"A CROSS-SECTIONAL STUDY OF PREVALENCE OF DIABETES, THYROID DYSFUNCTION AND HYPERPROLACTINEMIA IN WOMEN WITH RECURRENT PREGNANCY LOSS"

KILPAUK MEDICAL COLLEGE & HOSPITAL, CHENNAI

Submitted to

The Tamil Nadu Dr. M.G.R. Medical University

In partial fulfillment of the requirements for the award of the degree of

M.D. DEGREE EXAMINATION

BRANCH – II
(OBSTETRICS & GYNAECOLOGY)

KILPAUK MEDICAL COLLEGE & HOSPITAL
THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI

APRIL 2013

BONAFIDE CERTIFICATE

Certified that the dissertation titled **"A CROSS-SECTIONAL STUDY OF PREVALENCE OF DIABETES, THYROID DYSFUNCTION AND HYPERPROLACTINEMIA IN WOMEN WITH RECURRENT PREGNANCY LOSS"** is a bonafide work of the candidate **Dr.S.NITHYA,** postgraduate student, Department of Obstetrics & Gynaecology, Kilpauk Medical College, Chennai – 10, done under my guidance and supervision, in partial fulfillment of regulations of **The Tamilnadu Dr.MGR Medical University** for the award of **M.D. Degree Branch II, (Obstetrics & Gynaecology)** during the academic period from May 2010 to April 2013.

Professor.Dr.P.RAMAKRISHNAN,
M.D., D.L.O

The Dean,
Kilpauk Medical College,
Chennai

Professor.A.KALA, M.D., D.G.O

Professor & Head of the Department
of Obstetrics & Gynaecology,
Kilpauk Medical College,
Chennai.

DECLARATION

I **Dr. S.NITHYA** solemnly declare that this dissertation **"A CROSS-SECTIONAL STUDY OF PREVALENCE OF DIABETES, THYROID DYSFUNCTION AND HYPERPROLACTINEMIA IN WOMEN WITH RECURRENT PREGNANCY LOSS"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Prof. Dr. G.GEETHA, M.D., D.G.O.,** Professor, Department of Obstetrics and Gynaecology, Govt. Kilpauk Medical College and Hospital, Chennai.

This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch II (Obstetrics and Gynaecology).**

Place : Chennai
Date : **(Dr. S.NITHYA)**

ACKNOWLEDGEMENTS

I take this opportunity to thank all those who have been instrumental in the successful completion of this work.

I would like to thank my **Dean, Professor. Dr.P.RAMAKRISHNAN, M.D. DLO** for giving me permission to carry out this research work.

I would like to express my profound gratitude and regards to my esteemed teacher and Head of the Department of obstetrics and gynaecology, **Professor.Dr.A.KALA, M.D.DGO**, for her painstaking supervision and invaluable suggestions throughout the period of this study.

I would like to express my deep gratitude and regards to my Guide, **Professor**.**Dr.G.GEETHA, M.D.DGO,** Department of obstetrics and gynaecology, KMCH, Chennai for her guidance, invaluable suggestions and constant encouragement

I would like to express my deep sense of gratitude to**, Professor. Dr.ANAND MOSES. M.D,** Head of the Department of Diabetology, for his excellent advice and interesting discussions on this subject

I would like to express my deep and sincere gratitude to **Professor. Dr. SREELAKSHMI D.C.H, Ph.D.,** Head of the Department of Genetics, I am heartily thankful for her constant encouragement, guidance for the fulfillment of this work.

I would like to express my gratitude to my other **Professors Dr.V.Sumathi M.D., D.G.O., Dr.T.K.Shaanthy Gunasingh M.D., D.G.O., Dr.PS.Jikki Kalaiselvi M.D., D.G.O.,** my co-guide Assistant Professor **Dr.Vilvapriya M.D., O.G.,** and all my **assistant professors** for giving their support and guidance.

I would like to thank **Mr.Padmanaban**, for his help in statistical analysis

My acknowledgment will be incomplete if I do not thank all **my patients** without whose co- operation, I would not have been able to conduct this study.

Finally nothing is possible without the blessings of the omnipotent **Almighty.**

turnitin

Your digital receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

Paper ID	291531071
Paper title	Thesis on recurrent pregnancy loss
Assignment title	Medical
Author	Nithya 20101585
E-mail	drnithi14@gmail.com
Submission time	25-Dec-2012 09:59PM
Total words	12961

First 100 words of your submission

"A CROSS-SECTIONAL STUDY OF PREVALENCE OF DIABETES, THYROID DYSFUNCTION AND HYPERPROLACTINEMIA IN WOMEN WITH RECURRENT PREGNANCY LOSS" KILPAUK MEDICAL COLLEGE & HOSPITAL, CHENNAI Submitted to The Tamil Nadu Dr. M.G.R. Medical University In partial fulfillment of the requirements for the award of the degree of M.D. DEGREE EXAMINATION BRANCH – II (OBSTETRICS & GYNAECOLOGY) KILPAUK MEDICAL COLLEGE THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI APRIL 2013 BONAFIDE CERTIFICATE Certified that the dissertation titled "CROSS-SECTIONAL STUDY OF PREVALENCE OF DIABETES, THYROID DYSFUNCTION AND HYPERPROLACTINEMIA IN WOMEN WITH RECURRENT PREGNANCY LOSS" is a bonafide work of the candidate Dr....

Turnitin Originality Report

A STUDY CO COGNITIVE FUNCTIONING IN AGING by Arya Chandran 20105701 M.D. Geriatrics From Medical (TNMGRMU APRIL 2013 EXAMINATIONS)

- Processed on 26-Dec-2012 22:35 IST
- ID: 294852004
- Word Count: 8059

Similarity Index
19%
Similarity by Source

Internet Sources:
9%
Publications:
12%
Student Papers:
5%

sources:

1 3% match (publications)
Antony J. Bayer. "Memory Clinics", Principles and Practice of Geriatric Medicine, 12/12/2005

2 2% match (Internet)
http://www.mindstreamshealth.com/content/TestDescriptions.pdf

3 1% match (publications)
Peggy A. Szwabo. "Psychological Aspects of Aging", Principles and Practice of Geriatric Medicine, 12/12/2005

4 1% match (Internet from 7/9/09)
http://web.uvic.ca/psyc/coursematerial/psyc315.m01/315/LectureMaterial/Memory%20Part%20II.ppt

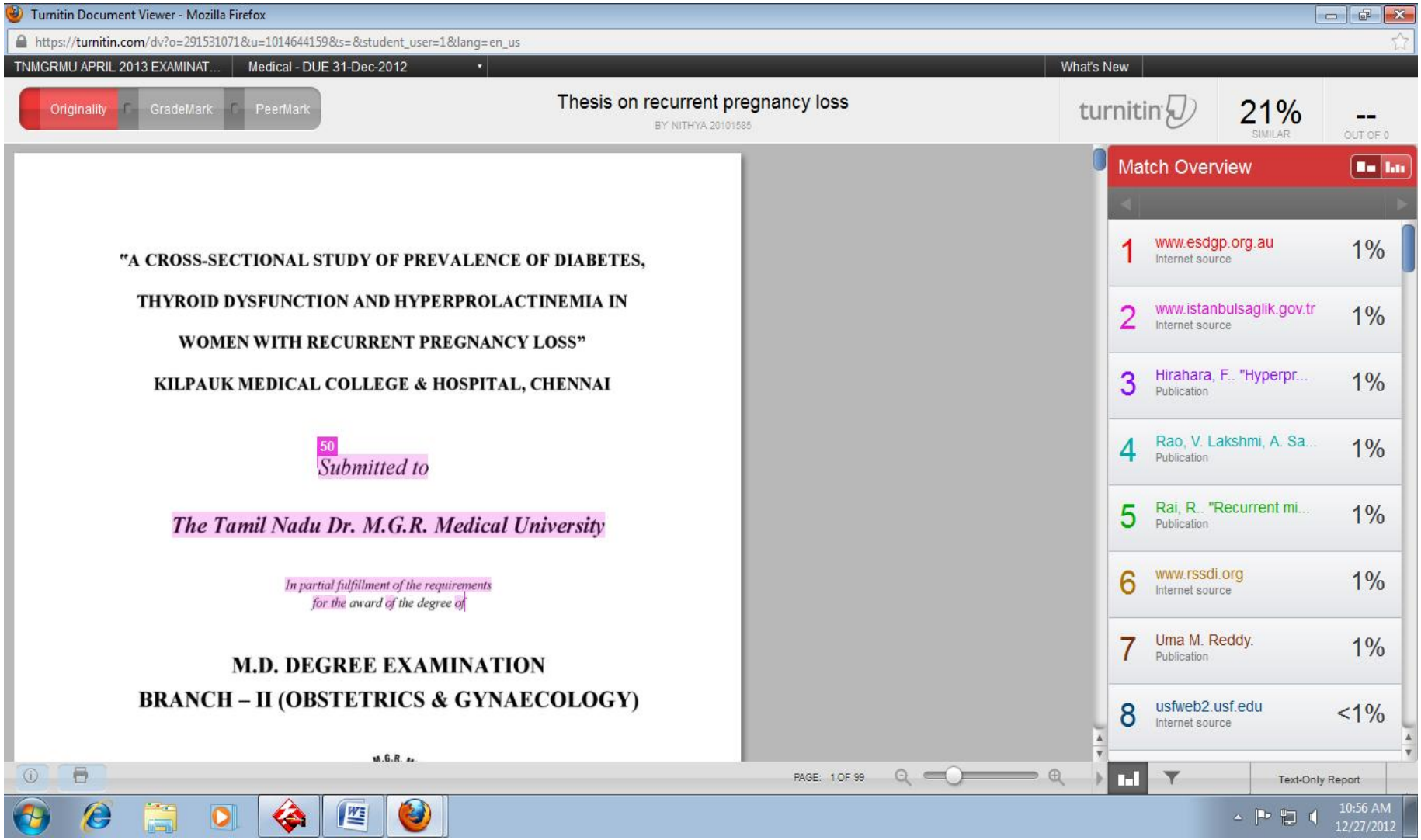
5 1% match (Internet from 10/21/11)
http://www.accessmedicine.com/content.aspx?aID=5121585

6 1% match (publications)
Stephanie Cosentino. "Clock Drawing Errors in Dementia", Cognitive and Behavioral Neurology, 06/2004

7 1% match (Internet from 8/10/12)
http://www.mhprofessional.com/downloads/products/007149992X/RopperCh29.pdf

8 1% match (student papers from 12/03/12)
Submitted to Bridgepoint Education on 2012-12-03

9 1% match (Internet from 3/7/12)
http://www.citeulike.org/user/elena_m/tag/consolidation


Turnitin Document Viewer - Mozilla Firefox
https://turnitin.com/dv?o=291531071&u=1014644159&s=&student_user=1&lang=en_us
TNMGRMU APRIL 2013 EXAMINAT...
Medical - DUE 31-Dec-2012
What's New
Originality
GradeMark
PeerMark
Thesis on recurrent pregnancy loss
BY NITHYA 20101585
turnitin
21%
SIMILAR
--
OUT OF 0
"A CROSS-SECTIONAL STUDY OF PREVALENCE OF DIABETES,
THYROID DYSFUNCTION AND HYPERPROLACTINEMIA IN
WOMEN WITH RECURRENT PREGNANCY LOSS"
KILPAUK MEDICAL COLLEGE & HOSPITAL, CHENNAI
Submitted to
The Tamil Nadu Dr. M.G.R. Medical University
In partial fulfillment of the requirements
for the award of the degree of
M.D. DEGREE EXAMINATION
BRANCH – II (OBSTETRICS & GYNAECOLOGY)
Match Overview
1 www.esdgp.org.au Internet source 1%
2 www.istanbulsaglik.gov.tr Internet source 1%
3 Hirahara, F.. "Hyperpr... Publication 1%
4 Rao, V. Lakshmi, A. Sa... Publication 1%
5 Rai, R.. "Recurrent mi... Publication 1%
6 www.rssdi.org Internet source 1%
7 Uma M. Reddy. Publication 1%
8 usfweb2.usf.edu Internet source <1%
PAGE: 1 OF 99
Text-Only Report
10:56 AM
12/27/2012

CONTENTS

INTRODUCTION

Spontaneous abortion or miscarriage is defined as the involuntary termination of pregnancy before 20 weeks of gestation or below fetal weight of 500 g.

Traditionally, Recurrent pregnancy loss was defined as three or more consecutive spontaneous miscarriages. In 1930s and 1940s, Malpas and Eastman suggested that the proportion to pregnancy losses in next pregnancy after three consecutive losses was as high as 73 - 84%[1]. Incidence 1 in 300 pregnancies[2]. Years later, clinical studies demonstrated that the risk of miscarriage is actually lower than predicted.

In the recent era, investigation and treatment is considered in couples with two consecutive spontaneous miscarriages, documented by ultrasound or histopathological examination (Leon Speroff et al). Evaluation is indicated when any of the following are present

- Embryonic heart activity observed before any earlier pregnancy loss
- Normal karyotype of the products of conception obtained from an earlier loss
- Female partner over 35 years of age, Women with previous history of infertility

The risk of recurrent pregnancy loss in young women

Women who have had at least one live born infant [3]

Number of prior miscarriages	**% risk of miscarriage in next pregnancies**
0	12%
1	24%
2	26%
3	32%
4	26%
6	53%

Previous reproductive history is a significant individual predictor of future outcome of a pregnancy. Women with a history of live births have a reduced risk of miscarriage in their subsequent pregnancy when compared to women whose pregnancy ended in miscarriage.

Women who have not had at least one live born infant [4]

Number of prior miscarriages	% risk of miscarriage in next pregnancies
2	24%
3	30%
4	40-50%

ETIOLOGY OF RECURRENT PREGNANCY LOSS

1) Genetic factors : 3.5 – 5 %
2) Anatomical factors : 12 -16 %
3) Endocrine factors : 17 – 20 %
4) Infectious factors : 0.5 – 5 %
5) Immunologic factors : 20 -50 %
6) Thrombotic factors
7) Others: 10 % (environmental, placental abnormalities, male factors, medical illness, altered uterine receptivity, exercise, yssynchronous fertilization).

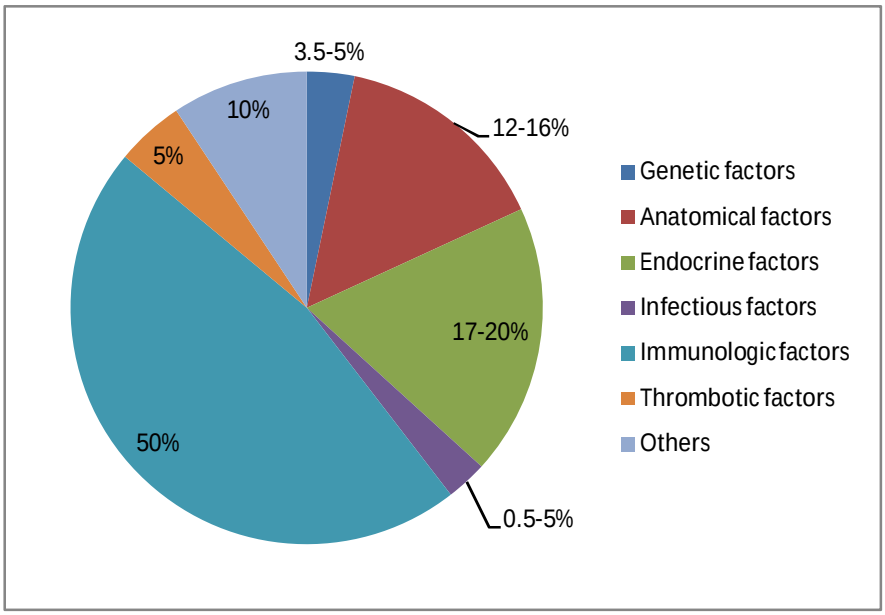


Figure 1: Etiology of Recurrent Miscarriage

The prognosis for successful pregnancy depends both on the underlying cause and the number of previous losses. The chance of a viable birth even after four pregnancy losses is as high as 60%.

Prognosis for a viable birth After

One spontaneous loss	76%
Two spontaneous loss	70%
Three spontaneous loss	65%
Four spontaneous loss	60%

When a causative factor is identified, specific treatment can help in improving the prognosis for a successful pregnancy.

Of all the causative factors described, an average success rate of 70-80% is achieved after correcting the abnormalities. Only with the early diagnosis and treatment of the Endocrinological dysfunction a success rate of more than 90% is achieved.

AIM OF THE STUDY

1. To evaluate the prevalence of diabetes both preconceptionally and antenatally in a women with previous history of recurrent miscarriage.

2. To evaluate the association of thyroid dysfunction in a women with history of recurrent miscarriage.

3. To evaluate the prevalence of hyperprolactinemia in recurrent miscarriage.

REVIEW OF LITERATURE

EPIDEMIOLOGY OF PREGNANCY LOSS

Early pregnancy loss is a very common traumatic event. Almost all chromosomally abnormal conception aborts spontaneously before 10 weeks of gestation, and 90% of conception with a normal karyotype continue [5]. Miscarriage may be viewed as a natural selection process for quality control.

Over all, approximately 12 – 15% of clinically recognized pregnancies results in spontaneous miscarriage before 20 weeks of gestation. Nearly about 30 - 60% of all conceptions will spontaneously get aborted within first 12 weeks of gestation; out of which half of the losses go unnoticed and this loss occurs even before a first missed menses.

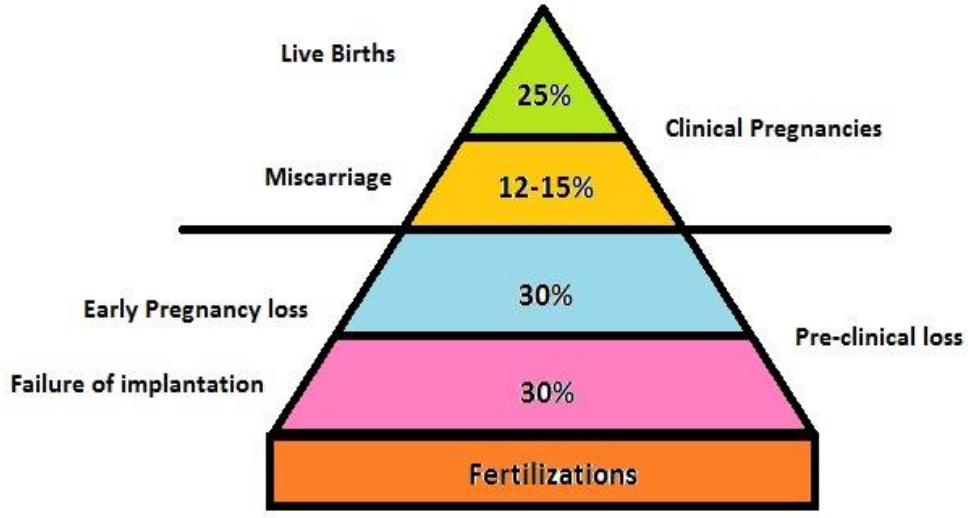


Figure 2: Epidemiology of Pregnancy loss

AGE AND MISCARRIAGE

Maternal age acts as a risk factor for miscarriage, due to the formation of chromosomally abnormal conceptions [6]

As age increases, there is increase in the incidence of mitotic segregation errors, rapid rise on number of aneuploid oocyte . Women with a demonstrated low ovarian reserve have an extremely higher rate of miscarriage, regardless of age [7].

In women with history of previous losses, advancing age adds to the risk related to previous losses. If both occult and recognized losses are considered, total pregnancy wastage in women over age 40 may exceed 75% [2]

PROGNOSTIC VALUE OF TRANSVAGINAL ULTRASOUND OBSERVATIONS

The risk of miscarriage decreases as the duration of pregnancy advances. The risk of pregnancy loss falls progressively after appearance of gestational sac (12%), yolk sac (8%), as crown rump length increases, (greater than 5mm – 7%, 6 – 10mm – 3%, more than 10 mm – less than 1%)

Appearance of embryonic cardiac activity by approximately 6 weeks is another important developmental mile stone and good prognostic indicator. In both normal and infertile asymptomatic young women, the appearance of embryonic heart activity decreases with the risk of pregnancy losses from 12% - 15% to 3 – 5%. [8]

GENETIC FACTORS

Most spontaneous miscarriages occur due to the chromosomal abnormalities in the embryo or fetus. Large number of abortuses have been cultured and karyotype suggested that approximately 50 % of all first trimester pregnancy losses, 30% of second trimester abortuses, and 3 % of still births are chromosomal abnormal [9]

Chromosomal abnormalities

90% - numerical (aneuploidy, polyploidy)

10% - structural abnormality (translocation , inversion and mosaicism)

Autosomal trisomy are the most common usually involving chromosome 13 – 16, 21 or 22, followed by monosomy X (45 X).42,44,45,21 The likelihood of euploid abortus increases with the number of previous miscarriages and after a previous abortion having a normal karyotype.

Parental chromosomal abnormality

However, in 4 -8 % of couples with recurrent pregnancy loss, one or other partner harbours a chromosomal abnormality that markedly increases the probability of a chromosomally abnormal conceptus.[10] Balanced translocation (Reciprocal, Robertsonian) are the most common abnormalities.

The chance of a livebirth rate in couples with a structural chromosome abnormality who conceive spontaneously is higher (50–65%) than couples who conceive after assisted reproductive methods.

Inversions

Pericentric inversion 9 occurs in 1 – 1.5 % in general population, this is a normal variant with no importance. Paracentric inversion results in abortion and anomalous fetus.

Karyotyping data likely underestimated the prevalence of chromosomal abnormalities due to unrecognized maternal cell contamination; normal euploid cells are less likely to fail culture than abnormal cell lines. [11]

Some genetic abnormality cannot be detected using standard Cytogenic techniques like isolated gonadal / germ line mosaicism/single gene defects.

Analyses using newer techniques not dependent on cell culture (FISH – fluorescence in situ hybridization, CGH – comparative genomic hybridization) suggest that the true incidence of chromosomal abnormalities in miscarried early pregnancies is closer to 75%.

ANATOMIC FACTORS

CONGENITAL UTERINE MALFORMATIONS

The prevalence of uterine anomaly in general population is 2%, and in patients with recurrent miscarriage accounts for about 6 – 7%.[12]

Unicornuate Uterus

Pregnancy outcomes are generally poor; approximately half of all recognized pregnancies fail. Since 40 % of the cases are associated with an ipsilateral renal agenesis. Further evaluation with intravenous pyelogram or renal sonogram is also indicated in the inter pregnancy period. Evidence suggest that most pregnancies in women with unicornuate uterus are best managed expectantly with cervical circlage

reserved for those with previous second trimester losses or evidence of progressive cervical shortening. [13]

Uterine Didelphys

40 % of women with uterine didelphys end in spontaneous miscarriage. Unification procedures are usually unnecessary, but can benefit some women with numerous miscarriages or previable births. When surgery is performed, the recommended technique unifies the two fundi and leaves the two cervices intact

Bicornuate Uterus

Data reveals miscarriage and overall fetal loss rates of 30% & 40% respectively. Surgery is generally unnecessary and best reserved for those with a well established history of otherwise unexplained recurrent pregnancy loss or previable . The incidence of cervical incompetence is highest in this group and evidence suggests that cervical circlage improves fetal survival rates. [14]

Septate Uterus

The most common uterine developmental anomaly accounting for 80 - 90% in both women with recurrent miscarriage (3.5%

prevalence) and in general population. Miscarriage rate associated with septate uteri is 65 %.

Hysteroscopy septoplasty dramatically improved post operative pregnancy outcomes. (80% term, 5% preterm, 15% miscarriage). [15]Arcuate uteri are a normal variant. Residual septal defect less than 1 cm has no adverse effect on pregnancy.

DES Exposure

70 % of women exposed to DES have uterine abnormality. Most common uterine abnormality is T shaped uterus, others include hypoplastic uterus, irregular intrauterine filling, constriction rings. Most exposed women are now beyond their reproductive period, affected women are occasionally encountered. The risk of spontaneous miscarriage in such women accounts about 24 % and 9 fold increased risk of ectopic pregnancy.

Uterine Leiomyoma

Uterine fibroids are reported in up to 30% of women, but their effect on reproductive outcome is unclear. Uterine fibroid impedes embryonic implantation and causes poor regional blood flow. The expression of *HOX10,* a gene that controls differentiation and is

involved in implantation, is found to be low in uterus with fibroids.[16] Hysteroscopic Myomectomy should be considered in cases of submucosal fibroids or any type fibroids larger than 5 cm. Resection has been shown to significantly improve live birth rates from 57% to 93%.

When myoma does not distort the uterine cavity, surgery is not indicated in the absence of any other symptoms specific to fibroid.

INTRAUTERINE ADHESIONS

Decreased functional intrauterine volume, endometrial fibrosis and inflammation predispose to placental insufficiency. Pregnancy outcomes are generally poor. 40 – 80 % results in spontaneous miscarriage and 25 % ends in preterm delivery.[17] The prognosis generally correlates with the severity of the disease. Hysteroscopic adhesiolysis dramatically improves the pregnancy outcome.

CERVICAL INCOMPETENCE

The diagnosis is based on a history of late second trimester miscarriage characterized by painless cervical dilatation followed by ballooning of membranes and ultimately resulting in expulsion of fetus. Efficient treatment helps in preventing future miscarriage.

IMMUNOLOGICAL PHENOMENON

Pregnancy is a immunotolerance state. A subset of CD4 cells that describe CD25 on their cell surface. These CD4, CD25 cells are called Regulatory T Lymphocytes (T reg cells). T reg cells when activated by autoantigens can suppress activated inflammatory cells.

Cellular Immune Mechanisms

Decidual NK cells compromises 70-80% of the total endometrial population at the implantation site.

Human reproductive tract is populated by TCR γ δ +; they are increased in early pregnancy; their functions are direct, Non – MHC registered recognition of antigens within tissues. Suppressor macrophages helps in pregnancy maintenance. They help in promotion of anti – inflammatory effect. T reg cells suppress maternal responses to self and to the fetus.

Antigen Presentation at the Maternal Fetal Interface

Implanting trophoblastic allograft causes down regulation of its expression of the MHC – encoded transplantation antigens and avoid recognition as non – self. Current theory, in placental trophoblast MHC class I and II molecules are not expressed.[18]

Extravillous trophoblast express classical MHC class I HLA – C and non – classical HLA – E and G products. They are characterized by their invasive potential deep into the maternal decidua, an activity essential for proper placental development. Aberrant expression of class II MHC; over expression of class I MHC leads to cytotoxic Tcell attack, could enhance abortion. MHC II genotypes appear to affect susceptibility to a variety of diseases, like diabetes and other auto immune diseases and adverse pregnancy outcome.

Regulation of maternal decidual cells

Regulatory mechanisms include

i) Alterations in T- helper cell phenotypes

ii) Reproductive hormones and immunosuppression

iii) Tryptophan metabolism

CDT4 cells are divided into TH1 responses and TH2 responses. TH1 cells are associated with inflammation. They are harmful to the implanting embryo.

TH2 cells are associated with IL – 4,5,6,10 and antibody production; they are important for pregnancy maintenance. [19]

The dysregulation of their T-helper cellular immune response accounts for about 60-80%. Leukemia inhibitory factor is absolutely essential for pregnancy maintenance.

Humoral Immune Response

Patients with recurrent pregnancy loss display altered humoral responses to endometrial and trophoblast antigens; Historicaly these IgG and IgM antibodies (cardiolipin and phosphatidylserine) are thought to be directed against negatively charged phospholipids. More recently the high tire of antibodies directed against a protein cofactor, called β 2 glycoprotein I alone is sufficient for diagnosis.

LABORATORY ASSESSMENT (SAPPORO CRITERIA) [20]

Antiphospholipid antibody syndrome requires presence of at least 1 clinical and 1 laboratory Criterion

• Clinical

1. One or more confirmed episodes of vascular thrombosis (venous, arterial, or small vessel).

2. Pregnancy morbidity

- Pregnancy complications including

  - 1 or more fetal deaths at greater than 10 weeks of gestation of a morphologically normal fetus.
  - One or more premature birth of a normal neonate before 34 th week because of pre eclamosia, or placental insufficiency .
  - 3 or more consecutive pregnancy losses at less than 10 weeks of gestation.

• Laboratory (repeated at least 2 times, more than 12 weeks apart)

- Positive plasma levels of the anticardiolipin antibodies (IgG orIgM) at medium to high levels
- Positive plasma levels of the lupus anticoagulant
- Anti β2 – glycoprotein 1 antibody of IgG or IgM isotype in 99^{th} percentile titer

The incidence of APAs in patients with RPL was between 3-5%; Less favourable pregnancy outcome was noted among patients with known Systemic Lupus Erythematosus. Anti-thrombotic molecule (annexin V) are reduced within the placental villi resulting in atherosclerosis in decidual spiral arteries.

THROMBOPHILIAS

Abnormal placental vascularisation and inappropriate placental thrombosis would relate these thrombophilic states to pregnancy loss.

The incidence of inherited thrombophilic mutations in Caucasians – 15%;

The most common are

I) Factor V leiden – 5%

II) Prothrombin promoter region mutation – 2-3%

III) Mutation in gene MTHFR – 11-15% .They are associated with mild thrombotic risks

The rare causes are

I) Anti-Thrombin and protein S deficiency. They are associated with more severe thrombophilic deficiencies.

INFECTIOUS CAUSES

Spontaneous miscarriage has found to be associated with Chlamydia trachomatis, Ureaplasma urealyticum or Mycoplasma hominis infection. Toxoplasma gondii, Listeria monocytogenes,

Campylobacter species, herpes virus, and cytomegalovirus has also been implicated.

Many studies has been conducted to correlate the association between miscarriage risk and Bacterial vaginosis. There is 5 fold increased risk of pregnancy loss before 20 weeks of gestation when Bacterial Vaginosis was diagnosed at the first prenatal visit before 14 weeks.[21]Chronic subclinical endometritis in women with symptomatic lower genital tract infection explains association between infection and miscarriage.

ENVIRONMENTAL FACTORS

SMOKING: Smokers who consume 10 cigarettes / day has adverse pregnancy outcome. The anti metabolite composition of cigarette like nicotine, carbondioxide and cyanide may predispose to placental insufficiency .

ALCOHOL: Consumption exceeding two drinks / day increases the risk. It adds to the additive risk with smoking.

CAFFEINE: Heavy caffeine consumption more than 300 mg / day, equivalent to 3 cups / day 2 fold increased risk of spontaneous miscarriage.

OBESITY: A body mass index equal to or greater than 25 is associated with greater risk of miscarriage.[22]

Others

- Anaesthetic gases (Perchorethylene)
- Exposure to heavy metals (Mercury,Lead)
- Isotretinoin (Accutane)
- Painters and factory workers

UNEXPLAINED RECURRENT PREGNANCY LOSS

Even after thorough evaluation, half of the women with recurrent miscarriage have no identified predisposing factors. Frequent communication, cautious optimism and emotional support during the first trimester of the next pregnancy have their own therapeutic value. 70 -75 % of women ultimately achieve successful pregnancy. Empiric treatment with exogenous progesterone or aspirin in women with unexplained recurrent pregnancy loss has no proven value.

ENDOCRINE FACTORS

LUTEAL PHASE DEFECT

Early pregnancy depends upon the secretion of progesterone from corpus luteum till 7 weeks of gestational period. Corpus luteal shift do not occur suddenly, it occurs gradually over a period of 7-9 weeks of pregnancy.[23] The human implantation window is relatively narrow approximately 6-10 days after ovulation. Low levels of circulating progesterone causes delayed endometrial maturation and causes shift in implantation window leading to failed or late implantation.

Luteal phase defect is diagnosed when there is a persistent delay of longer than 2 days in the histologic development of the endometrium compared with the respective day of the menstruation.

A low progesterone concentration during early pregnancy reflects defective corpus luteum, an intrinsically abnormal conceptus or both. Serum progesterone concentration fluctuates throughout the day as the corpus luteum progesterone secretion is pulsatile. Measurement of serum progesterone in early pregnancy to assist the quality of luteal function and supporting the risk pregnancy with exogenous progesterone therapy are futile.

Some of the cases of luteal phase defect are associated with hyper secretion of luteinizing hormone (LH). Abnormal LH causes premature aging of oocyte, dyssynchronous maturation of endometrium, improperly timed endometrium at potential implantation sites.[24]

The Luteal phase deficiency is considered as a subtle form of ovulation dysfunction . Some prefer to treat with exogenous progesterone supplementation starting from 2-3 days after ovulation.[25]

POLYCYSTIC OVARIAN DISEASE

Polycystic ovarian disease are not a characteristic feature of a specific endocrine disorder, results from functional derangement in follicular development, or by sustained increased intraovarian androgen levels as a consequence of chronic anovulation.

The National Institute of Child Health and Human Development (NICHD) in 1990.

1. Hyperandrogenism

2. Menstrual dysfunction

3. Exclusion of other disorders having a same clinical presentation .

The European society for Human Reproduction And Embryology (ESHRE) and The American Society Of Reproductive Medicine (ASRM) – Rotterdam criteria -2003, at least two of three major criteria including,

1. Oligo/anovulation

2. Clinical or biochemical signs of hyperandrogenism

3. Polycystic ovaries as identified by ultrasound (total number of follicles, 12 or more measuring 2 – 9 mm in diameter ; ovarian volume > 7 – 7.5 m l)

Excluding other androgen excess disorders.

PCOS and INSULIN RESISTANCE

The overall prevalence of insulin resistance among with PCOS is 50 -75%, greater in obese than in lean individual.

Methods of measuring insulin sensitivity

1. Hyperinsulinemic euglycemic clamp insulin sensitivity is defined as the ratio of glucose disposal rate to the steady state insulin concentration

2. Fasting serum insulin concentration values more than 20 -30 µIU /ml suggest insulin resistance.

3. Fasting glucose / insulin ratio less than 4.5 indicates resistance.

4. Homeostatic model assessment of insulin resistance (HOMA – IR) values greater than 3.2-3.9 indicates insulin resistance

5. Quantitative insulin sensitivity check index (QUICKI)

Inverse of the sum of the fasting glucose and insulin concentrations expressed logarithmically; values greater than 0.33 indicates insulin resistance[26]

A baseline 2 hour OGTT is recommended for all women with PCOS, as up to 35 % exhibit impaired glucose intolerance and up to 10 % have diabetes. Hyperinsulinemia and high levels of Plasminogen Activation Inhibitor(PAI) activity for the increased incidence of miscarriage (30-50%) among women with PCOS. Metformin has also found to reduce PAI activity.[27]

Metformin treatment can reduce or eliminate the higher risk of miscarriage in women with PCOS relating to an underlying metabolic disorder.

THYROID HORMONES IN PREGNANCY

Physiological changes in pregnancy

Moderate enlargement of thyroid gland by glandular hyperplasia and increased vascularity during pregnancy, but normal pregnancy does not typically cause thyromegaly.

In early first trimester, oestrogen increases the synthesis of thyroxine binding globulin. Serum levels of total thyroxine T4 increases beginning from

7 and 9 weeks, and plateau at 18 weeks. Rise in Free serum T4 levels peaks with hCG levels, later returns to baseline . T3 levels starts increasing and reaches peak at 18 weeks later plateaus. TRH levels are not increased during normal pregnancy.

TSH levels get supressed during pregnancy. This results in failure to diagnose women with early hypothyroidism. Inverse relationship exists between TSH and hCG . TSH levels drops to a nadir at 10 weeks and at the same time hCG reaches the peak. As hCG decreases later, TSH raises in later part of pregnancy. Fetal thyroid gland starts secreting insulin only after 10 – 12 weeks of pregnancy,

since then the entire supply and fetal brain development depends on maternal source.

Hypothyroidism in pregnancy (LEON SPEROFF et al) [28]

Hypothyroidism, even subclinical have increased risk of spontaneous miscarriage. Mechanism being impaired function of endometrium, corpus luteum and the placenta. Preconceptional screening with achievement of euthyroid state before pregnancy is necessary for successful outcome.

Universal screening is not routinely recommended. But those with elevated TSH levels needs estimation of anti thyroid antibodies. Women with positive thyroid antibodies have has an increased risk of becoming hypothyroid as pregnancy advances. Women treated for hypothyroidism requires an increase in thyroxine during pregnancy starting as early as 5 th week of gestation.

The causes for such an effect are

1. estrogen induced increase of thyroid binding globulin,

2. dilutional effect of increase in vascular volume ,

3. and the increase in placental transport and metabolism.

As soon as pregnancy is diagnosed, 30 % increase in levothyroxine dose is required . TSH levels should be monitored monthly and adjust levels in lower limit of normal range for trimester specific levels .

Weiwei Wang et al, [29] in his clinical study included 2899 pregnant women in their first trimester were enrolled in the study to find the prevalence of thyroid dysfunction and effectiveness between case – finding and universal screening strategies. According to The Endocrine Society Clinical Practice Guideline, the high risk group are excluded .

The results of the study states that the prevalence of hypothyroidism was higher among the high risk group significantly when compared to those with no risk factors (10.7 Vs 7 %) . Patients with positive titre for thyroid antibodies and those with risk factors had increased risk of thyroid dysfunction. If a case-finding strategy is followed for screening thyroid function in patients with risk factors, approximately 81.6% pregnant women with hypothyroidism were missed.

N Benhadi et al, [30] In this study, he compared the association of maternal TSH and free thyroxine (FT4) concentrations in early pregnancy and the risk of miscarriage.

2497 Dutch women were included in this cohort study. TSH, FT4, and thyroid peroxidase antibodies(TPO-Ab) concentrations were determined at first booking. Miscarriage was observed in 27 cases and there was an increase in level of mean TSH and FT4 level in cases when compared with control group. The risk of miscarriage increased by 60% for every doubling in TSH concentration. This association remained even after excluding all the confounding factors .

There was no relation between Maternal FT4 concentrations and miscarriage. Nearly 5.8% had TPO-Ab positive status but none of them had an adverse pregnancy outcome. TPO-Ab positive group had associated higher TSH values and their risk for miscarriage decreases after treatment with thyroxine. It finally concludes that adverse pregnancy outcome in thyroid antibody positive status either with or without elevated TSH can be improved with treatment.

Indian Journal of Medical Sciences, Vol. 62, No. 9, September, 2008, [31]

The prevalence of hypothyroidism in women with recurrent first trimester are evaluated. 163 non-pregnant women with recurrent first trimester miscarriage were included in this case – control study. Thyroid

function tests are done and after analysis Hypothyroidism was observed in seven cases of miscarriage group (4.12%) and one in control group.

If the thyroid levels were insufficient in women, they have a higher risk of miscarriage. Most of the women confirms pregnancy only during the last weeks of first trimester, during which the insult has already occurred .

Children born as a result of consanguineous marriage, has a higher risk of harbouring defective genes and results in greater risk of miscarriage. Consanguinity was observed in 30.67% of miscarriage group. Women with personal or family history of thyroid disease or with symptoms suggestive of hypothyroidism should be tested for thyroid hormone .

They concluded that early diagnosis and treatment of hypothyroidism in women with recurrent first trimester miscarriage will help in achieving a better outcome in subsequent pregnancies.

Negro R et al**,** [32] This study evaluated the association of recurrent first trimester miscarriage and preterm delivery between the thyroid antibody negative women whose TSH values were between 2.5 and 5.0 mIU/liter. They observed a higher incidence of recurrent miscarriage in

women with TSH levels more than 2.5 mIU/liter. There was no significant differences in the preterm delivery rate.

Chen L et al, [33] Thyroid autoimmunity(TAI) and miscarriage a meta-analysis.

This study compared the association of thyroid autoimmunity and miscarriage rate with normal thyroid status in women and the effect of supplementation with thyroxine in altering their pregnancy outcomes .

A systematic review of the studies was done to compare the association between TAI and miscarriage . The prevalence of thyroid autoantibodies in women with recurrent miscarriage was around 17-33%, and in women with subfertility it accounts about 10-31%. Even in women with euthyroid status, the presence of thyroid peroxidase antibodies, can lead to adverse pregnancy outcomes. The proposed are;

1) Thyroid autoantibodies causes a subtle deficiency, either decrease in free thyroxine levels because of chronic lymphocytic thyroiditis or inability of the thyroid secretion to meet the demands raised by pregnancy and this minor alterations can lead to adverse pregnancy outcomes.

2) Presence of thyroid autoantibodies denotes an underlying autoimmune state. Thyroid hormones influence the production of angiogenic growth factor, cytokine production, trophoblast proliferation, and invasion. Dysregulation of such inflammatory processes and alterated cytokine expression leads to miscarriage. These women develop subclinical or overt hypothyroidism.

3) Age is more important as antibody positive status is more common in older women than in young.

There was a significant association in twenty eight of the 31 studies between thyroid autoantibodies and spontaneous miscarriage. The odds ratio of miscarriage was tripled in women with thyroid autoantibodies and doubled in women with subfertility. TSH levels were elevated in thyroid autoantibody positive women. Data on serum free thyroxine (fT4) and free triiodothyronine (T3) concentrations were insufficient. Effect of levothyroxine treatment on pregnancy outcomes, two studies were compared, there was 52% risk reduction after treatment

De Vivo A et al**,** [34] **216** pregnant women who had history of miscarriages were included in the study. Patients with known thyroid disorders are excluded. Type of miscarriage was divided in to two

groups very early (embryonic loss – CRL < 10 mm) and early (fetal loss – CRL > 10 mm) .

TSH levels were higher among women in very early pregnancy losses. Outcome of the study postulated that subclinical hypothyroidism and autoimmune disease were independently associated with embryo loss, but those who tested positive for subclinical hypothyroidism had abortion onset at an early gestation.

Vaidya B et al, [35] The efficacy of screening thyroid disorders among pregnant women in their early trimester who belongs to high risk group. TSH was found to be higher in high risk women (6.8 % Vs 1 %) than in low risk. They concluded that about one third of cases will be missed if such a screening strategy was followed .

Haddow JE et al, [36] Maternal hypothyroidism in early trimester of pregnancy is harmful to fetal brain development and causes mental retardation, correction of such disorders lead to improvement in the IQ scores of children. Maternal thyroid function gains more importance in view of screening and early treatment during the first trimester of pregnancy.

DIABETES AND PREGNANCY

Diabetes is one of the oldest, but most common complication of pregnancy and emerging health concern in developing countries as it influence the health of mother and the outcome of the fetus.

"In earlier days even before the introduction of insulin, Diabetes in pregnancy was thought to be incompatible with life and hence diabetic women were not allowed to conceive"

Later in 1823 HG Bennewitz, stated "Diabetes as a symptom of pregnancy as the disease appeared along with pregnancy, lasted till the duration of pregnancy, and it terminated with delivery".

In 1882, **J Mathews Duncan et al,** [37] was the first to recognize Diabetes in pregnancy as a serious problem with adverse maternal and fetal outcome. His observations holds good even today.

In 1909, **Whitfield Williams et al**,[38] screened the urine samples of all pregnant women and concluded that pregnancy can occur in a diabetic women and Diabetes can occur in pregnancy, although both remains a serious problem.

In 1915, **Elliot P Joslin et al**, [39] he concluded that with improvements of treatment in diabetes, pregnancy is less likely to develop complications .

In early 1970, Norbert Frienkel formed "Diabetes in pregnancy Centre (DPC)" and he was the one to introduced the concept of "Accelerated starvation and facilitated anabolism." He demonstrated that the poor metabolic control at different phases of gestation; In early phase of pregnancy–spontaneous abortion and congenital malformations, in the middle – psychomotor development, and in late pregnancy – macrosomia.

Maternal Diabetes affects Pre implantation Embryo development and oocyte maturation, it causes decreased ovulation, mitotic spindle defects, chromosomal misalignments and aneuploidy. Oocyte and embryo are vulnerable to acute and chronic hyperglycemia.

Ryan Ennes et al, [40] In early normal pregnancy there will be a rise in both oestrogen and progesterone. Their actions over insulin is counter balanced as progesterone results in insulin resistance, whereas ostrogen is protective. Diabetes complicates about 10 % of all the pregnancies. Diabetes exerts a negative effect on implanting fetus by its inflammatory nature, due to oxidative stress and activation of Protein

kinase C and Mitogen – activated protein Kinase resulting in improper trophoblastic penetration.

Claudan TD et al, [4] among women with type 2 diabetes only 5 % of 61 pregnacies were planned, and in more than 50 % of women they entered the antenatal clinic only in their first trimester.

Roland et al, [42] observed only 29 % of diabetic women attended pre pregnancy counseling.

Leptin: Leptin is a 16 kDa protein encoded by obesity gene which is secreted from adipose tissue. It is a good marker of insulin resistance, it causes both central and peripheral insulin resistance.

Laivuori et al, [43] maternal plasma leptin levels increases during pregnancy due to associated insulin resistance, and thus any alteration in leptin action may lead to development of Diabetes. They also found a significant positive correlation between leptin levels and glycosylated haemoglobin.

Dunne et al, [44] out of 182 pregnancies with type 2 diabetes, they observed a miscarriage rate of 8.8 % when compared to 15.7 % in women with poor diabetic control, a nearly two fold increased risk.

The most often associated teratogenic factors in diabetes are hyperglycemia and ketonemia. They lead to alteration in the metabolism of inositol, sorbitol, arachidionic acid/ prostaglandins, reactive oxygen species and folic acid . This embryonic glycated proteins along with the genetic inheritance determines the chance of embryopathy in pregnancy.

Organogenesis occurs before 8 weeks of pregnancy before which most of the women are unaware of their pregnancy.

Miller et al, [45] Increase in the level of HbA1c was positively correlated with the risk of occurrence of malformation during early pregnancy.

HbA1c	Risk of malformation
7 – 8.5 %	5.1 %
8.6 -9.9 %	22.9 %
Above 10 %	21.7 %

Sheffield et al, [46] in his study concluded that women with pre gestational or gestational diabetes in accordance with fasting hyperglycemia has 2 to 3 fold increased risk of developing malformed fetus.

Strotmeyer et al, [47] Diabetic women has increased menstrual problems before 30 yrs than control. There was two fold increased risk of menstrual problems. Women aged less than 20 yrs and 20 -29 yrs, was related to long cycles and increased menstruation. No differences was noted after 30 years of age. The results postulated that diabetes was an independent risk factor for young women with menstrual abnormalities.

Obesity is associated with both diabetes and polycystic ovarian disease. They generally takes a long time to conceive, irrespective of their age and menstrual irregularities .

Metwally et al, [48] observed that oocytes of women with increased body mass index would give rise to poor quality of blastocysts.

Robker et al , [49] found that women with increased body mass index have increased levels of intrafollicular insulin and triglycerides, free androgen profile, C – reactive protein and increased expression of lipoprotein receptors which contributes to the poor obstetric outcome.

Mille JL et al,[50] This study was conducted to determine the association whether women with insulin dependent diabetes have an

increased risk of spontaneous abortion and to know the relationship between good glycemic metabolic control and loss of pregnancy in diabetics.

Miscarriage was observed in 16 % of both diabetic and non-diabetic women. After excluding the other known confounding factors that would cause spontaneous miscarriage, still there was no significance. But things observed in this study are, among the diabetic women with good glycemic control, and who ended in abortion had both an increase in their fasting and postprandial blood sugar levels in the first trimester when compared to those women who achieved their good glycemic control before conception .

In diabetic women with poor glycemic control, there was an associated increase of 3.1% rate of miscarriage with increased glycosylated hemoglobin.

This study concludes by confirming that women in their first trimester with a poor glycemic control have a higher risk of miscarriage.

The Multicenter Diabetes in Early Pregnancy (DIEP) study observed increased risk of spontaneous miscarriage from 9 % to 45 % in women with poor glycemic control in first trimester .

Temple et al, [51]among 242 patients, glycosylated hemoglobin > 7.5 % results in four fold increased risk of spontaneous abortion than control .

Ivanisevic et al, [52] delayed embryonic growth in women with type 1 diabetes has eight fold higher risk of miscarriage than women with normal fetal growth . Their HbA1c levels were 9.34 % in women with poor metabolic control

Schoenfeld et al, [53] Diabetes causes reduction in the turn over of phosphatidyl inositol, disruption of arachidionic acid cascade, and later prostaglandin deficiency. Undetectable prostaglandin levels in the yolk sac was observed in diabetic women who had a spontaneous abortion in their early trimester. The free radical oxidative process leads to conceptus damage, embryonic death and abortion .

Ben – haroush A, Fisch B et al,[54] increased glucose levels alters the gene expression, resulting in programmed cell death of key progenitor cells which ends in miscarriage .

Miodovnik M et al,[55] Good levels of glycemic control in between pregnancies was associated with better obstetric outcomes and prevents the mental agony of the mother resulting in miscarriage. 43 women with diabetes were enrolled in this study. Fasting and postprandial blood sugars, HbA1c were collected at 9 weeks of gestation. 20 women resulted in term pregnancies and 15 ended in abortion. In women who had term pregnancies, the levels of postprandial blood sugar and glycosylated haemoglobin levels were significantly lower than who ended in abortion .

Strotmeyer et al,[47] more than 40 % of women with type 1 diabetes had associated Hashimoto's thyroiditis (type 2 polyglandular failure associated with antibodies to multiple endocrine organs). women with corrected thyroid abnormalities were less likely to develop menstrual disturbances.

PROLACTIN AND PREGNANCY

Prolactin is secreted by anterior pituitary lactotrophs. It is an unique hormone among others, as its secretion is controlled by tonic inhibition.

Stimulating factors

- Thyroid-releasing hormone (TRH),
- Gonadotropin-releasing hormone (GnRH)
- Hypothalamic serotonergic pathway
- g-aminobutyric acid (GABA)
- Estrogens,
- Pregnancy, and
- Breast suckling
- Chronic renal disease
- Pituitary adenoma /hypothalamic tumours

Pharmacologic agents that cause prolactin release act either by blockade of dopamine receptors (e.g., haloperidol, phenothia-zines) or by dopamine depletion in the tuberoinfundibular neurons (e.g., reserpine).

Other factors: Angiotensin II, Histamine (H2) antagonists, and opiates. Prolactin secretion has a diuranal variation with increase in pulsatile secretion during sleep.

Inhibiting factors

Increased levels of dopamine.

Human prolactin has partial structural similarity to Growth Hormone, this accounts for the lactotropic activity of growth hormone. Two forms of prolactin are found in the circulation- Non-glycosylated (monomeric & polymeric) and glycosylated. 85 % of prolactin (23 kDa) secreted into serum is non-glycosylated,.

The polymeric forms of prolactin (big prolactin) have reduced rates of binding to the prolactin receptor and possess decreased bioactivity when compared to monomeric. Some patients with elevated prolactin levels can have normal reproductive function; this group of patients have increased polymeric forms.

Certain isotypes of prolactin, specifically iso-B prolactin, is found to be elevated in the patients with infertility and pregnancy wastage. This isotype is also found to be more resistant to bromocriptine therapy when compared with normal . Circulating prolactin in turn

stimulates the hypothalamic dopaminergic neuronal activity, which suppresses both prolactin and GnRH neurons.

Grades of hyperprolactinemia (Leon speroff et al,)

Mild	20 -50 ng/ml	short luteal phase, poor preovulatory folliculogenesis
Moderate	50 -100 ng/ml	oligo /amennorhoea
Severe	>100ng/ml	Frank hypogonadism (decreased estrogen).

In normal pregnancy, prolactin increases by 10 fold reaching about 200 – 400 ng/ ml by term. The levels of increased estrogen in turn cause a rise in prolactin by stimulating pituitary lactotrophs. Both the rise of prolactin and estrogen nearly parallels by 7 – 8 weeks, this occurs as estrogen inhibits the prolactin inhibiting factor, Dopamine and leads to activation of transcription gene promoter gene of prolactin.

The source of prolactin in pregnancy comes from maternal pituitary, uterine decidua, and the fetal pituitary. Uterine decidual synthesis of prolactin is also secreted in to amniotic fluid. This levels reaches a peak at 26 – 28 weeks of gestation it later falls to a nadir after

34 weeks. Prolactin prevents water from being transferred from the fetal to the maternal circulation thereby preventing fetal dehydration.

TREATMENT OF HYPERPROLACTINEMIA

Bromocriptine

It is a dopamine agonist. It is used to normalize the prolactin irrespective of the etiology leading to the disorder. Treatment with Bromocriptine showed return of ovulatory menstrual cycles in 80 – 90 %, diminished prolactin levels, return of reproductive function (**Molitch ME et al**)[56]

Onset of action is rapid within 1 -2 hours ; starts decreasing as soon as initiation of theraphy. Sudden discontinuation may lead to return to elevated levels. They are usually started at the lowest dose 1.25mg daily at night and gradually increased until the dose that cause a decrease in prolactin level is reached. Gastrointestinal side effects are common. It can be reduced by administering the drug vaginally and the efficacy is relatively higher with vaginal route(**Vermesh M et al**)[57]

Cabergoline ,an ergot derivative, long acting dopaminergic properties, less side effects, less frequent dosing (1mg once or twice weekly), higher compliance rate. Normalization of prolactin leval occurs

in 95 % (**Bassetti M et al**).[58] This drug plays an important role in patients intolerant or resistant to Bromocriptine

Seppala M et al, [59] This study demonstrated a diminished plasma progesterone levels in women with hyperprolactinemia than their control in the ovulatory cycles. They had onset of symptoms which occurred in a specific sequence like 1) short luteal phase 2) galactorrhoea 3) ovulatory disturbances 4) Menstrual irregularities which forms the typical amenorrhoea-galactorrhoea syndrome. They found that these symptoms resolved with the initiation of treatment with bromocriptine.

Homburg R,et al, [60] it was previously thought that only short luteal phase and polycystic ovaries played a role in spontaneous miscarriage, but recently hypersecretion of luteinizing hormone has been implicated to play a key role in recurrent pregnancy loss.

Ando N, Gorai I et al, [61] In their study, they found many women with elevated prolactin levels duing their routine comprehensive screening for recurrent miscarriage.

Asukai K et al, [62] Hypothalamic – pituitary ovarian system is affected by hyperprolactinemia or occult hyperprolactinemia. This causes impaired folliculogenesis and abnormal maturation of oocyte.

This impaired process is found to be reversed with administration of Bromocriptine.

Yamaguchi M et al,[63] They concluded that patients with hyperprolactinemia ultimately in due course of time develops luteal insuffiency, galactorrhoea and dysfunction in reproductive endocrinology. Those patients who has both elevated prolactin levels and luteal phase defect responds better with Bromocriptine.

Fumiki Hirahara, M.D et al, [64] They reported that a profound group of women with repeated miscarriage had abnormal prolactin levels with no disturbances in their ovarian or menstrual function . They initially evaluated serum prolactin in two different menstrual cycles during the mid-follicular phase in the day time, women with abnormal values were subjected to endometrial biopsy.

12 women were found in hyperprolactinemia and occult hyperprolactinemia. They were started on Bromocriptine and prolactin levels were brought down to normal levels. Patients who conceived during the course of theraphy were continued with bromocriptine till 9 weeks of gestation. The success rate of 85.7 % and 52.4 % of livebirths were observed in those who were treated and not treated respectively.

They concluded that maintenance of normal levels of prolactin is essential in early pregnancy and Bromocriptine has a significant role in the therapeutic strategy of such patients with recurrent miscarriage.

MATERIALS AND METHODS

This study was conducted among 100 patients who attended the Genetic clinic, The Department of Obstetrics and Gynaecology in Government Kilpauk Medical College Hospital, Chennai. Ethical committee clearance obtained on Febraury 2011. Study period : February 2011 to September 2012.

This study was done after obtaining ethical committee clearance conducted in Kilpauk Medical College Hospital.

Sample size: 100, sample size was calculated by,

$n = Z^2_{1-\alpha/2} \quad P(1 - P) / d^2$

where, n – sample size

Z- table value, 1.96

P- proportion in a given population

d- desired precision, 0.05

About 100 patients are selected, after a complete evaluation of history, clinical examination and all basic investigations, they are subjected to the study.

INCLUSION CRITERIA

Women with previous history of two or more abortions that occurred in the first trimester among the reproductive age group were included

EXCLUSION CRITERIA

1) Second trimester abortions.
2) Women who conceived after Assisted Reproductive Technologies.
3) Previous ectopic pregnancies.
4) Previous molar pregnancies.
5) Known diabetic patients.
6) Known patients with thyroid disorders.
7) Women taking Anti – psychotics.

METHODOLOGY

After selection of 100 women based on the inclusion criteria, the patient was explained about the study and after obtaining the consent,

they are subjected to the study. Detailed history was taken to evaluate the presence of risk factors . A thorough general and systemic examination was done. All basic clinical investigations were performed .

Blood samples are collected and assayed for the following tests

1.Thyroid stimulating hormone.

2.Serum prolactin.

3.Glucose Tolerance test.

Reports are evaluated and the prevalence of each disorder is correlated with the casuation of Recurrent pregnancy loss.

Patients were advised to come in their fasting states. They were advised not to eat, drink, or exercise strenuously for atleast 8hours and be in rest during the test.

Thyroid stimulating hormone assay (**LEON SPEROFF et al**)

- Non-pregnant adult 0.34- 4.25 µIU/ml
- 1^{st} trimester 0.3 -2.30µIU/ml

PROLACTIN

- Non –pregnant adult 20 ng/ml
- 1st trimester 36- 213 ng/ml

GLUCOSE TOLERANCE TEST

- NON – PREGNANT WOMEN : ADA recommends a 75g OGTT with plasma glucose measurement at fasting and 2hr. Blood sugar was estimated by GOD-POD method.

	Normal	**Impaired glucose Intolerance**	**Diabetes Mellitus**
Fasting	<100	100 -126	>126
2 hour	<140	140 - 200	>200

- PREGNANT - WOMEN: 2 hour 75gm oral glucose, a venous blood glucose level of 140mg % or more is considered diagnostic. (Journal of Obstetrics and Gynaecology of India,Vol – 62).

The final data of all risk factors were expressed in percentages . statistical analysis was done with chi–square test and students independent T – test. The analysis was taken as statistically significant if pvalue < 0.05.

RESULTS AND ANALYSIS

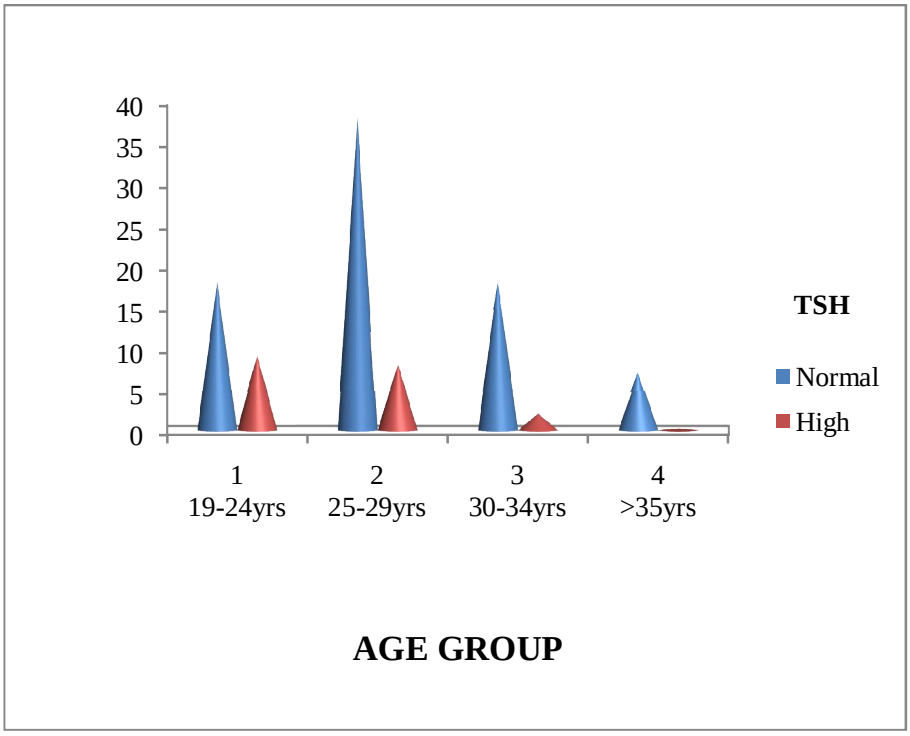
THYROID AND RECURRENT MISCARRIAGE

Table: 1 Distribution of Thyroid Dysfunction among different age groups

			TSH		Total
			0	1	
AGE GROUP	1 19-24yrs	Count	18	9	27
		% within TSH	22.20%	47.40%	27.00%
		% of Total	18.00%	9.00%	27.00%
	2 25-29yrs	Count	38	8	46
		% within TSH	46.90%	42.10%	46.00%
		% of Total	38.00%	8.00%	46.00%
	3 30-34yrs	Count	18	2	20
		% within TSH	22.20%	10.50%	20.00%
		% of Total	18.00%	2.00%	20.00%
	4 >35yrs	Count	7	0	7
		% within TSH	8.60%	0.00%	7.00%
		% of Total	7.00%	0.00%	7.00%
	Total	Count	81	19	100
		% within TSH	100.00%	100.00%	100.00%
		% of Total	81.00%	19.00%	100.00%

Pearson chi-square value: 6.376; p value 0.095 (not significant).

Figure 3: Distribution of Thyroid Dysfunction among different age groups



Patients with hypothyroidism comprises of about 47.4 % in the age group 1, 42.1 % among age group 2, 10.5 % among age group 3.

MENSTRUAL ABNORMALITY

Table 2: Relationship between Menstrual abnormality and Thyroid Dysfunction

			TSH		
			0	1	Total
MENSTRUAL	0	Count	59	7	66
		% within TSH	72.80%	36.80%	66.00%
		% of Total	59.00%	7.00%	66.00%
	1	Count	22	12	34
		% within TSH	27.20%	63.20%	34.00%
		% of Total	22.00%	12.00%	34.00%
	Total	Count	81	19	100
		% within TSH	100.00%	100.00%	100.00%
		% of Total	81.00%	19.00%	100.00%

Pearson value 8.887; p value 0.004 (significant)

Among patients with recurrent pregnancy loss, in women without menstrual irregularities 36,8 % had hypothyroidism ,whereas in women who had menstrual disturbances,63.2 % had hypothyroidism. The association of menstrual disturbances among women with hypothyroidism in recurrent pregnancy loss is statistically significant.

INFERTILITY

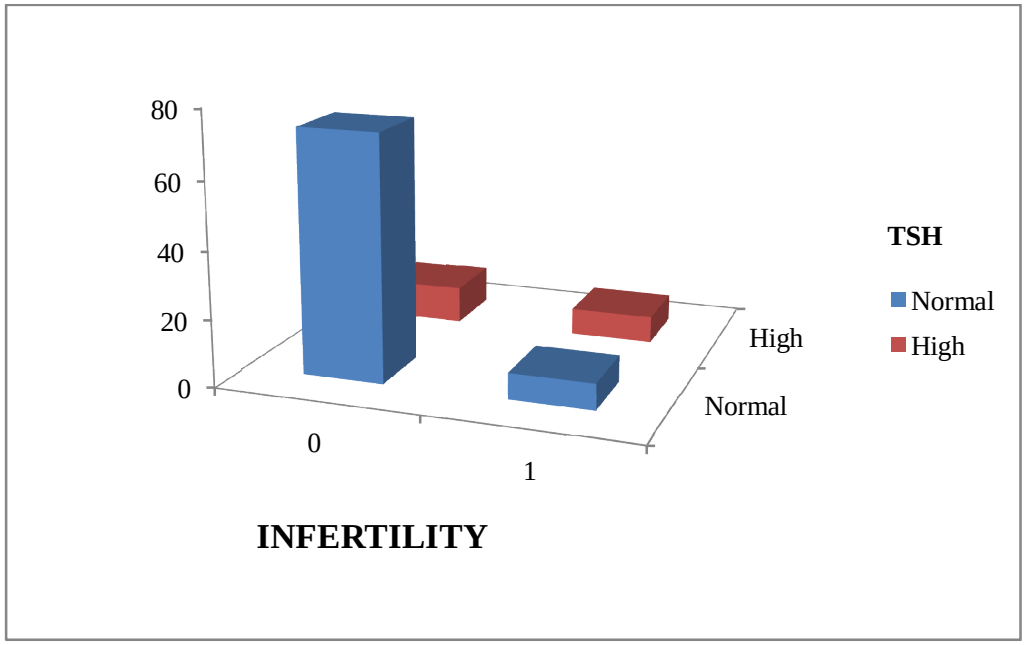
Table 3: Relationship between Infertility and Thyroid Dysfunction

			TSH		
			0	1	Total
INFERTILITY	0	Count	73	11	84
		% within TSH	90.10%	57.90%	84.00%
		% of Total	73.00%	11.00%	84.00%
	1	Count	8	8	16
		% within TSH	9.90%	42.10%	16.00%
		% of Total	8.00%	8.00%	16.00%
	Total	Count	81	19	100
		% within TSH	100.00%	100.00%	100.00%
		% of Total	81.00%	19.00%	100.00%

Pearson Chi-Square 11.894 ; p value 0.002 (significant)

In women with recurrent pregnancy loss, with previous h/o infertility hypothyroidism was observed in 42 .1 %, and in patient with no such risk factors hypothyroidism was observed in 57.9% .

Figure 4: Relationship between Infertility and Thyroid Dysfunction



In women with recurrent pregnancy loss with previous history of infertility almost half of the women had thyroid dysfunction. There exists statistical significance between occurrence of thyroid dysfunction among women with infertility and recurrent pregnancy loss.

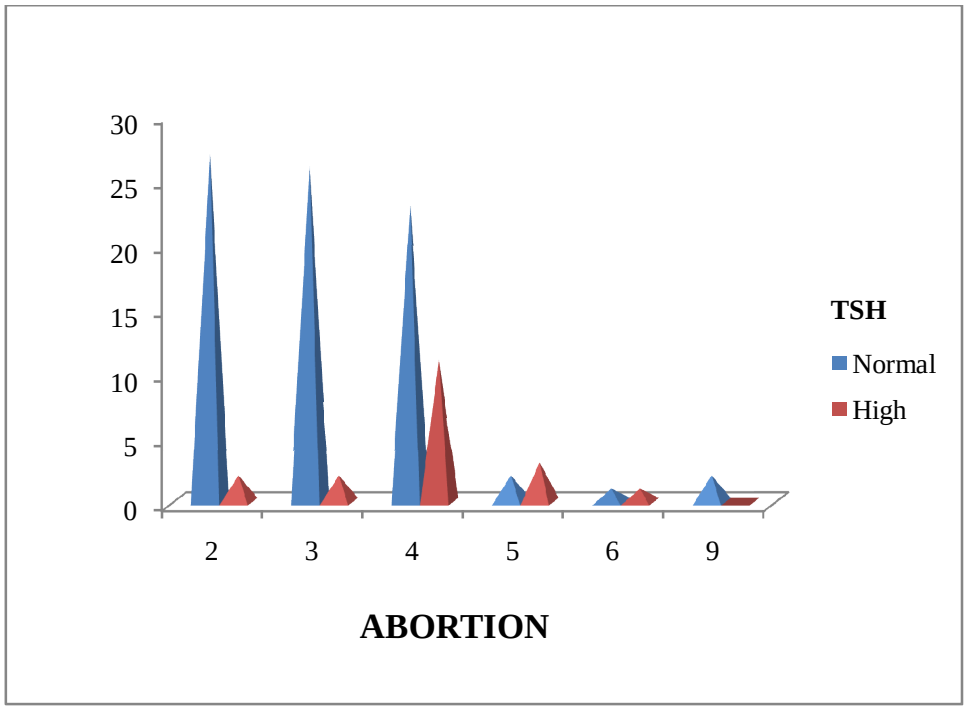
Table 4: Association of Thyroid Dysfunction and Recurrent Miscarriage

			TSH		
			0	1	Total
PREVIOUS NUMBER OF ABORTION	2	Count	27	2	29
		% within TSH	33.30%	10.50%	29.00%
		% of Total	27.00%	2.00%	29.00%
	3	Count	26	2	28
		% within TSH	32.10%	10.50%	28.00%
		% of Total	26.00%	2.00%	28.00%
	4	Count	23	11	34
		% within TSH	28.40%	57.90%	34.00%
		% of Total	23.00%	11.00%	34.00%
	5	Count	2	3	5
		% within TSH	2.50%	15.80%	5.00%
		% of Total	2.00%	3.00%	5.00%
	6	Count	1	1	2
		% within TSH	1.20%	5.30%	2.00%
		% of Total	1.00%	1.00%	2.00%
	9	Count	2	0	2
		% within TSH	2.50%	0.00%	2.00%
		% of Total	2.00%	0.00%	2.00%
	Total	Count	81	19	100
		% within TSH	100.00%	100.00%	100.00%
		% of Total	81.00%	19.00%	100.00%

Pearson Chi-Square Value 16.437 ; p value 0.006 (significant)

In recurrent miscarriage population , women with previous two and three abortions, hypothyroidism was noted in 10.5% of each group ; women with previous four abortions, hypothyroidism was noted in 57.9% ; and in women with previous five abortions, hypothyroidism was observed in 15.8 %, women with more than 6 abortions, hypothyroidism was noted in 5.3 %

Figure 5: Association of Thyroid Dysfunction with Recurrent Miscarriage



In women with recurrent pregnancy loss, the number of abortions has a statistical significance with the occurrence of hypothyroidism, especially there is an higher association of hypothyroidism when the number of abortion is more than four.

FAMILY HISTORY OF THYROID

Table 5: Association of Thyroid Dysfunction in women with Family History of Thyroid

			TSH		Total
			0	1	
FH/THYROID	0	Count	72	13	85
		% within TSH	88.90%	68.40%	85.00%
		% of Total	72.00%	13.00%	85.00%
	1	Count	9	6	15
		% within TSH	11.10%	31.60%	15.00%
		% of Total	9.00%	6.00%	15.00%
	Total	Count	81	19	100
		% within TSH	100.00%	100.00%	100.00%
		% of Total	81.00%	19.00%	100.00%

Pearson chi – square value : 5.057 ; p value 0.036 (significant)

In women with family history of thyroid dysfunction, nearly 31.6 % had hypothyroidism in patients with recurrent miscarriage.

Family history of thyroid is a significant risk factor for development of hypothyroidism in women with recurrent pregnancy loss

Group Statistics

Table 6: The correlation between the occurrence of abortion and its association with hypothyroidism

	TSH	N	Mean	Std. Deviation	Std. Error Mean
ABORTION	1	19	3.95	0.97	0.223
	0	81	3.19	1.305	0.145

Independent Samples Test						
		Levene's Test for Equality of Variances		t-test for Equality of Means		
		F	Sig.	T	Df	Sig. (2-tailed)
ABORTION	Equalvariances assumed	1.71	0.19	2.39	98	0.019
	Equal variances not assumed			2.87	35.09	0.007

The association between the women with recurrent miscarriage and hypothyroidism was analyzed with independent T – test and was also found to be statistically significant.

DIABETES AND RECURRENT MISCARRIAGE

AGE GROUP

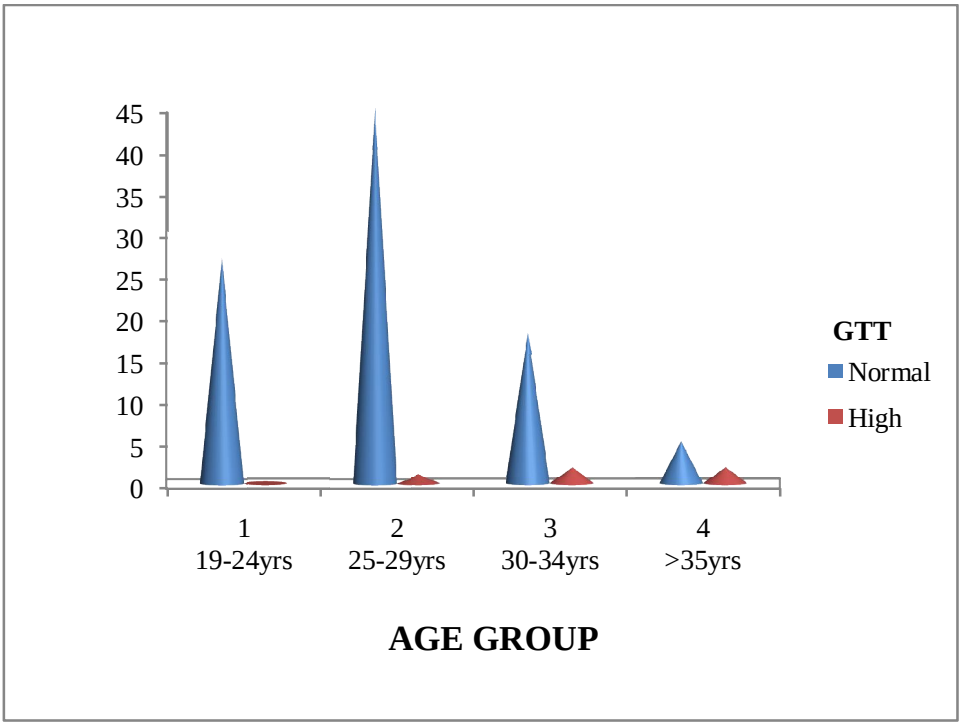
Table 7: Distribution of Diabetes Mellitus among different age groups

			GTT		Total
			0	1	
AGE GROUP	1 19 - 24 Yrs	Count	27	0	27
		% within GTT	28.40%	0.00%	27.00%
		% of Total	27.00%	0.00%	27.00%
	2 25 - 29 yrs	Count	45	1	46
		% within GTT	47.40%	20.00%	46.00%
		% of Total	45.00%	1.00%	46.00%
	3 30 - 34 yrs	Count	18	2	20
		% within GTT	18.90%	40.00%	20.00%
		% of Total	18.00%	2.00%	20.00%
	4 >35 Yrs	Count	5	2	7
		% within GTT	5.30%	40.00%	7.00%
		% of Total	5.00%	2.00%	7.00%
	Total	Count	95	5	100
		% within GTT	100.00%	100.00%	100.00%
		% of Total	95.00%	5.00%	100.00%

Pearson chi – squarevalue: 11.435; p value: 0. 010 (significant).

In women with recurrent miscarriage, 20 % of Diabetes was observed among age group 2 and 40% of Diabetes belongs to age group 3 & 4.

Figure 6: Distribution of Diabetes Mellitus among different age groups



From this data, it is inferred that diabetes occurs mainly in the age group above 30. Diabetes has a significant association in women with recurrent pregnancy group especially among older age group.

MENSTRUAL ABNORMALITY

Table 8: Association between Menstrual abnormality and Diabetes Mellitus

			GTT		Total
			0	1	
MENSTRUAL	0	Count	65	1	66
		% within GTT	68.40%	20.00%	66.00%
		% of Total	65.00%	1.00%	66.00%
	1	Count	30	4	34
		% within GTT	31.60%	80.00%	34.00%
		% of Total	30.00%	4.00%	34.00%
	Total	Count	95	5	100
		% within GTT	100.00%	100.00%	100.00%
		% of Total	95.00%	5.00%	100.00%

Pearson Chi-Square value: 4.963; pvalue: 0.026 (significant)

Among women with menstrual disturbances, 80 % had diabetes, whereas in women without menstrual disturbances, 20 % had diabetes. There exists statistical significance between menstrual disturbances and Diabetes in women with recurrent miscarriage especially this was observed in women with higher body mass index which causes ovulatory dysfunction.

INFERTILITY

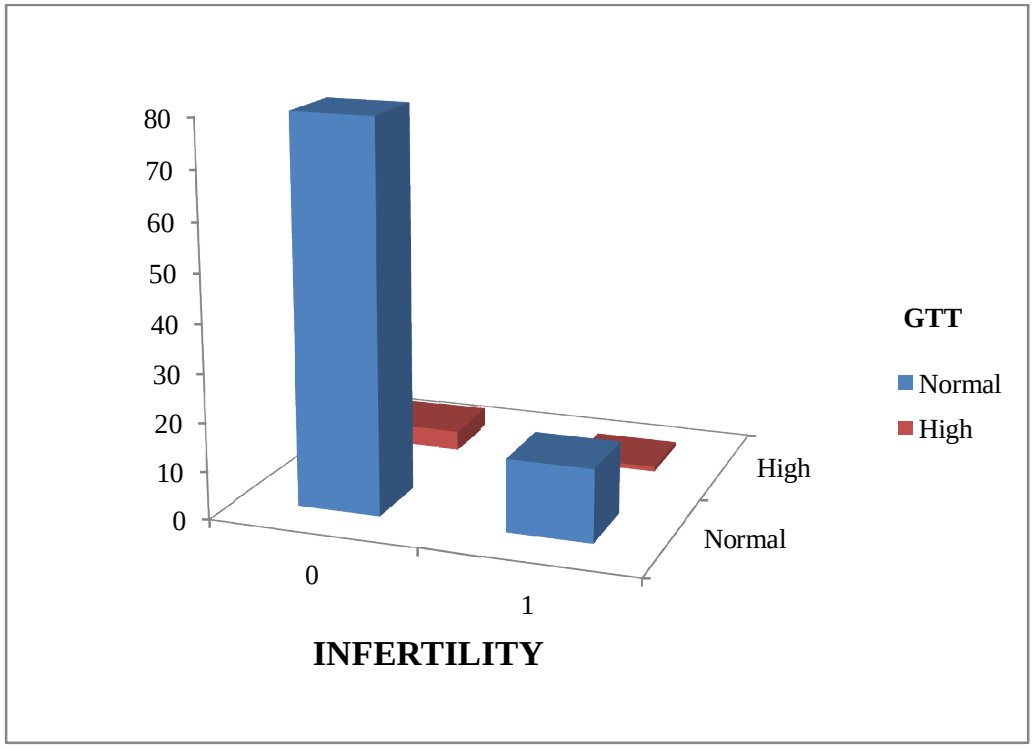
Table 9:Relationship between Infertility and Diabetes Mellitus

			GTT		Total
			0	1	
INFERTILITY	0	Count	80	4	84
		% within GTT	84.20%	80.00%	84.00%
		% of Total	80.00%	4.00%	84.00%
	1	Count	15	1	16
		% within GTT	15.80%	20.00%	16.00%
		% of Total	15.00%	1.00%	16.00%
	Total	Count	95	5	100
		% within GTT	100.00%	100.00%	100.00%
		% of Total	95.00%	5.00%	100.00%

Pearson Chi-Square value: 0.063; pvalue: 0.082 (not significant)

In women with recurrent miscarriage, patients with previous history of infertility. Diabetes was observed in 20% , in patient with no such risk factors Diabetes was reported in 80% .

Figure 7:Relationship between Infertility and Diabetes Mellitus



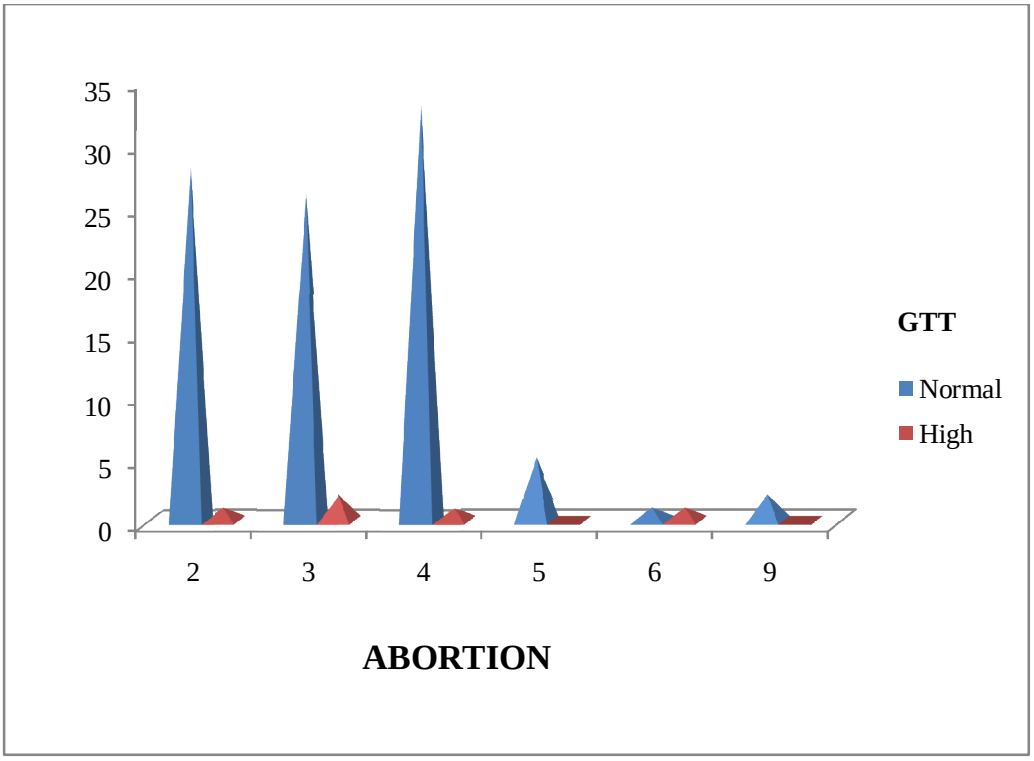
There is no statistical significance between infertility and Diabetes in women with recurrent pregnancy loss

Table 10: Association of Diabetes Mellitus with Recurrent Miscarriage

			GTT		Total
			0	1	
PREVIOUS NUMBER OF ABORTION	2	Count	28	1	29
		% within GTT	29.50%	20.00%	29.00%
		% of Total	28.00%	1.00%	29.00%
	3	Count	26	2	28
		% within GTT	27.40%	40.00%	28.00%
		% of Total	26.00%	2.00%	28.00%
	4	Count	33	1	34
		% within GTT	34.70%	20.00%	34.00%
		% of Total	33.00%	1.00%	34.00%
	5	Count	5	0	5
		% within GTT	5.30%	0.00%	5.00%
		% of Total	5.00%	0.00%	5.00%
	6	Count	1	1	2
		% within GTT	1.10%	20.00%	2.00%
		% of Total	1.00%	1.00%	2.00%
	9	Count	2	0	2
		% within GTT	2.10%	0.00%	2.00%
		% of Total	2.00%	0.00%	2.00%
	Total	Count	95	5	100
		% within GTT	100.00%	100.00%	100.00%
		% of Total	95.00%	5.00%	100.00%

Pearson chi – square value 9.616 p value 0.087 (not significant)

Figure 8: Association of Diabetes Mellitus with Recurrent Miscarriage



There is no significant association between the occurrence of abortion and Diabetes in women with recurrent pregnancy loss

FAMILY HISTORY OF DIABETES

Table 11: Association of Diabetes Mellitus in women with Family History of Diabetes

			GTT		Total
			0	1	
FH/DM	0	Count	84	4	88
		% within GTT	88.40%	80.00%	88.00%
		% of Total	84.00%	4.00%	88.00%
	1	Count	11	1	12
		% within GTT	11.60%	20.00%	12.00%
		% of Total	11.00%	1.00%	12.00%
	Total	Count	95	5	100
		% within GTT	100.00%	100.00%	100.00%
		% of Total	95.00%	5.00%	100.00%

Pearson Chi – Square value : 0.319; pvalue: 0.572(not significant)

In women without family history of Diabetes ; diabetes was observed in 80 % of patients, And in those with family history, it was observed in 20 %.

In this study, there is no statistical significance between family history of diabetes and occurrence of diabetes among patients with recurrent pregnancy loss .

Table 12:Association between Menstrual abnormality and Prolactin Disorders

MENSTRUAL IRREGULARITIES					
			PROLACTIN		Total
			0	1	
MENSTRUAL	0	Count	66	0	66
		% within PROLACTIN	68.00%	0.00%	66.00%
		% of Total	66.00%	0.00%	66.00%
	1	Count	31	3	34
		% within PROLACTIN	32.00%	100.00%	34.00%
		% of Total	31.00%	3.00%	34.00%
	Total	Count	97	3	100
		% within PROLACTIN	100.00%	100.00%	100.00%
		% of Total	97.00%	3.00%	100.00%

Pearson Chi-Square value: 6.004; pvalue: 0.014 (significant)

All women who were diagnosed to have hyperprolactinemia in this population, there was 100% association with menstrual disturbances. Menstural disorders in woman with recurrent pregnancy loss have a statistically significant association with prolactin disorders.

INFERTILITY

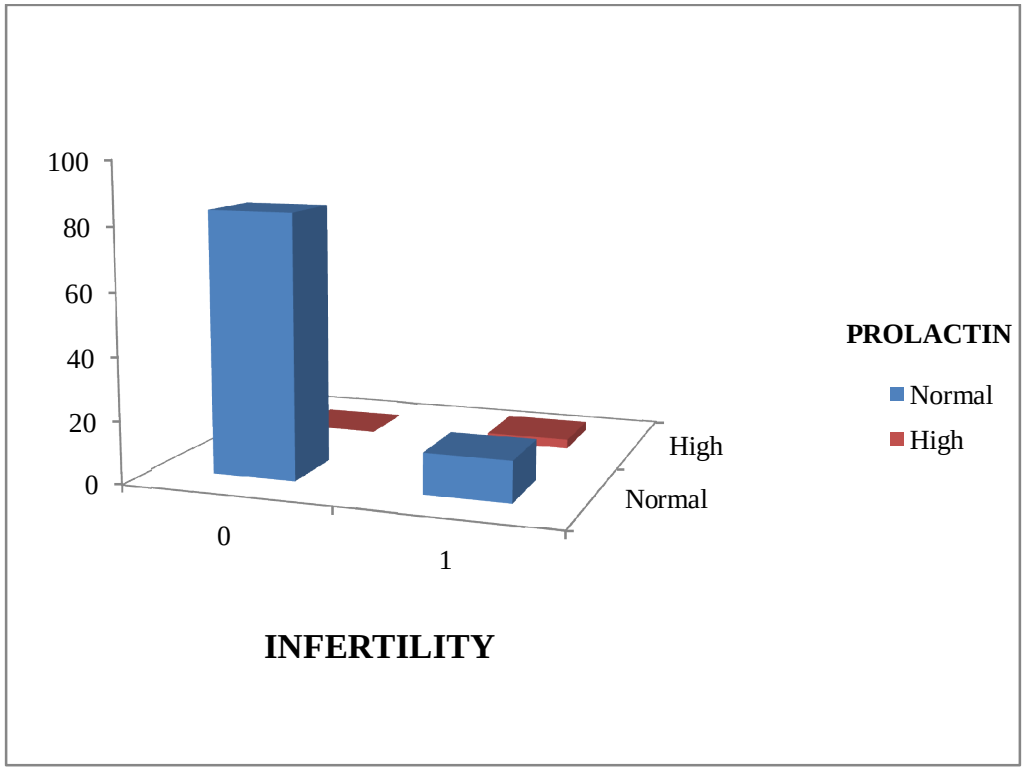
Table 13:Association between Infertility and Prolactin disorders

			PROLACTIN		Total
			0	1	
INFERTILITY	0	Count	84	0	84
		% within PROLACTIN	86.60%	0.00%	84.00%
		% of Total	84.00%	0.00%	84.00%
	1	Count	13	3	16
		% within PROLACTIN	13.40%	100.00%	16.00%
		% of Total	13.00%	3.00%	16.00%
	Total	Count	97	3	100
		% within PROLACTIN	100.00%	100.00%	100.00%
		% of Total	97.00%	3.00%	100.00%

Pearson chi – square value: 16.237; pvalue: 0.000 (significant)

Among woman with recurrent pregnancy loss with previous history of infertility, there was 100% association with elevated prolactin levels.

Figure 9: Association between Infertility and Prolactin disorders



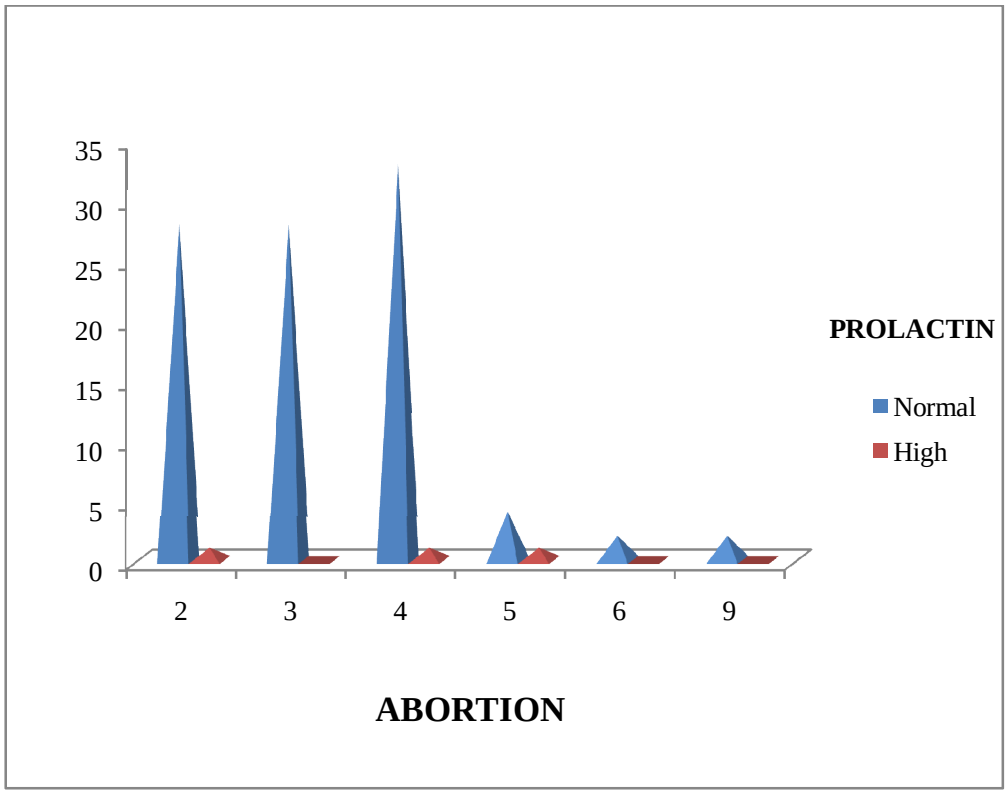
There exists a higher statistical significance with previous history of infertility and hyperprolactinemia in woman with recurrent pregnancy loss.

Table 14: Association of Hyperprolactinemia with Recurrent Miscarriage

			PROLACTIN		
			0	1	Total
PREVIOUS NUMBER OF ABORTION	2	Count	28	1	29
		% within PROLACTIN	28.90%	33.30%	29.00%
		% of Total	28.00%	1.00%	29.00%
	3	Count	28	0	28
		% within PROLACTIN	28.90%	0.00%	28.00%
		% of Total	28.00%	0.00%	28.00%
	4	Count	33	1	34
		% within PROLACTIN	34.00%	33.30%	34.00%
		% of Total	33.00%	1.00%	34.00%
	5	Count	4	1	5
		% within PROLACTIN	4.10%	33.30%	5.00%
		% of Total	4.00%	1.00%	5.00%
	6	Count	2	0	2
		% within PROLACTIN	2.10%	0.00%	2.00%
		% of Total	2.00%	0.00%	2.00%
	9	Count	2	0	2
		% within PROLACTIN	2.10%	0.00%	2.00%
		% of Total	2.00%	0.00%	2.00%
	Total	Count	97	3	100
		% within PROLACTIN	100.00%	100.00%	100.00%
		% of Total	97.00%	3.00%	100.00%

Pearson chi – square value 5.976 ; p value 0.309 (not significant)

Figure 10: Association of Hyperprolactinemia with Recurrent Miscarriage



Hyperprolactinemia was observed in 33.3% in woman with previous history of 2, 4 and 5 abortions. There is no statistically significant association between number of abortion and hyperprolactinemia

FAMILY HISTORY OF THYROID

Table 15: Association of Prolactin Disorders in women with Family History of Thyroid

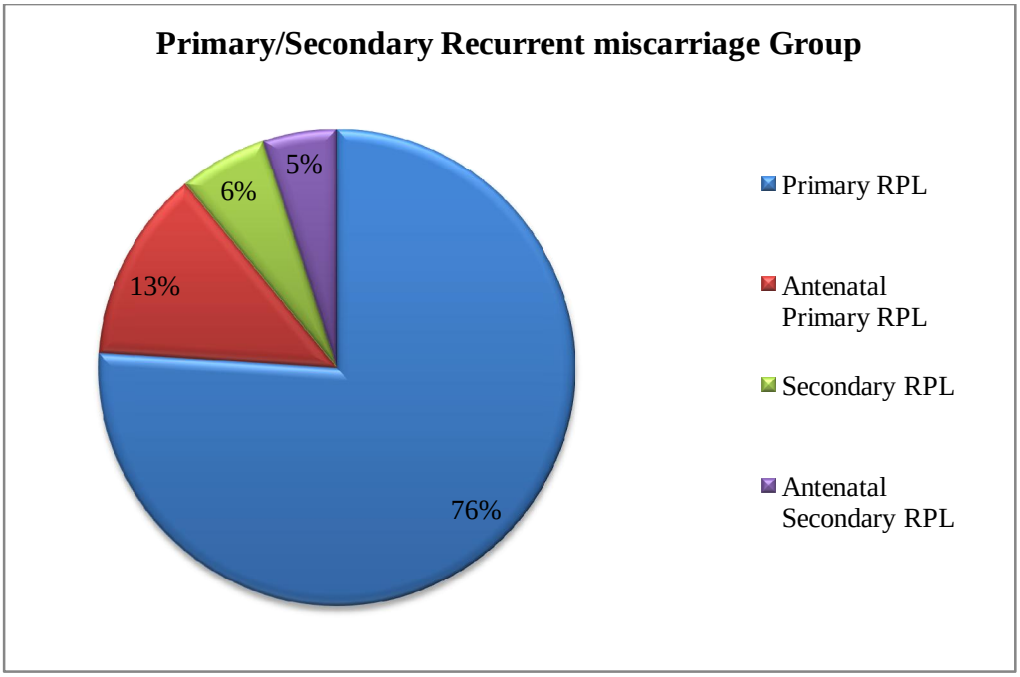
			PROLACTIN		
			0	1	Total
FH/THYROID	0	Count	84	1	85
		% within PROLACTIN	86.60%	33.30%	85.00%
		% of Total	84.00%	1.00%	85.00%
	1	Count	13	2	15
		% within PROLACTIN	13.40%	66.70%	15.00%
		% of Total	13.00%	2.00%	15.00%
	Total	Count	97	3	100
		% within PROLACTIN	100.00%	100.00%	100.00%
		% of Total	97.00%	3.00%	100.00%

Pearson chi – square value: 6.475; pvalue: 0.058 (significant)

In women with family history of hypothyroidism, hyperprolactinemia was observed in 66.7 % of individuals, whereas it was noted only in 33. 3 % of individuals with no family history of thyroid dysfunction

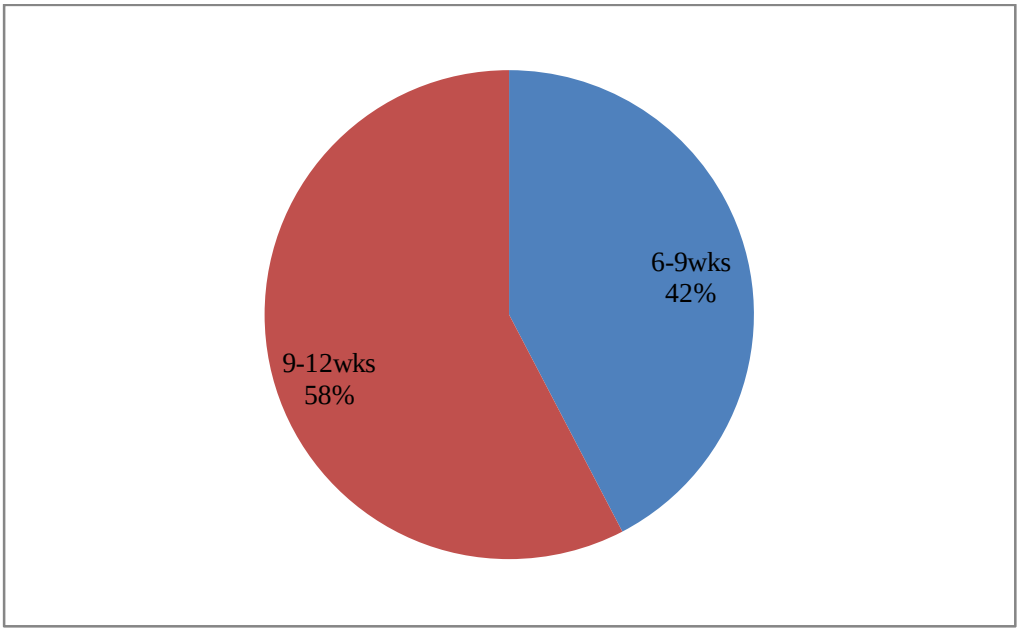
PRIMARY AND SECONDARY MISCARRIAGE

Figure 11



89 patients of primary and 11 patients of secondary miscarriage were included 19 antenatal patients were included, of which13 delivered term, 4 preterm, one intra uterine death, and one patient had recurrent miscarriage

Figure 12: GESTATIONAL AGE AT ABORTION



Among the study group, the gestational age of abortion is divided in to two groups, 42% of miscarriage occurred in 6 – 9 weeks and 58% of the miscarriage occurred in 9 -12 weeks.

Table 16: The correlation between the age group and the occurrence of abortion

Age group and abortion								
					95% Confidence Interval for Mean			
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound	Mini-mum	Maxi-mum
1	27	2.74	0.813	0.156	2.42	3.06	2	4
2	46	3.09	0.939	0.138	2.81	3.37	2	5
3	20	4.35	1.785	0.399	3.51	5.19	2	9
4	7	4.29	0.951	0.36	3.41	5.17	3	6
Total	100	3.33	1.28	0.128	3.08	3.58	2	9

ANOVA					
ABORTION					
	Sum of Squares	**Df**	**Mean Square**	**F**	**Sig.**
Between Groups	39.294	3	13.098	10.238	0.00
Within Groups	122.816	96	1.279		
Total	162.11	99			

The association of recurrent pregnancy loss among women with higher age group was found to be statistically significant.

Table 17: Correlation between BMI and abortion

Correlations			
		ABORTION	**BMI**
ABORTION	Pearson Correlation	1	.255*
	Sig. (2-tailed)		0.01
	N	100	100
BMI	Pearson Correlation	.255*	1
	Sig. (2-tailed)	0.01	
	N	100	100
*. Correlation is significant at the 0.05 level (2-tailed).			

The correlation between women with recurrent pregnancy loss and those with higher body mass index was found to be statistically significant.

DISCUSSION

Among women with recurrent pregnancy loss, 100 patient was evaluated and results that were obtained were tabulated and subjected to analysis. The following results are observed at the end of the study.

In this study; in relation to age group and recurrent pregnant loss; Hypothyroid was higher among 19 – 24 age groups (47.4%) and Diabetes was found to occur in age group of population more than 30 years (80%).

Considering the age of the patients included in this population, there was an associated higher statistical significance between the age of the patient and the occurrence of abortion (pvalue 0.000). As the age increases, patients with previous history of recurrent pregnancy loss are highly susceptible to recurrent abortions.

Anne Marie et al., (conducted a population based register – linear study) BMJ, 24, June 2000; [65] which also inferred that as Maternal age increases, the risk of spontaneous abortion also increases proportionally. They observed 8.9% risk of miscarriage in women of 20 – 24 years. 74.7% risk in women more than 45 years.

In women with menstrual irregularities among recurrent pregnancy loss group; there observed statistically significant association of 63.2% with hypothyroidism; 80% with Diabetes; and 100% with prolactin disorders. In women with Diabetes, 80% of the population with irregular menstrual cycles had an average Body Mass Index of more than 28 which attributes to their menstrual disturbances.

This finding is also compared with the latest study conducted by **Neha Sharma et al**, [66] International Journal of Science and Research, 2012 they found that Thyroid Stimulating Hormone had a higher statistical significance (pvalue <0.01) in women with menstrual disturbances and infertility.

In recurrent miscarriage women; with previous history of infertility, there was a statistical significance associated with Thyroid and prolactin disorders (100%- pvalue: 0.000).

Hakim et al; [67] observed that women who are infertile have a greater risk of recurrent miscarriage when compared to women who are fertile.

The same result was observed in the study performed by **Azima Kalsum et al**; [68] which reported 69.51% of women who had

prolactin disorders reported with infertility; and **Homburg R et al** [60] implicated the role of prolactin disorders in women with recurrent pregnancy loss.

The number of abortion has a higher statistical correlation (pvalue: 0.006) in women who tested positive for Thyroid dysfunction, especially in women with previous history of 4 abortions.

Ashoor et al, [69] women with miscarriage had higher TSH levels (5.9 vs 2.5%, pvalue < 0.05). Indian Journal of Medical Sciences, observed that the association of hypothyroidism with recurrent miscarriage were found to be statistically significant (pvalue < 0.001).

Vinita et al, [70] found hypothyroidism in 1.4% of women with recurrent miscarriage in Indian population.

Stray Pederson et al, [71] observed thyroid dysfunction in 2% of women with recurrent miscarriage.

This was also observed in the study performed by **Regan et al**; [4] He stated that the outcome of a women's first pregnancy is also considered as a predictive factor and this also influence the outcome of subsequent pregnancies.

Family history of Thyroid also had a statistical significance between the occurrence of hypothyroidism (pvalue: 0.036) and prolactin disorders (pvalue: 0.058) in women of Recurrent Pregnancy Loss group.

2 out of 3 patients with hyperprolactinemia had associated hypothyroidism, this was also observed by **Van Gaal et al**, where decrease in thyroid levels stimulates lactotrophs resulting in hyperprolactinemia.

89 patients of primary and 11 patients of secondary miscarriage were included.19 antenatal patients were included, of which13 delivered term, 4 preterm, one intra uterine death, and one patient had recurrent miscarriage.

The other correlation was between the Body Mass Index and the number of abortion which has got a statistical significance of (0.010).

This was also implicated in the study performed by **Metwally M et al** [48], in women with Body Mass Index of more than 25; there exists increased cha1nces of spontaneous abortion(OR – 1.67).

Hamiton Fairley et al, [72] observed an increased miscarriage when Body Mass Index is increased when compared to normal. (60% vs 27%, pvalue < 0.05).

SUMMARY

About 100 patients with previous history of 2 or more miscarriage who reported to Kilpauk Medical College and who fulfilled the inclusion and exclusion criteria were included in the study

In recurrent miscarriage group of my study,

There was 19% incidence of hypothyroidism, of which 57.9% are distributed among women with previous 4 losses.

Diabetes has been reported in 5% of population in this group, of which 80% were in the age group more than 30.

Menstrual disturbances were observed in 63.2% of hypothyroid patients, 80% of diabetic patients and in all patients who had hyperprolactinemia.

In women with previous history of infertility, 42.1% had hypothyroidism and 20% had Diabetes. In women with family history of thyroid, 31.6% had hypothyroidism and 66.7% had hyperprolactinemia.

In my study, there is no statistical significance between Diabetes and hyperprolactinemia with the occurrence of abortion.

Age and Body mass Index has a significant association with recurrent miscarriage.

CONCLUSION

Recurrent miscarriage is a distressing situation both to the patient and the investigator until and unless the cause is established. The evaluation of endocrinological causes has been simple, easy and cost effective for the general population.

1) Women with endocrinological dysfunction, majority of them will have some form of menstrual abnormality which could be evaluated by a proper history

2) Hypothyroidism has a significant association with recurrent miscarriage group, hence early routine screening, diagnosis, treatment of subclinical and overt forms has a better obstetrical outcome reducing the mental agony of the patient.

3) Women with positive family history of thyroid abnormality along with hypothyroidism are those candidates who need thyroid antibody evaluation. Routine screening for all cases is not necessary.

4) Though, Diabetes mellitus as such do not cause abortion, women with poor glycemic control and those with elevated fasting blood glucose level are still considered as risk factors. This group of

women also has an associated insulin resistance which influences their future outcome.

5) Thyroid function test is done before confirming the diagnosis of hyper prolactinemia, and initiation of thyroxine substitution would correct subtle abnormalities in prolactin levels.

BIBLIOGRAPHY

1. Malpas P, A study of abortion sequence, J Obstet Gynaecol Br Emp 45:932, 1938.

2. Wilcox AJ, Weinberg CR, O'Connor JF, et al. Incidence of early loss of pregnancy. N Engl J Med 1988;319:189–194.

3. Roman E, Fetal loss rates and their relation to pregnancy order, J Epidemiol Community Health 38:29, 1984.

4. Regan L, Braude PR, Trembath PL. Influence of post reproductive performance on risk of spontaneous abortion. BMJ 1989;299:541–545

5. Quenby S, Vince G, Farquharson R, Aplin J, Recurrent miscarriage: a defect in nature's quality control?, Hum Reprod 17:1959, 2002.

6. Nybo Andersen AM, Wohlfahrt J, Christens P, Olsen J, Melbye M. Maternal age and fetal loss: population based register linkage study. BMJ 2000; 320: 1708–12

7. Levi AJ, Raynault MF, Bergh PA, Drews MR, Miller BT, Scott RT, Jr., Reproductive outcome in patients with diminished ovarian reserve, Fertil Steril 76:666, 2001.

8. Simpson JL, Mills JL, Holmes LB, Ober CL, Aarons J, Jovanovic L, Knopp RH, Low fetal loss rates after ultrasound-proved viability in early pregnancy, JAMA 258:2555, 1987.

9. Guerneri S, Bettio D, Simoni G, Brambat B, Lanzani A, Fraccaro M, Prevalence and distribution of chromosome abnormalities in a sample of fi rst-trimester internal abortions, Hum Reprod 2:735, 1987.

10. Portnoi M-F, Joye N, van den Akker J, Morlier G, Taillemite JL, Karyotypes of 1142 couples with recurrent abortion, Obstet Gynecol 72:310, 1988.

11. Lomax B, Tang S, Separovic E, Phillips D, Hillard E, Thomson T, Kalousek DK, Comparative genomic hybridization in combination with flow cytometry improves results of cytogenetic analysis of spontaneous abortions, Am J Hum Genet 66:1516, 2000

12. Simon C, Martinez L, Pardo F, Tortajada M, Pellicer A, Mullerian defects in women with normal reproductive outcome, Fertil Steril 56:1192, 1991

13. Propst AM, Hill JA, 3rd, Anatomic factors associated with recurrent pregnancy loss, Seminars Reprod Med 18:341, 2000.

14. Golan A, Langer R, Wexler S, Segev E, Niv D, David MP, Cervical cerclage—its role in the pregnant anomalous uterus, Int J Fertil 35:164, 1990.

15. Raga F, Bauset C, Remohi J, Bonilla-Musoles F, Simón C, Pellicer A, Reproductive impact of congenital Müllerian anomalies, Hum Reprod 12:2277, 1997.

16. Rackow BW, Taylor HS. Uterine leiomyomas affect endometrial HOX10 expression. J Soc Gynecol Investig 2006; 13 (suppl 2): 654.

17. Shaffer W, Role of uterine adhesions in the cause of multiple pregnancy losses, Clin Obstet Gynecol 29:912, 1986

18. Mattson R. The non-expression of MHC class II in trophoblast cells. Am J Reprod Immunol 1998;40:385–394.

19. O'Garra A, Arai N. The molecular basis of T helper 1 and T helper 2 cell differentiation. Trends Cell Biol 2000;10:542–550.

20. Lockshin MD, Sammaritano LR, Schwartzman S. Validation of the Sapporo criteria for antiphospholipid syndrome. Arthritis Rheum 2000;43:440–443.

21. Donders GG, Van Bulck B, Caudron J, Londers L, Vereecken A, Spitz B, Relationship of bacterial vaginosis and mycoplasmas to the risk of spontaneous abortion, Am J Obstet Gynecol 183:431, 2000.

22. Metwally M, Ong MKJ, Ledger WL, Li TC, Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception. A meta-analysis of the evidence, Fertil Steril 90:714, 2008.

23. Scott R, Navot D, Liu HC, Rosenwaks Z, A human in vivo model for the luteoplacental shift, Fertil Steril 56:481, 1991

24. Watson H, Kiddy DS, Hamilton-Fairley D, et al. Hypersecretion of luteinizing hormone and ovarian steroids in women with recurrent early miscarriages. Hum Reprod 1993;8:829–833

25. Haas DM, Ramsey PS, Progestogen for preventing miscarriage, Cochrane Database Syst Rev 16:CD003511, 2008.

26. Skrha J, Haas T, Sindelka G, Prazny M, Widimsky J, Cibula D, Svacina S, Comparison of the insulin action parameters from hyperinsulinemic clamps with homeostasis model assessment and QUICKI indexes in subjects with different endocrine disorders, J Clin Endocrinol Metab 89:135, 2004.

27. Glueck CJ, Wang P, Fontaine RN, Sieve-Smith L, Tracy T, Moore SK, Plasminogen activator inhibitor activity: an independent risk factor for the high miscarriage rate during pregnancy in women with polycystic ovary syndrome, Metabolism 48:1589, 1999.

28. Clinical gynecologic Endocrinologic and Infertility, Marc A,Fritz and Leon Speroff et al, eighth Edition

29. European Journal of Endocrinology (2011) 164 263–268 ed. Weiwei Wang, Weiping Teng, Zhongyan Shan, Sen Wang, Jianxin Li

30. European Journal of Endocrinology (2009) 160 985–991 N Benhadi1, W M Wiersinga1, J B Reitsma2, T G M Vrijkotte3 and G J Bonsel

31. Indian Journal of Medical Sciences, Vol. 62, No. 9, September, 2008, pp. 359- 363 Prevalence of hypothyroidism in recurrent pregnancy loss in first trimester

32. Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, Stagnaro-Green A 2010 Jun 9.

33. Thyroid autoimmunity and miscarriage: a meta-analysis. Chen L, Hu R Clin Endocrinol (Oxford). 2011 BMJ. 2011

34. Thyroid. 2010 Jun;20(6):633-7.Thyroid function in women found to have early pregnancy loss. De Vivo A, Mancuso A, Giacobbe A, Moleti M, Maggio Savasta L, De Dominici R, Priolo AM, Vermiglio F

35. Vaidya B, Anthony S, Bilous M, Shields B, Drury J, Hutchison S, Bilous R Detection of thyroid dysfunction in early pregnancy: Universal screening or targeted high-risk case finding? J Clin Endocrinol Metab. 2007 Jan;92(1):203-7. Epub 2006 Oct 10.

36. Haddow JE, Palomaki GE, Allan WC, Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. New England Journal of Medicine 1999 341 549–555

37. Dun can JM. on puerperal sepsis Trans obs soc London 1882,24:256-85

38. Williams JW. The clinical significance of glycosmia in pregnant woman Am J Med sci 1909:137;1-26

39. EP Joslin. Pregnancy and Diabetes Mellitus Boston Med surg J1915 173: 841-9

40. Ryan EA,Ennesi; Role of gestation and hormones in induction of insulin resistance J clin Endicrinol metab 1988; 67:341 – 7

41. Clausen TD, Ekbom P, Mathiesen Et al, Poor pregnancy outcome in women with Type 2 Diabetes.Diabetes Care 2005;28:323 – 8

42. Roland JM, Murphy HR et al, The pregnancies of women with Type 2 Diabetes poor outcomes by opportunities for imps relation to improvement. Diabet Med 2005; 22:1774 - 7

43. Laivuori H; kuaju R; Et al Lepten ; its relation to serum insulin and insulin sensitivity. Metabolism 2000; 49:259 – 63

44. Dunne F;Brydon P, Smith K,Gee H. Pregnancy in women with Type 2 Diabetes; 12 years outcome data 1990 – 2002 Diabet Med 2003; 20: 734 – 8.

45. Miller E, Hare JW; Cloherty Jp et al; Elevated Maternal HbA1c in early pregnancy and fetal Malformations in women with Type 1 Diabetes Diabetologia 2000; 43:79-82.

46. Sheffield Js, Butler Koster EG; Casey BM et al; Maternal Diabetes and infant malformations, obstet Gynecol 2002;100:925-30.

47. Strotmeyer SE, Steen Kiste AS, Fole TP, et al; Menstural cycle differences between women with Type 1 Diabetes and women without Diabetes. Diabetes Care 2003; 26: 1016 – 21.

48. Metwally M, Cutting R, Tipton A1 et al; Effect of increased body mass index on oocyte, embryo quality in Invitro fertilization patients. Reprod Biomed 2007; 15: 532 – 8.

49. Robker RL, Akison LK, Bennett BD; Obese women exhibit differences in ovarian Metabolites; harmones and gene expression compared with moderate weight women J clin Endocrinol Metab 2009 : 94(5) :1533 – 40

50. INTNL. J. Diab. dev. countries (1991), vol. 11Mille JL, Simpson JL, Driscoll SC, Jovanovic-Peterson R. Incidence of spontaneous abortion among normal women and insulin dependent diabetic women whose pregnancies were identified within 21 days of conception. N Engl J Med 1988;319:1617-23.

51. Temple R, Aldridge V, Greenwood R et al; Association between outcome of pregnancies and glycemic control in early pregnancy in Type 1 Diabetes populated Based study Br Med J 2002; 325: 1275 – 6.

52. Ivaniseic M, Bukovic D, Starcevic V et al, Influence of hyperglycemia on early embryonic growth in IDDM pregnant women.Coll Antropol 1999 ; 23:183 - 8

53. Schoenfeld A, Erman A, Warchaizer S et al; Yolk sac concentration of prostaglandin E2 in diabetic pregnancy, further clues to etiology of diabetic embryopathy. Prostaglandins 1995; 50: 121 – 6.

54. Ben – Hallroush A; Fisch B, Diabetes and infertility. Textbook of Diabetes and pregnancy, 2nd Edition London, UK; Informa Healthcare 2008: PP: 482 – 92

55. Miodovnik M, Mimouni F, Siddiqi TA, Khoury J, Berk MA. Spontaneous abortions in repeat diabetic pregnancies: a relationship with glycemic control. Obstet Gynecol 1990;75:75-8.

56. Molitch ME. Pathologic hyperprolactinemia. Endocrinol Metab Clin North Am 1992; 21:877).

57. Vermesh M, Obstet Gynecol 1988; 72:693.

58. Bassetti M, J Clin Endocrinol Metab 1984; 58:268

59. Lancet. 1976 Jan 31;1(7953):229-30. Hyperprolactinaemia and luteal insufficiency. Seppala M, Ranta T, Hirvonen E

60. Homburg R, et al, Amar NA, Eshel A, Adams J, Jacobs HS. Influence of luteinizing hormone concentration on ovulation, conception and early pregnancy loss in polycystic ovary syndrome. Br Med J 1988;297: 1024–6.

61. Ando N, Gorai I et al, Prolactin disorders in patients with habitual abortion. Acta Obstetricia et Gynaecologica Japon 1992;44:650–6.

62. Asukai K, Uemura T, Minaguchi H. Occult hyperprolactinemia in infertile women. Fertil Steril 1993;60:423–7.

63. Yamaguchi M, Aono T, Koike K, Nishikawa Y, Ikegami H, Miyake A, et al. Effects of nocturnal hyperprolactinemia on ovarian luteal function and galactorrhea. Eur J Obstet Gynecol Reprod Biol 1991; 39:187–91

64. FERTILITY AND STERILITY : Hyperprolactinemic recurrent miscarriage and results of randomized bromocriptine treatment trials. Fumiki Hirahara, M.D., Noriko Andoh, M.D., Kaori Sawai, M.D., Tomoo Hirabuki, M.D., (vol. 70, no. 2, August 1998).

65. Maternal age and fetal loss: population based register linkage study Anne-Marie Nybo Andersen, Jan Wohlfahrt, Peter Christens, Jørn Olsen, Mads Melbye ; BMJ volume 320 24 June 2000 :1708-12.

66. Prevalence of serum thyroid hormones and menstrual irregularities with infertility in Uttar Pradesh,Iindia, Neha Sharma et al Journal: International Journal of Pharmaceutical Sciences and Research Volume: 3; Issue: 9; Start page: 3454; Date: 2012;

67. Hakim RB, Gray RH, Zacur H. Infertility and early pregnancy loss. Am J Obstet Gynecol 1995;172:1510-7.

68. Vol. 41, 3, 2002 ; Role of hyperprolactinemia in fertility. Azima Kalsum, Samina Jalali. Department of Biological Sciences, Quaid-e-Azam University Islamabad, Pakistan.

69. Ashoor G, Maiz N, Rotas M, Jawdat F, Nicolaides KH 2010. Maternal thyroid function at 11 to 13 weeks of gestation and subsequent fetal death. Thyroid 20:989–993.

70. Vinita D, Anjoo A, Premlata Y, Agarwal CG. Endocrinological factors and recurrent abortion. J Obstet Gynecol India 2003;53:234-6.

71. Stray-Pedersen B, Stray-Pedersen S. Etiologic factors and subsequent reproductive performance in 195 couples with a prior history of habitual abortion. Am J Obstet Gynecol 1984;148:140-6.

72. Hamilton-Fairley D, Kiddy D, Watson H, Paterson C & Franks S 1992 Association of moderate obesity with a poor pregnancy outcome in women with polycystic ovary syndrome treated with low dose gonadotrophin. British Journal of Obstetrics and Gynaecology 99 128–131

PROFORMA

Name: IP.No:

Age: PH.No:

Address:

MENSTRUAL HISTORY:

Age at Menarche:

Cycles: Regular/Irregular:

Duration: LMP:

MARITAL HISTORY:

Married for

Consanguinity:

OBSTETRIC HISTORY:

PAST HISTORY: not a known diabetic/ hypertension/thyroid disorders.

Family History:

Abortion

Infertility

Diabetes

PERSONAL HISTORY:

HUSBAND:

Age:

Occupation:

Smoking/alcohol:

MEDICAL HISTORY:

GENERAL EXAMINATION:

Height			
Weight	BMI	Breast	
Thyroid		BP	
Pulse		Cvs/Rs:	P/A: P/S: P/V:

INVESTIGATIONS

Hb%

Urine Routine

Blood sugar:

S.urea:

S.creatinine:

Blood group:

VDRL:

HIV:

HBsAg:

Pelvic Ultrasonogram:

SPECIFIC INVESTIGATIONS:

Glucose Tolerance Test:

Thyroid Stimulating Hormone:

S.Prolactin:

ABBREVATIONS USED IN MASTER CHART

R	–	Regular cycles
IR	–	Irregular cycles
CM	–	consanguineous marriage
NCM	–	Non consanguineous marriage
G	–	Gravida
P	–	para
L	–	live birth
A	–	Abortion
FH/DM	–	Family history of Diabetes Mellitus
FH/Thyroid	–	Family history of Thyroid
BMI	–	Body Mass Index
GTT	–	Glucose Tolerance Test
FBS	–	Fasting Bloog Sugar
TSH	–	Thyroid Stimulating Hormone
PCOS	–	Polycystic Ovarian Disease
SLE	–	Systemic Lupus Erythematosus
LAC	–	Lupus AntiCoagulant
LN	–	Labour Naturale
LSCS	–	Lower Segment Ceasarean Section
IUD	–	Intrauterine Death
AP Eclampsia	–	Antepartum Eclampsia

MASTER CHART

Name	Age	IP No	Menstrual History	Marital History	Infertility	Score	6-9wks	9-12wks	FH/ DM	FH/ THYROID	BMI	GTT		TSH	Prolactin	Others
												FBS	2HR			
Suganya	20	2486	R	CM	NO	A3	2	1	0	0	19.3	92	120	3.4	14	PCOS
Sasikala	20	2811	R	CM	YES	A2	1	1	0	0	27.3	86	132	5	8	N
Sivagami	20	7824	R	NCM	NO	A2	0	2	0	0	27.3	82	114	3.8	18	N
Revathy	21	6978	R	NCM	NO	A3	1	2	0	1	21.3	96	112	3.2	9	N
Rubini	22	9285	IR	CM	NO	A3	0	3	1	0	27.8	85	124	3.9	14	PCOS
vanitha	22	6394	IR	NCM	NO	A2	2	0	0	0	23.6	90	125	2.8	16	N
Gayathri	22	12749	R	NCM	NO	A4	1	3	0	0	24.8	83	110	6.5	12	PCOS
Sheela	22	9633	IR	NCM	NO	A2	2	0	0	0	18.9	82	126	5.5	17	PCOS
Pattu	22	9318	R	NCM	NO	A2	0	2	0	0	22	78	125	3.9	8	N
Pavithra	22	8649	R	NCM	NO	A2	1	1	0	0	23.4	82	132	2.8	14	N
Manimegalai	22	8310	IR	NCM	NO	A4	2	2	0	1	26.4	81	112	6.8	13	N
Nirmala	23	4111	R	CM	NO	A3	0	3	1	0	23.6	95	125	2.7	15	N
Lakshmi	23	2096	R	NCM	NO	A2	0	2	0	0	22.1	91	136	3.5	18	N
Rasathi	23	6729	R	NCM	NO	A2	2	0	1	0	22	92	128	3.6	6	N
radhika	23	6295	IR	NCM	NO	A3	1	2	0	0	24.1	86	132	2	16	N
sathya	24	4148	IR	CM	YES	A4	3	1	0	1	27.8	88	115	8.7	14	N
Meena	24	5762	R	CM	NO	A3	0	3	0	0	19.7	79	125	4.8	18	N

Name	Age	IP No	Menstrual History	Marital History	Infertility	Score	6-9wks	9-12wks	FH/ DM	FH/ THYROID	BMI	GTT		TSH	Prolactin	Others
												FBS	2HR			
Shalini	24	3720	IR	NCM	YES	A4	2	2	0	0	19.2	81	133	6.8	14	N
Nethravathi	24	11365	R	NCM	NO	A2	0	2	0	0	26.8	85	128	4.2	12	N
Jeeva	24	6743	R	NCM	NO	A2	1	1	0	0	21	82	138	3.5	18	N
Menaga	24	6049	IR	NCM	NO	A4	1	3	0	1	19.4	83	129	9.2	14	N
Nirmaladevi	24	5461	R	NCM	NO	A2	1	1	1	0	19.7	92	138	3.8	18	N
Sathya	25	14390	IR	NCM	NO	A3	2	1	0	0	27.2	91	125	3.5	12	N
Susheela	25	4739	R	NCM	NO	A2	0	2	0	0	24.8	73	113	3.5	11	N
Devi	25	2904	R	NCM	NO	A2	0	2	0	0	23.2	84	136	3.8	14	N
Umadevi	25	2098	R	NCM	NO	A3	1	2	0	1	26.2	86	132	2.9	17	N
Kumari	25	12081	R	NCM	NO	A2	2	0	0	0	25.8	82	126	4.2	8	N
Revathy	26	7810	R	CM	NO	A3	0	3	0	0	19.4	75	119	3.6	12	N
Jeyalakshmi	26	4710	R	NCM	NO	A3	1	3	0	0	20.8	71	132	3.4	9	N
Malar	26	11057	R	NCM	NO	A2	1	1	1	0	25.4	86	128	2.8	11	N
Sagayamary	26	8120	IR	NCM	YES	A4	3	1	0	0	19.6	98	126	8.5	26	N
Nirmala	27	2151	R	NCM	NO	A4	1	3	1	0	28.6	94	119	6.7	11	N
Priya	27	7218	R	NCM	NO	A3	3	0	0	0	29.3	86	123	3.2	14	N
Rekha	27	3711	R	CM	YES	A4	3	1	0	0	28.4	84	138	35	12	N
Valli	27	3011	IR	NCM	YES	A4	1	3	0	0	29.5	72	133	3.1	9	PCOS
Malliga	27	9483	IR	NCM	NO	A3	2	1	0	0	21	128	238	2.6	14	N

Name	Age	IP No	Menstrual History	Marital History	Infertility	Score	6-9wks	9-12wks	FH/ DM	FH/ THYROID	BMI	GTT		TSH	Prolactin	Others
												FBS	2HR			
Kamala	27	10241	R	NCM	NO	A2	1	1	0	0	26.8	86	120	2.5	6	N
Shenbegam	27	4127	R	CM	NO	A4	2	2	0	0	25.2	81	125	2.9	15	N
Mahalakshmi	27	9285	IR	CM	yes	A3	1	2	0	0	23.4	88	108	10	12	N
Anandhi	27	7924	R	NCM	NO	A3	1	2	0	0	21.8	91	135	2.3	8	N
Jaya	28	7010	IR	NCM	NO	A5	3	2	0	0	24.2	92	138	6	15	N
valarmathy	28	7111	IR	NCM	NO	A4	2	2	0	0	27.8	75	125	3.6	9	PCOS
Nirmala	28	3618	R	NCM	NO	A2	0	2	0	0	20.8	78	124	2.6	16	N
Kamali	28	5230	R	NCM	NO	A3	2	1	0	0	22.6	94	108	3.2	13	N
sumathi	28	6840	R	NCM	NO	A5	2	3	0	0	20.5	72	114	12	14	N
Nithya	28	3528	R	NCM	NO	A2	1	1	0	0	26.3	68	126	3.2	18	PCOS
Pownamal	28	4697	R	NCM	NO	A4	2	2	0	0	19.2	70	135	2.6	11	N
Devi	28	8446	IR	NCM	NO	A4	2	2	0	1	21.2	88	122	5.2	10	N
Janaki	28	11016	R	CM	NO	A3	1	2	0	0	23.6	98	116	2.3	9	N
Latha	28	10235	R	NCM	NO	A2	0	2	1	0	23.3	89	103	2.6	12	N
Neela	28	8341	R	NCM	NO	A2	2	0	0	1	21.3	84	128	3.5	14	N
Dhanalakshmi	28	8340	R	NCM	NO	A5	1	4	0	0	28.9	91	138	3.6	12	N
mythili	29	4309	R	CM	NO	A4	0	4	0	0	25.2	92	124	6	17	N
Maheshwari	29	8156	IR	NCM	YES	A2	2	0	0	1	26.9	88	126	3.2	33	N
Banumathy	29	9624	R	NCM	NO	A3	0	3	0	1	23.8	85	124	3.5	13	N

Name	Age	IP No	Menstrual History	Marital History	Infertility	Score	6-9wks	9-12wks	FH/ DM	FH/ THYROID	BMI	GTT		TSH	Prolactin	Others
												FBS	2HR			
Sudha	29	7924	IR	CM	NO	A3	1	2	0	0	24.1	86	132	3.4	17	PCOS
Kumudha	30	6910	R	NCM	NO	A3	3	0	0	0	20.8	75	132	4	8	N
Nagalakshmi	30	8502	R	CM	NO	A4	2	2	0	0	29.6	72	120	3.5	12	N
Savithri	30	7051	IR	NCM	YES	A6	2	4	0	0	28.3	88	115	6.2	14	PCOS
Rekha	30	12091	IR	NCM	NO	A3	0	3	0	0	22	86	126	3.2	9	SLE
Rajeshwari	30	6284	R	CM	NO	A4	2	2	0	0	28.4	81	132	3.5	15	N
vanitha	30	5983	R	NCM	NO	A4	2	2	0	0	22.1	83	138	2.9	14	N
Reshma	30	10947	IR	NCM	NO	A4	2	2	1	0	22.6	94	106	3.5	16	N
Jaya	31	7020	IR	NCM	NO	A4	2	2	1	0	28.2	132	224	2.9	15	N
Sangeetha	31	9371	IR	NCM	NO	A2	2	0	0	0	25.6	158	242	3.2	9	N
Bharathi	31	7205	R	NCM	NO	A4	1	3	0	0	26.2	88	138	3.5	17	N
Leelavathy	31	15293	IR	NCM	NO	A4	1	3	0	1	25.8	84	132	3.6	14	N
Kamatchi	32	6581	R	NCM	NO	A4	0	4	0	0	25.2	91	108	3	13	N
Uma	33	7639	IR	NCM	YES	A5	2	3	0	1	27.8	91	132	6	26	N
Sasikala	34	4238	R	NCM	NO	A4	2	2	0	0	25.8	88	138	3.5	12	N
Thilagavathy	34	10283	R	NCM	NO	A4	2	2	0	0	28.6	91	116	3.1	16	N
Hemalatha	35	6811	R	NCM	NO	A6	3	3	0	0	30.2	138	253	2.9	7	N
Rani	35	4323	R	NCM	NO	A4	0	4	0	0	31.2	82	128	2.6	9	N
Anjugam	36	1089	R	CM	NO	A4	2	2	1	0	27.8	88	119	2.4	15	N

Name	Age	IP No	Menstrual History	Marital History	Infertility	Score	6-9wks	9-12wks	FH/ DM	FH/ THYROID	BMI	GTT		TSH	Prolactin	Others
												FBS	2HR			
Rajathi	36	7493	R	NCM	NO	A4	2	2	0	0	27.6	86	127	3.2	10	N
Kanagavalli	38	13268	R	NCM	NO	A5	2	3	0	0	28.8	89	128	3.4	14	N
Revathy	24	3529	IR	NCM	YES	P1L1A4	2	2	0	0	28.4	78	136	8.6	8	PCOS
Priya	27	3611	IR	NCM	YES	P1L1A4	2	2	0	0	24.1	95	132	3.6	13	N
Rajeshwari	27	5092	R	NCM	NO	P1L1A2	2	0	0	0	18.6	83	128	3.5	15	N
Hemalatha	36	8212	R	NCM	YES	P1L1A4	1	2	0	0	23.8	92	138	3.6	16	N
Amaramma	32	8410	IR	CM	YES	P1L1A3	2	1	0	0	25.6	95	121	3.9	16	PCOS

Name	Age	IP No	Menstrual History	Marital History	Infertility	Score	6-9wks	9-12wks	FH/DM	FH/ THYROID	BMI	GTT 2hr	TSH	Prolactin	Others
Suganya	19	13211	R	NCM	NO	G3A2	1	1	1	0	19.7	120	2.2	34	PRETERM LN
Kalpana	20	13204	IR	CM	NO	G3A2	1	1	0	0	19.4	132	1.9	32	TERM ,LN
Radhika	24	14410	R	CM	NO	G4A3	1	2	0	1	23.4	126	3.4	33	LAC +VE TERM LN
Valli	24	2111	R	NCM	NO	G4A3	2	1	0	0	26.4	113	2.1	36	PRETERM LN
Anjali	26	6061	R	NCM	NO	G3A2	1	1	0	0	28.3	136	2.1	33	TERM LSCS
Saraswathy	26	5293	R	CM	NO	G3A2	0	2	0	0	26.4	116	2	36	TERM LN
Sathya	27	4111	IR	NCM	NO	G4A3	2	1	0	0	27.8	127	2	33	TERM LN
Karthika	28	8210	IR	NCM	NO	G5A4	2	2	0	0	22.6	134	1.9	34	TERM LN
Geetha	28	9205	R	NCM	NO	G5A4	2	2	0	0	28.8	130	3	38	TERM LN
Komala	28	6577	R	NCM	NO	G3A2	0	2	0	0	22.1	129	1.6	33	TERM LSCS
Hemavathy	30	4011	R	NCM	NO	G10A9	4	5	0	0	22.6	122	2	33	TERM LSCS
Chitra	31	5396	IR	NCM	NO	G10A9	3	6	0	1	26.5	112	2.1	35	ABORTED AT 6mA
Alice	38	4261	IR	CM	YES	G4A3	2	1	0	0	29.5	160	1.9	37	TERM LSCS
Subedha begum	26	1039	R	NCM	NO	G5P1L1A3	1	2	0	1	21.9	128	1.9	35	TERM LSCS
Sasikala	27	14469	IR	NCM	NO	G5P1L1A3	0	3	0	0	26.8	112	2.1	37	AP ECLAMSIA IUD
Girija	28	13627	R	NCM	YES	G6P1L1A4	2	2	0	1	25.2	113	2.1	35	LAC +VE TERM LN
shyamala	28	9838	R	NCM	NO	G3P1L1A2	1	1	0	0	24	129	1.5	36	TERM LN
Mariammal	32	6396	R	NCM	NO	G5P1L1A3	1	2	0	0	25.5	132	1.8	35	PRETERM LN
Shyamala devi	33	3811	R	CM	NO	G6P1L1A4	3	1	1	0	22.4	127	2	34	PRETERM LN

ETHICAL COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE, KILPAUK,
CHENNAI- 10.
Venue: PANAGAL HALL, KMC
Dt: 01.02.2011

CHAIRPERSON
Prof. Dr.V.KANAGASABAI, MD.,
Dean
Govt. Kilpauk Medical College, Chennai-10

Sub: Ethical Committee project work - approved – regarding.
Ref: Lr.No.3944/Audit/E1/09 Dt. 30.11.2010

****

With above reference, the Institutional Ethical committee meeting for the following students was conducted at our Institution on 01.02.2011.

S.NO.	Name	Topic
1.	Dr.Navin Kumar, MS(Ortho), PG., Govt. Royapettah Hospital, Chennai.	1.To Identify a Safe Zone to approach proximal Humerus 2.To study Anatomical relations of Axillary nerve, its course & its Variations
2.	Dr.T.Satheesh Kumar, D.Ortho., PG., Govt. Royapettah Hospital, Chennai	Heriditary Multiple Exostosis
3.	Dr.J. Jeya Shambavi, MD(Pathology), PG., Kilpauk Medical College, Chennai-10	Clinicopathological Histomorphological and Immunohistochemical Study of Neuroendocrine Tumors of GIT
4.	Dr.L. R. Saranya. MD., (Paed.)PG., Kilpauk Medical College, Chi-10	Cord Blood Zinc Level in Term-Small for Gestational Age Neonates
5.	Dr.A.Satheesh Kumar, MS(ENT), PG., Kilpauk Medical College, Chennai	Study on Cases of Chronic Suppurative Otitis Media in Tubo Tympanic Type Due to Sinusitis as Focal Sepsis
6.	Dr.R.Parthiban,(Msc.,Physiology), PG., Kilpauk Medical College,Ch-10	Prevalence of Cardiac Dysautonomia in Type I Diabetes mellitus
7.	B. Manikandan, (Msc., Physiology), PG., Kilpauk Medical College, Chennai-10	A Comparative Study of Left Ventricular Structure and Function in Obese and Non Obese Subjects
8.	G. Selvakumar, (MSc., Physiology),	A Study of the Intraocular Pressure In

9.	R. Ragulji, (Msc.,Physiology), PG., Kilpauk Medical College, Ch-10	A Study of Pulmonary function in insulin dependent diabetes mellitus
10.	V.M. Jenila Vemy, (Msc..Physiology). PG..Kilpauk Medical College, Chennai-10	Cardiovascular Autonomic Dysfunction in Chronic Kidney Disease
11.	Dr.G. Lakshmi, MD(O&G), PG., Kilpauk Medical College, Ch-10	A Study of Association of Thyroid Disorders in Abnormal Uterine Bleeding
12.	Dr.R. Harini, MD(O&G), PG., Kilpauk Medical College, Chennai	Single Dose Antibacterial treatment for Asymptomatic Bacteriuria in Pregnancy
13.	Dr.E.Geetha, MD(O&G), PG., Kilpauk Medical College, Chennai	A Study of the incidence course of Pregnancy and Pregnancy outcome in Obstetric Cholestasis and to evaluate the efficiency of UDCA in relieving the Symptoms and Improving the Perinatal outcome in these Patients
14.	Dr.S. Nithya, MD(O&G), PG., Kilpauk Medical College, Chennai	Prospective Study of Prevalence of diabetes Mellitus, Thyroid Dysfunction and Hyperprolactinemia in Recurrent Pregnancy loss
15.	Dr.Mohideen Fathima, MD(O&G), PG., Kilpauk Medical College, Chennai	A Study of evaluation of multi system changes in Gestational hypertension / severe pre-eclamptic/eclampasia patients
16.	Dr.M.Padma Priya, MD(O&G), PG., Kilpauk Medical College, Chennai	Dyslipidemia – as a Predictor of PIH
17.	Mrs.G. Savitha, (Msc.,Medical Bio Chemistry), Kilpauk Medical College, Chennai-10	Association of subclinical hypothyroidism in metabolic syndrome patients
18.	Dr.K. Bharadhwaj, MD(G.M.), PG., Kilpauk Medical College, Ch-10	A Study on Peripheral Vascular Disease in Type 2 Diabetes Mellitus
19.	Dr.B.Priya, MD(G.M.), PG	Study of Serum Bilirubin Concentration in Established Coronary Artery Disease
20.	Dr.R.Hema, MD(G.M.), PG.,	Study of Troponin I level in Supraventricular Tachycardia in Non Cad Patients
21.	Dr.P.Manoj Kumar, MD(G.M.), PG., Kilpauk Medical College, Ch-10	A Study on Pulmonary Functions in Type 2 Diabetes Mellitus
22.	Dr.M.Dhanasekar, MD(G.M.), PG.,	Prognostic Risk Stratification of Acute Coronary Syndrome – Role of Highly Sencitive – Reactive Protien
23.	Dr.N. Karthik, MD(G.M.), PG., Kilpauk Medical College, Chennai-10	A Study of Comparison of QT Dispersion in Acute Myocardial Infraction Between Early Reperfusion and Late Reperfusion Therapy

24.	Dr.H. Anuradha, MD(G.M.), PG., Kilpauk Medical College, Ch-10	A Study of Stress Hyperglycemia in Moderate Degree Burns
25	Dr. V. Nandakumar, MD(G.M.), PG.,	A Prospective Study of Clinical Profile of Emphysematous Pyelonephritis in Type Two Diabetes Mellitus
26.	Dr.S.Sasikumar, MS(G.S.), PG., Govt. Royapettah Hospital, Chennai	A Study of Unusual Presentations of Appendicitis.
27.	Dr.S.R.Padmanabhan, MS(GS), PG., Govt. Royapettah Hospital, Chennai	A Comparative Study Between Autologous Platelet Rich Plasma and Saline Dressing for Diabetic Ulcer
28.	Dr.C.Rose, Scientist-G and Head, Biotechnology, Central Leather Institute, Chennai.	Wound healing efficacy of the chitosan –containing collagenous biomaterial on burn wound
29.	E.K. Lavanya,B.Tech, Biotechnology, PG., Prathyusha Institute of Technology and Management, Tiruvallur.	Isolation and Characterization of Bacterial Pathogens from Eye Infection

We are glad to inform you that at the Ethical Committee meeting, the documents were discussed and the above short term projects are Ethically approved.

9/2/11

CHAIRPERSON
DEAN
Govt. Kilpauk Medical College,
Chennai-10.

To: The Individuals

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு :

மகளிர் மற்றும் மகப்பேறு மருத்துவத்துறை :

கீழப்பாக்கம் மருத்துவக்கல்லூரி :

பங்கு பெறுபவரின் பெயர் :

பங்கு பெருபவரின் வயது :

பங்கு பெருபவரின் எண் :

பங்கு பெறுபவர் இதனை (√) குறிக்கவும்.

- ❖ மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும் அதற்கான தகுந்த விளக்கற்களை கேட்க வாய்ப்பளிக்கப்பட்டடுள்ளது என அறிந்து கொண்டேன். ☐
- ❖ நான் இவ்வாய்வில் தன்னிச்சையாகத் தான் பங்கேற்கிறேன்.எந்த காரணத்தினாலோ எந்த சட்டசிக்களுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.ஷ ☐
- ❖ இந்த ஆய்வு சம்பந்தமாகவோ அதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போது இந்த ஆய்வில் பங்கு பெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறோன். ☐
- ❖ இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ முடிவையோ பயன்படுத்திக் கொள்ள மறுக்கமாட்டோன். ☐
- ❖ இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உன்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். ☐
- ❖ இந்த ஆய்வில் ஒருமுறை 5 மி இரத்த பரிசோதனைக்காக எடுத்தக் கொள்ளப்படும் என்பதை அறிவேன்.

பங்கேற்பவரின் கையொப்பம்_____

இடம்_____ தேதி_____

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்
சாட்சியாளரின் கையொப்பம்

இடம்_____ தேதி_____

சாட்சியாளரின் பெயர் மற்றும் விலாசம்

ஆய்வாளரின் கையொப்பம்

இடம்_____ தேதி_____

ஆய்வாளரின் பெயர்_____