SERUM PROGESTERONE AS A SINGLE HORMONE TO DETECT FETAL VIABILITY IN CASES OF THREATENED ABORTION

Dissertation submitted in Partial fulfilment of the regulations required for the

award of M.S. Degree in Obstetrics and Gynaecology

THE TAMIL NADU Dr.M.G.R. MEDICAL UNIVERSITY CHENNAI,

TAMIL NADU

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CERTIFICATE

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COIMBATORE, TAMILNADU, INDIA - 641 014

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Course : M.S. OBSTETRICS AND GYNAECOLOGY.

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Dissertation Topic : SERUM PROGESTERONE AS A SINGLE MARKER TO ASSESS FETAL VIABILITY IN THREATENED ABORTION.

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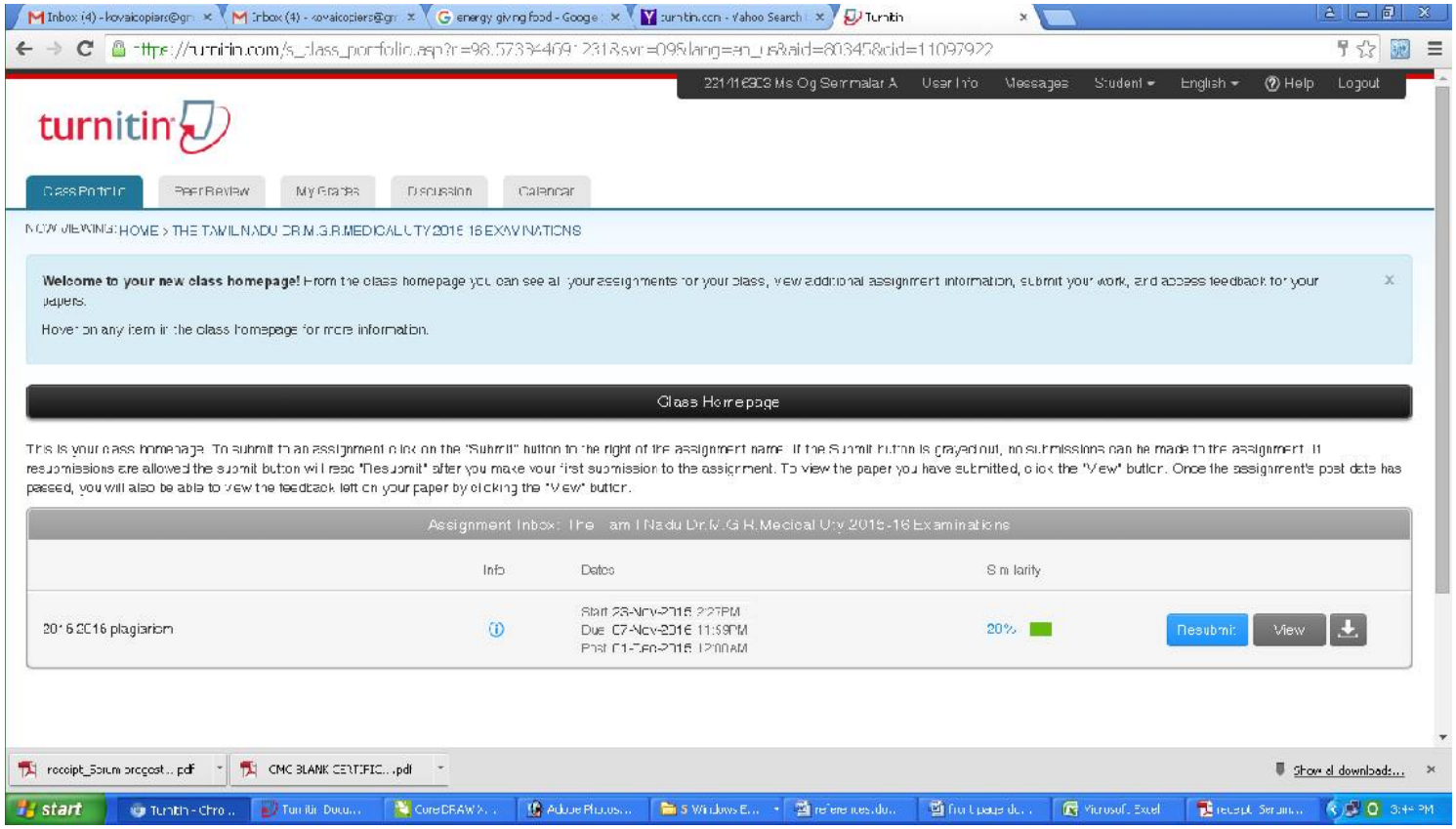
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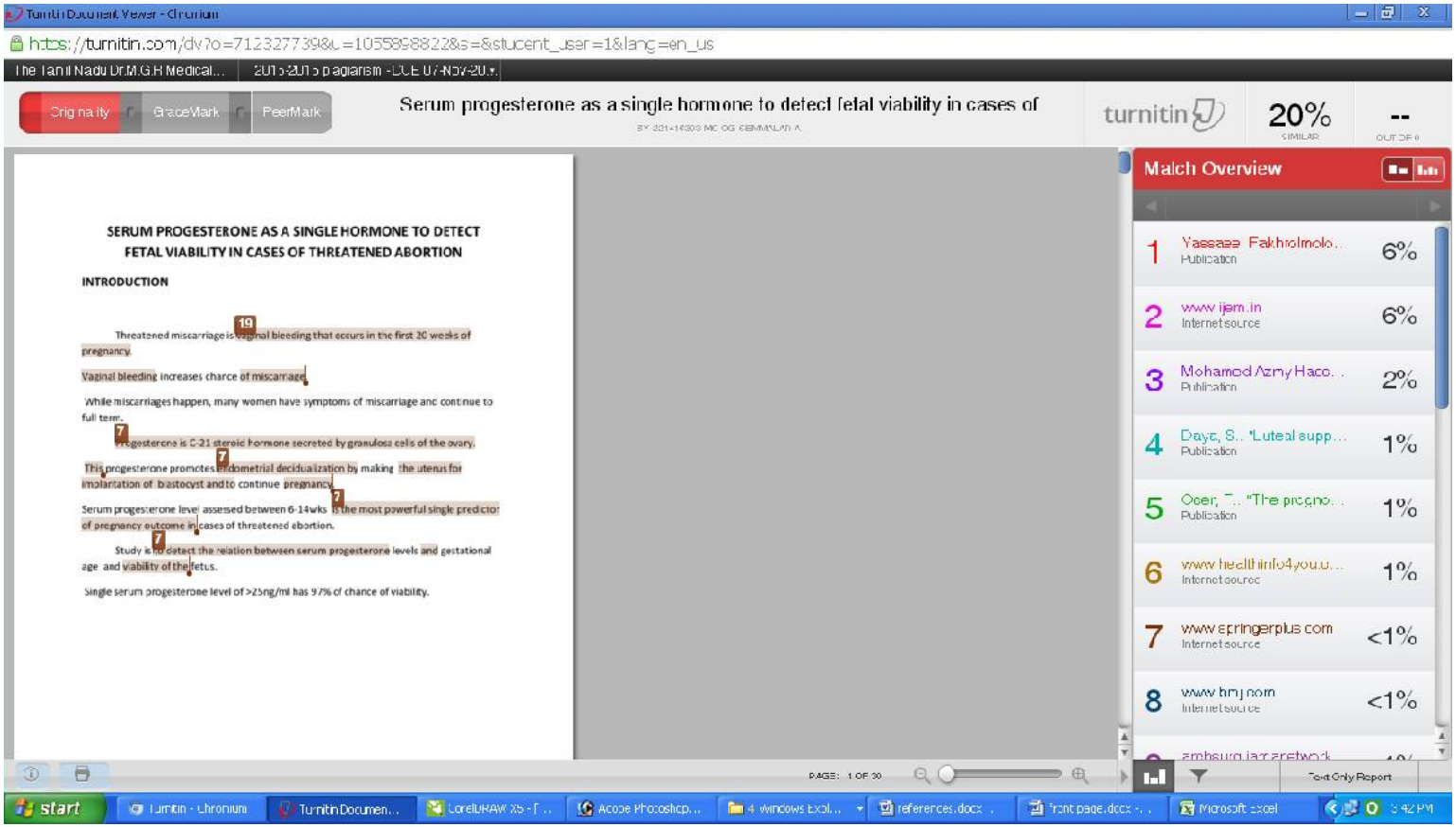
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OUT OF
SERUM PROGESTERONE AS A SINGLE HORMONE TO DETECT FETAL VIABILITY IN CASES OF THREATENED ABORTION
INTRODUCTION
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Vaginal bleeding increases charce of miscarriage.
While miscarriages happen, many women have symptoms of miscarriage anc continue to full term.
Progesterone is C-21 steroic hormone secreted by granulosa cells of the ovary.
This progesterone promotes endometrial decidualization by making the uterus for implantation of blastocyst and to continue pregnancy.
Serum progesterone level assessed between 6-14wks is the most powerful single predictor of pregnancy outcome in cases of threatened abortion.
Study is to detect the relation between serum progesterone levels and gestational age and viability of the fetus.
Single serum progesterone level of >25ng/ml has 97% of chance of viability.
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SERUM PROGESTERONE AS A SINGLE HORMONE TO DETECT FETAL VIABILITY IN CASES OF THREATENED ABORTION

INTRODUCTION

CERTIFICATE

This is to certify that the dissertation entitled "**SERUM PROGESTERONE AS A SINGLE HORMONE TO DETECT FETAL VIABILITY IN CASES OF THREATENED ABORTION** " is a bonafide and genuine research work Carried out by **Dr. A.SEMMALAR** in partial fulfilment of the requirement for the degree of Master of **Obstetrics and Gynaecology**

.

Date

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Date

Dr.Edwin Joe
The Dean,
Coimbatore Medical College Hospital.

DECLARATION

DECLARATION

I, Dr.A.Semmalar declare that the Dissertation titled "**SERUM PROGESTERONE AS A SINGLE HORMONE TO DETECT FETAL VIABILITY IN CASES OF THREATENED ABORTION** " Submitted to the Dr.MGR Medical university Guindy, Chennai is an original work done by me during the academic period from June 2015- July – 2016 at the Department of Orthopaedics, Coimbatore Medical College Hospital, Coimbatore, under the guidance and direct supervision of DR.R.MANONMANI M.D.D.G.O., Head of the department and associate professor, Department of Obstetrics and Gynaecology, Coimbatore Medical College Hospital, Coimbatore.

All the details of the patients, the materials and methods used are true to the best of my knowledge.

I assure that this dissertation has not been submitted to or evaluated by any other Medical University.

Dr.A.Semmalar

INTRODUCTION

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Vaginal bleeding increases chance of miscarriage.

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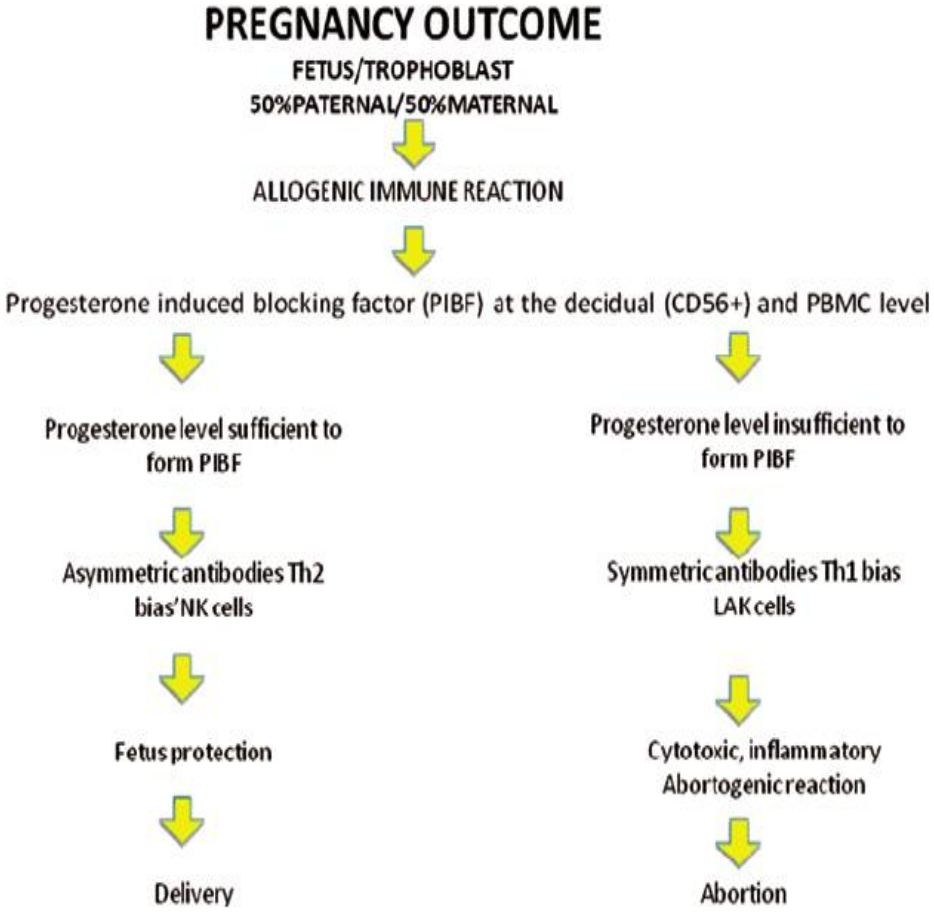

PREGNANCY OUTCOME
FETUS/TROPHOBLAST
50%PATERNAL/50%MATERNAL
ALLOGENIC IMMUNE REACTION
Progesterone induced blocking factor (PIBF) at the decidual (CD56+) and PBMC level
Progesterone level sufficient to form PIBF
Asymmetric antibodies Th2 bias'NK cells
Fetus protection
Delivery
Progesterone level insufficient to form PIBF
Symmetric antibodies Th1 bias LAK cells
Cytotoxic, inflammatory Abortogenic reaction
Abortion

Classification of miscarriage

1. Threatened
2. Inevitable
3. Complete
4. Incomplete
5. Missed
6. Septic

TYPES OF MISCARRIAGE

1. Spontaneous
2. Induced

Spontaneous types

1. Sporadic {isolated}
2. Recurrent

INDUCED

1.Legal {medical termination of pregnancy}

2.illegal – Septic

Threatened miscarriage is where the onset of miscarriage has started but has not progressed to the level where recovery is impossible

Symptoms

1 bleeding per vaginum – usually very minimal

Brownish or reddish

2. pain - very mild pain in abdomen

Painless

3. Mild backache

Signs

- Very gentle pelvic examinations reveal

1 spotting per vaginum

2 external os is closed

3 uterus size corresponds to period of gestation

4 cervix and uterus feel soft

- Trans vaginal uitrasonography reveals

1.well formed gestational sac with healthy embryo

2.fetal cardiac activity

3.fetal echoes –central

Bed rest , pain relief and serum progesterone may be beneficial

Advice given are

1. To avoid strenuos work for atleast 2 weeks
2. Repeat usg after 3-4 weeks

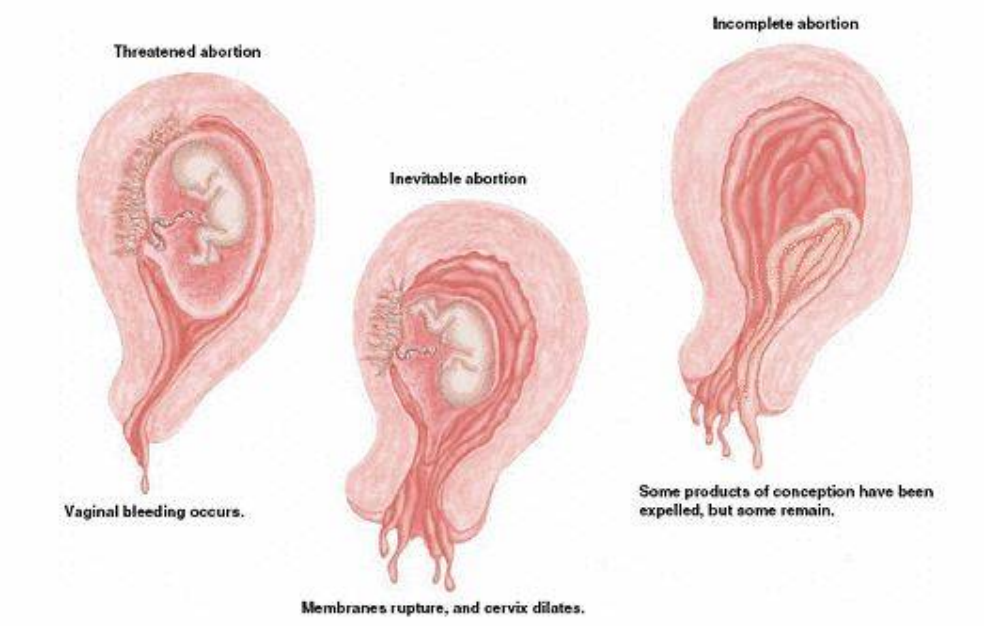
There is increased chances of

placenta previa

preterm labor

intra uterine growth restriction

fetal anomalies


Threatened abortion
Vaginal bleeding occurs.
Inevitable abortion
Membranes rupture, and cervix dilates.
Incomplete abortion
Some products of conception have been expelled, but some remain.

OBJECTIVES

- To assess the levels of serum progesterone in patients with threatened abortion and follow up the patients to find the pregnancy outcome.
- Single serum progesterone value of > 25ng/ml has 97% chance of fetal viability

METHODOLOGY

SELECTION CRITERIA

a) Inclusion Criteria

- All antenatal patients presenting with spotting per vaginum before 20 weeks of gestation.

b) Exclusion Criteria

- All antenatal cases above 20 weeks.
- All antenatal patients presenting with profuse bleeding per vaginum before 20 weeks of gestation.

TYPE OF STUDY

Short-term prospective study.

Approximate sample size is 100.

Period of study: From Jan - 2015 to Jan - 2016.

Study was conducted at the department of Obstetrics and Gynecology in Coimbatore Medical College and Hospital.

About 100 patients presenting to the antenatal/ Gynecology OP with history of spotting per vaginum were taken into study.

During the first visit to alleviate the anxiety of the patients with history of spotting, reassurance was given and a 2ml sample of blood was collected in serum test tube.

The serum was sent for progesterone assay and the serum progesterone levels were noted.

The patients were asked to come for follow up regularly.

At around 5 months of gestation, an ultrasound was done at the antenatal OP to check for fetal heart rate and thus viability of the fetus was noted.

These patients were further followed up regularly in the antenatal OP and the pregnancy outcome was monitored.

Of the 100 patients who presented to antenatal op 15 patients lost follow up and hence 85 persons were taken into study.

The 85 patients were serially followed up and their fetal viability was monitored.

Among them, few progressed to incomplete and complete abortion.

The patients who crossed the period of viability were serially followed up and their pregnancy outcome was monitored.

The following variables were taken into account

1.age

2.parity

3.gestational age

4.previous h/o miscarriage

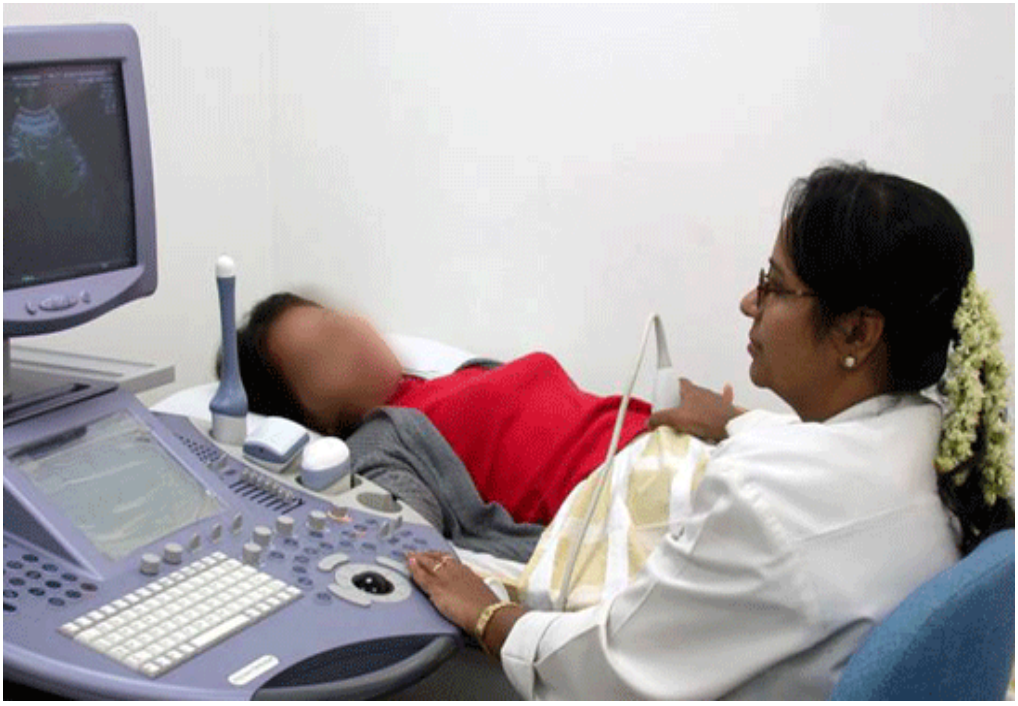
5.seum progesterone levels

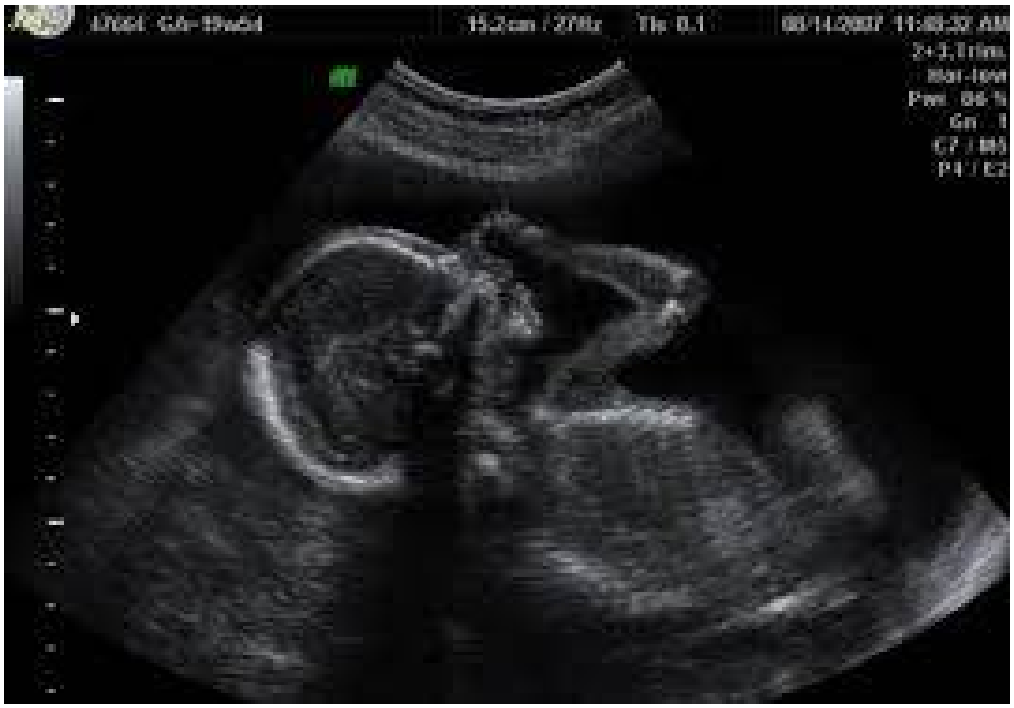
a. <10 ng/ml

b. 10-25 ng/ml

c. > 25 ng/ml

The patients were followed up with serial ultrasound at 20 wks fetal viability was confirmed using ultrasound. The patients were asked to come for further follow up .Again at 7 months fetal viability was confirmed, the pregnancy outcome was monitored

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Abortion is the natural failure of the fetus earlier than twenty weeks of conception. It will be a shocking happening that so it will have a psychological impact on both the husband and wife.

What is a threatened abortion, it is defined as a bleeding of vagina in the presence or absence of abdominal cramps, which is a frequent problem of pregnancy.

It has an incidence of 20 percent in women for the period of early gestation and roughly not whole of these pregnancies will terminate Even if abortion does not follow early bleeding, these foetuses are at augmented risk for delivery before term period, low birth weight and prenatal death.

Numerous studies recently suggest that, this hormone progesterone can lessen pregnancy failure in females with threatened abortion By development of conception, the function of inadequate progesterone level decline and uterine anatomical abnormality either with or without cervical incompetency is accountable more than hormonal shortage. Some approaches like cervical cerclage can be useful over medical interventions.

Hormone progesterone plays a vital role in the preservation of pregnancy. In the existence of adequate progesterone amount at the time of pregnancy, leucocytes produce a substance called progesterone induced blocking factor which protects against abortion in rats .In addition promoting secretary phase in the endometrium and also supports early pregnancy, it alters the mother's immune response to thwart fetal abortion and relaxes the smooth muscles of uterus. In spite of this sufficient evidence, which has led to progestogens being used in treatment of threatened abortion for several years, there is small data accessible to hold up their regular use in this matter The purpose of this research was to decide whether progesterone is efficient in allowing pregnancy to continue beyond twenty weeks in females with threatened abortion.

Review of Literature

Progesterone is very essential for the establishment and maintenance of pregnancy.

Progesterone's function is to transform the endometrium to attain the secretory function of endometrium which is essential for the implantation and the maintenance of pregnancy.

The placental steroidogenesis happens approximately during the fifth week gestation.

After this there will be a transfer of luteal support to placenta, this process starts happening between seventh and ninth week and this period is called luteal-placental shift.

Here the production of progesterone occurs from both sources. Production of progestrone by the corpus luteum is must essential for early human pregnancy.

Progesterone acts in two different ways one is by supporting the growth of the endometrium and also by improving the blood flow and o2 supply by rising the nitric oxide production.

It keeps the myometrium quiet by the relaxing effect on uterine musuculatre. Genes regulated by progesterone in the uterus during the pregnancy period will control the endometrial receptivity and differentiation and recruitment of natural killer cells in the decidua.These NK cells will act on vascularity i.e., angiogenesis and also trophoblast invasion.

This is established by the presence of lymphocyte progesterone receptors present on δ T cells and NK CELLS in the peripheral blood. Recognition of fetal antigens is by efficient progesterone lymphocyte receptor regulation mechanisms.

The one another factor which mediates the immune system is progesterone induced blocking factor which are regulated by the genes dependent on progesterone.

The incidence of unexplained miscarriages could have an immunological etiology .

For the PCOS patients with episodes of early pregnancy loss, progesterone supplementation, if low at 5-weeks gestation, during early pregnancy period might restore the fetal growth and then avoid recurrent miscarriages.

In a women with polcystic ovarion disease who had early pregnancy loss there seem to be decrease in serum progesterone levels. The time period is early gestation period of five weeks.

Women with frequent miscarriages during early pregnancies, progesterone supplementation during this period has resulted in survival of fetus.

The relation between thyroid and frequent miscarriages hypothesis relation to immunology has been postulated, which states that thyroid stimulating hormone and human choriono gonadotropins have glycoprotein receptors. There will be cross reactivity between hcg and tsh .

So if tsh receptors are able to act on the glycoprotein receptors of hcg , the thyroid antibodies will also able to act on the receptors of reproductive hormones so they will be terminate the pregnancy.

Insufficiency of corpus luteum is due to increase in prolactin secretion above the normal level .therefore, management with drugs that stimulate dopamine or act as agonists of dopamine and treatment with exogenous progesterone in them is necessary.

During assisted reproduction low progesterone environment is created in hospitals due to interventions in assisted reproduction.

Luteal phase defect is seen in women with PCOD, disorders with thyroid and prolactin use of hcg analogues and other aspiration techniques involving granulosa cells cause the corpus luteum to secrete less amount of progesterone. This may be one of the cause for miscarriage.

Luteal phase is the period starting after ovulation and formation of pregnancy otherwise onset of menstrual cycle 14 days later. After ovulation, the luteal phase of an ordinary natural cycle is featured by development of corpus luteum, which starts synthesizing reproductive hormones progesterone which is more in quantity and lesser amount of estrogen.

Luteal phase insufficiency is characterised by secreting lesser amount of progesterone. One of the reasons for implantation failure is the luteal phase defect, which is the culprit for unsuccessful reproduction and frequent miscarriages

Survival of the embryo is facilitated by changing the immune system towards production of Th2 response.

Rationale for Luteal Support in Pregnancy

Placental HCG and secretion of progesterone and estradiol by corpus luteum are the major endocrine events at the commencement of pregnancy, while the luteo-placental shift is a significant step in the later stages.

Progesterone affects not only decidualization, it is also the main immunological determinant in addition to it controls uterine contractibility and cervical capability. These property will contribute significantly in the direction of the correct maturity of pregnancy .

Successful pregnancy is connected not with a up regulation of Th1 cytokines such as IFN-γ and TNF-α but with up regulation of Th2 cytokines such as, IL-6 and IL-4 IL-10.

At the time of pregnancy, progesterone will increase the production of progesterone-inducing blocking (PIBF) 34-KDa protein, which will prevent immune reactions toward the trophoblast through the blockade of natural killer cell activation and a raise in asymmetric non cytotoxic-blocking antibodies.

Mitogen-stimulated peripheral monocytes from females with a normal pregnancy have been revealed to have notably elevated concentration of Th2 cytokines and poorer concentration of Th1 cytokines than those from females with a H/O unexplained recurrent spontaneous miscarriage.

Nevertheless, when PMBCs from females with recurrent spontaneous miscarriage were administered with progesterone, the production of Th1 cytokines was repressed and production of Th2 cytokines was improved, thus changing the Th1 : Th2 balance in good turn of pregnancy. [20]

females with threatened abortion that have exposed a decline in pregnancy loss with treatment using suppository containing progesterone

Cytokines which are Pro-inflammatory linked with mis-carriage ,progesterone- induced blocking factor (PIBF) had reduced or inhibited immune reaction and changing of cytokines from type 1 to type 2 cytokines caused a raise in the production of cytokines type 2.

Pregnancy is often troubled by immunological factors, neuroendocrine and luteinic deficiencies and hyper-contractility of myometrium. This shows the decrease in abortion in women managed with progesterone as prophylaxis

There are also few studies, yet, that show inadequate data on the consequence of progestogens on threatened miscarriage.

In a study, miscarriage toll were radically lesser in the group managed with progesterone derivatives than the untreated group. Progestogens also have a pharmacodynamic effect by dropping the production of prostaglandins; therefore it relaxes smooth muscles of uterus and preventing inappropriate contractions that may result in miscarriage and preterm labour pain

Some pregnant women have lower abdominal pain followed by missed period, but if lower abdominal pain is associated with uterine bleeding, it may predict impending abortion.

PCOS women showed exceptionally little progesterone production in early pregnancy which may result in degenerative changes in early fetal growth.

The bulk of corpus luteum remains somewhat stable for the first 8-9 weeks of conception which is followed by a marked decrease in the size of corpus luteum. Angiogenesis starts occuring after the ovulatory LH surge.

Vascularity of the corpus luteum starts increasing, leading to formation of one of the most heavily vascularized structure rich in cholesterol which are needed for the production and transport of the progesterone to the circulation.

The changes in the blood flow of corpus luteum during the luteal phase and earlier period of pregnancy.

During the late follicular phase there is high resistance index but after the time period the RI decreases ie towards the luteal phase.

During the midluteal phase the resistance index was low, thus showing a vast amount of blood flow to the corpus luteum.

There was an rise in RI and therefore decrease in the blood flow on degeneration of the corpus luteum. Females with luteal phase defect the resistance index was more thus showing a reduction in the blood flow.

At the time of gestation the resistance index remains at mid luteal phase level for the first seven to eight weeks and then rises when the corpus luteum degenerates.

The period starting from the luteal phase approximately around 8-10 weeks of pregnancy is the critical time.

The correct function of the GnRH pulse initiator in the hypothalamus is vital for both ovaries to function normally, therefore it also necessary for the normal function of corpus luteum. Around one-half of luteal phase deficiency are mostly due to inappropriate function of the GnRH pulse initiator.

After ovulation the rise in serum progesterone levels contain the GnRH pulse initiator, resulting in decrease in LH pulses and poor luteal function. The knowledge of paracrine and auto mechanisms between steroidogenic and nonsteroidogenic cells now allow subclassification of luteal phase defects of ovarian origin.

After performing the luteotomy procedure within 7 weeks of gestation, there was an abrupt reduction in the amount of serum progesterone concentration which lead to miscarriage.

Progesterone is well-known to make secretory changes in the lining of the uterus necessary for victorious implantation of a fertilized egg. It has been suggested that a causative factor in numerous cases of miscarriage may be insufficient secretion of progesterone.

For that reason, progestogens have been used, beginning in the first trimester of pregnancy, in an attempt to prevent spontaneous miscarriage.

In order to determine the efficacy and safety of progestogens as a prophylactic therapy, a meta-analysis was done of RCT comparing progestogens with placebo given in an attempt to stop miscarriage.

Although many serum biomarkers have been studied in an attempt to discriminate between viable,

failed intrauterine and ectopic pregnancies,

current practice involves serial measurements of serum quantitative hCG levels.

Habitually, physicians have expected hCG levels to increase twice the amount or raise the amount by sixty six percent every two days in normal pregnancies.

Instead if the rate of increase in HCG is not equal to the above mentioned values then it would have been associated with nonviable and ectopic pregnancies. Serial hCG trend, on the other hand, must be observed with vigilance because some of the ectopic pregnancies will have increasing hCG levels similar to normal pregnancies which is estimated to be around sixty four percent in some patients.

Between three and ten percent of normal intrauterine pregnancies will show signs of “abnormal” rises in hCG titres.

In addition, a latest study showed hCG curves in during early period of viable pregnancies and found that the very slow increase for a normal viable pregnancy was in fact fifty three percent at forty eight hours.

Therefore, these novel hCG curves emphasize the complicatedness in applying hCG only to differentiate between nonviable and viable pregnancies since there is important overlap in hCG trends between the two groups.

In reaction to the difficulties of the sequential hCG approach, researchers have observed both solitary serum biomarkers and combining several biomarkers.

Sex hormone progesterone’s serum level of less than ten nanograms per millilitre is usually indicative of a pregnancy which is nonviable, whereas a serum level of more than twenty five nanograms per millilitres is characteristically dependable with a viable one.

Regrettably, an roughly forty percent of gestations will have serum levels of progesterone in the undetermined range, between ten and twentyfive nanograms per millilitre.

In addition, several authors have recommended with a progesterone level of 5 ng/mL instead of ten nano/ml as a marker because the above mentioned value can make out nonviable pregnancies with almost a sensitivity of around 100%.

Inhibin A is also being observed as a potential biomarker and has been exposed to be lesser in ectopic pregnancies as compared with normal ones. In an attempt to enlarge on the facts from solitary biomarkers, multiple biomarkers have been observed.

Sadly, only partial information was integrated in those previous studies.

The reason of the present study was to improve findings from the earlier body of job by developing and evaluating a model that include appropriate clinical facts as well to serum biomarkers to predict pregnancy viability.

Beth J. Plante etal conducted a study in a pregnant women who were in the period of early period .

The aim of the study was to develop a multiple marker to detct the viability of pregnancy when the quantity of progesterone is indeterminate.

What is the objective of the study the objective is to form a model which

helps us to distinguish viable and nonviable pregnancies even at a single visit during the first trimester.

The design of the study is a prospective cohort study. Participants of the study are 256 pregnant women who are in the first trimester of pregnancy. Every one of them are symptomatic in the group.

The study was conducted between 2002 and 2004 in an urgent care providence which is located in Rhode Island.

Detailed history and clinical assessment was done in each and every pregnant women. Predictors of early gestation were collected.

This includes the above mentioned clinical history and assessment and serum samples of various biomarkers. The serum samples are collected by puncturing the vein. The predictors were analysed alone and then in combination with other variable using ROC which is called receiver operator characteristic curves.

The women are separated into two groups again, based on the values of reproductive hormone progesterone.one group is called extreme where the values of progesterone are in extreme that is it includes both the values first one

is women having serum progesterone level less than five nanogram per millilitre the second one is women having serum progesterone level morethan twenty five nanogram per millilitre.

The second group is called grey zone which includes serum progesterone level between five and twenty five nanogram per millilitre.

The results of the study is that among many biomarkers, progesterone had the maximum diagnostic precision in finding out the viability.

Sex hormone progesterone was extremely accurate in the extremes group but not as much of correct in the grey zone because the area under the curve is .71 where as the area under the curve in extremes is 0.99.

In order to correct this deficit a MMM was suggested the MMM is nothing but an abbreviation of multiple marker mode.MMM(multiple marker model) was suggested for the participants who were classified under grey zone.

This includes hormonal assay of serum progesterone and another important hormone human chorionic gonadotropin. It also includes symptoms and ultrasonographic findings and symptoms of pregnant women

A multiple marker model is able to predict pregnancy viability in ladies with symptoms. It had an accuracy of 90%.

Strategies concentrated on evaluating early gestation have increased over the past number of decades in reaction to elevated rates of ectopic pregnancy which is estimated to be 19.7/1,000 pregnancies in the year nineteen ninety two.

Responsive human chorionic gonadotropin hormonal assays and superior sonological techniques have helped us to find out the earlier recognition of ectopic pregnancies.

In spite of these advances, the very most symptomatic women who come in to the department of obstetrics and gynaecology during the early weeks of gestation keep on to require two or more evaluations before pregnancy viability and the location can be precisely determined.

This setback in diagnosis is of worry to both practitioners and patients. An evaluation tool with the capability to differentiate between nonviable and viable pregnancies at a first visit, will definitely decrease mortality and morbidity from unidentified ectopic pregnancies and minimize patient fear.

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Amal Darwish, M.D etal conducted a study the objective is to forecast pregnancy result by observing the relation linking serum CA125, progesterone and βHCG and the incidence of miscarriage in the pregnancy during the trimester, in patients with record of recurrent pregnancy loss. It is a prospective controlled study.

It was conducted at Kasr- El-Aini Hospital and Galaa Hospital. The methods and materials of this study are: Serum CA125, progesterone and βHCG levels in twenty women who are pregnant with history of frequent pregnancy loss and they were compared to 20 women who are pregnant but with no history of abortion, and there are a different group of women who were also 20 in number and they failed to complete the first trimester of pregnancy during the study.

The results of the study showed Serum B-hCG had a a sensitivity of 100%, specificity of 50%,a Positive predictive value of 50% and a negative predictive value of 100%.Followed by serum progesterone which has a specificity of 78%,sensitivity of 25%, positive predictive value is 36% and negative predictive value is 67%, and the least serum CA125 showed a specificity of 65%, a sensitivity of 10%, positive predictive value is 13% and a negative predictive value is of 59%.

From the above findings we conclude that the value of CA125 in frequent abortions is still uncertain and does not need to be recommended on routine basis. In contrast β-HCG is hundered% sensitive with a fifty% negative predictive value as a single serum measurement for the prediction of pregnancy ending

The frequencies of foetal death in clinically obvious pregnancies will be about 10-15%. The frequency will be clearly elevated if we think about the preclinical losses diagnosed by βHCG levels which start from three weeks following the LMP. Accordingly, the expected probability for a woman to have three consecutive abortions should be in the range of 0.3% to 0.4%.

The real frequency of habitual abortion, on the other hand, is significantly high, being in the range of 0.4% to 0.8%. These distinctions suggest that not only casual causes but also some definite factors should be involved in this type of reproductive failure (2).

Preterm labor is defined as Labor and delivery between 20 –37weeks incidence 5%-10%

ACOG defines preterm labor as regular contractions associated with cervical dilatation before 37 weeks

It is the leading cause of perinatal morbidity and mortality

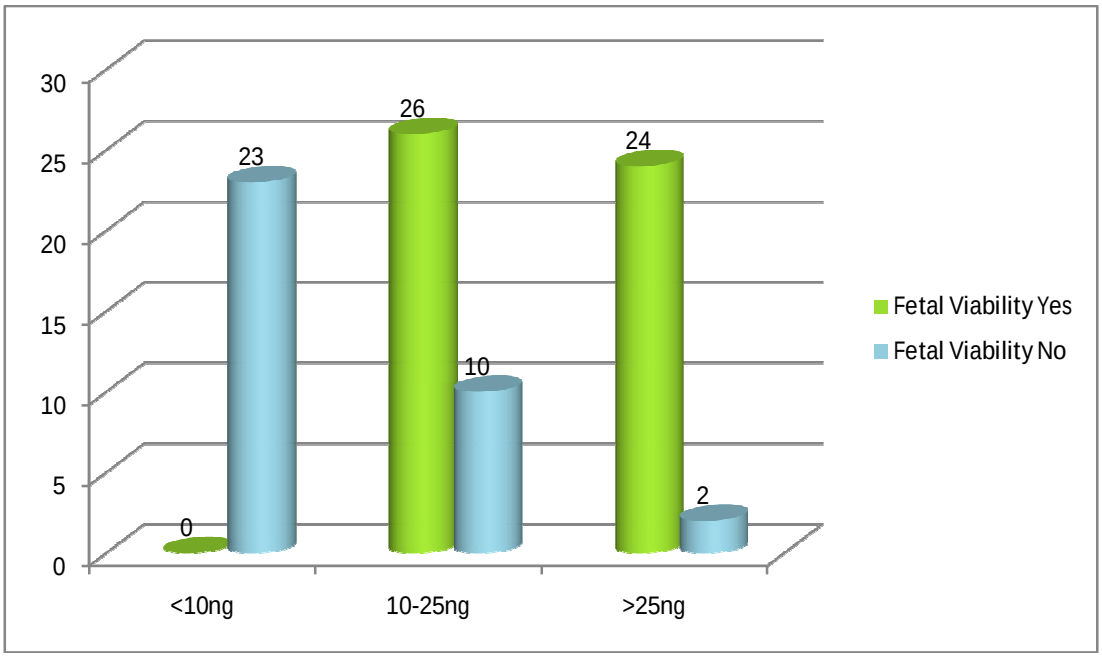
Survival rates have increased and morbidity has decreased because of technologic advances

- Definition (WHO) :Preterm labor is the presence of contractions of sufficient strength and frequency to effect progressive effacement and dilatation of the cervix between 20 and 37 weeks' gestation. Threatened miscarriage has more chances of preterm labor.

ANALYSIS AND RESULTS

Serum Progesterone * Fetal Viability

	Fetal Viability		Total	**Chi-square results**
	Yes	No		
<10ng	0	23	23	**0.000 P<0.01**
10-25ng	26	10	36	
>25ng	24	2	26	
Total	50	35	85	


30
25
20
15
10
5
0
0
23
26
10
24
2
<10ng
10-25ng
>25ng
Fetal Viability Yes
Fetal Viability No

Out of 26 patients who are in >25ng/dl group of serum progestrone, 24 patients have fetal viability. So it is concluded that with increase in serum progesterone there is more chance of fetal viability. Among the 23 patients of Serum progesterone values of < 10 ng/ml none of them had viable pregnancy

Among the 36 patients between 10-25ng/ml 26 had viable pregnancy and 10 had non viable pregnancy

Among the 26 patients of serum progesterone >25ng/ml 24 had viable pregnancy

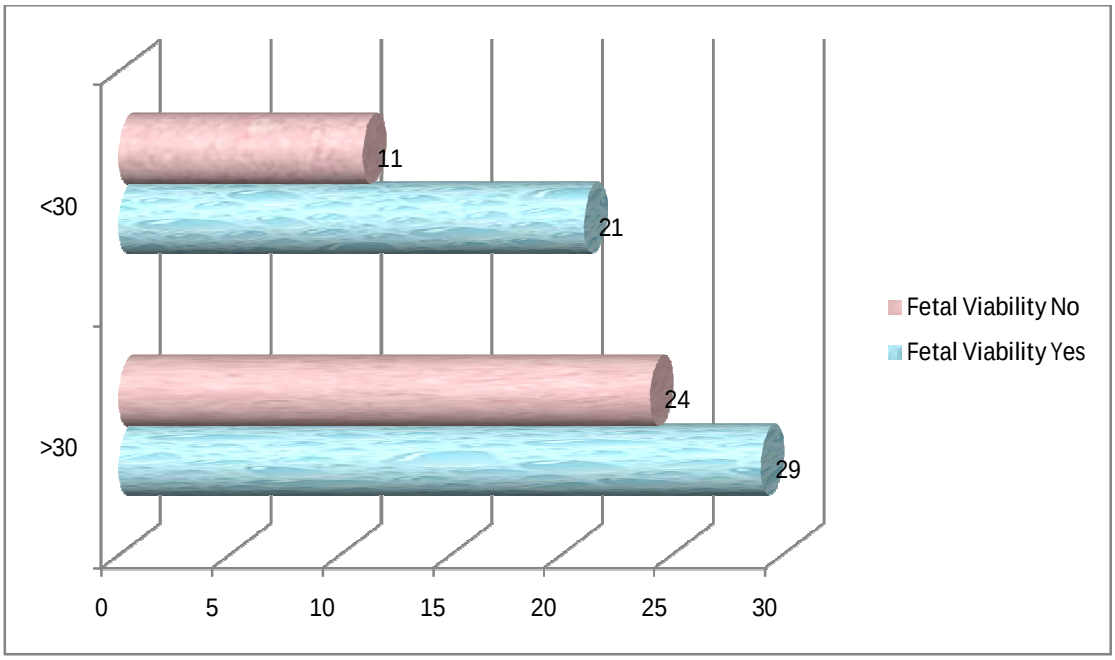
So a single serum progesterone value of >25ng/ml is a effective marker to say that the pregnancy will be viability

Chi-square results

0.000
P<0.01

Age * Fetal Viability

	Fetal Viability		Total	**Chi-sq result**
	Yes	No		
>30	29	24	53	
<30	21	11	32	**0.223**
Total	50	35	85	


<30
>30
11
21
24
29
0
5
10
15
20
25
30
Fetal Viability No
Fetal Viability Yes

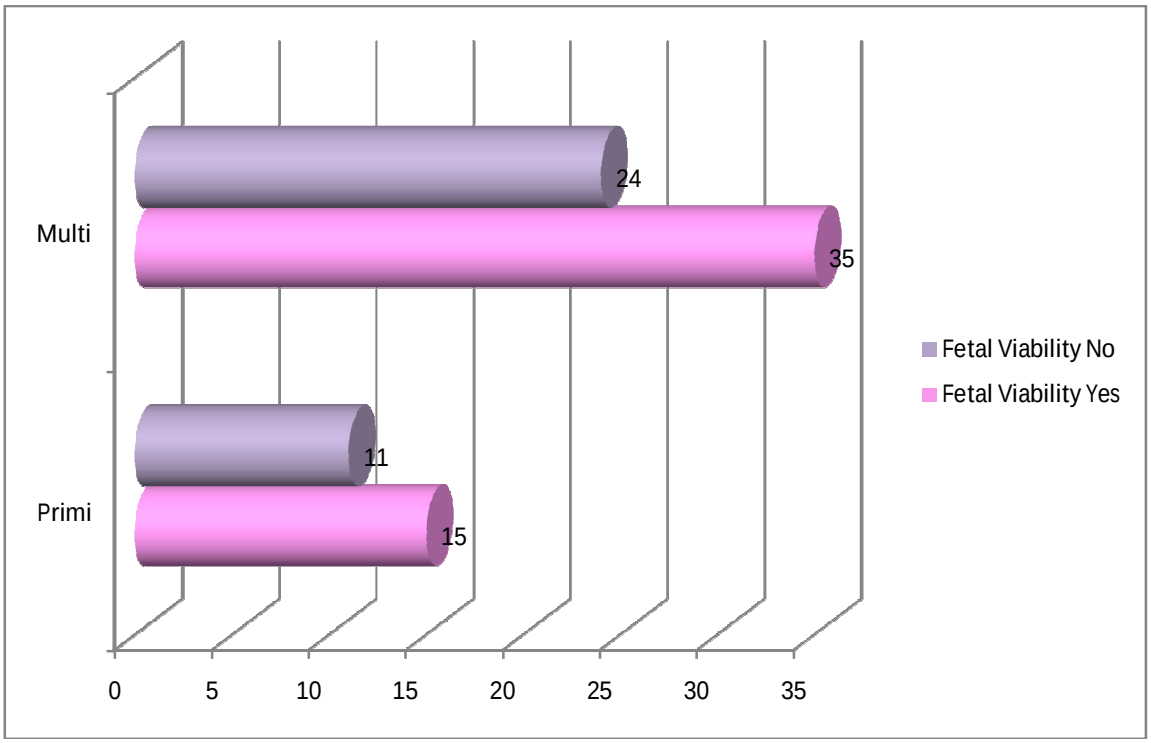
Regarding age factor

Age <30 among 32 patients 21 had viable pregnancy and 11 had non viable pregnancy

Among the 53 patients of age>30 29 had viable pregnancy and 24 had non viable pregnancy

Parity * Fetal Viability

	Fetal Viability		Total	**Chisq result**
	Yes	No		
Primi	15	11	26	**0.537**
Multi	35	24	59	
Total	50	35	85	


Multi
Primi
24
35
11
15
0
5
10
15
20
25
30
35
Fetal Viability No
Fetal Viability Yes

Regarding parity

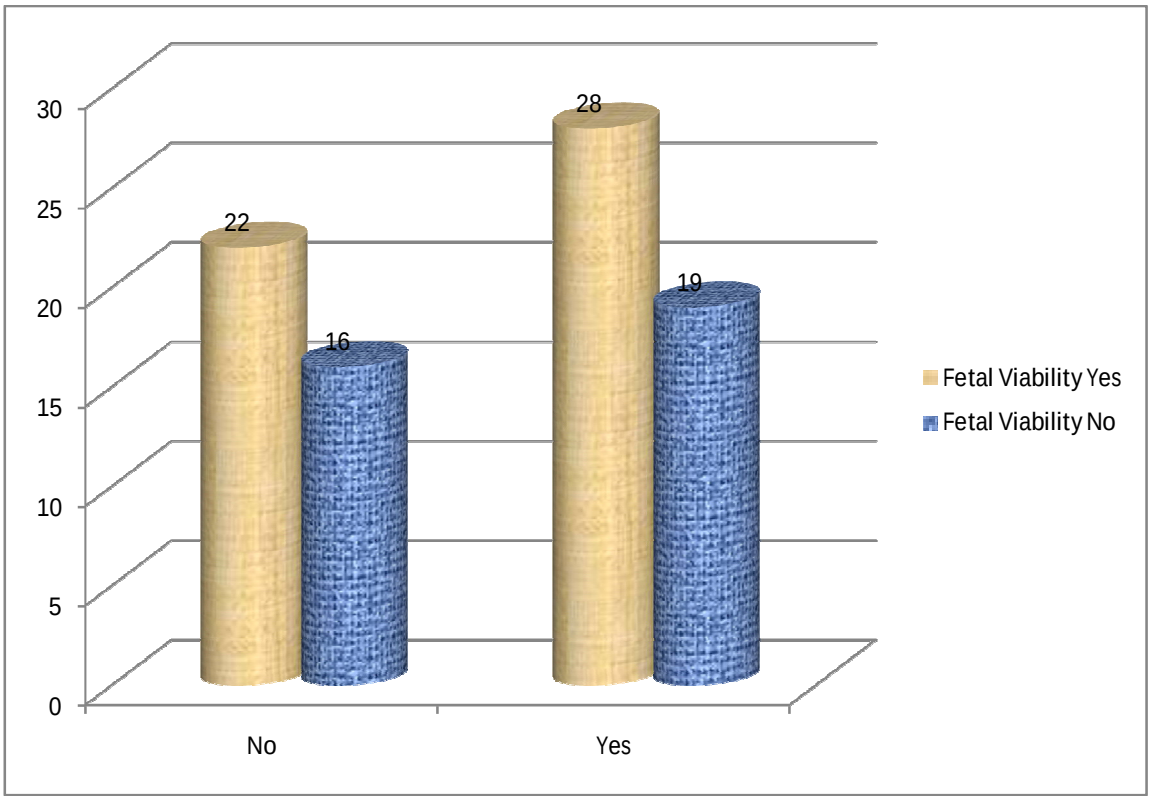
Among 26 primigravida 15 had viable foetus and 11 had non viable pregnancy

Among 59 multigravida 25 had viable foetus 24 had non viable pregnancy

Thus primi had more chances of viable pregnancy

Previous H/O Miscarriage

	Fetal Viability		Total	**Chisquare result**
	Yes	No		
No	22	16	38	
Yes	28	19	47	**0.525**
Total	50	35	85	


30
25
20
15
10
5
0
22
16
28
19
No
Yes
Fetal Viability Yes
Fetal Viability No

Regarding previous history of miscarriage

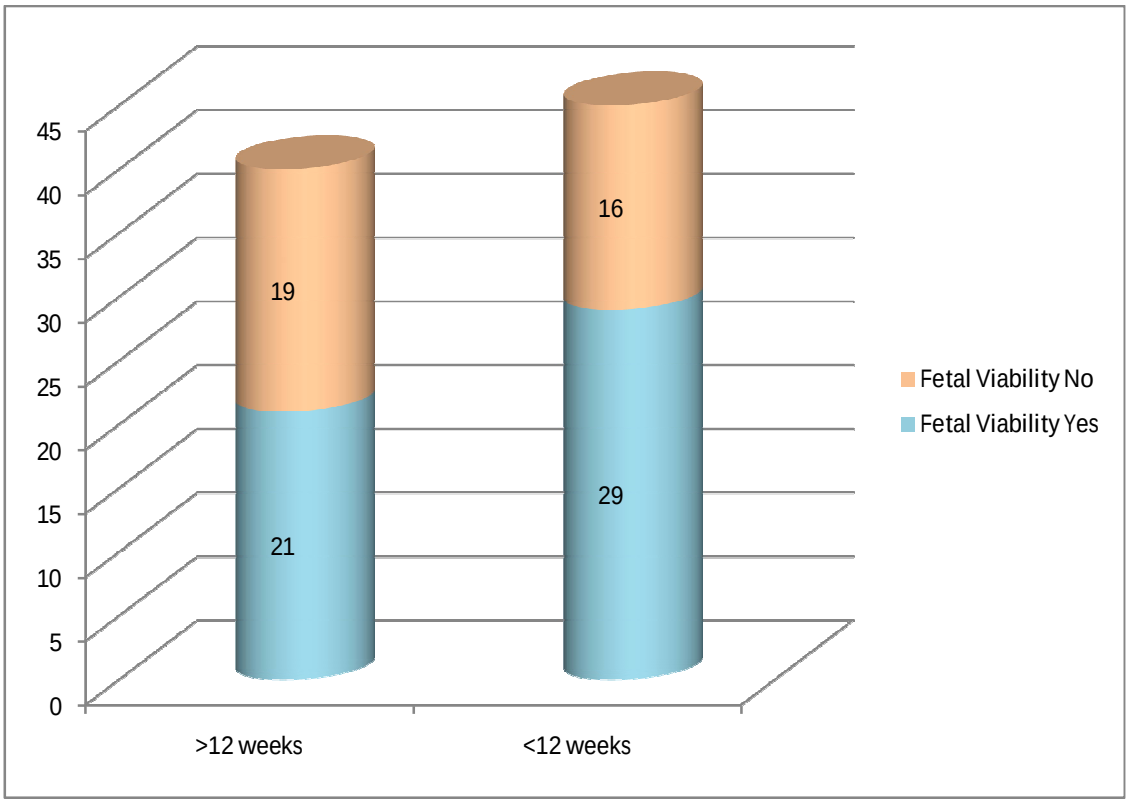
Among 47 patients with previous history of miscarriage 28 patients had viable foetus and 19 had non viable pregnancy

Among 38 patients with previous history of no miscarriage 22 patients had viable foetus and 16 had non viable pregnancy

Thus patients with previous history of miscarriage had a slight increase in chance of future miscarriage

Gestational Age * Fetal Viability

	Fetal Viability		Total	**Chisquare result**
	Yes	No		
<12 weeks	21	19	40	**.185**
>12 weeks	29	16	45	
Total	50	35	85	


45
40
35
30
25
20
15
10
5
0
19
21
16
29
>12 weeks
<12 weeks
Fetal Viability No
Fetal Viability Yes

Regarding gestational age

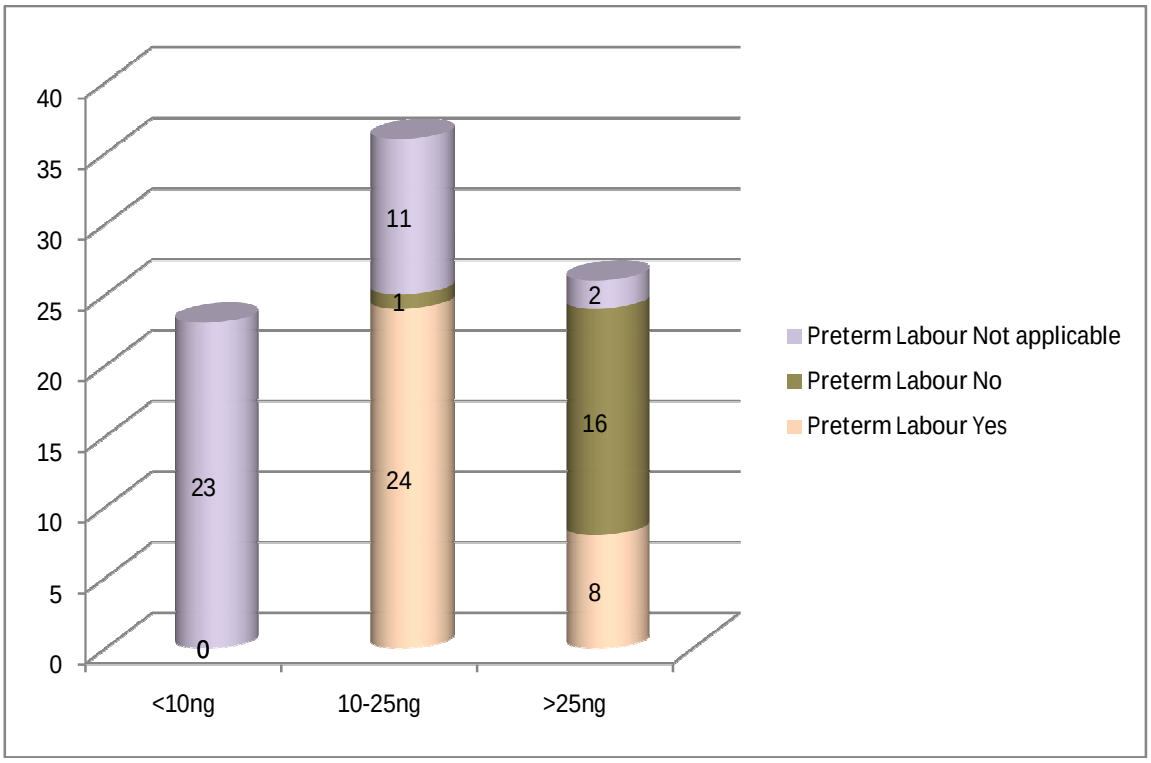
Among 40 patients with gestational age of <12 weeks 21 patients had viable foetus and 19 had non viable pregnancy

Among 45 patients with gestational age of >12 weeks 29 patients had viable foetus and 16 had non viable pregnancy

Thus as the period of gestation at which spotting occurs advances the chance of viability increases

Serum Progesterone * Preterm Labour

	Preterm Labour			Total	**Chisquare result**
	Yes	No	Not applicable		
<10ng	0	0	23	23	**0.000 P <0.01**
10-25ng	24	1	11	36	
>25ng	8	16	2	26	
Total	32	17	36	85	


40
35
30
25
20
15
10
5
0
23
0
11
1
24
2
16
8
<10ng
10-25ng
>25ng
Preterm Labour Not applicable
Preterm Labour No
Preterm Labour Yes

Regarding preterm labor

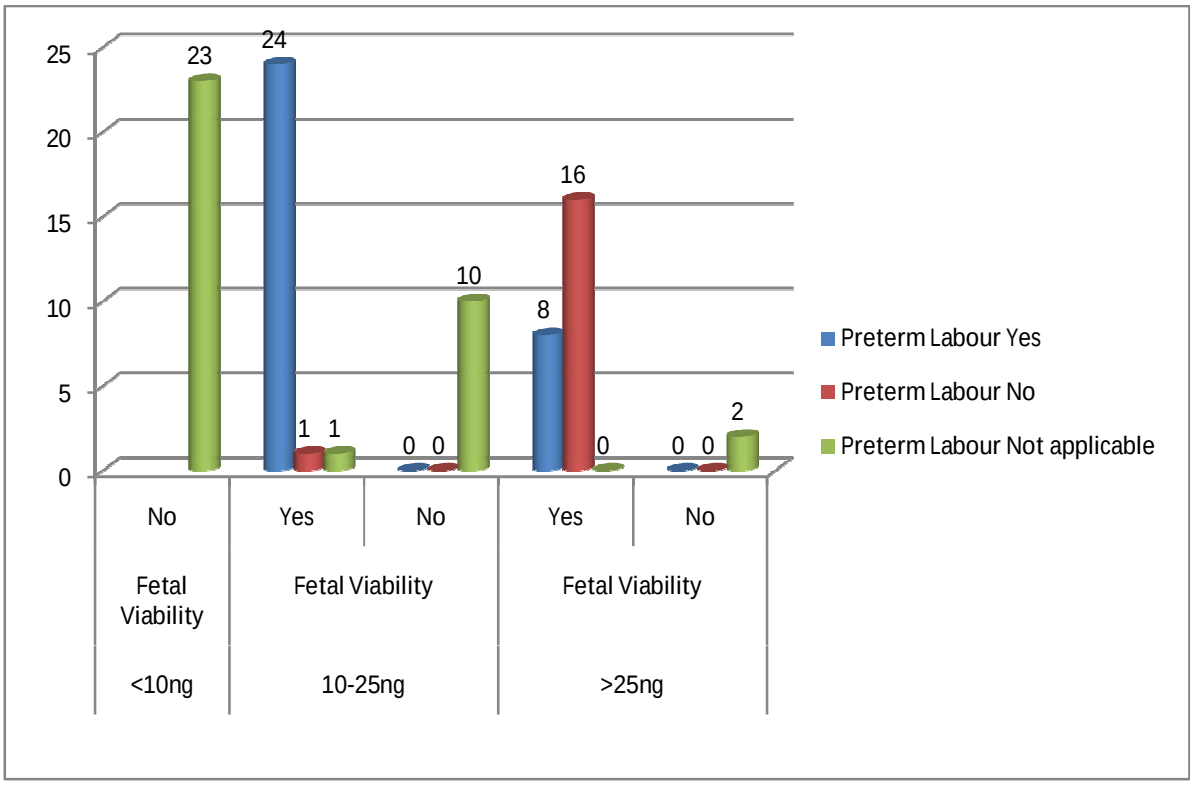
Amomg the 36 patients with serum progesterone values of 10-25ng/ml 24 patients had preterm labour

Among the 26 patients with serum progesterone values of > 25ng/ml 8 patients had preterm labour

Thus as the progesterone values increases the chances of preterm labour also increases

Fetal Viability * Preterm Labour * Serum Progesterone

Serum Progesterone			Preterm Labour			Total	**Chisquare result**
			Yes	No	Not applicable		
<10ng	Fetal Viability	No			23	23	
10-25ng	Fetal Viability	Yes	24	1	1	26	**0.000 P<0.01**
		No	0	0	10	10	
>25ng	Fetal Viability	Yes	8	16	0	24	**0.000 P<0.01**
		No	0	0	2	2	


25
20
15
10
5
0
23
24
1
1
0
0
10
8
16
0
0
0
2
No
Yes
No
Yes
No
Fetal Viability
Fetal Viability
Fetal Viability
<10ng
10-25ng
>25ng
Preterm Labour Yes
Preterm Labour No
Preterm Labour Not applicable

Thus when serum progesterone values are less than 10ng/ml then the chance of fetal viability is nil.

When values between 10-25ng/ml, chances of fetal loss is reduced but preterm labour chances are more.

Values of >25ng/ml, the chances of viability is increased also the occurence of preterm labour is reduced

DISCUSSION

In my study out of 100 patients 15 patients lost follow up.

Among the 85 patients 50 had viable pregnancy.

35 patients went in for incomplete miscarriage and non viable pregnancy.

Among the 23 patients of Serum progesterone values of < 10 ng/ml ,none of them had viable pregnancy

Among the 36 patients between 10-25ng/ml ,,26 had viable pregnancy and 10 had non viable pregnancy

Among the 26 patients of serum progesterone >25ng/ml,24 had viable pregnancy

Chi-square results

0.000

P<0.01

So a single serum progesterone value of >25ng/ml is a effective marker to say that the pregnancy will be viable

Regarding AGE FACTOR:

age <30 among 32 patients ,21 had viable pregnancy and 11 had non viable pregnancy

among the 53 patients of age>30,29 had viable pregnancy and 24 had non viable pregnancy

Chi-sq result

0.223

Regarding PARITY:

Among 26 primigravida, 15 had viable foetus and 11 had non viable pregnancy

Among 59 multigravida ,25 had viable foetus and 24 had non viable pregnancy

Thus primi had more chances of viable pregnancy

Chisq result

0.537

Regarding previous history of miscarriage:

Among 47 patients with previous history of miscarriage 28 patients had viable foetus and 19 had non viable pregnancy

Among 38 patients with previous history of no miscarriage 22 patients had viable foetus and 16 had non viable pregnancy

Thus patients with previous history of miscarriage had a slight increase in chance of future miscarriage

Chisquare result

0.525

Regarding gestational age:

Among 40 patients with gestational age of <12 weeks,21 patients had viable foetus and 19 had non viable pregnancy

Among 45 patients with gestational age of >12 weeks,29 patients had viable foetus and 16 had non viable pregnancy

Thus as the period of gestation at which spotting occurs advances,the chance of viability increases.

Chisquare result

.185

Regarding preterm labor:

Among the 36 patients with serum progesterone values of 10-25ng/ml,24 patients had preterm labour

Among the 26 patients with serum progesterone values of > 25ng/ml,8 patients had preterm labour

Chisquare result

0.000

P <0.01

Thus as the progesterone values increases,the chances of preterm labour also increases. As compared with the previous studies done in various departments in my study reveals that the seum progesterone is an effective marker to detect fetal viability in cases of threatened abortion

The levels of the three biomarkers that is progesterone, inhibin A and HCG differed appreciably between the nonviable and viable patients. Amongst solitary biomarkers, reproductive hormone progesterone single-handedly had the maximum utility.

As HCG levels have to be serially monitored and increase in serum HCG levels alone predicts the chances of viability. Hence multiple serum samples have to be taken, which is not cost effective. The sensitivity of Inhibin - A is not clearly known in previous studies.

Single serum Progesterone value is cost – effective and also sensitive to detect fetal viability in cases of threatened abortion.

LIMITATIONS

The patients coming to the antenatal op were taken samples at first visit but were started on progesterone supplements and hence in the group of 36 patients between 10-25ng/ml 26 had viable pregnancy and 10 had non viable pregnancy.

The cut off of gestational age was 12wks,but many patients presented only after 10 wks and there was difficulty in eliciting history of spotting and quantifying the amount of blood loss.

Fetal viability was confirmed only with fetal heart rate with ultrasound Doppler thus the possibilities of anomalous baby was not taken into study.

Similarly intra uterine growth restriction and oligohydramnios and Doppler abnormalities were not included.

Preterm babies birth weight and survival rate were not considered.

CONCLUSION

It is thus concluded that single serum progesterone value of >25ng/ml has 97% chances of fetal viability.

It is a sensitive tool to assess fetal viability in cases of threatened miscarriage.

The capability to differentiate between nonviable and viable gestation at an early visit has quite a lot of significant implications, which includes reducing couple’s anxiety, helping us in earlier prediction of viability and getting better couple’s satisfaction.

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3 **.** Are serum progesterone levels predictive of recurrent miscarriage in future pregnancies? **Mayumi Ogasawara, M.D.**

4. **Progesterone-mediated immunomodulation in pregnancy: its relevance to leukocyte immunotherapy of recurrent miscarriage**

4. **Luteal insufficiency in first trimester**

   DuruShah**,** NagadeeptiNagarajan

   Gynaecworld and Gynaecworld Assisted Fertility Unit Mumbai,

   Gynaecworld, Mumbai, India

5. The Effect of Progesterone Suppositories on Threatened Abortion: A Randomized Clinical Trial

   [1]Reza Shekarriz-Foumani, Masoumeh Fallahian Fakhrolmolouk Yassaee, and Shabnam Afsari,

6. Accuracy of single progesterone test to predict early pregnancy outcome in women with pain or bleeding: meta-analysis of cohort studies.

Verhaegen J[1], Gallos ID, van Mello NM, Abdel-Aziz M, Takwoingi Y, Harb H, Deeks JJ, Mol BW, Coomarasamy A.

7 Biochemical markers for prediction of pregnancy outcome in cases of recurrent pregnancy loss

Amal Darwish, M.D. Nabil Ghorab, M.D. Hazem El-Ashmawy, M.D. Manal Kamal, M.D. Ahmed Soliman, M.D. Department of Obstetrics and Gynecology, Cairo University, Galaa Teaching hospital, Cairo, Egypt

8. 1. Kutteh WH and Pasquarette MM. Recurrent pregnancy loss. In Advances in Obstetrics and Gynecology. Rock J, faro S, Gant N et al. (ed.) 1995; Vol.2 P: 147-165. 2. Babill SP. and Sverre SP. Etiologic factors and subsequent reproductive performance in 195 couples with a prior history of habitual abortion. Am J Obstet Gynecol 1984; 15: 140-6 3. Cunningham DS, Brodnik RM, Rayl DL, Brown AW, Hansen KA.Suboptimal progesterone production in pathologic pregnancies.J Reprod Med 1993;38(4):301-5

9. **A Multiple Marker Model to Predict Pregnancy Viability When Progesterone Is Indeterminate**

Beth J. Plante, M.D., Jeffrey D. Blume, Ph.D., Geralyn Lambert-Messerlian, Ph.D.,

Rebecca Shackelton, Sc.M., Jacob Canick, Ph.D., and Maureen G. Phipps, M.D., M.P.H.

ANNEXURE – IV

Xgg[j y;go t k;

bgah; :

ghypdk; :

taJ :

Kfthp :

muR nfhi t kUj;J t f; f y;Y}hpapy; kfgngU kUj;J t J iwapy;gI;l nkwgo gapY k; khz tp brkkyh; m th;f s; nkwbfhs;S k; " fUrrpi j tpy; ,uj;j ghpnrhj i dapy;g[uh$! ;lujhd;ms t[f s;" Fwpj;j Ma;tpy;bra;K iw kwWk; m i d j;J tptu ';f i sa[k; nf I;L f; bfhz L vdJ renj f ';f i s bj spt[ggL j;jpf;bfhz nId;vdg i j bjhptpj;J f;bfhs;fpnwd;

ehd; ,e;j Ma;tpy; KG rkkjj;J I d/ Ra rpe;j i da[I Dk; fye;J bfhs;s rkkjpf;fpnwd;

,e;j Ma;tpy; vd;D i I a m i d j;J tpgu ';f s; ghJ fhf;fggL t J I d; , jd;Kot[f s;Ma;tpjHpy;bt spapIggL tjpy;M Inrg i d , y;i y vdg i j bjhptpj;J f;bfhs;fpnwd; ve;j neuj;jpYk; ,e;j Ma;tpyUe;J ehd; tpy fpf; bfhs;s vdf;F chpi k c z L vdg i ja[k;mwpnt d;

S. NO	NAME	AGE	PARITY	PREV H/O	GEST	PROGES	FETAL	PRETERM
				MISCARRIAGE	AGE	TERONE	VIABILITY	LABOUR
1	Kavitha	35	Primi	No	14	12	Yes	Yes
2	Poornima	31	Primi	No	7	18	Yes	Yes
3	Manju	25	Multi	No	11	29	Yes	No
4	Devi	33	Multi	Yes	12	5	No	NA
5	Amudha	35	Primi	No	14	13	Yes	Yes
6	Jansi	32	Multi	No	12	20	Yes	Yes
7	Priya	35	Multi	No	6	23	Yes	Yes
8	Sophia	34	Primi	No	16	30	Yes	No
9	Suganya	28	Multi	Yes	7	35	Yes	No
10	Saritha	26	Multi	No	9	38	Yes	No
11	Jamuna Rani	32	Primi	No	10	8	Yes	NA
12	Tamilarasi	21	Multi	Yes	11	12	Yes	Yes
13	Radha	25	Multi	No	8	14	No	NA
14	Sindhu	34	Multi	Yes	14	20	Yes	Yes
15	Thenmozhi	20	Primi	No	6	6	No	NA
16	Fareen Begum	35	Multi	Yes	10	8	No	NA
17	Rajamani	31	Multi	No	15	23	No	Yes
18	Saroja	22	Primi	No	9	40	Yes	No
19	Sumaina Banu	33	Primi	No	8	42	Yes	No
20	Rajeswari	34	Multi	Yes	12	14	No	NA
21	Mahalakshmi	28	Multi	No	16	16	Yes	Yes
22	Soundharya	27	Multi	No	13	18	Yes	Yes
23	Devika	35	Primi	No	9	7	No	NA
24	Selvi	31	Multi	Yes	7	9	No	NA
25	Kaviya	32	Multi	Yes	6	11	Yes	Yes

26	Manjula	26	Multi	No	16	21	No	NA
27	Lavanya	34	Multi	Yes	10	28	Yes	Yes
28	Karpagavalli	31	Multi	No	11	24	Yes	Yes
29	Poongodi	21	Primi	Yes	9	30	Yes	Yes
30	Thilagavadhi	33	Multi	Yes	10	8	No	NA
31	Muthuselvi	25	Multi	Yes	11	20	Yes	Yes
32	Bhuvaneswari	25	Multi	No	9	40	Yes	No
33	Anandhi	27	Primi	Yes	6	46	Yes	Yes
34	Saranya	26	Multi	Yes	7	29	Yes	No
35	Prema	21	Multi	No	6	15	Yes	Yes
36	Geethanjali	34	Primi	Yes	8	12	No	NA
37	Parasakthi	32	Multi	No	14	6	No	NA
38	Ranganayagi	35	Multi	No	16	11	Yes	Yes
39	Dhanalakshmi	25	Primi	Yes	10	42	Yes	Yes
40	Veeralakshmi	34	Multi	Yes	11	13	Yes	Yes
41	Sandhya	23	Multi	No	7	32	Yes	Yes
42	Anushya	28	Multi	Yes	6	8	No	NA
42	Mythili	31	Primi	Yes	8	9	No	NA
43	Nambidevi	19	Multi	No	12	7	No	NA
44	Brinda	33	Multi	Yes	8	14	Yes	Yes
45	Seetha	32	Multi	Yes	6	8	No	NA
46	Kowsalya	35	Primi	No	15	6	No	NA
47	Kamala	34	Multi	Yes	7	24	Yes	No
48	Kanaga	34	Primi	No	14	8	No	NA
49	Parameshwari	32	Multi	No	16	34	Yes	No
50	Kalaivani	25	Primi	No	12	18	Yes	NA
51	Shapna	35	Primi	No	8	7	No	NA

52	Logeshwari	31	Primi	No	9	22	Yes	Yes
53	Pushpa	35	Multi	Yes	10	24	No	NA
54	Uma Maheswari	27	Multi	Yes	11	18	Yes	Yes
55	Radha mani	32	Multi	No	12	17	No	NA
56	Gomadhi	34	Multi	Yes	16	38	Yes	No
57	Sasikala	24	Multi	No	9	23	Yes	Yes
58	Masilamani	33	Primi	No	8	26	Yes	Yes
59	Millimalik	35	Multi	No	13	6	No	NA
60	Yasoda	32	Multi	Yes	14	9	No	NA
61	Gowthami	22	Primi	No	16	42	No	NA
62	Sindhuja	33	Primi	No	7	48	Yes	Yes
63	Amsa	31	Multi	Yes	12	8	No	NA
64	Sasikala Rani	27	Multi	Yes	10	19	No	NA
65	Bala Sundari	33	Multi	No	8	16	Yes	Yes
66	Narmadha	26	Multi	No	10	22	No	NA
67	Menega	34	Multi	Yes	12	21	Yes	Yes
68	Ranjitha	25	Primi	Yes	14	6	No	NA
69	Rejina	35	Primi	No	8	9	No	NA
70	Chitra	32	Multi	Yes	13	7	No	NA
71	Jeyabharathi	25	Multi	No	16	20	No	NA
72	Agalya	35	Multi	No	12	13	No	NA
73	Lakhmi	26	Multi	No	14	30	Yes	No
74	Vennila	33	Multi	Yes	12	20	Yes	No
75	Sharadha	35	Primi	No	16	10	Yes	Yes
76	Charumadhi	29	Multi	Yes	6	24	Yes	Yes
77	Priyamani	33	Multi	Yes	15	28	Yes	No
78	Soorya	35	Multi	Yes	12	7	No	NA

79	Deepa	28	Primi	No	16	26	Yes	No
80	Vaidhegi	31	Multi	Yes	14	38	Yes	Yes
81	Eswari	25	Multi	Yes	13	34	No	NA
82	Nandhinipriya	32	Multi	Yes	13	40	Yes	No
83	Jessi Rani	35	Primi	No	12	8	No	NA
84	Saraswathi	34	Multi	Yes	12	42	Yes	No
85	Sushmitha	25	Multi	No	16	9	Yes	NA