±1.7 cm/s) and absence of diastolic flow which was obtained from all examined yolk sac. The pulsatility index showed the mean value of 3.24± 0.94. Vitelline vessels showed similar PSV (5.4 ± 1.8 cm/s) and PI values (3.14 ±0.91).[67]

Abnormalities of the yolk sac development:

It is evident from the formation and function of the yolk sac, that any deviation in these complicated processes could disturb the development of the embryo. It plays an important role in the nutritive, metabolic and hemopoietic processes of the first trimester.[68]

Absence of yolk sac is the first sonographic indicator of an early maldevelopment.

It is very important finding of a blighted ovum. In this case, we should distinguish between intrauterine and ectopic pregnancy.

Abnormal yolk sac size is also an indicator of maldevelopment. Lyons established that for a gestational sac diameter of less than 10mm, the yolk sac diameter should be less than 4 mm. A large yolk sac can indicate poor pregnancy outcome. The surviving embryos the probabilities for chromosomal aberrations increase.

Small yolk sac can also predict poor pregnancy outcome[61]. Green and Hobbins reported a similar outcome with diameter less than 2 mm.[69]

Kucuk and workers found that the yolk sac diameter out of 2SD of the mean for the gestational age allowed prediction of an abnormal pregnancy outcome with a sensitivity of 65%, specificity of 97%, and positive predictive value of 71% and negative predictive value of 95%.

Abnormal yolk sac shape allowed prediction of an abnormal pregnancy outcome with a sensitivity of 29%, specificity of 95%, positive predictive value of 47% and a negative predictive value of 90.5%.[70]

Changes in echogenicity can also be the same predicting factors. Presence of hyperechogenic yolk sac is highly associated with chromosomal aneuploidy between the 9 and 11 gestational weeks.[71]

Kurjak and workers demonstrated the characteristics of yolk sac circulation. They found a non continuous, low velocity waveform with absent diastolic flow. They also detected three different types of abnormal circulation signals in patients with missed abortions – irregular blood flow, permanent diastolic flow, and venous blood flow.[67]

Makikallio and workers examined the Doppler parameters of uterine, spiral, intraplacental, chorionic, umbilical and yolk sac hemodynamics in early pregnancies. They found that in patient who later had pre eclampsia at the 8th week the maternal intraplacental resistance index was higher, a week later, the yolk sac resistance index and umbilical artery mean velocity were lower. In late first trimester, increased velocities and RI were observed in chorionic arteries. No difference in uterine and spiral artery hemodynamics and in umbilical artery pulsatility index was observed.[72]

In diamniotic twin pregnancies the number of the embryos equals the number of the yolk sacs. In monochorionic-monoamniotic twin pregnancies a single yolk sac may be a normal finding, but cases of single yolk sac are highly associated with conjoined twins.[73]

ASSOCIATION BETWEEN DIFFERENT MORPHOLOGICAL TYPES AND ABNORMAL KARYOTYPES IN EARLY PREGNANCY LOSS [74]

Chromosomal abnormalities are the most common cause of early pregnancy loss, accounting for over 50% of fetal demise. In a study conducted by Angiolucci et al. the prevalence of chromosomal abnormalities was significantly higher when there were abnormal morphological features compared with cases having normal ultrasound (85.2% vs. 33.8%, $P < 0.0001$). Specifically, the highest prevalence of chromosomal abnormalities was found in the **early symmetrical arrested growth group** i.e., simultaneous arrest of growth of both gestational sac and CRL (100%), followed by the **small embryo-fetus group** i.e., CRL < 5th centile with normal gestational sac diameter (94.1%), the **enlarged yolk sac group (93.3%)** and the **empty sac group** (72.2%). The prevalence of chromosomal abnormalities in each of these four abnormal morphological types was significantly higher than that in early pregnancy loss with normal ultrasound.

They found the **enlarged yolk sac** feature in the vast majority of cases of early pregnancy loss that had a **trisomy 22 karyotype**. This association suggests that fundamental genes for embryonic development may be localized on chromosome 22, and their over expression might determine potentially lethal abnormalities in the

embryo-fetal circulation. The accumulation of fluid inside the yolk sac could be an early sign of such abnormalities in the embryo-fetal circulation. In all cases of early pregnancy loss with enlarged yolk sac, the abnormal increase in yolk sac size was already present before miscarriage and therefore this cannot be attributed to postmortem events.

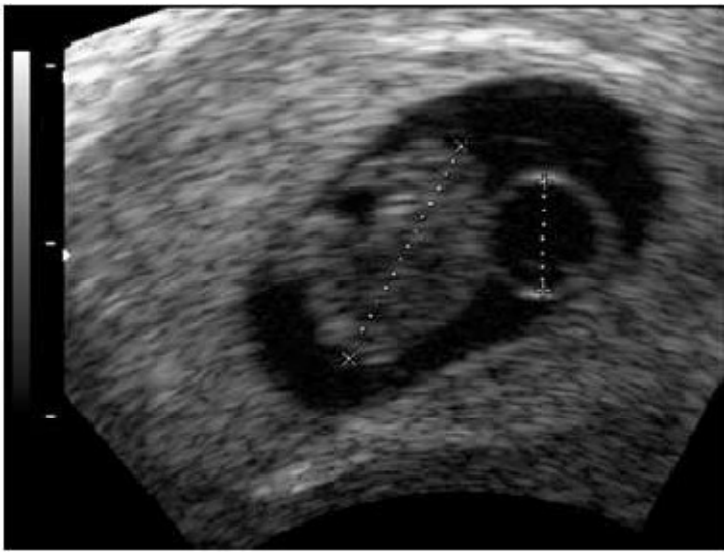


FIG 12: Sonographic appearance at 7 + 3 weeks of enlarged yolk sac in a case which then suffered early pregnancy loss, showing large yolk sac mean diameter (6.1 mm, +callipers) and normal crown–rump length (13.6 mm, × callipers)[74] The **small embryo-fetus** type was found to correlate with a **45, X karyotype.**

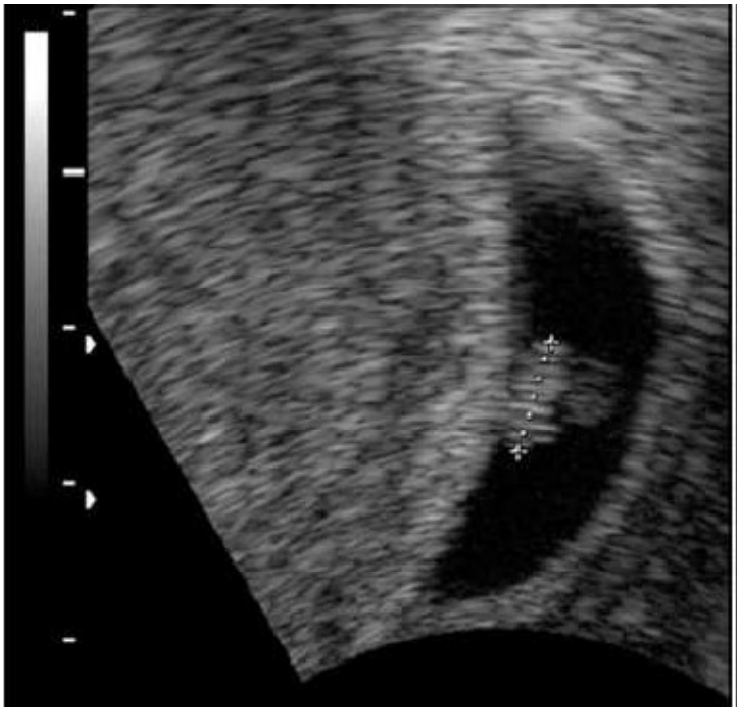


FIG 13: Sonographic appearance at 7 + 3 weeks of small embryo-fetus in a case which then suffered early pregnancy loss, showing small crown–rump length (5 mm, callipers) and normal/large mean gestational sac diameter (23 mm).[74]

A CRL : YSD measurement < 10th percentile, as well as an irregularly shaped echogenic yolk sac may be predictive of aneuploidy, particularly trisomy 18[75]

The exact etiology for the increased risk of miscarriage associated with enlarged YSD is unclear. In one study with karyotype information from products of miscarriage, the investigators concluded enlarged YS is a non specific finding of failed pregnancy.[76]

Persistent yolk sac:[77]

A persistent yolk sac has been defined as a yolk sac that has achieved a diameter of 5.6 mm or greater without losing its internal pressure at the 12th week of pregnancy or later. A persistent yolk sac was not associated with adverse perinatal outcomes,including abnormal sonographic findings, isolated structural defects, poor

obstetric outcomes, and perinatal mortality. Although yolk sacs mostly disappear toward the end of the first gestational trimester, they may sometimes persist even to the 13thweek of gestation. The persistence of the yolk sac seems to be unrelated to an adverse perinatal outcome.

MATERIAL AND METHODS

Source of data

Pregnant women attending obstetric OPD between 5-12 weeks of gestational age at BLDE University's Shri. B. M. Patil Medical College, Hospital and Research Center, Bijapur from Oct 2013 to June 2014.

Details of the study

Inclusion criteria

Pregnant women of gestational age less than 12weeks

Asymptomatic cases

Threatened abortion cases

Exclusion Criteria

Molar pregnancy

Multiple pregnancy

Ectopic pregnancy

Missed abortion

Incomplete and Inevitable abortion.

Women with known structural anomalies of uterus

Method of data collection

All patients attending Shri B. M. Patil Medical College between 5-12 week of gestational age were subjected to sonographic evaluation of yolk sac morphological

characteristics and followed up at 11-14week and for anomaly scan between 18-22 weeks and clinically till 28 weeks to look for abortions.

Yolk sac diameter was measured from inner to inner distance of yolksac.

PRIMARY OUTCOME - Correlation between abnormal yolksac diameter, shape, echogenicity with abortions.

SECONDARY OUTCOME - Correlation of abnormal and persistent yolksac with abortions.

SAMPLE SIZE

$$n=\frac{Z\alpha^2 xpxq}{Z^2}$$

$$=150$$

Statistical analysis

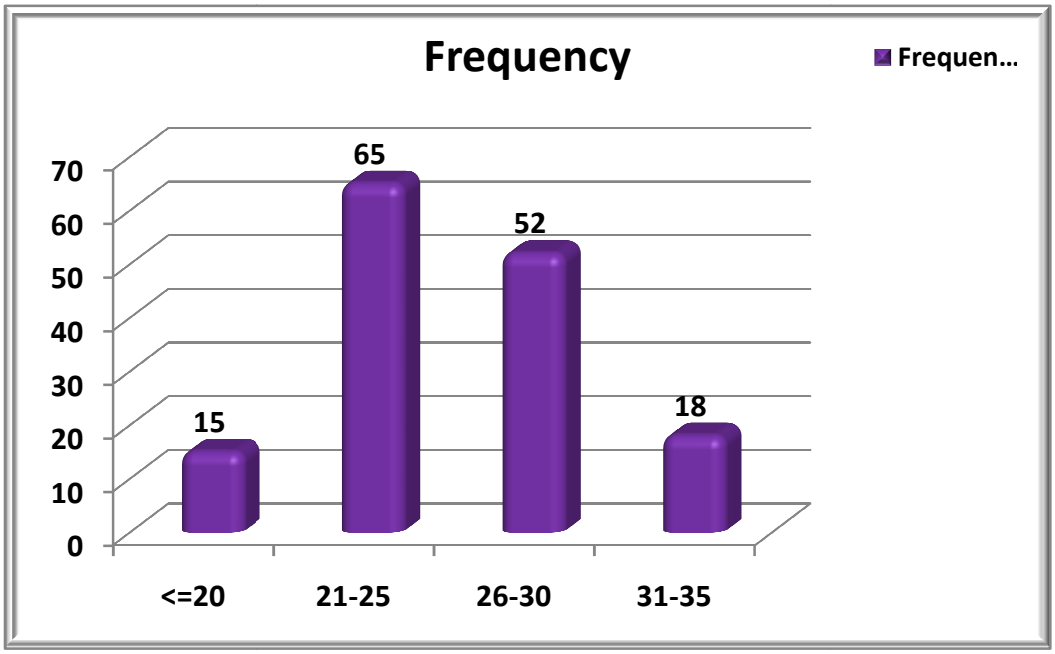
All the quantitative parameters such as yolk sac diameter, gestational age, CRL, Mean gestational sac diameter, age and parity of women etc will be described in terms of descriptive statistics such as mean and standard deviation. Upper and lower 95% confidence limits will also be estimated. Appropriate graphical presentation will be carried out to plot the yolk sac diameter with mean ± 2SD based on women with normal pregnancy outcome. Bivariate corelation will be estimated between different factors such as Yolk sac diameter v/s Gestational age, Yolk Sac diameter v/s Mean gestational sac diameter. To test for difference in Yolk sac diameter between abnormal and normal outcome t-test/non parametric tests of significance will be employed.

RESULTS

Table 4 Age distribution of study population

Number	Minimum	Maximum	Mean	SD
150	18	34	25.49	3.96

Graph 1 : Age distribution of patients



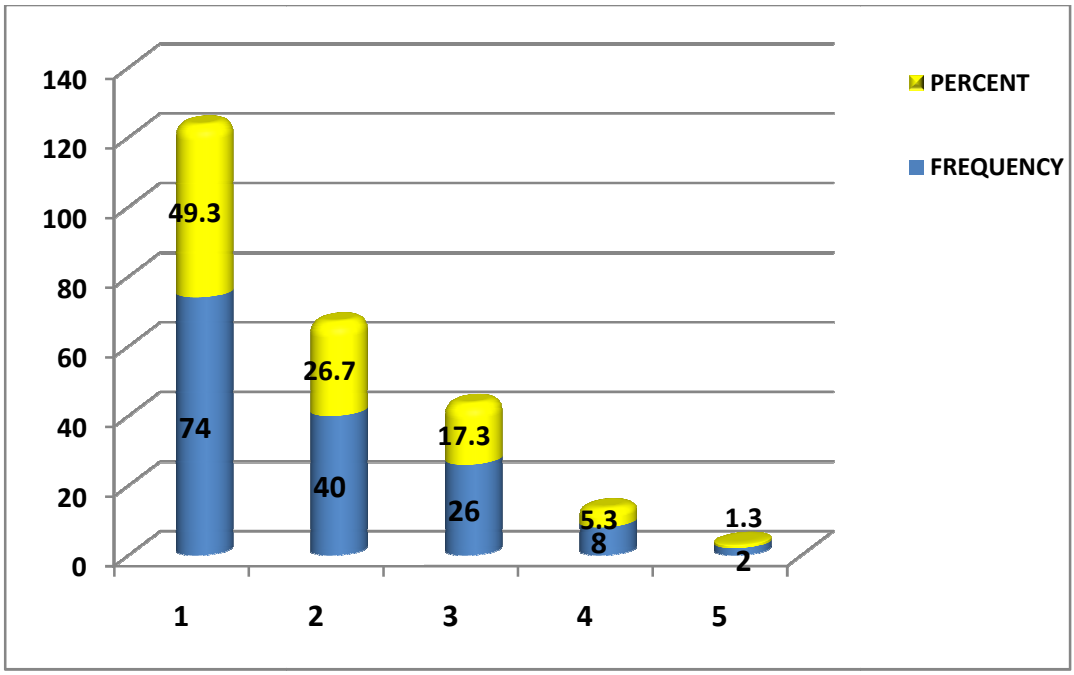
Age

The study population was mainly in the age group of 21 to 30 with an average percentage of 56%

Table 5 Distribution of gravidity in study population

Gravida	Frequency	Percent
1	74	49.3
2	40	26.7
3	26	17.3
4	8	5.3
5	2	1.3
TOTAL	150	100.0

Graph 2 : Distribution of study population according to gravidity



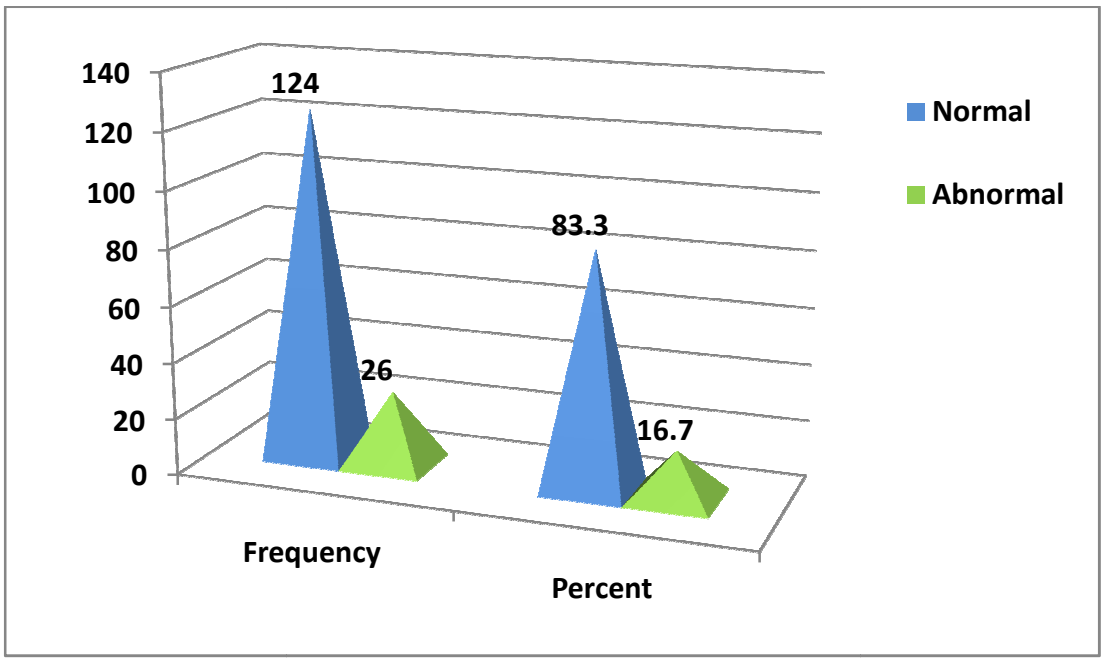
Gravidity

49.3% of the study population were primigravida.

Table 6 Pregnancy outcome in study population

Outcome	Frequency	Percent
Normal	124	83.3
Abnormal	26	16.7
Total	150	100

Graph 3 : Distribution of study patients according to pregnancy outcomes.

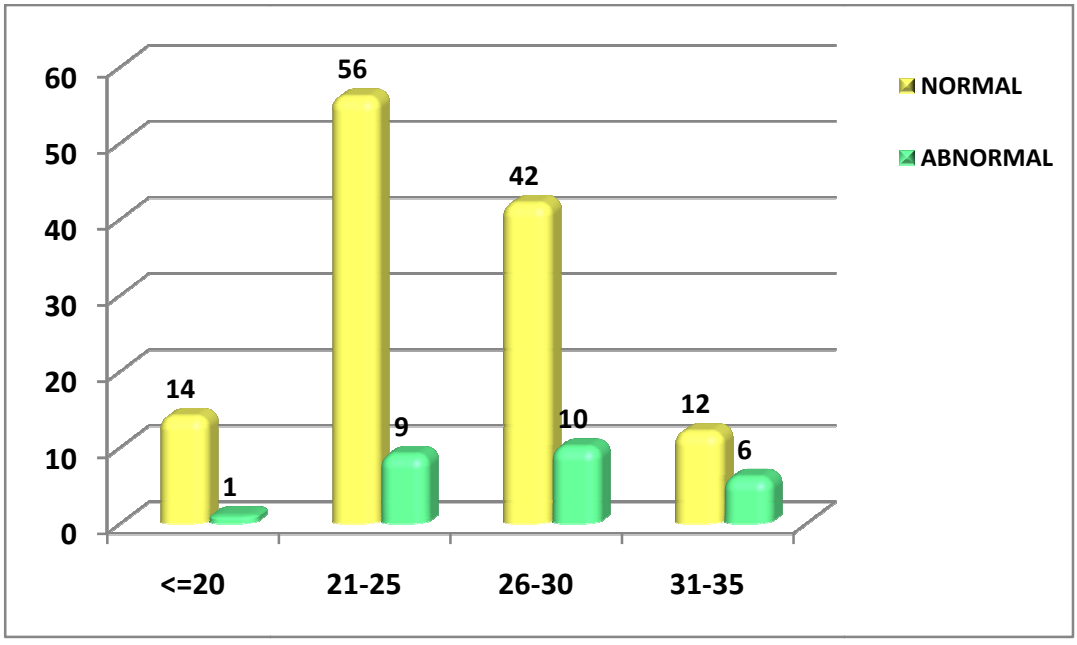


16.7% of the stuy population had an outcome of abortion.

Table 7 Distribution of normal and abnormal outcome with respect to maternal age

Maternal age	Normal	Abnormal	Total	p
<=20	14	1	15	0.012*
21-25	56	9	65	
26-30	42	10	52	
31-35	12	6	18	
Total	124	26	150	

Graph 4 : Distribution of maternal age according to preganancy outcome.



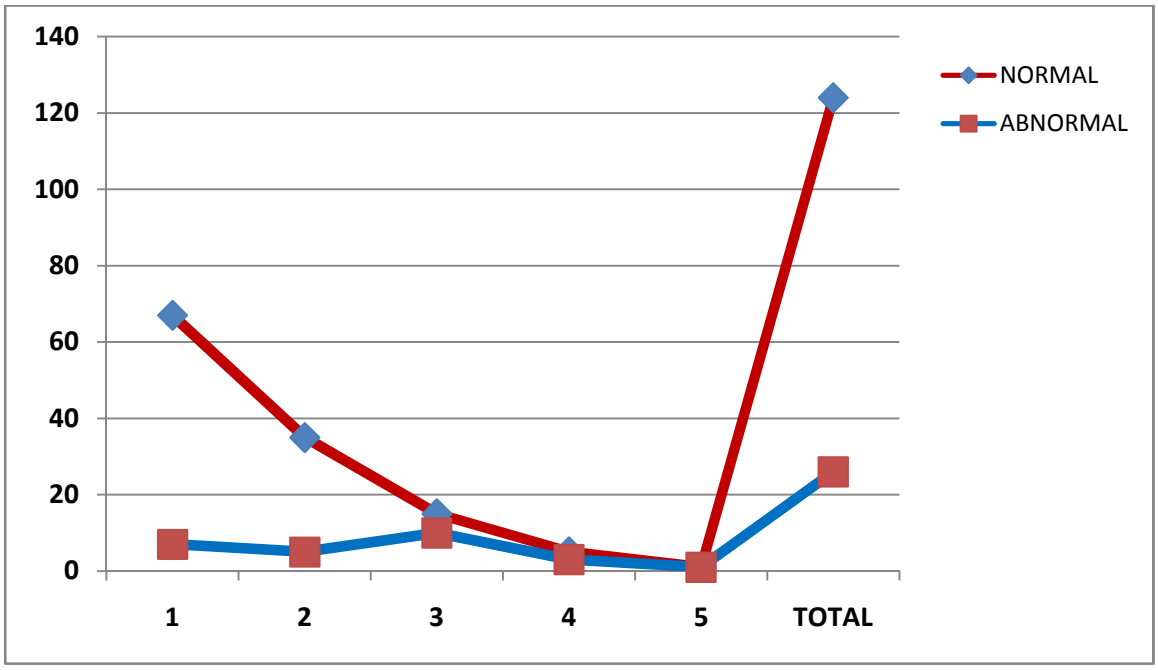
Maternal age

P value is 0.012 and is statistically significant and its found to be that the outcome of abortion increased with respect to maternal age.

Table 8 Gravidity among normal and abnormal outcome

Gravida	Normal	Abnormal	Total	p
1	67	7	74	0.01*
2	35	5	40	
3	15	10	26	
4	5	3	8	
5	1	1	2	
TOTAL	124	26	150	

Graph 5 : Distribution of study population according to pregnancy outcomes

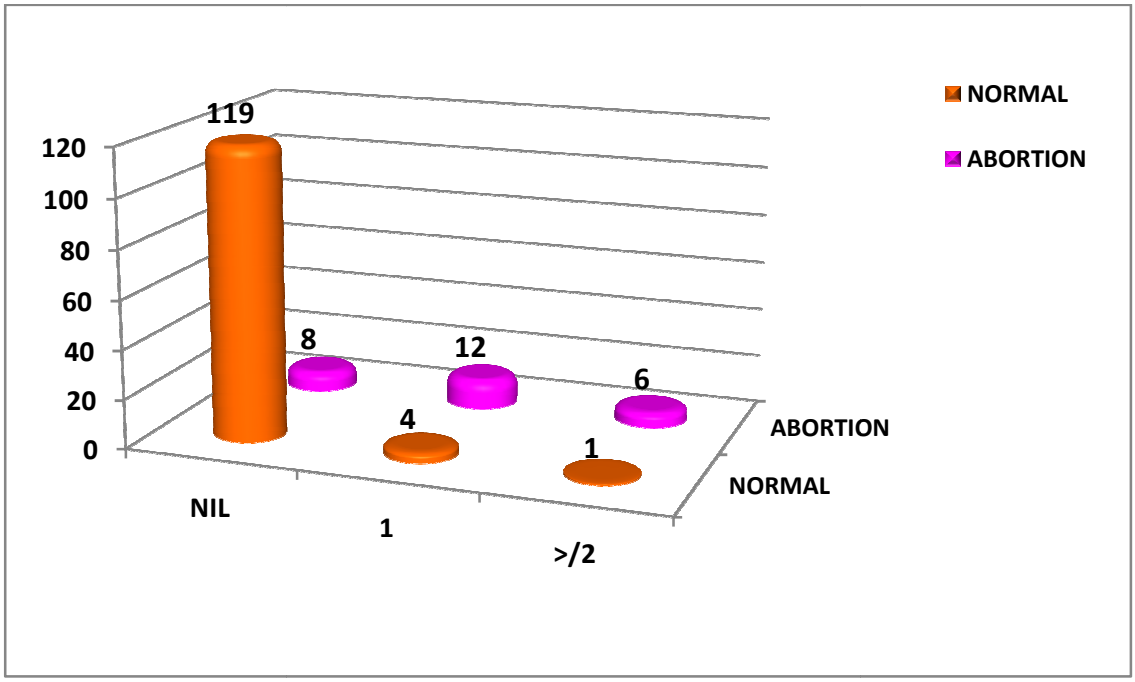


The probability of abnormal outcome increases with the increase in gravidity of the patient. P value was 0.01 and hence was statistically significant.

Table 9 Distribution of normal outcome and abortions with respect to previous abortions

Previous Abortions	Normal	Abortion	p
NIL	119	8	<0.0001*
1	4	12	
>/2	1	6	
TOTAL	126	24	

Graph 6 : Distribution of study population with respect to previous abortions



The probability of abnormal outcome in the current pregnancy increased with increase in the number of previous abortions.

Table 10 Yolk sac diameter at a particular gestational age in pregnancies with normal outcome

Gest age	N (no)	Min (mm)	Max (mm)	Mean	SD
5W-5W+6D	8	2.6	4.8	3.85	0.77
6W-6W+6D	25	2.2	6.2	3.64	1.04
7W-7W+6D	33	3.4	6.5	4.75	0.86
8W-8W+6D	34	2.7	5.7	4.49	0.52
9W-9W+6D	25	4.1	6.7	4.86	0.69
10W-10W+6D	13	3.5	5.2	4.06	0.49
11W-11W+6D	12	3.1	5.7	4.05	0.97

Graph 7 : Mean distribution of yolk sac diameter at particular gestational age with normal out comes.

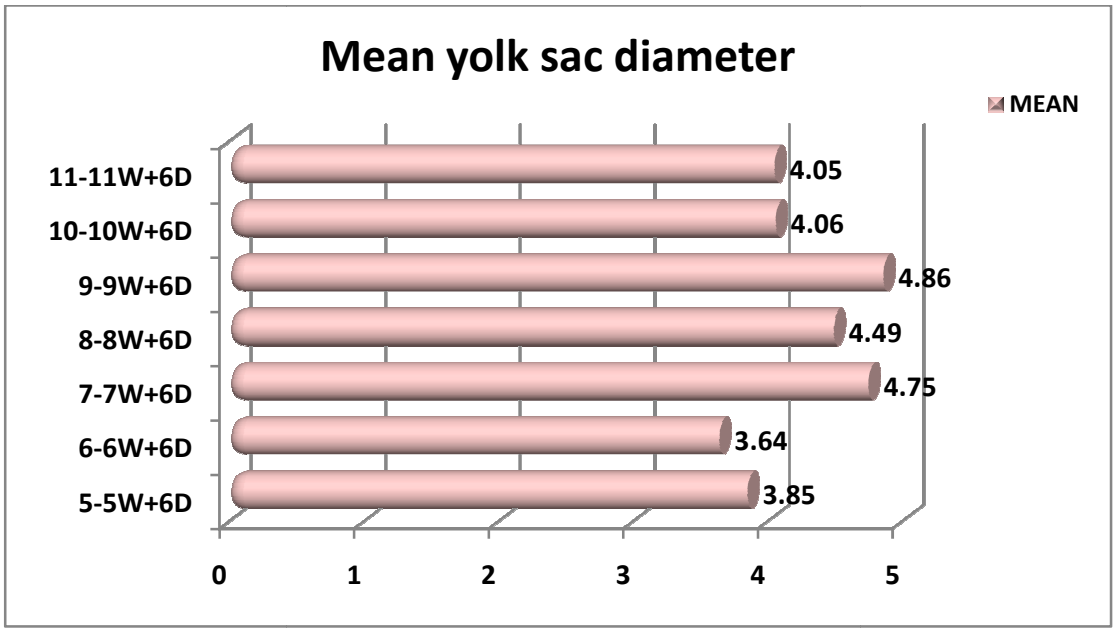


Table 11 Yolksac diameter at a particular gestational age with outcome of abortions

Gest Age	N (no)	MIN (mm)	MAX (mm)	MEAN	SD
5W-5W+6D	4	3.9	4.8	4.4	0.45
6W-6W+6D	3	5.8	6.0	5.9	0.10
7W-7W+6D	8	5.5	6.5	5.9	0.38
8W-8W+6D	3	2.7	4.7	3.86	1.04
9W-9W+6D	5	4.2	6.7	5.84	0.98
10W-10W+6D	-				
11W-11W+6D		5.3	5.7	5.56	0.23

Graph 8 : Mean distribution of yolk sac diameter at particular gestational age with abnormal outcomes.

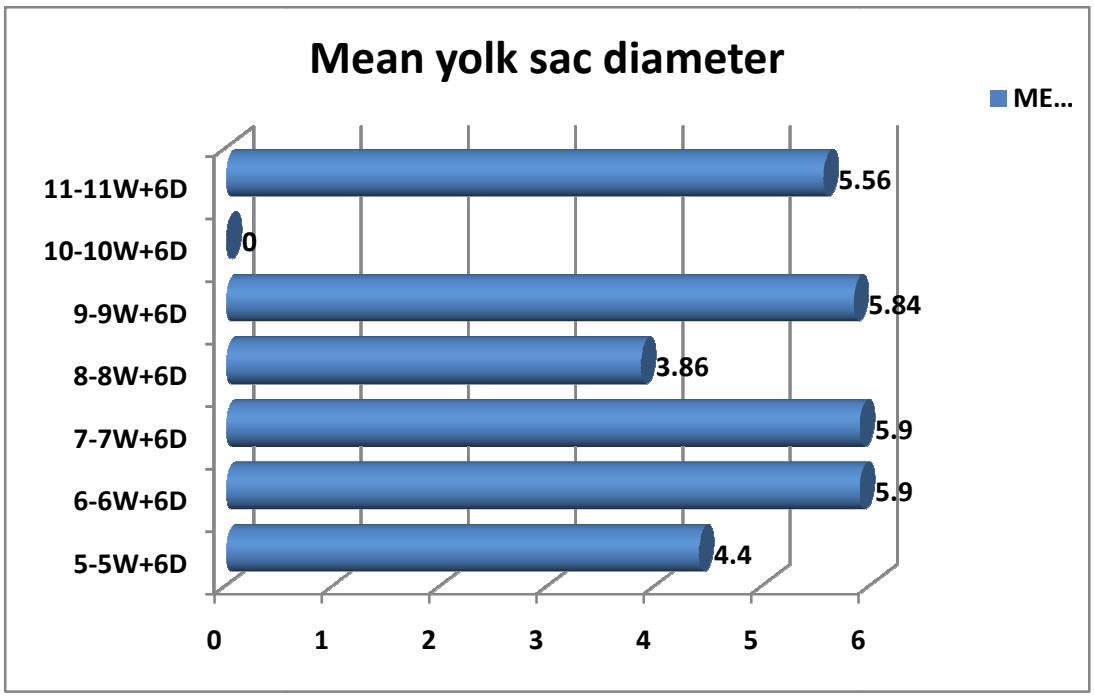


Table 12 Differences between means of normal and abnormal outcome

GEST AGE	MYSD-N/ABN	T	P
5w-5w+6d	1.15	3.21	0.018*
6w-6w+6d	2.55	7.41	<0.0001*
7w-7w+6d	1.57	7.32	<0.0001*
8w-8w+6d	-0.322	-1.025	<0.0001*
9w-9w+6d	1.22	5.01	0.012*
10w-10w+6d	---		
11w-11w+6d	2.02	9.10	<0.0001*

There is a significant difference in the mean yolksac diameter of normal and abnormal outcomes. Its significantly found in the study that as the MYSD increases from above the mean of that gestational age the outcome of abortion is significant with a significant p value of<0.0001.(as explained in the above table and graph)

Table 13 Yolksac as a predictor of pregnancy outcome

GEST AGE	SENSITIVITY	SPECIFICITY	PPV	NPV
5W-5W+6D	50	100	100	66.7
6W-6W+6D	66.7	100	100	95.65
7W-7W+6D	87.50	96.0	87.50	96.50
8W-8W+6D	50.0	93.55	33.33	96.67
9W-9W+6D	40.0	95.0	66.67	86.36
10W-10W+6D	----			
11W-11W+6D	66.67	88.89	66.7	89.0

Statistical analysis of yolk sac diameter as a predictor of pregnancy outcome was significant in all the weeks and very much significant when measured between 6th and 9th week of gestation, i.e. from 42 to 63 days of gestation, ($P < 0.001$)and from77 to 82 days. Sensitivity and NPV was highest at 7th week of gestation. Specificity and PPV was highest during 5th and 6th week of gestation

Table 14 Distribution of cases according to yolksac shape and its relation to abortions

Yolksac shape	Normal/Abortions	Total
Irregular	00/11	11
Regular	130/09	139

There is significance that whenever the yolksac shape was irregular the outcome was only abortions.

Table 15 Distribution of cases according to yolksac echogenicity and its relation to abortions

Yolksac Echogenicity	Abortions	Total
Normal	25	25
Hypo/hyperechoic	1	1

There was not much statistical significance of echogenicity of yolksac to abortions. there was only one case with hyperechogenicity related to abortion and that case was associated with trisomy 21 on karyotyping of the aborted material.

Table 16 Detection of anomalies in relation to yolksac

Anomaly detected	**Normal yolksac**	**Enlarged yolksac**	**Irregular yolksac**	**Echogenic yolksac**	**Serum markers**	**Autopsy**
Spina bifida	-	+	-	normal	AFP- increased	-
Meningocele		+	reg	hyperechoic	AFP- increased	Confirmed
Hydrocephalous with ventriculomegaly		+	-	normal	β- hcg - increased Maternal serum μE_3 - decreased	Confirmed

In our study 3 anomalies were detected with abnormal yolksac characteristics and were correlated with biochemical markers and autopsy.

DISCUSSION

The reliability of ultrasonographic visualization of the human yolk sac is well established.[63]

In this study 150 pregnancies in the 1st trimester were analyzed to determine the role of yolk sac as a predictor of abortion. This sample size was larger than that of the study by Stampone et al, conducted in Rome[79], which had a sample size of 117. But the sample size in the present study is much smaller than the study conducted by Lindsay et al[78] in Winnipeg, Canada, in which 486 consecutive intrauterine pregnancies were examined.

The mean age of the study population was 25.4 years and 56% of the study population belonged to the age group of 21- 30 years. In this study 49.3% of the study population were primigravidae.

INCIDENCE OF ABNORMAL PREGNANCY OUTCOME:

In the present study we had 16.7 % incidence of abortions. This is in concordance with the study by Roth et al[24] who estimated the frequency of spontaneous abortion to be 15% of recognizable pregnancies. In the study conducted by Lindsay et al[78] to evaluate the role of yolk sac size and shape as predictor of pregnancy outcome, the incidence of abnormal pregnancy outcome was 32.7%(159/486).

But the criteria for defining an abnormal outcome varies in different studies, for example in our study, abnormal outcome was defined as spontaneous abortion, before 24 weeks of gestation or demonstrable foetal anomalies whereas, Lindsay et al

considered abnormal outcome as first trimester embryonic or fetal death or demonstrable fetal anomaly.

In an Indian study Nawal Rajani et al[17] the incidence of abnormal outcome was 20% which included missed abortion and blighted ova before 12 weeks of gestation. In our study, the probability of abnormal pregnancy outcome was significant with maternal age. (P = 0.001). This is similar to the results of previous studies which show an increase in the incidence of miscarriage with increase in maternal age.[50,56,86] According to these studies, until age 30, the incidence of miscarriage is approximately 12%, thereafter the rate increases rapidly, exceeding 50% in the women older than 45 years.[86]

Our study indicates that the probability of abnormal outcome increases with the increase in gravidity of the patient, with significant increase in the risk of abortion with Gravida 3 and more (P = 0.012).

Also the present study shows that history of previous abortion increases the risk of abnormal outcome in the subsequent pregnancies (P<0.0001).

BIOMETRY OR GROWTH OF YOLK SAC WITH GESTATIONAL AGE IN PREGNANCIES WITH NORMAL OUTCOME:

In our study, progressively increasing mean YSD was found with advancing gestational age between 6th and 9th week of gestation, from 0.385 cm to 0.486 cm following which it starts decreasing in size by 10th week.

Cepni et al.[88] demonstrated the steady increase in YSD from 5 to 11 weeks of gestation in normal pregnancies after which it disappears by 12 weeks. Chama et al.[85]

reported a linear increament in mean YSD from 2.27 mm at 5 weeks of gestation to 5.61 mm at 11 weeks of gestation. Lindsay et al[78] reported that yolk sac grows at a rate of approximately 0.1 mm per mm growth of the MSD when the MSD is less than 15 mm and then slows to 0.03 mm per mm growth of MSD.

Our findings was also comparable to the Indian study by Nawal Rajani et al[17] in which progressively increased mean YSD was found with advanced gestational age between 5 – 9 weeks of GA, followed by either their disappearance (73.61%), or decreased size (26.38%) thereafter at 11 weeks of GA in cases with normal outcome.

In the present study Student t test was applied to test the significance of difference between the means of YSD of normal and abnormal pregnancy outcome. The difference between the mean yolk sac diameters between normal and abnormal outcomes is statistically significant (P<0.001).

This is similar to the study by Nawal Rajani et al[17] in which a highly significant difference was detected between mean YSD of both groups (P<0.001).

VALUE OF ABNORMAL YOLK SAC CHARACTERISTICS AS A PREDICTOR FOR

ABNORMAL PREGNANCY OUTCOME

For a yolk sac diameter which is lesser than the 2SD below the mean, the sensitivity of predicting an abnormal outcome was 22.58%, the specificity was 98.59 % and PPV was 77.78% (P < 0.001) in comparison to 15.6%, 95.3% and 44.4% respectively, reported by Lindsay et al.[78]

For a yolk sac diameter which is more than 2SD above the mean, the sensitivity of predicting an abnormal outcome was 38.7%, the specificity was 97.88 % and PPV was 80% ($P < 0.001$) in comparison to 15.6%, 97.4% and 60% respectively, reported by Lindsay et al.[78]

When both the groups are combined, the sensitivity of predicting an abnormal outcome was 61.29 %, specificity was 96.48 % and PPV was 79.17% ($P<0.001$) in comparison to 26.9%, 92.7% and 51.1% respectively, reported by Lindsay et al.[78] The results of our study are more likely comparable to the results of the study by Kucuk et al.[70] They found a yolk sac diameter out of 2 standard deviations of the mean for the menstrual age allowed prediction of an abnormal pregnancy outcome with a sensitivity of 65%, a specificity of 97%, a PPV of 71% and a NPV of 95%, which were comparable to 61.29 %, 96.48 %, 79.17% and 91.95% respectively, found in our study.

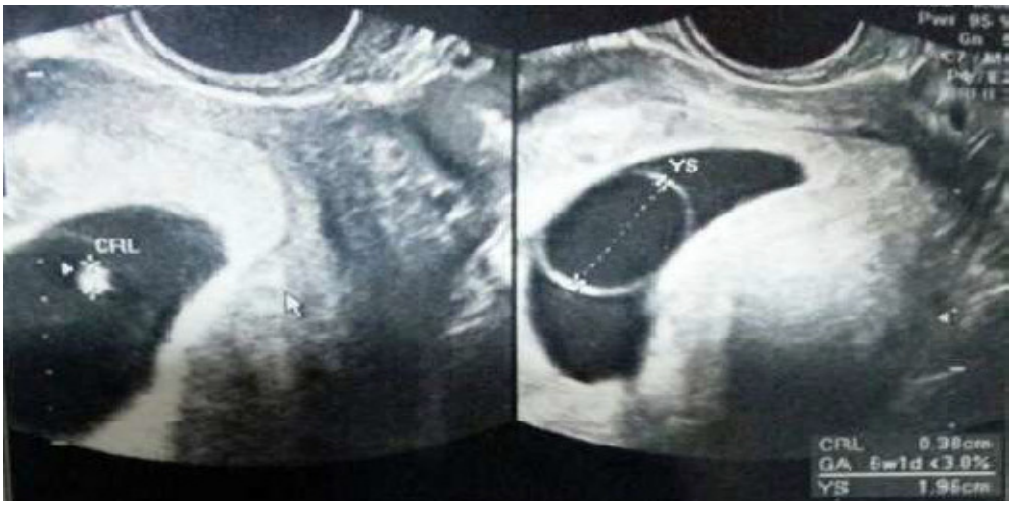
In our study we have also estimated the ideal time to perform the transvaginal scan, in order to achieve the highest possible sensitivity, specificity, positive and negative predictive value. Sensitivity and NPV was highest at 7th week of gestation. Specificity and PPV was highest at 6th week of gestation.

Statistical analysis of yolk sac diameter as a predictor of pregnancy outcome was significant when measured between 5th and 11th week of gestation ($P < 0.0001$). This is similar to the studies done previously in which yolk sac could be accurately evaluated from 5 completed weeks of GA.[17,78-79]

In a more recent study by Berdahl, D. M., J. Blaine, et al[79], the authors have examined the value of a specific cut-off (5 mm) to allow easier patient counselling. They concluded pregnancies with MSD≥ 5 mm on early ultrasound require

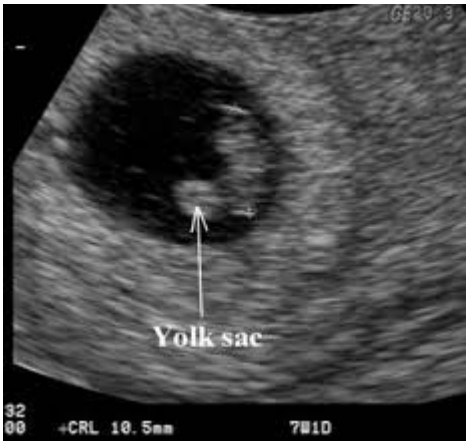
monitoring and counselling about a threefold increased risk for first-trimester loss independent of maternal risk factors such as age, body mass index, polycystic ovary syndrome, smoking, and diabetes. In addition, their study shows for the first time that enlarged yolk sac diameter may be associated with an increased risk of preterm delivery. However in our study we have not evaluated any specific cut-off for YSD. Lindsay et al[78] reported that no pregnancy with normal outcome had a yolk sac diameter of greater than 5.6 mm at less than 10 weeks of menstrual age. In 6 patients the yolk sac diameter was more than 5.6 mm. All 6 had abnormal outcome. In our study no pregnancy with a normal outcome had a yolk sac diameter greater than 6.4 mm between 5 – 10 weeks GA and 3 cases had yolk sac diameter more than 6.4 mm, all of whom had abnormal pregnancy outcome – spontaneous abortion

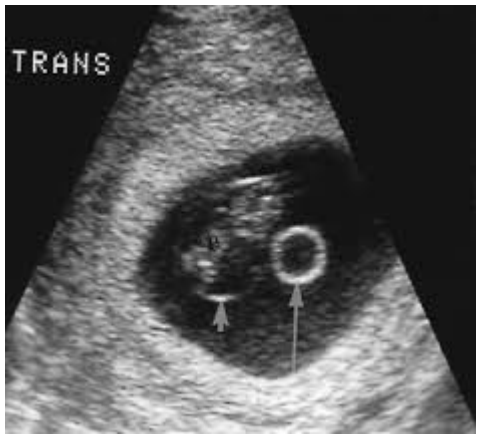
FIG 15: A transvaginal sonogram showing an abnormally large yolk sac (YSD = 1.96 cm) with a CRL of 0.38 cm corresponding to a GA of 5 weeks 4 days, at menstrual age of 70 days (10weeks). Cardiac activity was absent.

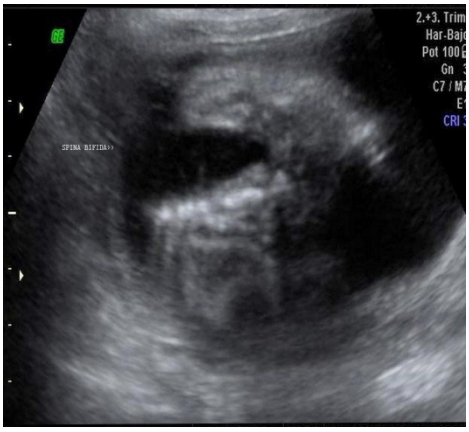


3 cases with abnormal yolksac diameters were diagnosed with anomalies in our study. The anomalies detected in our study are hydrocephalous with

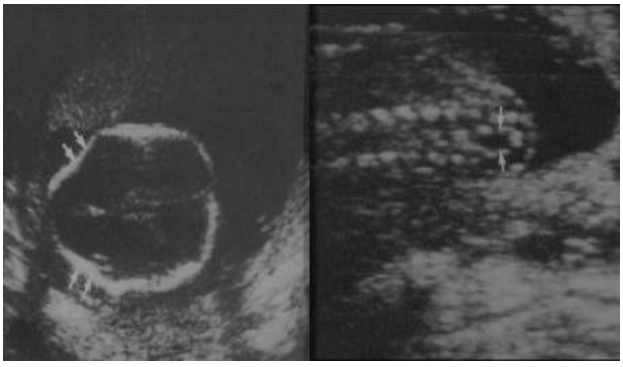
ventriculomegaly, meningocele an spina bifida.2of them had enlarged yolksac and 1 of them had a hyperechogenic yolksac.







Spina bifida



Meningocele

2 cases had absence of yolksac and were diagnosed with blighted ovum and which had an outcome of spontaneous abortion.

Irregularly shaped yolksac were associated with abortions significantly. Only 1 case had an hyprechoic yolksac and was associated with anomaly with chromosomal abnormality.

CONCLUSION

We can conclude from the present study that measurement of the secondary yolk sac diameter between 5th to 12th week of gestation can be used as a valuable tool to predict abortions.

As the yolk sac is the first structure to appear in the gestational sac, confirming an intra uterine pregnancy, using yolk sac measurement as a tool to evaluate pregnancy outcome, provides a mode of early prediction of pregnancy outcome, even before the detection of the embryo. This in turn helps in counselling the parents regarding the risk of miscarriage and the need for follow up ultrasound examinations. It is particularly helpful to counsel patients with history of threatened or recurrent abortion who abort despite resting in the hospital for many weeks. It also helps in pursuing a more active line of management if required.

Based on the results of this study and data available from the literature, it is certain that abnormal yolk sac diameter, shape and echogenicity is associated with poor pregnancy outcome. But there is uncertainty regarding the causality of the poor pregnancy outcome associated with abnormal yolk sac size. Very few authors suggest association of chromosomal abnormalities with abnormal yolksac size, some negotiate this association. Some suggest association of endocrine abnormalities such as Type 1 diabetes mellitus with enlarged yolk sac. Further studies are required to establish causality of poor pregnancy outcome with abnormal yolk sac size, so that a line of management can be planned for such patients, which may include karyotyping of the couple, karyotyping of the abortus, investigations for detecting any possible endocrine factors associated with such outcomes and to plan further line of treatment for such patients.

SUMMARY

This study was conducted to evaluate the role of yolk sac characteristics in predicting Abortions.

In this study 150 women who presented to the antenatal OPD of B.L.D.E Hospital, between 5 and 12 weeks of gestation were evaluated with transvaginal or transabdominal sonography and measurements such as MSD, CRL and YSD were taken.

Patients were followed up to 24 weeks of gestational age and classified as normal outcomes if pregnancy continues beyond 24 weeks and no anomalies of the foetus was noted.

The mean age of the study population was 25 years and 56% of the study population belonged to the age group of 21- 30 years. 49.3% of the study population were primigravidae.

We had 16.7% incidence of abnormal pregnancy outcome. The probability of bnormal pregnancy outcome increased with maternal age. (P = 0.012.). The probability of abnormal outcome increased with the increase in gravidity of the patient, with significant increase in the risk of abortion with Gravida 3 and more (0.0001).

In our study some anomalies were detected which were diagnosed earlier by abnormal yolk sac characteristics and correlated with biochemical markers and autopsy findings.

There was a significant positive correlation between YSD and CRL (r =0.613), MSD (r= 0.566) and GA (r = 0.553) [P<0.001].

A normal range of yolk sac diameter was established based on normal outcomes for each gestational week. Yolk sac diameter more than 2 standard deviations above or below the mean were considered as abnormal yolk sac diameter. Using these criteria of abnormal yolk sac diameter to predict abnormal pregnancy outcome, the sensitivity of predicting an abnormal outcome was 61.29 %, specificity was 96.48 % and PPV was 79.17% ($P<0.001$) The sensitivity and negative predictive value were highest when the scan was performed at 7^{th} week of gestation and specificity and positive predictive value was highest at 6^{th} week of gestation.

Significant correlation was seen with irregularly shaped yolksac and its incidence with abortions. Though echogenicity correlation with abortion was not significant in our study, the only case which had hyperechoic yolksac was associated with anomaly.

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SAMPLE INFORMED CONSENT FORM

TITLE OF THE TOPIC	**:**	**"EVALUATION OF YOLKSAC ABNORMALITIES IN PREDICTING ABORTIONS"**
PRINCIPAL INVESTIGATOR	**:**	**Dr. J.AISHWARYA.**
PG GUIDE NAME	**:**	**Dr. P. B. JAJU**

PURPOSE OF RESEARCH

The usage of sonography in determining the biometry of yolksac and predicting the pregnancy outcome in the first trimester.

PROCEDURE

I understand that I will be a part of this study. My history and physical findings will be taken from the case paper and will be evaluated in a systematic way.

RISK AND DISCOMFORTS

I understand that this procedure is not expected to aggravate any side effect or cause detrimental effect to me or my child.

BENEFITS

This study will help to know the pregnancy outcome in the early weeks of pregnancy.

CONFIDENTIALITY

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality and privacy regulation of BLDE University's Shri. B. M .Patil Medical College. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting names to numbers will be kept in a secured location**.**

If the data are used for publication in the medical literature or for teaching purpose no names will be used**.**

I understand that the relevant designated authority are permitted to have an access to my medical record and to the data produced by the study for audit purpose. However, they are required to maintain confidentiality**.**

Signature of candidate Signature of guardian

PROFORMA

Name :

Age :

Op.no/Ip. No/unit :

Address :

Occupation :

DOA :

DOD :

Time of admission :

Chief complaints :

History of present complaints :

Antenatal history :

BOOKED/UNBOOKED :

IMMUNISED/UNIMMUNISED :

1st Trimester :

2nd Trimester :

3rd Trimester :

Obstetrics history :

Married Life :

Obstetric Score :

Menstrual History :

PaMC :

LMP :

EDD : POG :

Past History :

Family History :

Personal History :

General Physical Examination

Build and Nourishment :

Height : Pulse :

Weight : BP :

Temp :

Breast : RR :

Thyroid :

Pallor / icterus / cyanosis / clubbing / edema / lymphadenopathy.

Systemic Examination

CVS :

RS :

PER ABDOMEN :

Per speculum Examination

(if required)

Per Vaginal Examination

INVESTIGATIONS

BLOOD INVESTIGATIONS

HAEMOGLOBIN :

HIV :

HBsAg :

VDRL :

BLOOD GROUPING AND TYPING :

BT :

CT :

RBS :

URINE ROUTINE :

ULTRASONOGRAPHY IN FIRST TRIMESTER:

GESTATIONAL AGE

YOLK SAC SHAPE

YOLK SAC DIAMETER

CRL

GESTATIONAL SAC DIAMETER

AND

FOLLOW UP OF ALL PATIENTS WITH CONGENITAL ANOMALY SCAN

(18-24 WEEKS)

BIOCHEMICAL MARKERS

KARYOTYPING IN SPECIFIED CASES

ETHICAL CLEARANCE CERTIFICATE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 52 2014
Date 04/8/14.
B.L.D.E.U's Shri B.M. Patil Medical College.

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 04-08-2014. *at* 11-00 am *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title Evaluation of Yolksac abnormalities in predicting abortions - A prospective study

—×—×—

Name of P.G. student J. Aishwarya.

Dept of Obstetrics & Gynecology [DGO]

Name of Guide/Co-investigator Dr P.B Jaju. Prof & HOD. OBG.

for

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

KEY WORDS TO MASTER CHART

YSD	–	YOLKSAC DIAMETER
CRL	–	CROWN RUMP LENGTH
GSD	–	GESTATIONAL SAC DIAMETER
NT	–	NUCHAL TRANSLUCENCY
ECHO	–	ECHOGENICITY
W	–	WEEK
D	–	DAY
IR	–	IRREGULAR
REG	–	REGULAR
HYD	–	HYDROCEPHALOUS
VENT	–	VENTRICULOMEGALY
AFP	–	ALPHA FETO PROTEIN
HCG	–	HUMAN CHORIONIC GONADOTROPIN
SERUM μE3	–	SERUM ESTRADIOL
INC	–	INCREASED
DEC	–	DECREASED
SPO ABORTION	–	SPONTANEOUS ABORTION

MASTER CHART

S NO	NAME	OPD NO	AGE	GRAVIDA	PARA	LIVING	ABORTION	MENSTRUAL AGE	GSD (mm)	CRL (cm)	YSD (mm)	YOLK SAC SHAPE	ECHOGENICITY	PROGNOSIS	NT	ANOMALY	BIO CHEMICAL MARKERS	AUTOPSY	CLINICAL HISTORY
1	Anupama	6931	23	1				5W+4D	8.6	2.1	4.8	Ir	Normal	Sp abortion	Normal	-	Normal	-	Pain Abdomen
2	Shantha	6938	18	1				6W	14.7	1.9	2.7	Reg	Normal	-	Normal	-	Normal	-	-
3	Ansubai	6927	28	2			1	7W+1D	16	1.1	4.2	Reg	Normal	-	Normal	-	Normal	-	-
4	Jyothi	2013	29	1				8W+2D	21	1.2	4.9	Reg	Normal	-	Normal	-	Normal	-	-
5	Girija	8474	33	1				9W+2D	26.2	1.7	5.9	Reg	Normal	Sp abortion	Normal	-	Normal	-	Known hypothyoid
6	Sharada	8472	18	2				10W	40.1	4.7	4.3	Reg	Normal	-	Normal	-	Normal	-	-
7	Revathy	9148	32	3	1	1	1	11W	43	5.4	3.7	Reg	Normal	-	Normal	-	Normal	-	-
8	Meenakshi	3827	28	1				9W+4D	38.1	3.9		Reg	Normal	Blighted ovum	Normal	-	Normal	-	-
9	Mangala	8735	28	1				8W+3D	27.6	3.1	4.4	Reg	Normal	-	Normal	-	Normal	-	-
10	Shobha	8743	33	1				7W+2D	23.1	2.7	3.8	Reg	Normal	-	Normal	-	Normal	-	-
11	Roopa	4611	34	4	2	2	2	8W+4D	26.7	2.6	4.8	Reg	Normal	-	Normal	-	Normal	-	-
12	Aarthi	4866	26	2	1	1	1	9W+2D	35.2	2.9	4.7	Reg	Normal	-	Normal	-	Normal	-	-
13	Chaya	10223	25	1				11W	42	5.1	3.6	Reg	Normal	-	Normal	-	Normal	-	-
14	Sumangali	9930	32	1				10W+1D	39	4.8	3.7	Reg	Normal	-	Normal	-	Normal	-	-
15	Vidya	10388	22	1				9W+2D	32.3	3.9	4.5	Reg	Normal	-	Normal	-	Normal	-	-
16	Anjana	12076	25	1				8W+5D	24.7	3.7	4.7	Reg	Normal	-	Normal	-	Normal	-	-
17	Anitha	11735	27	2	1			7W+4D	19.3	2.9	3.9	Reg	Normal	-	Normal	-	Normal	-	-
18	Pooja	7091	23	1				6W+2D	13.9	0.9	3	Reg	Normal	-	Normal	-	Normal	-	-
19	Deepa	13431	18	1				5W+6D	10.1	0.6	2.6	Reg	Normal	-	Normal	-	Normal	-	-
20	Shabana	13242	29	1				6W+4D	18	1.1	2.2	Reg	Normal	-	Normal	-	Normal	-	-
21	Poornima	13570	24	1				6W+3D	17.6	1	2.7	Reg	Normal	-	Normal	-	Normal	-	-
22	Parimala	9161	23	2			1	8W	21.1	3.1	4.1	Reg	Normal	-	Normal	-	Normal	-	-
23	Janaki	14478	24	1				8W+2D	23.7	3.3	4.2	Reg	Normal	-	Normal	-	Normal	-	-
24	Jyothi	8570	21	1				8W+1D	20.8	2.9	4.2	Reg	Normal	-	Normal	-	Normal	-	-
25	Seetha	15350	33	3	1	1	1	7W+5D	19.7	2.7	5.8	Ir	Normal	Spo abortion	Normal	-	Normal	-	-
26	Bharathi	15841	28	1				9W	27.3	3.7	4.4	Reg	Normal	-	Normal	-	Normal	-	-
27	Banu	15494	25	1				9W+2D	27.7	3.6	4.6	Reg	Normal	-	Normal	-	Normal	-	-
28	Shivamma	11082	25	1				10W	40	4.6	5.2	Reg	Normal	-	Normal	-	Normal	-	-
29	Deepika	16978	28	1				11W	44	4.9	4	Reg	Normal	-	Normal	-	Normal	-	-
30	Gowri	16567	20	1				9W+3D	38.4	4.2	4.6	Reg	Normal	-	Normal	-	Normal	-	-
31	Geethanjali	12249	31	1				9W	26.3	2.9	4.1	Reg	Normal	-	Normal	-	Normal	-	-

S NO	NAME	OPD NO	AGE	GRAVIDA	PARA	LIVING	ABORTION	MENSTRUAL AGE	GSD (mm)	CRL (cm)	YSD (mm)	YOLK SAC SHAPE	ECHOGENICITY	PROGNOSIS	NT	ANOMALY	BIO CHEMICAL MARKERS	AUTOPSY	CLINICAL HISTORY
32	Sudha	17653	22	1				10W+3D	40.1	3.7	5	Reg	Normal	-	Normal	-	Normal	-	-
33	Madhuri	17527	25	1				11W	42.1	4.9	4.1	Reg	Normal	-	Normal	-	Normal	-	-
34	Rekha	12128	29	4	1	1	2	7W+6D	26.3	2.4	6.5	Ir	Normal	Spo abortion	Normal	-	Normal	-	Pain Abdomen
35	Shilpa	18624	29	3	2	2		5W+5D	13.1	0.8	3.9	Reg	Normal	-	Normal	-	Normal	-	-
36	Kalpana	18625	28	2	1	1		8W+2D	23.6	3.7	4.2	Reg	Normal	-	Normal	-	Normal	-	-
37	Shakunthala	17908	29	2	1	1		7W+5D	19.8	2.1	4.4	Reg	Normal	-	Normal	-	Normal	-	-
38	Vidya	18425	28	2	1	1		8W	20.8	2.7	4.1	Reg	Normal	-	Normal	-	Normal	-	-
39	Anitha	13607	22	1				9W	26.8	3.4	5	Reg	Normal	-	Normal	-	Normal	-	-
40	Richa	19254	30	4	3	3		9W+3D	36.7	3.7	5.2	Reg	Normal	-	Normal	-	Normal	-	-
41	Mangala	19250	30	5	4	4		10W+1D	40.1	4.7	4.1	Reg	Normal	-	Normal	-	Normal	-	-
42	Kavitha	19447	19	1				6W+5D	19	1.7	3.9	Reg	Normal	-	Normal	-	Normal	-	-
43	Vandana	19294	25	1				6W+2D	18.6	1.3	4.6	Reg	Normal	-	Normal	-	Normal	-	-
44	Laxmi	23964	27	2	1	1		7W+4D	19.8	1.8	4.4	Reg	Normal	-	Normal	-	Normal	-	-
45	Ragini	23100	21	1				8W+3D	24.6	2.4	4.9	Reg	Normal	-	Normal	-	Normal	-	-
46	Pooja	20885	20	1				7W+5D	22.1	1,4	5.1	Reg	Normal	-	Normal	-	Normal	-	-
47	Surekha	19521	32	3			2	6W+6D	15.3	1.2	6	Reg	Normal	Spo abortion	↑	Spina Bifida	AFP-Inc	Spina Bifida	-
48	Nirmala	24288	23	1				8W+2D	23.7	2.7	4.2	Reg	Normal	-	Normal	-	Normal	-	-
49	Indira	24669	23	1				9W	27.6	3.1	4.6	Reg	Normal	-	Normal	-	Normal	-	-
50	Priya	24162	18	1				10W+1D	40.6	4.1	3.9	Reg	Normal	-	Normal	-	Normal	-	-
51	Jyothi	28115	19	1				11W	43	5.1	3.2	Reg	Normal	-	Normal	-	Normal	-	-
52	Lalitha	27915	28	2	1	1		11W+2D	42.4	5.3	3.4	Reg	Normal	-	Normal	-	Normal	-	-
53	Mudakamma	28480	28	3	1	1	1	5W+6D	4.8	0.8	4.2	Ir	Normal	Spo abortion	Normal	-	Normal	-	-
54	Aruna	28785	25	1				8W+4D	24.9	2.8	4	Reg	Normal	-	Normal	-	Normal	-	-
55	Keerthi	28713	25	1				9W+2D	33.1	2.7	4.6	Reg	Normal	-	Normal	-	Normal	-	-
56	Savithri	14627	24	1				10W+2D	42	3.9	3.9	Reg	Normal	-	Normal	-	Normal	-	-
57	Sunanda	17487	21	1				11W+1D	44	4.9	5.7	Reg	Normal	Spo abortion	↑	Meningocle	AFP-Inc	Meningocle	-
58	Ambika	25141	26	2	1	1		9W	34	3.4	4.3	Reg	Normal	-	Normal	-	Normal	-	-
59	Ramya	26126	28	2	1	1		8W+5D	32.3	2.7	4.9	Reg	Normal	-	Normal	-	Normal	-	-
60	Arthi	30896	23	1				7W+6D	26.8	2.3	4.7	Reg	Normal	-	Normal	-	Normal	-	-
61	Nirmala	31063	25	1				5W+4D	13.1	0.7	3.5	Reg	Normal	-	Normal	-	Normal	-	-
62	Chaya	32529	28	2	1	1		6W	17.1	1	3.9	Reg	Normal	-	Normal	-	Normal	-	-
63	Umadev	36516	25	1				6W+2D	16.8	1.1	3.7	Reg	Normal	-	Normal	-	Normal	-	-

S NO	NAME	OPD NO	AGE	GRAVIDA	PARA	LIVING	ABORTION	MENSTRUAL AGE	GSD (mm)	CRL (cm)	YSD (mm)	YOLK SAC SHAPE	ECHOGENICITY	PROGNOSIS	NT	ANOMALY	BIO CHEMICAL MARKERS	AUTOPSY	CLINICAL HISTORY
64	Radhika	31426	30	3	1	1	1	7W	18.8	1.3	6	Reg	Normal	Spo abortion	Normal	-	Normal	-	Pain Abdomen
65	Nirmala	37907	26	2	1	1		8W	24.6	1.9	4.1	Reg	Normal	-	Normal	-	Normal	-	-
66	Prema	36151	23	1				7W+4D	20.9	1.4	5	Reg	Normal	-	Normal	-	Normal	-	-
67	Jhanavi	34719	25	1				8W	22.8	2.3	4.6	Reg	Normal	-	Normal	-	Normal	-	-
68	Savithri	3553	23	1				9W+2D	35.4	3	4.5	Reg	Normal	-	Normal	-	Normal	-	-
69	Rani	39000	25	1				10W	41	4.1	3.9	Reg	Normal	-	Normal	-	Normal	-	-
70	Ganga	39324	21	1				9W+4D	38.2	3.7	4.8	Reg	Normal	-	Normal	-	Normal	-	-
71	Yashoda	39325	24	1				6W	15.8	1.4	3.1	Reg	Normal	-	Normal	-	Normal	-	-
72	Haseena	39591	24	1				6W+2D	16.8	1.3	3.4	Reg	Normal	-	Normal	-	Normal	-	-
73	Kanaka	37424	33	3	2	2		8W	21.8	2.3	4.2	Reg	Normal	-	Normal	-	Normal	-	-
74	Poonam	42743	34	4	3	3		9W+2D	36.3	3.3	5	Reg	Normal	-	Normal	-	Normal	-	-
75	Ragini	42374	24	1				7W+5D	19.7	2	4.4	Reg	Normal	-	Normal	-	Normal	-	-
76	Asha	44046	26	1				8W+4D	28.4	2.7	5	Reg	Normal	-	Normal	-	Normal	-	-
77	Jayada	40164	26	1				6W+6D	21.2	1.3	5.9	Reg	Normal	Spo abortion	Normal	-	Normal	-	-
78	Veena	44221	25	2	1	1		8W+4D	26.4	2.8	4.7	Reg	Normal	-	Normal	-	Normal	-	-
79	Sonakshi	44668	33	4	3	3		7W+5D	25.3	1.8	5	Reg	Normal	-	Normal	-	Normal	-	-
80	Ashwini	44722	25	1				8W	20.8	2.6	4.8	Reg	Normal	-	Normal	-	Normal	-	-
81	Kasturi	48564	27	2	1	1		8W+2D	22.6	2.7	4.9	Reg	Normal	-	Normal	-	Normal	-	-
82	Sangawwa	48492	30	2	1	1		7W+4D	20.3	1.8	4.7	Reg	Normal	-	Normal	-	Normal	-	-
83	Mahananda	2265	20	1				6W+5D	14.5	0.9	3	Reg	Normal	-	Normal	-	Normal	-	-
84	Jannat	2045	27	2	1	1		7W+4D	25	1.1	4.3	Reg	Normal	-	Normal	-	Normal	-	-
85	Basamma	49881	28	4	3	3		7W+5D	24.5	1.3	4.5	Reg	Normal	-	Normal	-	Normal	-	-
86	Neha	2839	26	2	1	1		6W+5D	21.3	1	3.1	Reg	Normal	-	Normal	-	Normal	-	-
87	Devaki	51574	25	1				7W	16.9	1	6.5	Reg	Normal	Spo abortion	Normal	-	Normal	-	-
88	Vimala	51069	27	2				8W	23.8	1.7	4.1	Reg	Normal	-	Normal	-	Normal	-	-
89	Surekha	3033	18	1				8W+2D	25.7	1.8	4	Reg	Normal	-	Normal	-	Normal	-	-
90	Sarika	4089	25	1				9W+1D	25	2.9	4.6	Reg	Normal	-	Normal	-	Normal	-	-
91	Vijaya	870	26	2	1	1		6W+4D	13.7	1.1	2.8	Reg	Normal	-	Normal	-	Normal	-	-
92	Rajani	893	25	2			1	5W+6D	19.9	0.9	3.9	Ir	Normal	Spo abortion	Normal	-	Normal	-	-
93	Yamini	4718	29	3			2	7W+4D	22.5	2.4	5.5	Ir	Normal	Spo abortion	Normal	-	Normal	-	-
94	Lavanya	4744	26	2	1	1		8W+3D	24.6	2.9	4.7	Reg	Normal	-	Normal	-	Normal	-	-
95	Geeta	4757	28	3	2	2		9W	28.6	3	5.9	Reg	Normal	Spo abortion	Normal	-	Normal	-	-

S NO	NAME	OPD NO	AGE	GRAVIDA	PARA	LIVING	ABORTION	MENSTRUAL AGE	GSD (mm)	CRL (cm)	YSD (mm)	YOLK SAC SHAPE	ECHOGENICITY	PROGNOSIS	NT	ANOMALY	BIO CHEMICAL MARKERS	AUTOPSY	CLINICAL HISTORY
96	Vani	4823	32	3	2	2		9W+4D	31.4	3.1	5.1	Reg	Normal		Normal	-	Normal	-	-
97	Ganga	4832	32	4	1	1	2	11W+2D	41.2	5.2	5.7	Reg	HYPERECHO	Spo abortion	Normal	Hyd/Ventri	β hcg inc,μ E3 dec	Tri 21	Pain abdomen
98	Neela	5330	28	3	2	2		7W+3D	18.6	2.1	3.7	Reg	Normal	-	Normal	-	Normal	-	-
99	Rekha	8413	18	1				8W+3D	22.7	2.9	ABSENC	Reg	Normal	Blighted ovum	Normal	-	Normal	-	-
100	Priyanka	3801	27	2	1	1		7W+5D	20.3	2	3.6	Reg	Normal	-	Normal	-	Normal	-	-
101	Seetha	8888	19	1				6W+3D	7.6	1.4	3.1	Reg	Normal	-	Normal	-	Normal	-	-
102	Lavanya	4744	26	2			1	7W+3D	24.1	1.3	5.6	Reg	Normal	Spo abor	Normal	-	Normal	-	-
103	Spandana	4974	28	3	2	2		9W+2D	44.3	3.1	4.4	Reg	Normal	-	Normal	-	Normal	-	-
104	Farida	285	23	1				10W	41.1	4.3	3.8	Reg	Normal	-	Normal	-	Normal	-	-
105	Mallamma	5853	26	2	1	1		11W+3D	44.1	5.3	3.6	Reg	Normal	-	Normal	-	Normal	-	-
106	Parvathi	10227	27	2	1	1		6W+4D	18.4	1.1	3.1	Reg	Normal	-	Normal	-	Normal	-	-
107	Kasibai	10228	26	2	1	1		7W+5D	22.1	1.7	4.2	Reg	Normal	-	Normal	-	Normal	-	-
108	Kaveri	9757	21	1				8W+6D	27.2	2.4	4.5	Reg	Normal	-	Normal	-	Normal	-	-
109	Bhuvana	9780	23	1				6W+6D	18.1	1	2.9	Reg	Normal	-	Normal	-	Normal	-	-
110	Parvathi	10227	27	2	1	1		5W+6D	17.8	0.9	3.1	Reg	Normal	-	Normal	-	Normal	-	-
111	Radhika	6031	31	5	3	3	2	8W+2D	25.7	3.7	5.7	Ir	Normal	Spo abortion	Normal	-	Normal	-	Pain abdomen
112	Sumitha	10410	26	2	1	1		7W+3D	20.4	2	3.4	Reg	Normal	-	Normal	-	Normal	-	-
113	Shoba	9793	22	1				8W+1D	22.1	2.7	4.1	Reg	Normal	-	Normal	-	Normal	-	-
114	Suman	6293	19	1				7W+2D	18.6	2.1	3.6	Reg	Normal	-	Normal	-	Normal	-	-
115	Vasthala	9832	31	4	1	1	2	8W+5D	24.5	2.7	2.7	Reg	Normal	Spo abo	Normal	-	Normal	-	-
116	Rohini	10203	22	1				9W	26.5	3.1	4.4	Reg	Normal	-	Normal	-	Normal	-	-
117	Neela	10636	25	1				10W+2D	40.4	4	3.9	Reg	Normal	-	Normal	-	Normal	-	-
118	Pallavi	7164	23	1				9W+4D	38.4	3.6	4.2	Reg	Normal	-	Normal	-	Normal	-	-
119	Geeta	10717	29	3	1	1	1	7W+5D	27.1	2.3	5.7	Ir	Normal	Spo abortion	Normal	-	Normal	-	-
120	Preethi	11335	21	1				6W+2D	11.7	1.1	3.6	Reg	Normal	-	Normal	-	Normal	-	-
121	Roopa	11764	32	3	2	2		7W+1D	16.7	1.6	3.7	Reg	Normal	-	Normal	-	Normal	-	-
122	Jyothi	12162	25	2	1	1		8W+3D	23.6	2	4.5	Reg	Normal	-	Normal	-	Normal	-	-
123	Indira	12197	21	1				10W	40.1	5	3.7	Reg	Normal	-	Normal	-	Normal	-	-
124	Shantha	12705	28	3	2	2		11W+1D	43.1	5.6	3.2	Reg	Normal	-	Normal	-	Normal	-	-
125	Laxmi	9474	23	1				9W+6D	40.2	4.8	4.7	Reg	Normal	-	Normal	-	Normal	-	-
126	Swetha	10073	22	1				8W+4D	24.4	3	5.1	Reg	Normal	-	Normal	-	Normal	-	-
127	Aarthi	13329	22	2			1	6W+5D	15.3	1	5.8	Ir	Normal	Spo abortion	Normal	-	Normal	-	-

S NO	NAME	OPD NO	AGE	GRAVIDA	PARA	LIVING	ABORTION	MENSTRUAL AGE	GSD (mm)	CRL (cm)	YSD (mm)	YOLK SAC SHAPE	ECHOGENICITY	PROGNOSIS	NT	ANOMALY	BIO CHEMICAL MARKERS	AUTOPSY	CLINICAL HISTORY
128	Laxmi	13255	24	3	2	2		7W+2D	18.6	1.8	4.9	Reg	Normal	-	Normal	-	Normal	-	-
129	Bhavana	14130	22	1				7W+5D	20.1	1.7	5.4	Reg	Normal	-	Normal	-	Normal	-	-
130	Kalavathy	10514	30	3	1	1	1	9W+6D	38.2	3.1	6.7	Reg	Normal	Spo abortion	Normal	-	Normal	-	-
131	Suhasini	16937	21	1				10W	41.1	4.1	3.5	Reg	Normal	-	Normal	-	Normal	-	-
132	Preethu\i	13824	21	2	1	1		11W+1D	44.1	5.2	3.1	Reg	Normal	-	Normal	-	Normal	-	-
133	Sameedha	10954	24	2	1	1		7W+5D	28.3	1.7	5.4	Reg	Normal	-	Normal	-	Normal	-	-
134	Sowmya	10724	25	2			1	11W+3D	44.1	5.8	5.3	Reg	Normal	Spo abo	Normal	-	Normal	-	-
135	Jyothi	13899	21	2	1	1		6W+6D	22.3	1.6	3.8	Reg	Normal	-	Normal	-	Normal	-	-
136	Neelamma	13929	24	3	1	1	1	5W+6D	14.8	0.6	4.8	Reg	Normal	Spo abo	Normal	-	Normal	-	Pain abdomen
137	Girija	13948	19	2	1	1		7W	21.3	1.4	4.1	Reg	Normal	-	Normal	-	Normal	-	-
138	Sanjana	14028	23	2	1	1		8W	28.3	2.4	4.6	Reg	Normal	-	Normal	-	Normal	-	-
139	Parvathy	14010	24	3	1	1	1	9W+2D	35.3	3.2	6.5	Ir	Normal	Spo abo	Normal	-	Normal	-	-
140	Sunitha	14065	32	3	2	2		8W+5D	32.3	2.7	4.7	Reg	Normal	-	Normal	-	Normal	-	-
141	Uma	14894	29	3	2	2		7W+4D	25.3	1.7	4.5	Reg	Normal	-	Normal	-	Normal	-	-
142	Shila	14905	29	3	2	2		6W+6D	24.7	1.1	3.9	Reg	Normal	-	Normal	-	Normal	-	-
143	Nanda	10191	31	3	2	2		7W+6D	25.6	1.6	4.4	Reg	Normal	-	Normal	-	Normal	-	-
144	Sumithra	15260	28	3	2	2		8W+4D	32.1	2.8	4.6	Reg	Normal	-	Normal	-	Normal	-	-
145	Rekha	15261	30	3	2	2		6W+5D	22.3	1	4	Reg	Normal	-	Normal	-	Normal	-	-
146	Anitha	15416	24	2			1	7W+4D	25.3	1.7	6	Ir	Normal	Spo abo	Normal	-	Normal	-	-
147	Bhavana	14785	25	3	2	2		6W+1D	14.7	1.1	2.9	Reg	Normal	-	Normal	-	Normal	-	-
148	Seetha	13854	22	2	1	1		8W+4D	31.1	2.2	5.4	Reg	Normal	-	Normal	-	Normal	-	-
149	Rekha	8413	18	1				10W+5D	42.6	5.1	4	Reg	Normal	-	Normal	-	Normal	-	-
150	Shantha	24153	21	1				6W	14.3	0.9	4.1	Reg	Normal	-	Normal	-	Normal	-	-