CORRELATION OF HYPERPROLACTINEMIA WITH HYPOTHYROIDISM IN INFERTILE WOMEN

A Dissertation Submitted to

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY

CHENNAI

In Partial fulfilments of the Regulations

for the Award of the Degree of

M.S. (OBSTETRICS & GYNAECOLOGY)

BRANCH – II

Reg. No. 221716054

GOVERNMENT STANLEY MEDICAL COLLEGE

CHENNAI

MAY 2020

CERTIFICATE BY THE INSTITUTION

This is to certify that dissertation titled **CORRELATION OF HYPERPROLACTINEMIA WITH HYPOTHYROIDISM IN INFERTILE WOMEN** is a bonafide work done by **Dr.T.RAMYA** at R.S.R.M. Lying in Hospital ,Stanley Medical College, .This dissertation is submitted to Tamilnadu Dr M.G.R. Medical University in partial fulfillment of university rules and regulations for award of M.S. Degree in Obstetrics and Gynaecology.

Prof.Dr .R. SHANTI MALAR, M.D, D.A.
DEAN
Stanley Medical College and Hospital,
Chennai -600001

Dr. K.KALAIVANI, M.D.,D.G.O.,DNB.
Superintendent
Government RSRM Lying In Hospital,
Stanley Medical College,
Chennai-600013

CERTIFICATE BY THE GUIDE

This is to certify that this dissertation entitled **"CORRELATION OF HYPERPROLACTINEMIA WITH HYPOTHYROIDISM IN INFERTILE WOMEN"** submitted by **Dr .T.RAMYA** appearing for Part II MS,Branch II Obstetricsand Gynaecology Degree Examination in May 2020 ,is a bonafide record ofwork done by her ,undermy direct guidance and supervision as per the rules and regulations of the Tamil Nadu Dr MGR Medical University,Chennai,Tamil Nadu India. I forward this dissertation to the Tamil Nadu Dr .MGR Medical University Chennai, India.

Dr. G.KUPPULAKSHMI,M.D,OG
Professor ,
Dept. of Obstetrics and Gynaecology
Government RSRM Lying in Hospital
Stanley Medical College, Chennai

DECLARATION

I **Dr .T.RAMYA**, solemnly declare that the dissertation entitled**,** **"CORRELATION OF HYPERPROLACTINEMIA WITH HYPOTHYROIDISM IN INFERTILE WOMEN"** is a bonafide work done by me at R.S.R.M. Lying in Hospital .Stanley Medical college ,Chennai-during April 2019-to November 2019 under the guidance and supervision of **Prof. Dr.K.Kalaivani M.D.,D.G.O.,D.N.B.,** Professor and Head of Department ,Obstetrics and Gynaecology. The dissertation is submitted to the Tamilnadu Dr.M.G.R.Medical University, in partial fulfillment of University rules and regulations for the award of M.S.Degree in Obstetrics and Gynaecology.

Place: Chennai

Date:

Dr.T.RAMYA

ACKNOWLEDGEMENT

I am grateful to Prof .**Dr.SHANTHI MALAR, M.D., D.A**. Dean , Govt. Stanley Medical College for granting me permission to undertake this study. I take this opportunity to express my sincere and humble gratitude to **Dr.K.Kalaivani , M.D., D.G.O., D.N.B.**, Superintendent, Govt. R.S.R.M. Lying in Hospital who not only gave me the opportunity and necessary facilities to carry out this work. I am deeply indebted to **Prof. Dr .G. KUPPULAKSHMI, M.D**. the mover behind the study for her able guidance and inspiration.

I am very grateful to RMO **Dr. ANITHA VIRGIN KUMARI M.D.,D.G.O** for her invaluable advice ,constant guidance and supervision during the study.

I am extremely grateful to all the Assistant Professors, for their advice and support during this study.

I thank my fellow postgraduates and friends for their support and cooperation.

I thank all my patients without whom this study would not have been possible.

Finally I thank Lord Almighty for showering blessings to complete this work.

TABLE OF CONTENTS

S.No.	Title	Page No.
1	INTRODUCTION	1 – 40
2	AIM OF STUDY	41
3	REVIEW OF LITERATURE	42 – 47
4	MATERIALS AND METHODS	48 – 54
5	RESULTS	55 – 73
6	DISCUSSION	74
7	SUMMARY	75
8	CONCLUSION	76
9	BIBLIOGRAPHY	77 – 81
10	ANNEXURES • Proforma • Consent Form • Ethical Committee Approval Form • Master Chart	82 – 97

ABBREVIATIONS

TSH	Thyroid Stimulating Hormone
TRH	Thyrotropin Releasing Hormone
HH	Hypogonadotropic Hypogonadism
GnRH	Gonadotropin Releasing Hormone
LH	Luteinizing Hormone
FSH	Follicle Stimulating Hormone
BMI	Body Mass Index
SD	Standard Deviation
IVF	Invitro Fertilisation
PCOS	Polycystic Ovaian Syndrome
POI	Primary Ovarian Insufficiency
POF	Premature Ovarian failure
S.NO	Serial Number.
OP.NO	Outpatient number
IP.NO	Inpatient number

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **CORRELATION OF HYPERPROLACTINEMIA WITH HYPOTHYROIDISM IN INFERTILE WOMEN** of the candidate **Dr.RAMYA T.** with Registration Number **221716054** for the award of **MASTER OF SURGERY** in the branch of **OBSTETRICS AND GYNAECOLOGY.**

I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **7** percentage of plagiarism in the dissertation.

GUIDE AND SUPERVISOR SIGN WITH SEAL

URKUND

Urkund Analysis Result

Analysed Document: theziz2.docx (D58483690)
Submitted: 11/8/2019 9:14:00 AM
Submitted By: jahnavi3636@gmail.com
Significance: 7 %

Sources included in the report:

new thyroid final copy 2.docx (D42475965)
1 Sunita Ramanand Draft thesis 26-05-2018.pdf (D47845823)
https://www.ijmedicine.com/index.php/ijam/article/view/225
https://www.ncbi.nlm.nih.gov/pubmed/2129207
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4188020/
https://www.researchgate.net/publication/324522754_CORRELATION_OF_PROLACTIN_LEVELS_WITH_THYROID_HORMONE_LEVELS_IN_THYROID_DISORDERS_INFERTILITY_AND_MENSTRUAL_DISORDERS
https://www.ijrcog.org/index.php/ijrcog/article/download/383/371
https://www.researchgate.net/publication/26502528_Study_of_Primary_Infertility_in_females_by_Diagnostic_Laparoscopy
https://www.researchgate.net/publication/10793116_Thyroid_disorders_in_infertile_women

Instances where selected sources appear:

17

INTRODUCTION

INTRODUCTION

DEFINITION OF INFERTILITY

Failure to conceive within one or more years of regular unprotected coitus.

Primary infertility patients have never conceived ,while secondary infertility indicates previous pregnancy but failure to conceive subsequently.

Under ordinary circumstances 80-90%of normal couples conceive during one year of attempting pregnancy.

DEFINITION OF FECUNDABILITY

It is the probability of achieving a pregnancy within one menstrual cycle. In a healthy couple it is 20%.

Fecunditity deals with child bearing ability and fertility deals with childbearing performance.

DEFINITION OF CHILDLESSNES

It is defined as women who are currently married for more than 5 years, currently not pregnant, having no terminated pregnancy, never used contraceptives and have no living children portrays similar levels and patterns to that of infertility.

AVERAGE CONCEPTION RATES FOR COUPLES

PERCENTAGE OF COUPLES	LENGTH OF TIME BEFORE CONCEPTION
20	Conceive in 1 month
60	Conceive in 6 months
75	Conceive in 9 months
80	Conceive in 12 months
90	Conceive in 18 months

ESSENTIAL FACTORS FOR CONCEPTION

- Healthy spermatozoa to be deposited high in vagina or near cervix- male factor
- Changes should occur in spermatozoa like capacitation and acrosome reaction and they acquire motility- cervical factor.
- Motile spermatozoa should ascend through cervix into uterine cavity
- Ovulation has to occur
- Patent fallopian tubes and oocyte should be picked up by fimbria- fimbrial factor.
- Fertilisation of oocyte by spermatozoa in the ampulla

For this to occur, male and female reproductive systems must be anatomically and physiologically intact, coitus must occur with sufficient frequency and at proper time i.e few hours before ovulation.

Even when fertilisation occurs, about 70% of embryos are abnormal and fail to develop or become nonviable soon after implantation.

PATHOPHYSIOLOGY OF INFERTILITY

Etiology	Incidence (%)
Male factor	***33***
Hypothalamic–pituitary disease	2
Testicular disease	35
Post-testicular defects in sperm transport	15
Idiopathic	45
Female factor	*45–55*
Ovulatory and ovarian factors	47
Peritoneal/tubal factors	13
Endometriosis	9
Uterine and cervical factors	6
Multiple female factors	12
Combined male and female factors	17
Unexplained infertility	***13***

Male partner brings to the union sperm laden semen, which is deposited in vagina during intercourse.

The ejaculate has volume of between 1 and 15 ml and contains more than 20 million spermatozoa.

Sperms survive in female genital tract for atleast 96 hours and sometimes for as long as 8 days.

Sperms are capable of fertilising an egg for 24-48 hours after ejaculation.

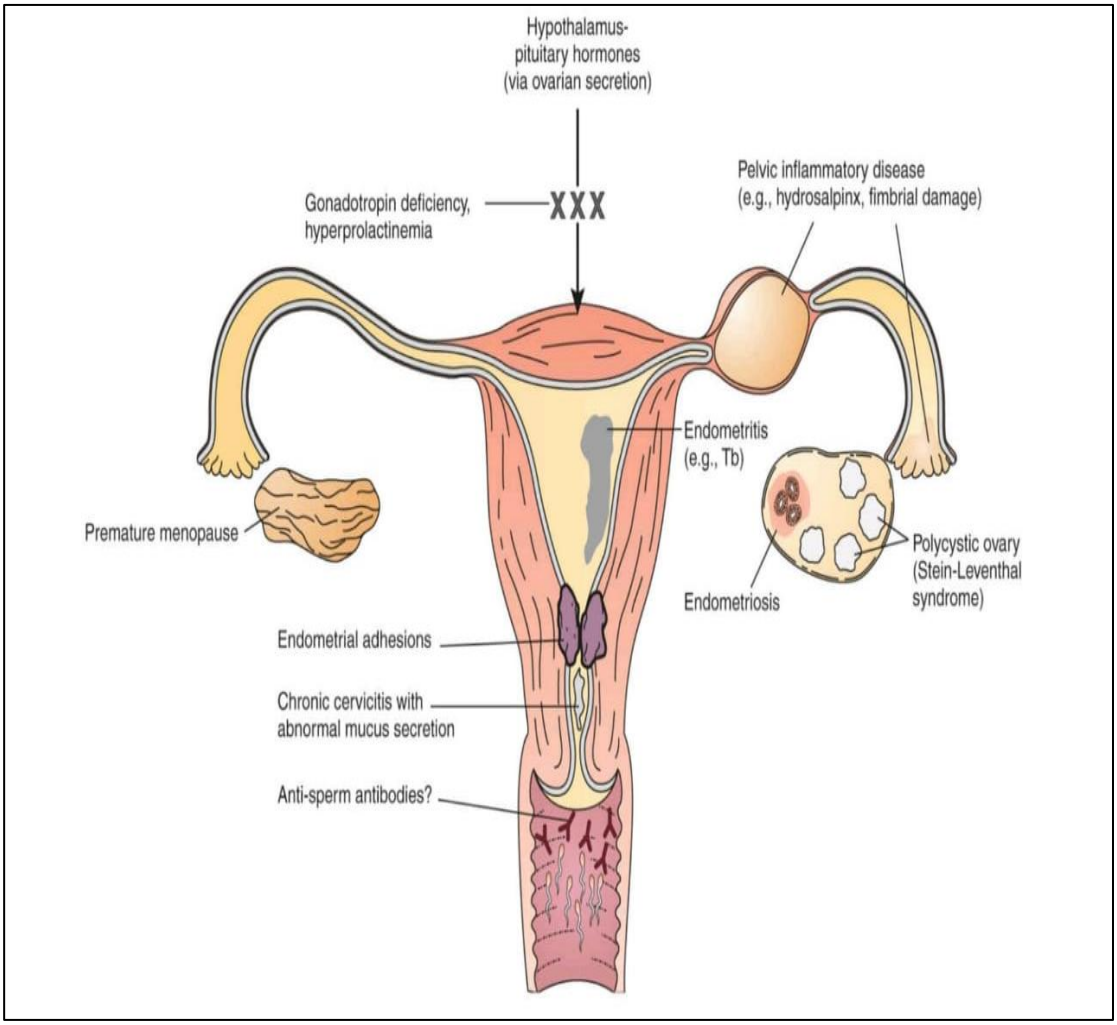
The oocyte is released from ovary during ovulation, i.e 14 days before onset of menstruation.

Progesterone is produced by luteinised follicle, causing increase of 0.5-1 Fahrenheit basal body temperature.

The oocyte may be fertilised during the first 24 hours after ovulation. It occurs in the distal fallopian tube.

For pregnancy to occur zygote passes into uterine cavity 3-5 days after fertilisation,and encounters a receptive endometrium.

CAUSES OF FEMALE FACTOR INFERTILITY



1.OVULATORY/OVARIAN

- Polycystic ovarian syndrome
- Advanced maternal age
- Primary ovarian insufficiency
- Hypothalamic amenorrhea
- Hyperprolactinemia

2.TUBAL FACTORS

- Pelvic inflammatory disease/Salphingitis
- Tubal ligation
- Endometriosis
- Pelvic adhesions

3.UTERINE FACTORS

- Congenital malformations
- Fibroids
- Uterine polyps
- Intrauterine Synechiae(Asherman syndrome)

4.CERVICAL FACTORS

- Mullerian duct abnormalities
- Cervical stenosis

OVULATORY/ OVARIAN DISORDERS

Disruption in hypothalamic-pituitary-gonadal axis at any level can result in menstrual disorders and infertility through impairment of folliculogenesis, ovulation ,and endometrial maturation

WHO CLASSIFICATION OF OVULATORY DISORDERS

Group1. Hypogonadotropic hypogonadal anovulation e.g hypothalamic amenorrhea

Group 2. Normogonadotropic normoestrogenic anovulation e.g. PCOS.

Group 3. Hypergonadotropic hypoestrogenic anovulation e.g. primary ovarian insufficiency (POI) and decreased ovarian reserve.

Group 4. Hyperprolactinemic anovulation

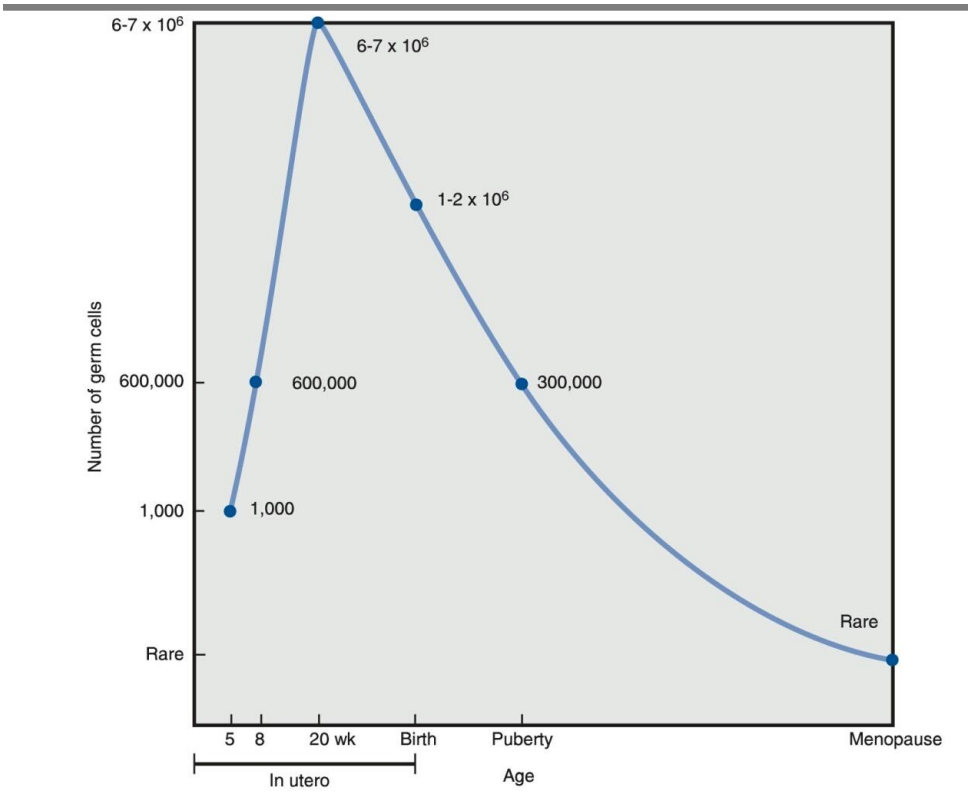
The most common ovulatory disorders causing infertility are PCOS and decreased ovarian reserve.

Oocyte aging is an important factor affecting female fertility.

During fetal life, the greatest number of germ cells are present in ovary, approximately 6-7 million in midgeststion.

The germ cell population then begins to decline exponentially by gene mediated apoptosis, numbering 1-2 million at birth and 30,000 at onset of puberty.

The number of viable follicles declines throughout reproductive years and rate of loss accelerates after mid30s.



During menopause ,ovary contains fewer than 1,000 follicles.

Factors that lead to decreased ovarian reserve include tobacco smoking, viruses, radiation, chemotherapy, autoimmune and genetic disorders.

When store of oocytes decreases to a point where a woman undergoes menopause before 40 years, the diagnosis is POI, known as premature ovarian failure(POF).

The age related decline in fecundability is due to both the decline in quantity and quality of oocytes.

The age related decrease in fertility is due to increase in rate of aneuploidy.

CAUSES OF ANOVULATORY INFERTILITY

1,Central

- Pituitary Insufficiency- trauma,tumour,congenital
- Hypothalamic insufficiency
- Hyperprolactinemia- drug,tumour,empty sella

2..Peripheral defects

- Gonadal dysgenesis
- Primary ovarian insufficiency(POI)
- Ovarian tumour
- Insulin resistance

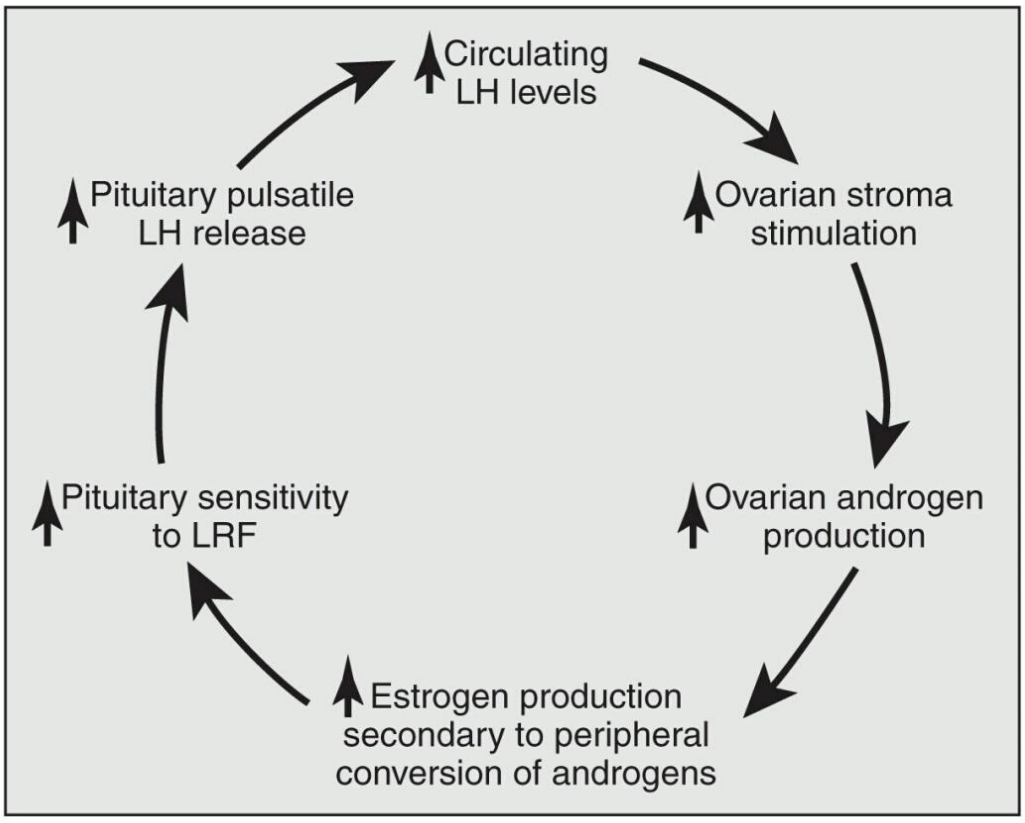
3.Metabolic disease

- Polycystic ovarian syndrome
- Thyroid disease
- Liver disease
- Obesity
- Androgen excess(adrenal,neoplastic)
- PCOS is the most common cause of oligo and anovulation in all women and those with infertility.

ROTTERDAM CRITERIA FOR DIAGNOSIS OF PCOS

Require the patient to have 2 of 3 findings once other causes of anovulation are ruled out

- Menstrual irregularity caused by oligoovulation or anovulation.
- Clinical or biochemical evidence of hyperandrogenism (hirsuitism, acne, male pattern balding, or elevated serum androgen concentration, and /or
- Presence of polycystic appearing ovaries



RISK FACTORS FOR PCOS

- Obesity.
- Insulin resistance
- Diabetes
- Premature adrenarche
- Positive family history of PCOS in first degree relatives.
- PCOS results in hyperinsulinemia which results in hyperandrogenism by stimulating androgen biosynthesis by ovary and decreasing sex hormone binding globulin.
- Hyperandrogenism leads to disruption of HPGA which manifest as infrequent or absent meses due to chronic anovulation.

STRATEGIES OF INVESTIGATING INFERTILITY

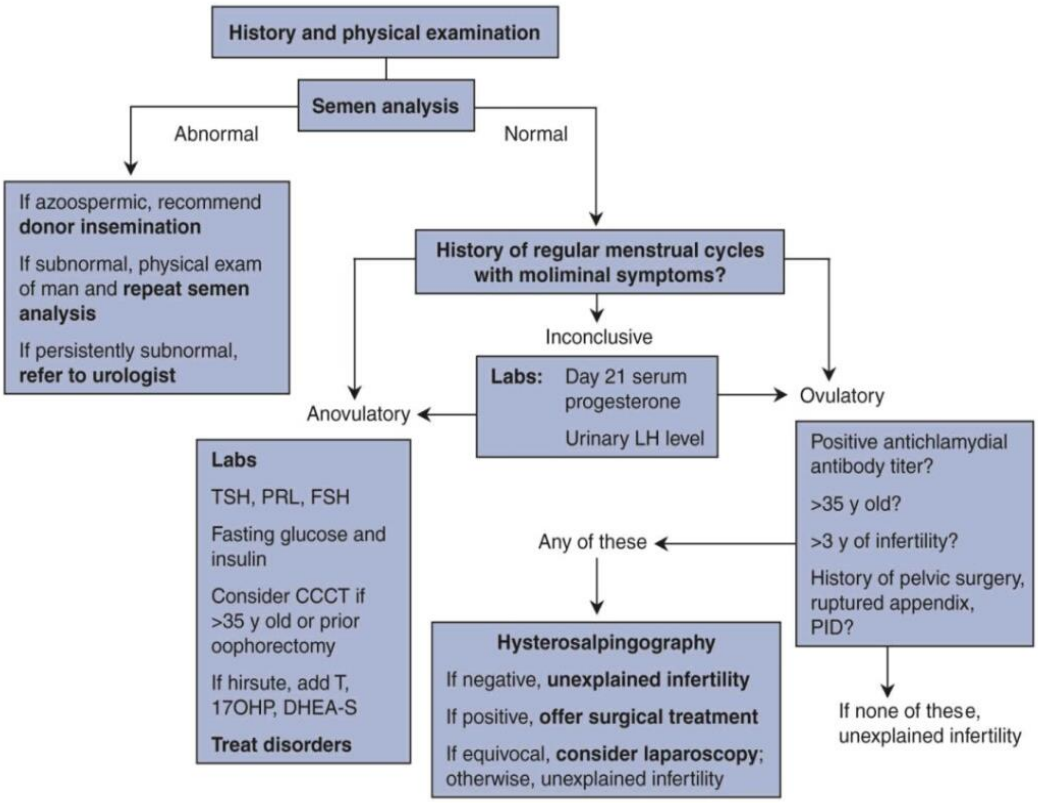
3 elements are necessary to achieve pregnancy.

- Sperm has to be available.
- Egg has to be available
- Egg and sperm must meet in a place conducive to fertilisation.

It is the investigation of these 3 elements that constitutes evaluation of infertile couple.

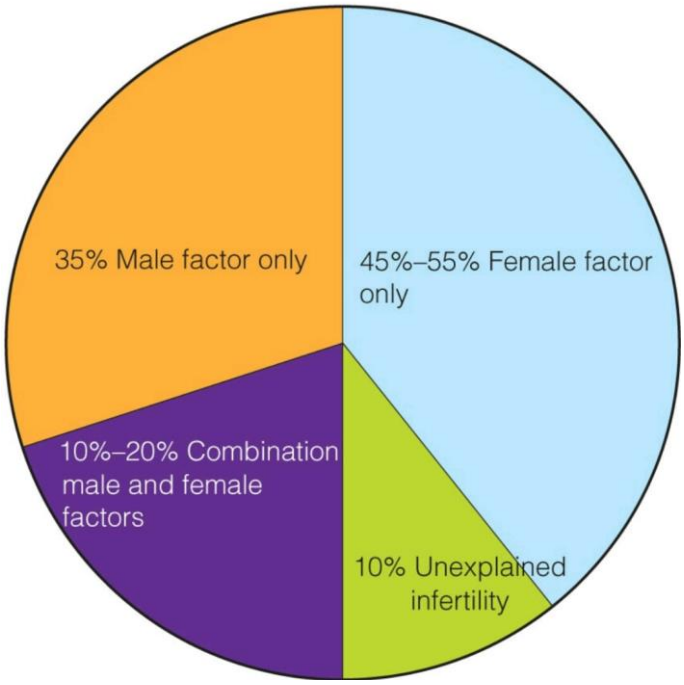
Age substantially decreases the rate of conception by lower embryo quality, reduced ovulation and reduced coital frequency.

It is reasonable to begin basic evaluation at 6 months in older patients and start treatment for unexplained infertility in women older than 35 years of age.



CAUSES OF INFERTILITY

- Male is responsible in 30-40% of cases.
- Female is responsible in 40-55% of cases.
- Both 10%
- Unexplained 10%



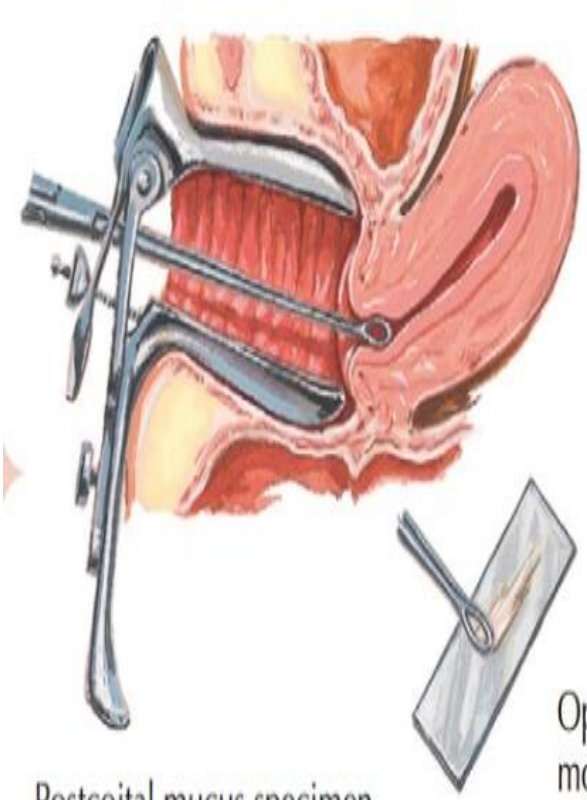
INVESTIGATION OF INFERTILITY

COMMON INFERTILITY FACTORS		
Factor	**Incidence (%)**	**Basic Investigations**
Male, coital	40	Semen analysis Postcoital test
Ovulatory	15-20	Urinary luteinizing hormone self-test*; serum progesterone*
Cervical	5	Postcoital test
Uterine, tubal	30	Hysterosalpingogram Laparoscopy
Peritoneal	40	Laparoscopy

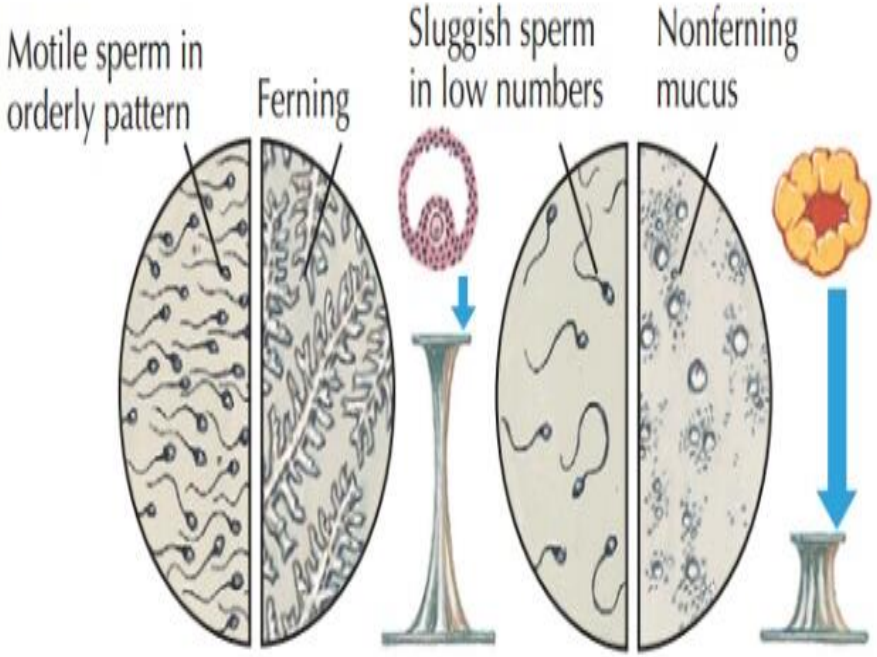
*Investigations only when menses are regular (every 22 to 35 days); oligomenorrhea generally requires treatment.

Evaluation and therapy is started earlier when obvious effects are identified, or they can be delayed when a correctable factor, like infrequent intercourse is identified.

First six to eight months of evaluation involves relatively simple and non-invasive tests and performance of radiologic evaluation of tubal patency by hysterosalphingography or hsg.



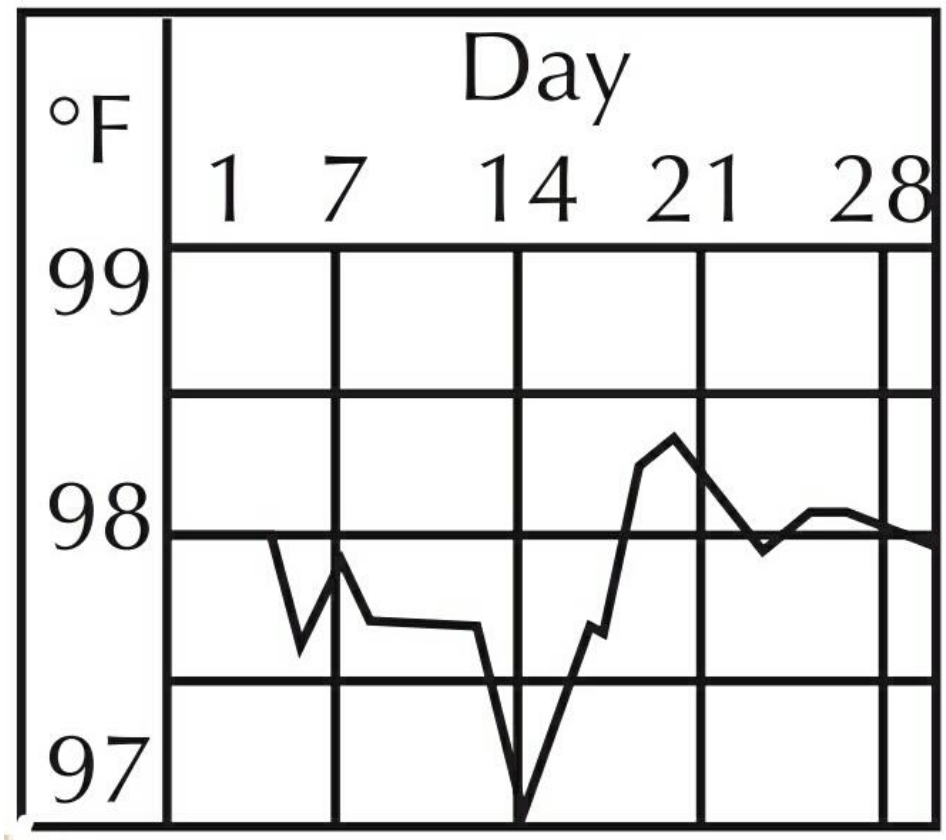
Postcoital mucus specimen from endocervical canal placed on slide for testing



Optimal postcoital test. Adequate motile sperm and cervical mucus with high water content. Increased ferning and spinnbarkeit

Suboptimal postcoital test. Few sluggish sperm in thick, cellular mucus. Decreased ferning and spinnbarkeit

Use of oil based dye in some cases doubled the success rate after HSG. Laproscopy is for a small proportion of couples who have not conceived after 18-24 months or have specific indications or a probable pelvic factor.

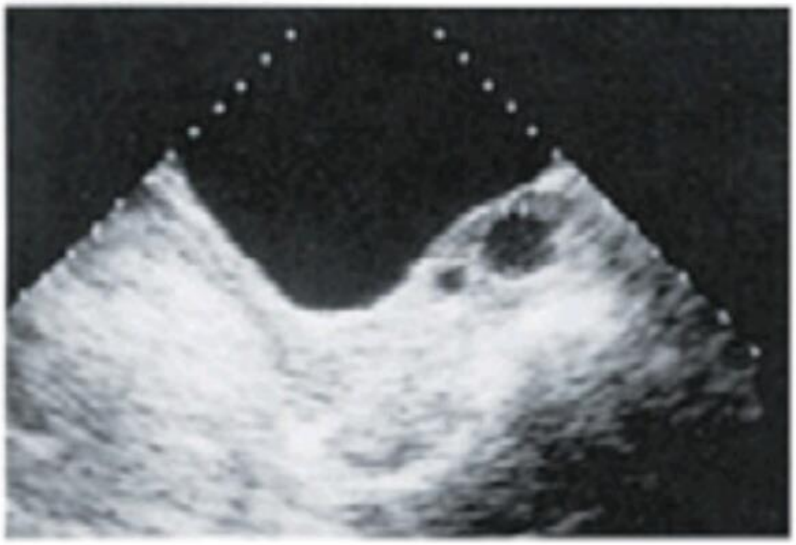


BBT chart

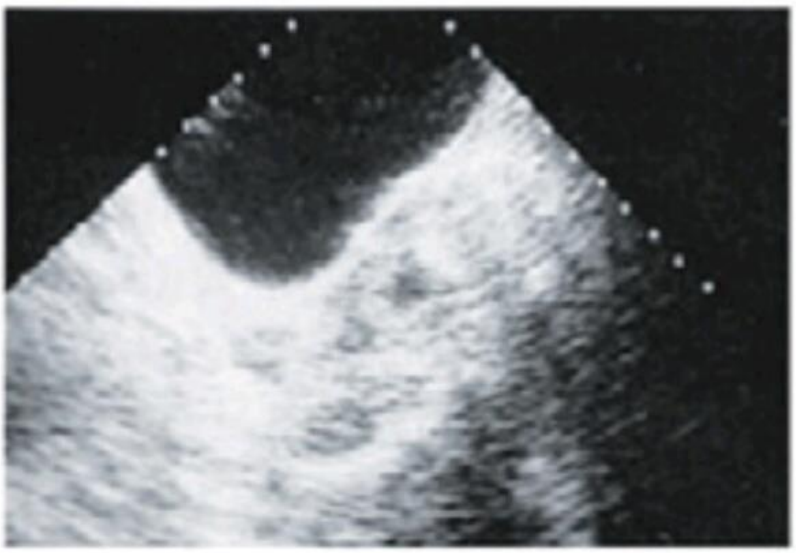
SEMEN ANALYSIS

A semen analysis can be performed following a 2-4 day period of abstinence. Entire ejaculate is collected in a clean ,nontoxic container. An excessive number of leucocytes more than 10 per high power field can predict infection.Special stains are required to differentiate polymorphonuclear leucocytes from immature germ cells. Accurate appraisal of abnormal semen requires at least 3 analyses.

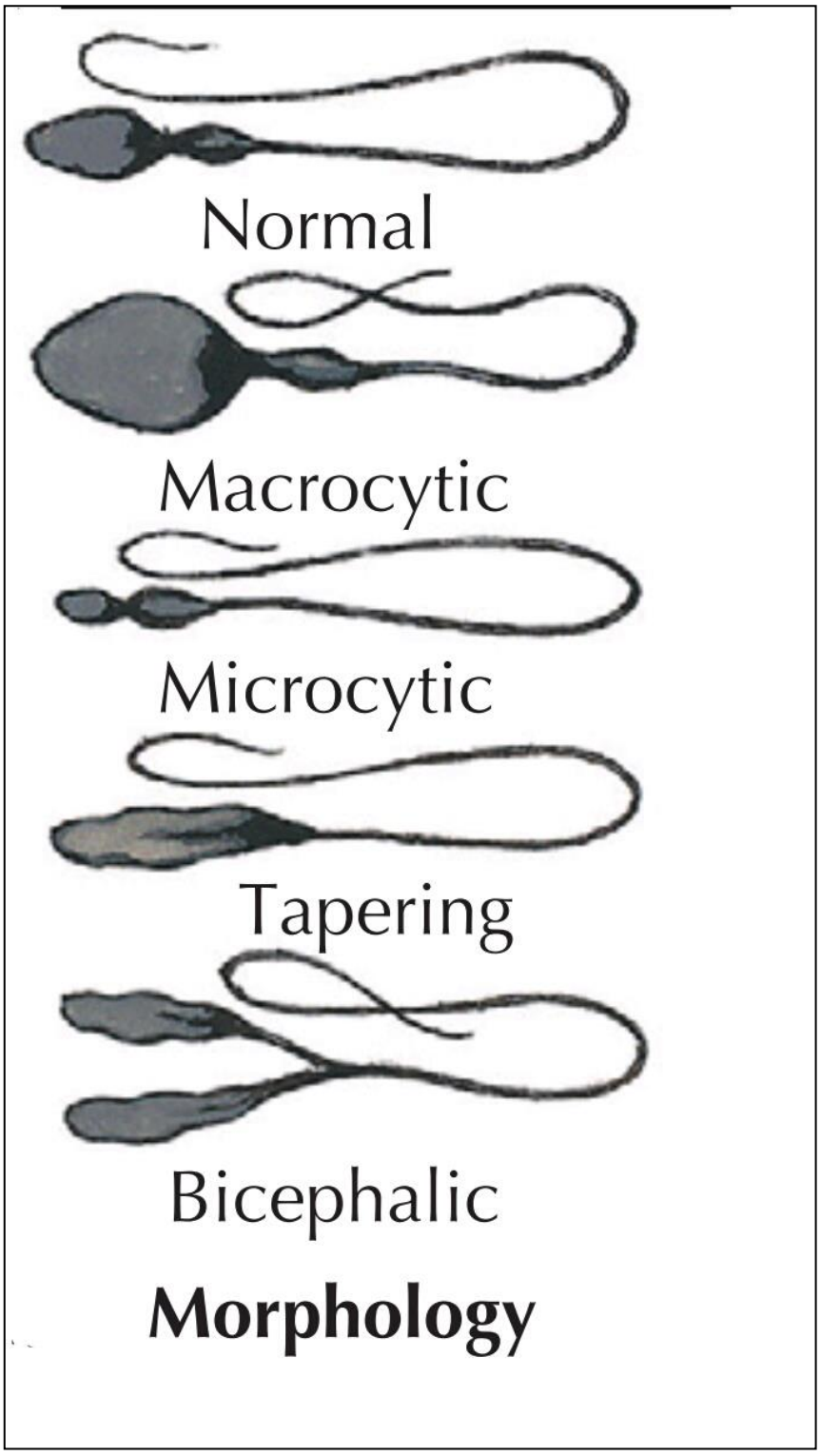
Preovulatory follicle



Ruptured follicle



Serial follicular ultrasound monitors follicular rupture


Normal
Macrocytic
Microcytic
Tapering
Bicephalic
Morphology

Periodic reassessment is necessary.

Endocrine evaluation is necessary .Hypothyroidism can cause infertility but thyroxine cannot be used empirically.

Low levels of gonadotropins may indicate hypothalamic pituitary failure. An elevated prolactin may indicate the presence of prolactin secreting pituitary tumor.

Elevated level of follicle stimulating hormone indicates damage of testicular parenchyma, since Inhibin produced by Sertoli cells provides feedback control of FSH secretion.

No response is likely in presence of elevated FSH.

Normal ovulation is confirmed by serial measurements of urinary LH ,which assess duration of luteal function,midluteal level of serum progesterone, which assess luteal function.

UTERINE AND CERVICAL FACTORS

Uterine and cervical factors account for less than 10% of female factor infertility cases .Uterine conditions like submucosal fibroids, polyps, intrauterine synechiae and congenital malformations can result in infertility.

Endometrial abnormalities like hyperplasia out of phase endometrium ,hyperplasia, and carcinomas can result in infertility.

They distort uterine cavity ,prevent implantation and affect endometrial development.

Conditions that predispose to intrauterine adhesions ,history of PID, infection after pregnancy loss and multiple curettages can result in infertility.

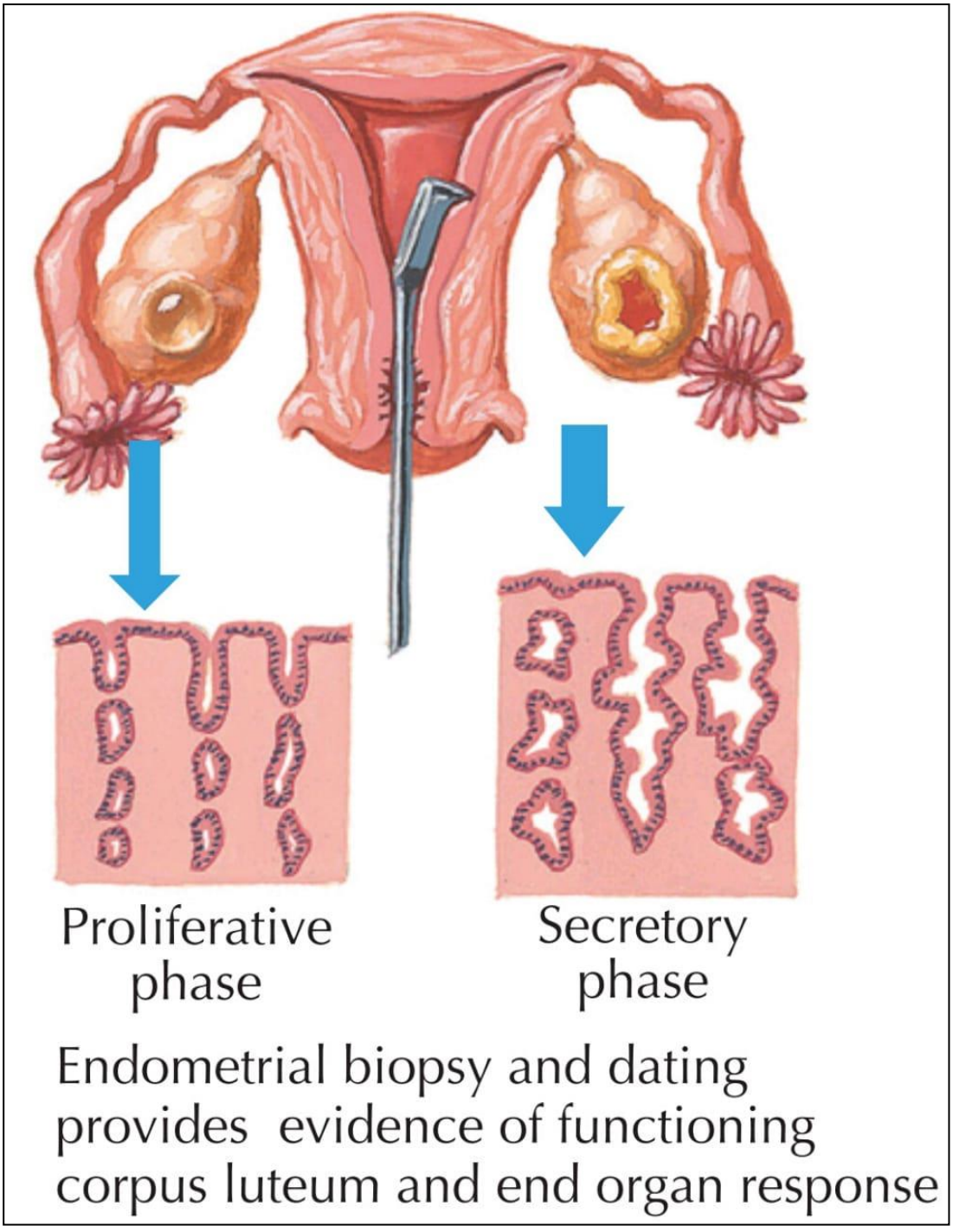
Diethyl stilbestrol exposure in utero increases uterine factor infertility.

Cervical structural abnormalities, cervicitis, abnormal cervical mucous production can cause infertility.

Cervical stenosis is iatrogenic and result from scarring after LEEP conisation, mechanical dilatation i.e. for miscarriage, termination of pregnancy, or hysteroscopy ,and from extensive laser cauterisation of cervix.

These procedures can stenosis and also destruction of endocervical epithelium, causing inadequate mucus production.

As normal midcycle mucus facilitates transport of sperm into endometrial cavity,disruption in mucus production can result in infertility.



Endometrial biopsy and dating provides evidence of functioning corpus luteum and end organ response

OTHER FACTORS

Luteal phase defect may begin with disruption of HPGA, causing deficient production of progesterone by corpus luteum and delay in endometrial maturation .This causes impaired implantation after fertilisation.

Genetic abnormalities like trisomies, mosaics, translocations is attributed in couples where no other cause can be determined.

The most common aneuploidy associated with female infertility is 45 X i.e Turner Syndrome.

PREVALENCE

Infertility affects 10-14 % of Indian population, the rate is higher in urban areas where one in six couples is impacted. According to WHO the overall prevalence of primary infertility in India is 6.6%and secondary infertility is 2.1%

TREATMENT OF INFERTILITY

Couple is advised intercourse every 1 to 2 days in periovulatory period i.e days 12-16 of a 28 day cycle. As infrequent coitus is a common contributing factor advice in this aspect is essential.

Woman is advised to lie on her back for 15 minutes after coitus to prevent rapid loss of semen from vagina.

Lubricants are toxic to sperm. Hence, PRESEED, a nontoxic lubricant has been developed for infertile couples.

Smoking and alcohol should be stopped or atleast reduced.

Factors that raise scrotal temperature like saunas, hot tubs, tight underwear must be discouraged.

HISTORY

The effects of ageing on female fertility are best done in natural population where couples reproduce without voluntary restrictions.

The Hutterites of North America is an example.

Contraception is condemned in them who migrated from Switzerland in 16th century .Studies of fertility in them shows fertility declines with advancing age

It showed that-

- Women who bear children when young are less inclined to conceive again.
- Coital frequency often declines as age increases, showing decreasing desire or lack of partner.
- Fertility rates are 4-8% lower in women aged 25-29 years,15-19% lower in aged 30-34,26-46% lower in women aged 35-39, 95% lower for women aged 40-45 years.

A Dutch study observed that the probability of livebirth decreased by approximately 3.5% per year after age 30.

PROLACTIN

Prolactin is a single chain polypeptide of 199 aminoacids, similar in structure to growth hormone and placental lactogen.Many hormones ,growth factors, and neurotransmitters affect prolactin gene.

Prolactin is encoded by a single gene on chromosome 6.

Most variants of prolactin are result of posttranslational modifications. Little prolactin represents splicing variant resulting from proteolytic deletion of amino acids.

Big prolactin has little biologic activity .

Big variants of prolactin are due to separate molecules of prolactin binding covalently or by interchain disulphide bonding.

High levels of inactive prolactin in absence of tumor can be due to creation of macromolecules of prolactin by antiprolactin autoantibodies.

Big prolactin accounts for 10-25% of hyperprolactinemia.

Enzymatic cleavage of prolactin yields fragments with biologic activity.

Prolactin gene is expressed in lactotropes of anterior pituitary,decidualised endometrium and myometrium.Prolactin secretion from all these sites is identical .

Differences in mRNA indicate differences in prolactin gene regulation.

Transcription is regulated by transcription factor binding to 5" promoter region that is also required for TSH and growth harmone secretion.

Gene transcription for prolactin is regulated by interaction of estrogen and glucocorticoid with 5" flanking sequences.

The prolactin receptor is encoded by gene on chromosome 5 near gene for growth hormone receptor.

The cardinal function of prolactin in mammals is for lactogenesis.In fish it is for osmoregulation.

Human pituitary prolactin contains 199 amino acid residues and disulphide bridges and has structural similarity to human growth harmone and human chorionic somatomammotropin.

Half life of prolactin is 20 minutes.

PROLACTIN RECEPTOR

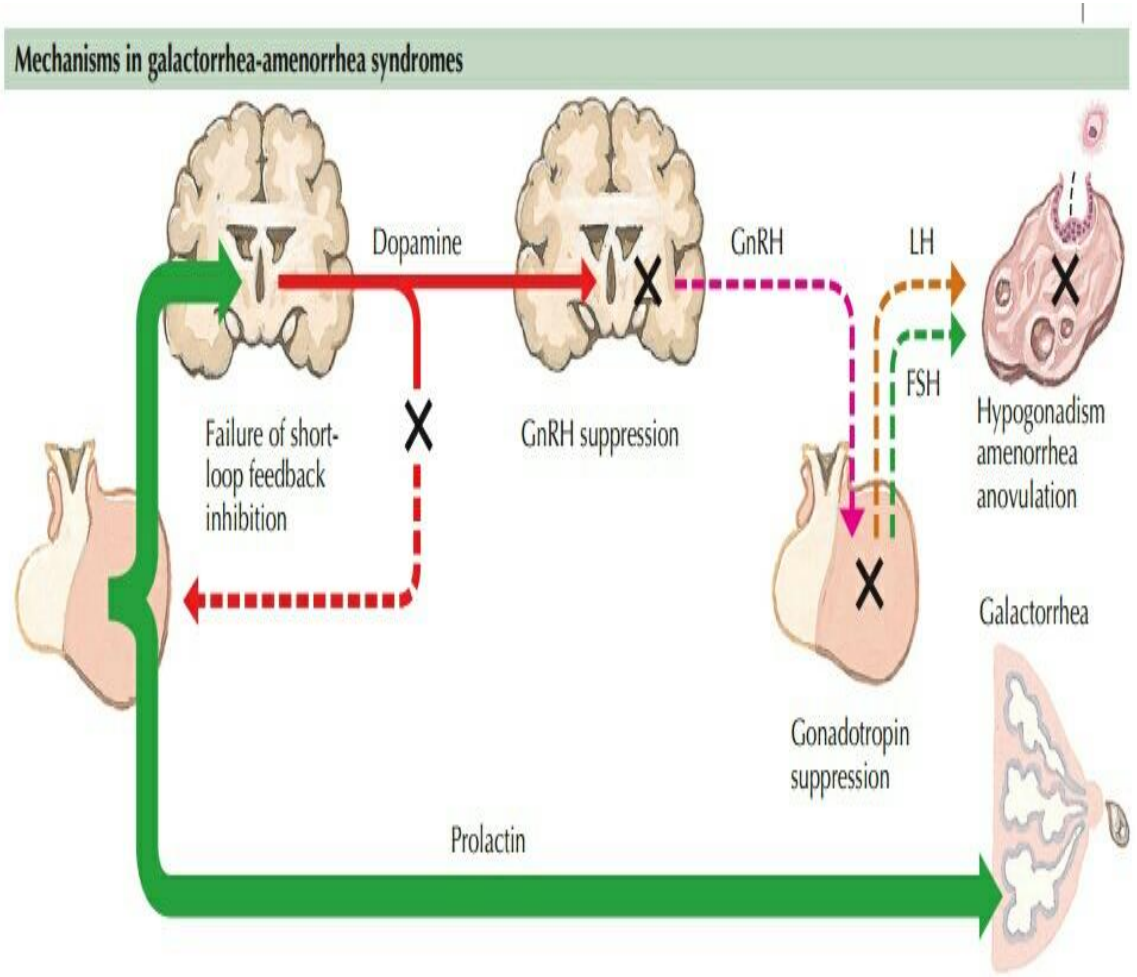
The prolactin receptor resembles growth hormone receptor and belongs to superfamily of receptors that includes growth hormone receptor and receptor for many cytokines and haematopoietic growth factors.

It dimerizes and activates Janus kinase/signal transducers and activators of transcription pathway and other intracellular enzyme cascades.

HYPOTHYROIDISM AND HYPERPROLACTINEMIA CAUSING INFERTILITY

Hypothyroidism can affect fertility due to anovulatory cycles,luteal phase defects, hyperprolactinemia and sex hormone imbalance.

Elevated prolactin may impact reproduction through inhibitory effects on hypothalamic Gonadotropin Releasing Hormone directly or on pituitary to reduce secretion of Gonadotropins i.e .Luteinising Hormone(LH) and Follicle Stimulating Hormone(FSH) ,resulting in reduction in both amplitude and frequency of LH pulses.

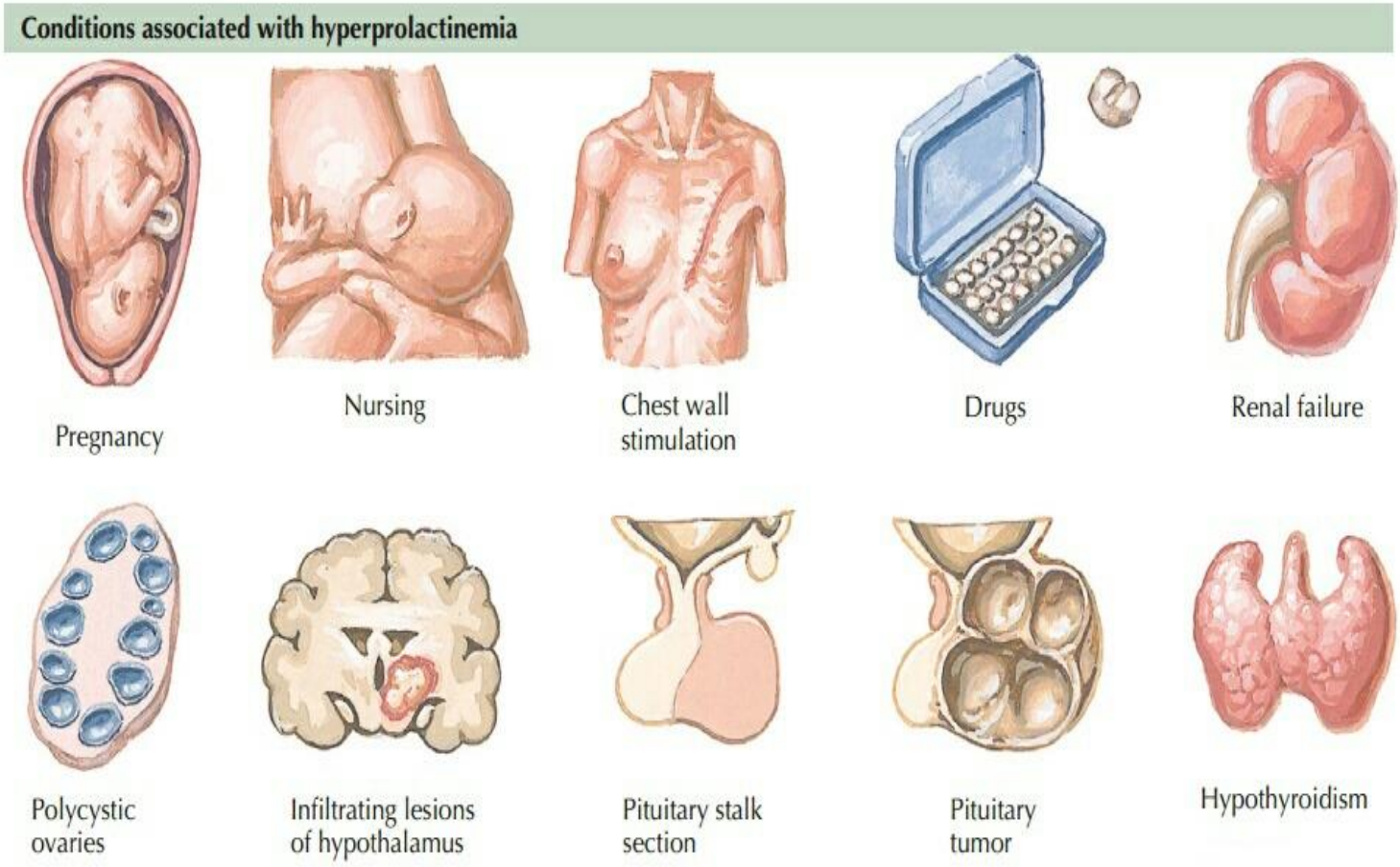


Galactorrhea results from direct effect of prolactin on breast; amenorrhea and hypogonadism result from secondary prolactin effects (via dopamine) on GnRH and gonadotropin production and release

Prolactin causes milk secretion from breast after priming by estrogen and progesterone.Its effect on breast involves increased action of mRNA and produces casein and lactalbumin.Prolactin inhibits effect of gonadotropins by action at the level of ovary.Excess prolactin secreted by tumors in males causes impotence.

Normal plasma concentration in men is 5 ng/mL and women is 8ng/mL.

CAUSES OF HYPERPROLACTINEMIA



1. PHYSIOLOGIC

These include pregnancy, nursing, nipple stimulation ,sleep, stress and seizures.

2.PHARMACOLOGIC

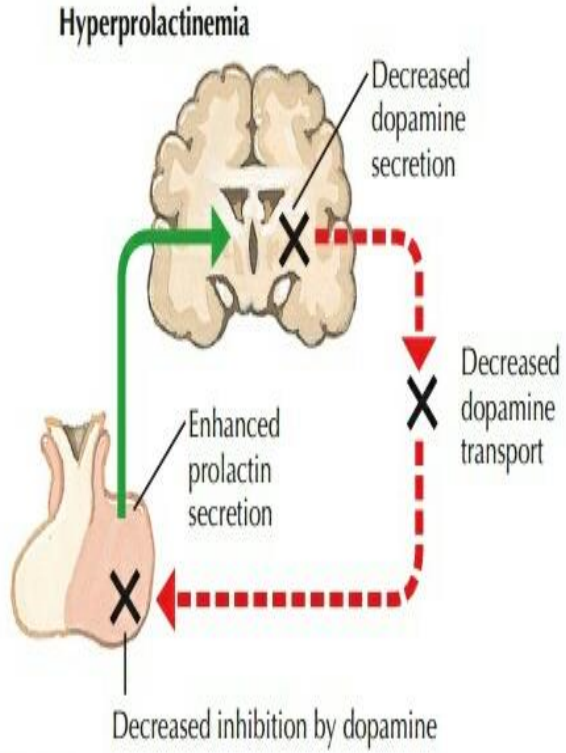
- Dopamine antagonist – Phenothiazines, haloperidol, risperidone, metoclopramide, reserpine, methyldopa, opiods
- Monoamine oxidase inhibitors-Clorgyline
- Cimetidine
- Verapamil

3. PATHOLOGIC

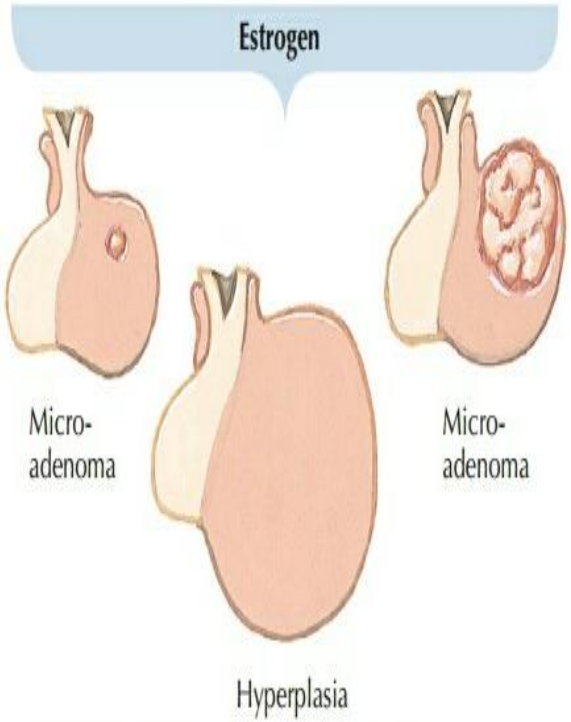
- Pituitary tumors
- Hypothyrouidism
- Chronic renal insufficiency
- Severe liver failure
- Hypophyseal stalk lesion
- Neuraxis irradiation
- Spinal cord lesions
- Hypophysitis

REGULATION OF PROLACTIN SECRETION

It is tonically inhibited by hypothalamus as section of pituitary stalk leads to an increase in circulating prolactin. Its secretion is increased by exercise ,surgical and psychological stresses and nipple stimulation. Plasma prolactin rises during sleep, rise starting after onset of sleep and persisting throughout sleep. Secretion increases in pregnancy, peaks at parturition and falls to nonpregnant levels in about 8 days postdelivery.



Conditions in which normal dopamine short-loop inhibition is blocked or prolactin secretion is enhanced cause clinically evident hyperprolactinemia



Conditions that increase estrogen levels may cause pituitary hyperplasia and induce growth of adenomas, causing hyperprolactinemia

Conditions associated with hyperprolactinemia

L-Dopa increases formation of dopamine and decreases prolactin secretion, Bromocriptine and other dopamine agonists inhibit secretion by stimulating dopamine receptors. Chlorpromazine and related drugs that block dopamine receptors increase prolactin secretion. Thyrotropin releasing hormone stimulates secretion of prolactin in addition to thyroid stimulating hormone. Polypeptides with prolactin releasing activity are present in hypothalamus. Estrogen acts directly on lactotropes and produces a slow increase in prolactin secretion.15-20% of women with secondary amenorrhea have elevated prolactin and when prolactin is restored to normal level normal menstrual cycle and fertility resumes.

CLINICAL FEATURES

Hyperprolactinemia is associated with ovulatory and menstrual disorders like amenorrhoea, oligomenorrhoea, anovulation. luteal phase defects and galactorrhoea. .About 2/3rd of women with galactorrhoea and amenorrhea will have hyperprolactinemia. They might have primary hypothyroidism. It is characterised by low serum levels of thyroxine T4 and decreased negative feedback over the hypothalamopituitary axis. This inturn results in increased secretion of Thyrotropin releasing hormone which stimulates thyrotropes and lactotrophs,increasing the levels of TSH and prolactin .

THE THYROID

The nuclear receptor for thyroid belongs to the steroid hormone receptor superfamily. The nuclear T3 receptor is ubiquitous. The thyroid axis is stimulated by thyrotropin releasing hormone (TRH) .It is inhibited by somatostatin and dopamine. Pituitary secretion of TSH is sensitive to changes in circulating levels of thyroid hormone.TSH secreting cells are regulated by T4 but after it is converted to T3.Some tissues depend on blood T3 for intracellular T3,brain and pituitary convert T4 to T3 intracellularly. Accurate measurement of thyroid function is by measurement of T4 and TSH.

Estrogen increases TRH receptor content of pituitary.TSH response to TRH is greater in women than in men, also in women taking estrogen – progesterone contraceptives. TRH stimulates prolactin secretion by pituitary. Small doses of TRH capable of increasing TSH are also capable of increasing prolactin .

Risk of pregnancy loss is increased in women with overt or subclinical hypothyroidism.

The risk of pregnancy loss is low in treated women with hypothyroidism having normal thyroid indices but increased in women with increased TSH levels including those with untreated subclinical disease and those with overt disease who required inadequate exogenous thyroid hormone .

Subclinical hypothyroidism is not benign and TSH screening is essential for evaluation of women with recurrent pregnancy loss. The goal is to maintain TSH in lower half of normal range i.e 0.45-2.0 microunits/mL.

A patient treated with thyroid hormone should be evaluated every year with TSH assay. If TSH is low then freeT4 has to be measured for dose adjustment..The response of TSH to changes in T4 is slow.A period of 8 weeks is required between dose adjustment and assessment of TSH.

CLINICAL FEATURES

Menstrual irregularities and bleeding problems are common in hypothyroidism. Amenorrhoea can occur due to TRH induced increase in prolactin or normal prolactin levels. Patients are generally asymptomatic, features include constipation, psychomotor retardation, cold intolerance, decreased exercise tolerance and carpel tunnel syndrome

CAUSES OF HYPOTHYROIDISM

1) Autoimmune disease

The most common cause of hypothyroidism is an autoimmune disorder, namely Hashimoto's thyroiditis.

2) Overresponse to hyperthyroidism treatment

Treatment of hyperthyroidism with antithyroid medications can result in hypothyroidism.

3) Radiation therapy

Commonly used for treatment of cancers of head and neck can lead to hypothyroidism.

4) Iodine deficiency

As iodine is required for production of thyroid hormones deficiency of iodine can result in hypothyroidism

5) Drug therapy

Treatment with lithium, amiadarone, interferons can result in hypothyroidism

6. Infiltrative diseases

Sarcoidosis, amyloidosis, scleroderma and hemochromatosis can result in hypothyroidism.

AIM OF STUDY

AIMS AND OBJECTIVES

- To study the correlation of hypothyroidism with hyperprolactinemia in infertile women .
- To study the correlation of other factors like age, duration of marriage and BMI with prolactin and thyroid levels.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

CORRELATION OF HYPERPROLACTINEMIA WITH HYPOTHYROIDISM IN INFERTILE WOMEN

Verma et al (2012) studied the prevalence of hypothyroidism in infertile women and evaluated the response of treatment for hypothyroidism on infertility. They observed that treatment of hypothyroidism t for 3 months to 1 year can help otherwise asymptomatic infertile women conceive.

Sonigo et al (2012) developed a hyperprolactinemic mouse model simulating human pathology by insertion of micropumps releasing prolactin over a period of 28 days. Control animals had normal estrous cycles every 5 days, prolactin treated mice were acyclic or had irregular cycles following their first estrous cycle. Other group of mice receiving prolactin for the first 14 days showed a resumption of normal estrous cycles after cessation of prolactin delivery.

Kokay et al (2011) used dual label insitu hybridisation for identification of prolactin sensitive GABA and Kisspeptin neurons in regions of hypothalamus involved in control of fertility.

Arojoki et al (2009) studied hypothyroidism in infertile women by measuring serum thyroid stimulating hormone levels and prolactin levels and noted the prevalence of abnormal TSH was highest in ovulatory dysfunction and lowest in tubal infertility and male infertility groups.

Bahar et al (2011) studied the prevalence of hyperprolactinemia and clinical symptoms in patients with subclinical hypothyroidism. They showed that the prevalence of hyperprolactinemia in subclinical hypothyroidism is notable and the disorder is commoner in female subclinical hypothyroidism than men.

Avasthi et al (2006) studied the incidence of hyperprolactinemia in female infertility after excluding tubal factor and studied the correlation with hypothyroidism.

Goswami et al (2009) studied correlation of prolactin and thyroid hormone concentration with menstrual patterns in women with infertility .They observed a significant association between abnormal menstrual patterns and

anovulatory cycles, as observed by endometrial examination of infertile women with elevated prolactin.

Ernst B et al (2009) performed a cross-sectional study and also reassessed serum prolactin levels in a subsample around 1 year after gastric bypass surgery. They could not detect any significant association between basal prolactin levels and the degree of obesity or related metabolic disturbances or systematic changes in basal concentrations of hormone after massive weight loss.

Saranya et al(2015) studied the prevalence of hyperprolactinemia in infertile women and its association with hypothyroidism.They observed a significant association of galactorrhoea with hyperprolactinemia and concluded that serum prolactin estimation is essential in infertile women with obesity or galactorrhoea.

Seth et al (2013) studied association of obesity with hormonal imbalance in infertility using anthropometric indices i.e height, weight, BMI, waist circumference and waist hip ratio. Positive correlation between serum FSH and markers of obesity like body weight, hip circumference and BMI was

observed in women with primary infertility. Serum prolactin and TSH showed positive correlation with body weight and BMI in secondary infertility.

Grimaldi et al(1990) studied basal levels of serum prolactin and prolactin response after thyrotropin releasing hormone in obese and age and sex matched healthy subjects. They observed that obese patients had higher basal levels of serum prolactin than healthy subjects. They observed no significant difference in prolactin concentration during TRH stimulating test.

Singh et al (1990) studied thyroid profile along with endocrine status of infertile women and observed that patients with hyperthyroidism had high estradiol levels ,while patients with hypothyroidism had high levels of testosterone thereby causing anovulation.

Tirgar et al (2016) evaluated hirsute women in crosssectional study and hormonal tests were performed on 2^{nd} or 3^{rd} day after menstruation using questionnaire in women without Polycystic ovarian syndrome. They observed no significant relation between marital statuses, galactorrhoea, family history and infertility with hyperprolactinemia. Significant correlation was present between irregular menses and hyperprolactinemia.

Shibli et al (2011) studied the management of hyperprolactinemia in the infertile woman reviews the effect of pregnancy on tumor size ,the usage of dopamine agonist, and effects of dopamine agonist on fetal development. They recommend for treatment when fertility is not an issue and issues related to follow up of prolactinomas.

Sharma et al (2012) studied biochemical association of hyperprolactinemia with hypothyroidism in infertile women and found a high incidence of hyperprolactinemia in infertile women and noted a positive correlation between hyperprolactinemia and hypothyroidism.

Ganguly et al (2010) studied trends of infertility and childlessness in India from NFHS data and concluded that with increase in age at first marriage, the capacity of women to bear children decreases. Infertility was higher among urban women. Standard of living has inverse relation with infertility rate. Working women have high infertility rate.

Akhtar et al (2015)studied the prevalence of hypothyroidism in infertile women an evaluation of response of treatment for hypothyroidism on infertility. They observed that infertile subclinical hypothyroid women conceived within 6 weeks to 2 year period .

MATERIALS AND METHODS

MATERIALS AND METHODS

AIMS OF STUDY

- To study the correlation of hypothyroidism with hyperprolactinemia in infertile women .
- To study the correlation of other factors like age, duration of marriage and BMI with prolactin and thyroid levels.

STUDY DESIGN

Observational study comprising of 100 samples of women with infertility in the age group of 20-35 years ,both primary and secondary infertility included.

STUDY POPULATION

Infertile women of 20-35 years of age attending the gynaecology OPD in the study centre meeting inclusion criteria after approval of local ethical committee and obtaining informed consent.

SAMPLE SIZE

According to qualitative analysis sample size is 100.

STUDY PLACE

GOVERNMENT RSRM LYING IN HOSPITAL,

ROYA PURAM

CHENNAI

STUDY PERIOD

8 months

INCLUSION CRITERIA

1. Infertile women age between 20-35 years and marriage duration more than 2 years.
2. Infertile women with husband having near normal sperm count.

EXCLUSION CRITERIA

1. Women age more than 35 years
2. Women with husbands with grossly abnormal semen analysis.
3. Women who have anomalies of genital tract, tubal blockade.

STUDY METHODS AND WORK PLAN

Demographics, baseline characteristics and other clinical risk factors of infertile women who consented for the study and meeting inclusion criteria were noted.

Blood samples were taken and levels of serum prolactin and thyroid hormones-freeT3,freeT4,TSH were measured.

Values of prolactin more than 25 microgram/L is termed as hyperprolactinemia.

Based on Canadian medical association, Hyperprolactinemia was categorised into:

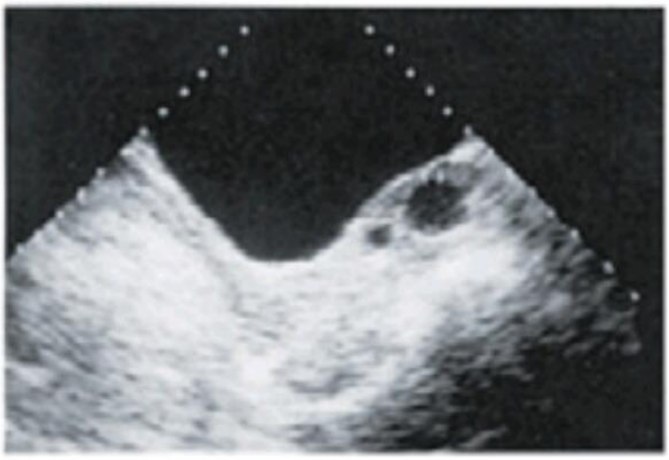
1. Mild 26-50 microgram/L
2. Moderate 51-75 microgram/L
3. Marked > 100 microgram/L

Other laboratory tests

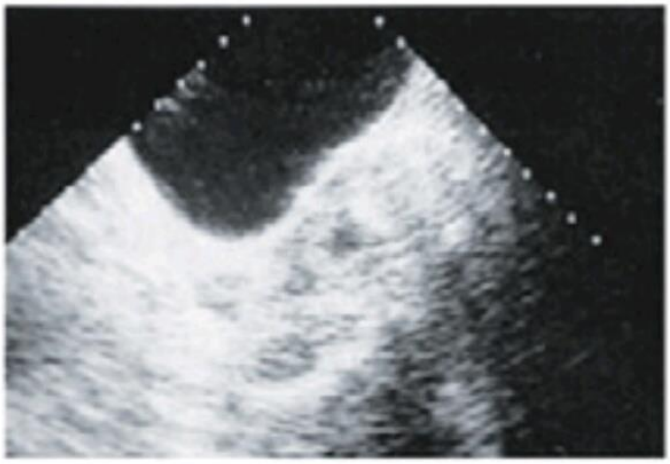
- Haematology-Haemoglobin level, total and differential count and platelet count.
- Biochemistry- Renal function test and random blood sugar levels.
- Blood samples of 6-8ml were taken for the above tests.
- Semen analysis-To look for Volume, appearance, Liquefaction time, Ph, total sperm count, colour, viscosity, motility, pus cells, RBCs, morphology.
- Sample obtained by ejaculating into a collection cup following a period of abstinence of atleast 72 hours
- Hysterosalphingogram- to rule out tubal blockade.
- Ultrasound

\

Preovulatory follicle



Ruptured follicle



Serial follicular ultrasound monitors follicular rupture

FOLLOW UP

The patient is followed up every month as a part of infertility workup and the hypothyroidism or hyperprolactinemia if detected is treated.

SCOPE OF STUDY

Early pickup of hypothyroidism and hyperprolactinemia in infertile women.

Initiation of appropriate management

Achieving normoprolactinemic and euthyroid state.

EXPECTED OUTCOME

PRIMARY OUTCOME

- To detect any hypothyroidism and hyperprolactinemia in infertile women at the earliest.
- To correlate hypothyroidism and hyperprolactinemia with other factors influencing it.

SECONDARY OUTCOME

To detect hypothyroidism and hyperprolactinemia and treat it at the earliest ,helping infertile couples conceive early

RESULTS

RESULTS

The information collected was tabulated in master chart in excel sheet. The correlation of hypothyroidism with hyperprolactinemia and BMI in women with both primary and secondary infertility was done by Spearmans correlation analysis. The correlation analysis was done using SPSS statistical tool (version 20.0)

If the P value is 0.000 to 0.010 ,it imply significant at level 1 i.e. Highly significant

If the P value is 0.011 to 0.050 ,it imply significant at level 5 i.e. Significant

If the P value is 0.051 to 1.000 ,it implies not significant at level 5.

TABLE-1: AGE IN YEARS

T-TEST

Group Statistics					
	Type of Infertility	N	Mean	Std. Deviation	Std. Error Mean
Age in years	Primary	77	26.69	4.378	.499
	Secondary	23	27.17	4.271	.891

Of the total 100 women with infertility,77 belonged to primary infertility group and 23 belonged to secondary infertility group.

The mean age in years of primary infertility group was 26.69 years, while in secondary infertility group the mean age was 27.17.

The standard deviation of age among primary infertility group was 4.378, while the standard deviation of age in secondary infertility group was 4.271

The standard error of mean for primary infertility was .499and secondary infertility was.891

TABLE 2

Independent Samples Test										
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Age in years	Equal variances assumed	.180	.673	-.469	98	.640	-.486	1.035	-2.539	1.568
	Equal variances not assumed			-.476	36.922	.637	-.486	1.021	-2.554	1.583

In this table, Levene's test for equality of variances for age in years ,P value obtained is .640 .This is more than significance level 0.05 ,thus null hypothesis is accepted and it is concluded that there is no difference between variance in population..

TABLE 3

GROUP STATISTICS OF DURATION OF MARRIAGE IN YEARS

Group Statistics					
	Type of Infertility	N	Mean	Std. Deviation	Std. Error Mean
Duration of marriage in years	Primary	77	4.57	2.319	.264
	Secondary	23	5.48	1.780	.371

The mean duration of marriage in years in primary infertility was 4.57 among women with primary infertility.

The mean duration of marriage in years in secondary infertility was 5.48.

The standard deviation from mean of marriage in years among primary infertility group was 2.319 and among secondary infertility group was 1.780.

The standard error of mean of primary infertility group was .264 and secondary infertility was .371.

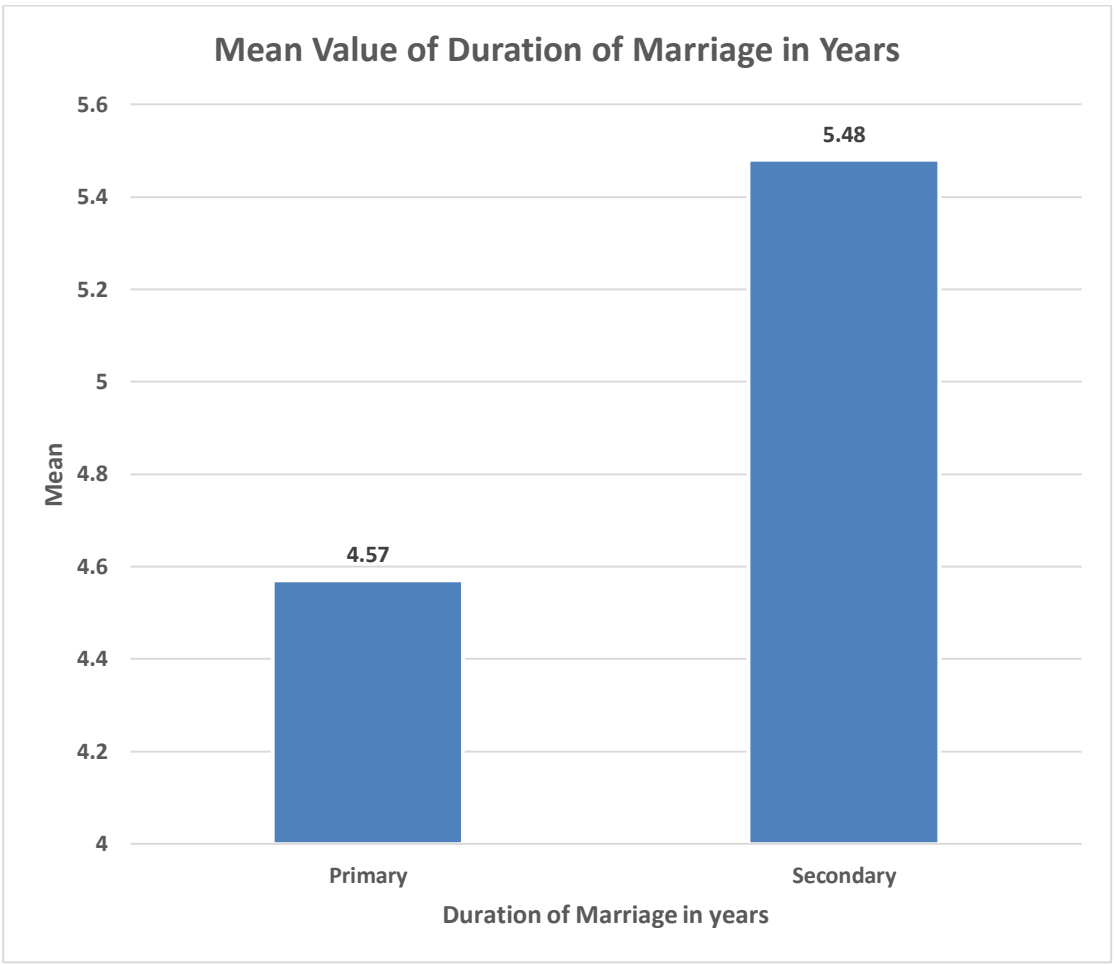

Mean Value of Duration of Marriage in Years
5.6
5.4
5.2
5
4.8
4.6
4.4
4.2
4
Mean
4.57
5.48
Primary
Secondary
Duration of Marriage in years

TABLE 4

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Duration of marriage in years	Equal variances assumed	1.142	.288	-1.727	98	.087	-.907	.525	-1.949	.135
	Equal variances not assumed			-1.990	46.499	.053	-.907	.456	-1.824	.010

In this table for Levenes test for equality of variances for duration of marriage in years ,the P value obtained is 0.087 .This is more than the significant P value of .05 .

Hence null hypothesis is accepted and homogenity of variance is present in population.

TABLE -5

GROUP STATISTICS OF TSH VALUES

T-TEST

Group Statistics					
	Type of Infertility	N	Mean	Std. Deviation	Std. Error Mean
TSH	Primary	77	3.4811	3.09880	.35314
	Secondary	23	5.4492	8.00030	1.66818

The mean TSH values of primary infertility women was found to be 3.4811 and among women with secondary infertility it was found to 5.4492.

The standard deviation from the mean of TSH values of women with primary infertility was 3.0988,among women with secondary infertility was found to 8.0003.

The standard error of mean among primary infertility women was .35314 and among women with secondary infertility was 1.68818

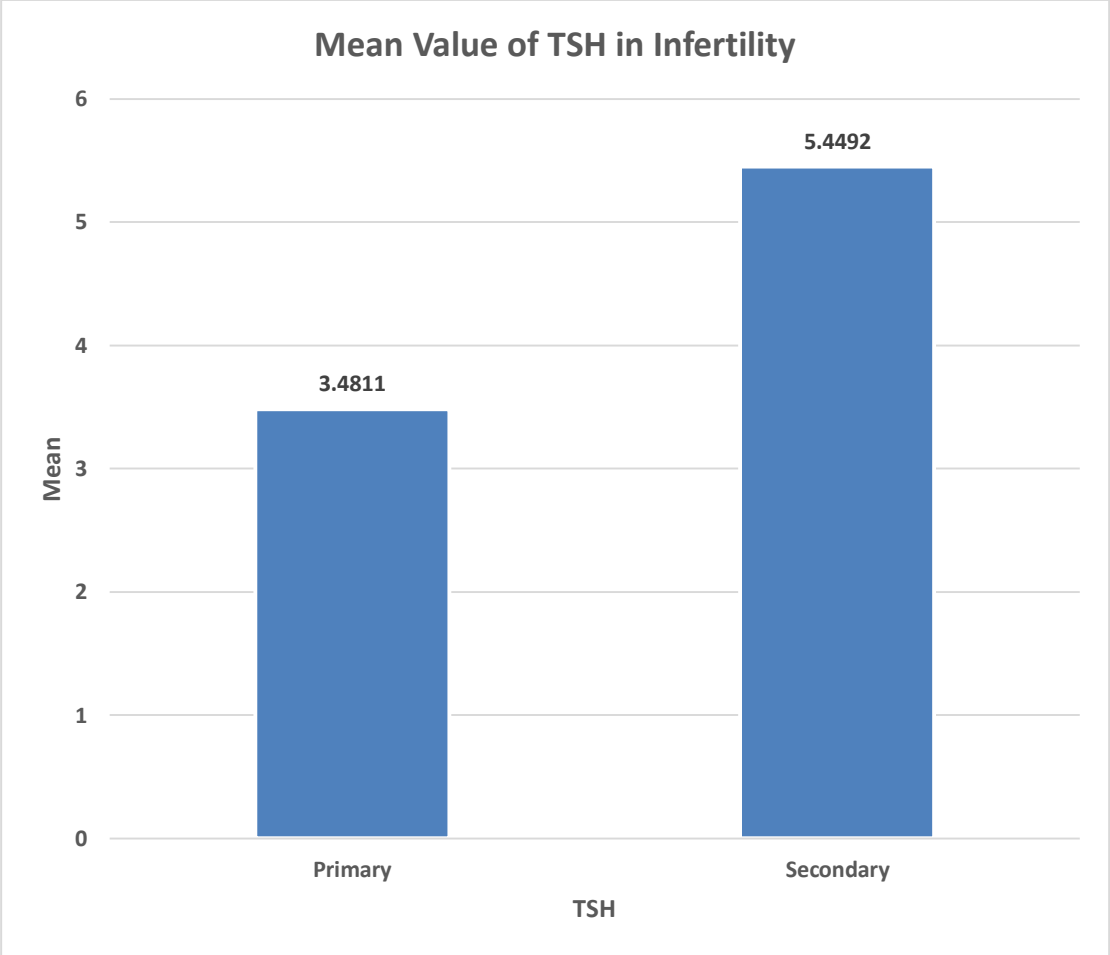

Mean Value of TSH in Infertility
6
5
4
3
2
1
0
Mean
5.4492
3.4811
Primary
Secondary
TSH

TABLE 6

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
TSH	Equal variances assumed	4.668	.033	-1.773	98	.079	-1.96809	1.10987	-4.17058	.23441
	Equal variances not assumed			-1.154	24.002	.260	-1.96809	1.70515	-5.48732	1.55115

In this table on Levene's test for equality of variances done for TSH values ,the P value obtained was .079 ,which is more the significant value of .05

Hence null hypothesis is accepted and homogeneity of variance is present in the population.

TABLE 7

GROUP STATISTICS OF PROLACTIN VALUES

Group Statistics					
	Type of Infertility	N	Mean	Std. Deviation	Std. Error Mean
Prolactin	Primary	77	19.6287	9.04658	1.03095
	Secondary	23	26.6217	19.95157	4.16019

The mean prolactin values of women with primary infertility was found to be 19.6287.

The mean prolactin values of women with secondary infertility was 26.6217.

The standard deviation from the mean of prolactin values among women with primary infertility was 9.04658 and secondary infertility was 19.95157

The standard error of mean of prolactin values among women with primary infertility was 1.03095 and secondary infertility women was 4.16019

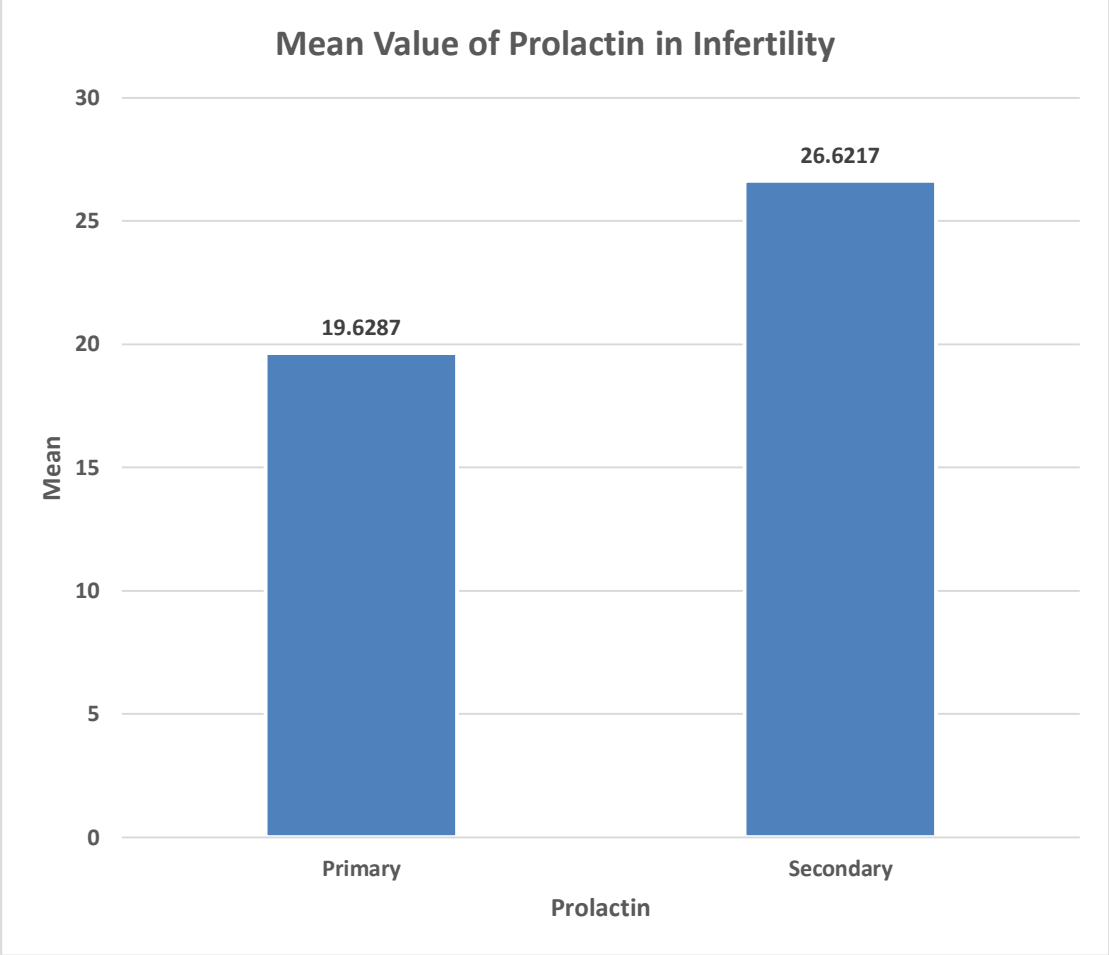

Mean Value of Prolactin in Infertility
30
25
20
15
10
5
0
Mean
19.6287
26.6217
Primary
Secondary
Prolactin

TABLE 8

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Prolactin	Equal variances assumed	3.027	.085	-2.381	98	.019	-6.99304	2.93761	-12.82264	-1.16344
	Equal variances not assumed			-1.632	24.758	.115	-6.99304	4.28603	-15.82466	1.83858

In this table of Levene's test for equality of variance for prolactin values, the P value obtained is .019.

This this less than the significant value .05 .

Hence null hypothesis is rejected and homogeneity of variance is not present.

TABLE 9

GROUP STATISTICS OF BMI

Group Statistics					
	Type of Infertility	N	Mean	Std. Deviation	Std. Error Mean
BMI	Primary	77	26.1906	4.03054	.45932
	Secondary	23	27.1739	3.61376	.75352

The mean BMI of women with primary infertility was 26.1906

The mean BMI of women with secondary infertility was 27.1739

The standard deviation from the mean of BMI in primary infertility group was 4.03054

The standard deviation of BMI among secondary infertility group was 3.61376

The standard error of mean among primary infertility group was .45932

The standard error of mean among secondary infertility group was .75352

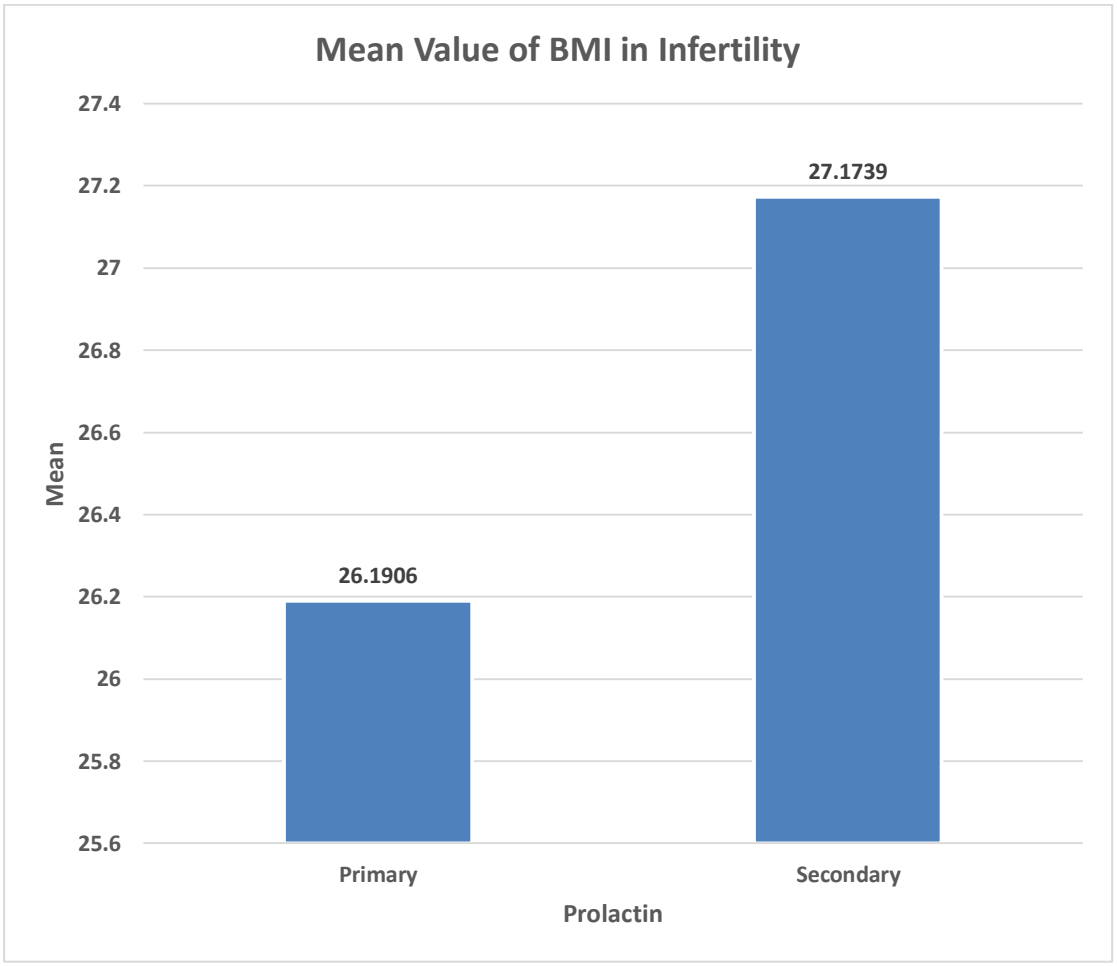

Mean Value of BMI in Infertility
27.4
27.2
27
26.8
26.6
26.4
26.2
26
25.8
25.6
Mean
26.1906
27.1739
Primary
Secondary
Prolactin

TABLE 10

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
BMI	Equal variances assumed	.532	.467	-1.050	98	.296	-.98326	.93643	-2.84159	.87506
	Equal variances not assumed			-1.114	39.796	.272	-.98326	.88248	-2.76711	.80058

In this table of Levenes test for equality of variance for BMI the P value obtained is .296

This is more than than the significant value .05

Hence null hypothesis is accepted and homogeneity of variance is present in the given population

CORRELATIONS FOR PRIMARY INFERTILITY

Correlations						
		Age in years	Duration of marriage in years	TSH	Prolactin	BMI
Age in years	Pearson Correlation	1	.373**	-.039	.003	-.031
	Sig. (2-tailed)		.001	.733	.979	.791
	N	77	77	77	77	77
Duration of marriage in years	Pearson Correlation	.373**	1	.049	-.052	-.143
	Sig. (2-tailed)	.001		.670	.656	.216
	N	77	77	77	77	77
TSH	Pearson Correlation	-.039	.049	1	.765**	.587**
	Sig. (2-tailed)	.733	.670		.000	.000
	N	77	77	77	77	77
Prolactin	Pearson Correlation	.003	-.052	.765**	1	.664**
	Sig. (2-tailed)	.979	.656	.000		.000
	N	77	77	77	77	77
BMI	Pearson Correlation	-.031	-.143	.587**	.664**	1
	Sig. (2-tailed)	.791	.216	.000	.000	
	N	77	77	77	77	77
**. Correlation is significant at the 0.01 level (2-tailed).						

In the primary infertility group the Pearson correlation coefficient value for TSH and prolactin is .765 and sig (2 tail value) is .001 which indicates correlation of TSH values with prolactin values.

The Pearson correlation coefficient for TSH and BMI .587 among primary infertility group and sig (2 tailed) is .000 indicating correlation of TSH with BMI.

The Pearson correlation coefficient value of prolactin and BMI is .664 among primary infertility group and sig(2 tailed) value .000 indicating correlation of prolactin with BMI.

CORRELATIONS FOR SECONDARY INFERTILITY

Correlations						
		Age in years	Duration of marriage in years	TSH	Prolactin	BMI
Age in years	Pearson Correlation	1	.658**	.413*	.393	.290
	Sig. (2-tailed)		.001	.050	.064	.180
	N	23	23	23	23	23
Duration of marriage in years	Pearson Correlation	.658**	1	.629**	.519*	.559**
	Sig. (2-tailed)	.001		.001	.011	.006
	N	23	23	23	23	23
TSH	Pearson Correlation	.413*	.629**	1	.867**	.611**
	Sig. (2-tailed)	.050	.001		.000	.002
	N	23	23	23	23	23
Prolactin	Pearson Correlation	.393	.519*	.867**	1	.624**
	Sig. (2-tailed)	.064	.011	.000		.001
	N	23	23	23	23	23
BMI	Pearson Correlation	.290	.559**	.611**	.624**	1
	Sig. (2-tailed)	.180	.006	.002	.001	
	N	23	23	23	23	23
**. Correlation is significant at the 0.01 level (2-tailed).						

The Pearson correlation coefficient for age in years and duration of marriage among secondary infertility group is .658 and sig(2 tailed) value is .001 indicating correlation of age with duration of marriage.

The Pearson coefficient of correlation of duration of marriage and TSH values among secondary infertility group is .629 sig(2 tailed) is .001 ,indicating correlation of duration of marriage with TSH .

The Pearson coefficient of correlation of duration of marriage with prolactin among secondary infertility group is .519 and sig(2 tailed) value is .011 indicating correlation of prolactin with duration of marriage.

The Pearson coefficient of correlation of duration of marriage with BMI among secondary infertility group is.559 and sig(2 tailed) is .006 indicating correlation of duration of marriage with BMI.

DISCUSSION

DISCUSSION

This is a prospective observational study done in 100 infertile women attending the gynaecology OPD in GOVT RSRM LYINGIN HOSPITAL, ROYAPURAM ,CHENNAI.

The study population of 100 was tested for prolactin and thyroid hormone levels after excluding male factor infertility and tubal factors.

The demographic factors, duration of marriage , BMI, age, freeT3, freeT4, TSH were studied to know their impact on causing infertility. The early detection of these conditions and correction of these hormonal imbalance can help couples conceive early.

In our study we find that increasing age, BMI,, period of infertility were associated with high prolactin levels.

SUMMARY

SUMMARY

In the 100 patients recruited into study 77 were under primary infertility category and 23 belonged to secondary infertility category.

The mean age of primary infertility women was 26.69 and secondary infertility women was 27.17 ,showing that women with secondary infertility were of higher age.

The mean duration of marriage in primary infertility was 4.57 and secondary infertility was 5.48

The mean TSH values for primary infertility was 3.4811 and secondary infertility was 5.4492,showing that both primary and secondary infertile women had higher than normal TSH values.

The majority of women with high TSH values also had high prolactin values.

The majority of women with raised TSH and prolactin also had raised BMI.

CONCLUSION

CONCLUSION

TSH values and prolactin values showed a positive correlation in women with both primary and secondary infertility.

Positive correlation of BMI with both prolactin and TSH was observed.

BMI also showed a positive correlation with duration of age in years after marriage.

This implies that infertile women in general have raised TSH and prolactin values, their BMI is on the higher side.

As the duration of years following marriage increases infertility also increases.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Grimaldi F ,Mazzolini A ,Paterniti BR,TorossiI,Proto G, Bertolissi F.Changes in secretion of prolactin in obesity.Minerva Endocrinology1990;15(4):267-71.

2. Nallusamy S ,GracelynLJ.Prevalence of hyperprolactinemia in infertile women and its association with hypothyroidism.Int J Adv Med 2016;3:33-8.

3. Ernst B,Thurnheer M,Schultes B.Basal serum prolactin levels in obesity-unrelated to parameters of metabolic syndrome and unchanged after massive weight loss.Obes Surg.2009;19(8):1159-62.

4. Crosignani PG.Management of hyperprolactinemic infertility.Middle east Fertility Society Journal.2012;17:63-69.

5. Seth B,Arora S,Singh R .Association of obesity with hormonal imbalance in infertility.A Crosssectional study in north Indian women.Ind J clin Biochem.2013;28(4):342-7.

6. Souter I , Baltagi LM, Toth TL, Petrozza JC.Prevalence of hyperprolactinemia and abnormal magnetic resonance imaging findings in a population with infertility.Fertil Steril 2010;94:1159-62

7. Crosignani PG.Management of hyperprolactinemic infertility.Middle East Fertility Society Journal.2012;17:63-69.

8. Singh L ,Agarwal CG,Chowdhary SR.Thyroid profile in infertile women.J.Obstet Gynecol India.1990;40;248-53.

9. Shibli-Rahhal A, Schlechte J.Hyperprolactinemia and infertility.Endocrinol Metab Clin N Am.2011;40:837-46.

10. Dizerega GS,Ross GT.Luteal phase dysfunction.Clin Obstet Gynecol.1981;8:733-51.

11. Sharma N, Baliarsingh S,Kaushik GG. Biochemical association of hyperprolactinemia with hypothyroidism in infertile women .Clin Lab.2012;58(7-8):805-10.

12. Verma I, Sood R,Juneja S, Kaur S.Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility.Int J Appl Basic Med Res.2012;2(1):17-9.

13. Muhammad o ,Bushra J.Physiological study of some Hormonal Parameters in Infertile Hyperprolactinemic Women in Pre and Post Treatment with Cabergoline and Bromocriptine.Medical journal of Babylon.2012;9(2):349-61.

14. Akhter N ,Hassan S .Subclinical hypothyroidism and hyperprolactinemia in infertile women:Bangladesh perspective after universal salt iodination.The internet journal of endocrinology.2008;5(1).

15. Goswami B,Patel S,Saxena A .Correlation of prolactin and thyroid hormone concentration with menstrual pattern in infertile women.J Reprod Infertility.2009;10(30:207-12.

16. Misra A,Chowbey P,Makkar BM,Vikram NK,Wasir JS,Chadha D.Consensus statement for diagnosis of obesity,abdominal obesity and metabolic syndrome for Asian Indians and recommendations for physical activity,medical and surgical management.J Assoc.Physicians India.2009;57:163-70.

17. Choudhary SD,Goswami A.Hyperprolactinemia and reproductive disorder a profile from north east.J Assoc Physicians India.1995;43:617-8.

18. Unuane D, Tournaye H,Velkeniers B,Poppe K.Endocrine disorders and female infertility.Best Prac Res Clin Endocrinol Metab.2011;25(6):861-73

19. Ratner LD,Gonzalez B,Ahtiainen P,Di Giorgio NP,Poutanen M. Short-term pharmacological suppression of the hyperprolactinemia of infertileHCG –overproducing female mice persistently restores their fertility.Endocrinology.2012;153(12):5980-92.

20. Rosato F ,Garofalo P.Hyperprolactinemia;from diagnosis to treatment. Minerva pediatricia.2002;54960:547-52.

21. Berinder K, Hulting AL, Granath F,Hirschberg AL,Akre o.Parity,pregnancy and neonatal outcomes in women treated for hyperprolactinemia compared with a control group.Clin Endocrinol.2007;67(3)393-7.

22. Poppe K ,Velkeniers B.Thyroid disorders in infertile women.Ann Endocrinol (Paris02003;64(1):45-50.

23. Zollner U,Lanig K ,Steck T, Dietl J.Assessment of endocrine status in patients undergoing IVF treatment.Is it necessary?Arch Gynecolo Obstet.2001;265(1):16-20.

24. Avasti Kumkum,Kaur Jasmine,Gupta Shweta.Hyperprolactinemia and its correlation with hypothyroidism in infertile women.J Obstet Gynaecol India.2006;56:68-71.

25. Eldin S ,Abdelghani A,Elmagadum A.Hyperprolactinemia as a cause of female infertility and its prevalence in central Sudan.Egypt Acad.j.Biolog.Sci.2013;5(1):31-6.

26. Serri O,Chik CL, Ehud Ur,Ezzat S.Diagnosis and management of hyperprolactinemia.Canadian Medical Association Journal.2003;169(60575-81.

27. Shoupe D,Mishell DR.Hypoprolactinemia:Diagnosis and treatment.In :Mishell's textbook of Infertility,Contraception and Reproductive Endocrinology.Massachusetts.Blackwell Science.1997;4:323-41.

28. Melmed S,Casanueva FF,Hoffman AR,Klienberg DL,Montori VM,Schlechte JA.Diagnosis and treatment of hyperprolactinemia:an Endocrine Society Clinical Practice guideline.J Clin Endocrinol Metab.2011;96:273-88.

29. Barclay L, Lie D.Endocrine Society Issues Guidelines for Management of Hyperprolactinemia.J Clin Endocrinol Metabol.2011;96:273-88.

ANNEXURES

- **Proforma**
- **Consent Form**
- **Ethical Committee Approval Form**
- **Master Chart**

APPENDIX I : PROFORMA

"CORRELATION OF HYPERPROLACTINEMIA WITH HYPOTHYROIDISM - AN OBSERVATIONAL STUDY"

1. Name:
   Age:
   Occupation:
   Income:

2. ADDRESS:

3. Menstrual history

4. Marital history :

5. H/O Galactorrhea YES/NO
   H/O discharge PV YES/NO
   H/O pruritis vulva YES/NO
   H/O genital ulcer YES/NO
   H/O chronic cough YES/NO
   H/Oweight loss/tremors/ palpitation YES/NO
   H/O intolerance to cold/hoarseness of voice / weight gain/ constipation YES/NO
   H/O contraception (if any) YES/NO

6. Coital history :

7. Andrological history:

   Name

   Age

   Occupation

   H/O smoking / alcohol /drug abuse YES/NO

   H/O genital ulcer YES/NO

   H/O chronic chest infection YES/NO

   H/O Diabetes/ hypertension YES/NO

   H/O medications YES/NO

   H/O previous genital or inguinal surgeries/trauma YES/NO

   H/O sexual dysfunction YES/NO

8. Obstetric H/O :

9. Past History :

   H/O any drug intake YES/NO

   K/C/O DM / HT/ TB/ Thyroid YES/NO

   H/O previous pelvic surgery YES/NO

   H/O PID YES/NO

   H/O postabortal curettage YES/NO

10. Personal history : H/O smoking/ alcohol/ drug abuse YES/NO

11. Family history :

12. Examination :

    General examination

    Breast

    Thyroid

    Abdominal examination

    Gynaecological examination

Local examination

Per Speculum

PV

13. Investigations done :
    - Hb%:
    - Blood sugars
        - FBS
        - PPBS
    - Chest X Ray
    - Mantoux :
    - USG Findings:
    - HSG
    - Semen Analysis
    - **Free T3**
    - **Free T4**
    - **TSH**

Prolactin levels

Follicular study

"CORRELATION OFHYPERPROLACTINEMIA WITH HYPOTHYROIDISM IN INFERTILE WOMEN- AN OBSERVATIONAL STUDY"

Purpose of the study:

To determine if there is increased occurrence of hypothyroidism and hyperprolactinemia among infertile woman

Procedure:

100 infertile patients are subjected to Thyroid function tests and their prolactin levels are estimated

Outcome -

Correlation of hypothyroidism with hyperprolactinemia if any is observed

Benefits:

The information from the study may prove to be of great importance in increasing fertility by correction of hypothyroidism and hyperprolactinemia

Confidentiality:

Utmost priority will be given to protect the privacy and confidentiality of your personal information. The collected information will not be shared with anyone not involved in the study and reporting will be done in aggregate form only

Voluntary participation:

Your participation in this study is voluntary and you have the right to withdraw your participation at any time during the interview without any explanation. Refusal to participate will not involve any penalty or loss of benefits to which you are otherwise entitled. There might be certain questions which you may not wish to answer. You can choose to decline answering these questions.

APPENDIX II : INFORMED CONSENT FORM

Title of the study:

CORRELATION OF HYPERPROLACTINEMIA WITH HYPOTHYROIDISM IN INFERTILE WOMEN - AN OBSERVATIONAL STUDY

I agree to participate in the study entitled and have been informed about the details of the study in my own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I understand that I can withdraw from the study at any point of time and even then, I can receive the medical treatment as usual.

I understand that I will not get any money for taking part in the study.

I will not object if the results of this study are getting published in any medical journal, provided my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my full cooperation for this study.

Name of the participant :	Name of the investigator: Dr. T. Ramya
Signature / Left thumb print:	Signature of investigator :
Date :	Date :

APPENDIX III : ETHICAL COMMITTEE APPROVAL FORM

GOVERNMENT STANLEY MEDICAL COLLEGE & HOSPITAL,CHENNAI -01
INSTITUTIONAL ETHICS COMMITTEE

TITLE OF THE WORK : CORRELATION OF HYPERPROLACTINEMIA WITH HYPOTHYROIDISM IN INFERTILE WOMEN – AN OBSERVATIONAL STUDY.

PRINCIPAL INVESTIGATOR : DR. RAMYA T,
DESIGNATION : PG IN MS (O&G),
DEPARTMENT : DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY, GOVT. STANLEY MEDICAL COLLEGE.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 03.04.2019 at the Council Hall, Stanley Medical College, Chennai-1 at 10am.

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

26/4/19

MEMBER SECRETARY,
IEC, SMC, CHENNAI

APPENDIX IV : MASTER CHART

S.NO.	NAME	AGE	OP/IP NO	TYPE OF INFERTILITY	DURATION OF MARRIAGE	TSH	PROLACTIN	BMI	COMORBIDITIES	TREATMENT	HSG	SEMEN ANALYSIS
1	KUMARI	27	7360	PRIMARY	5 YEARS	7.68	22.1	35.59	-	-	NORMAL	NORMAL
2	SUDHA	30	7529	PRIMARY	5 YEARS	0.62	5.7	20.1	-	-	NORMAL	NORMAL
3	PRIYA	22	6987	PRIMARY	2 YEARS	2.8	20	35.15	-	-	NORMAL	NORMAL
4	ANANDHI	35	6656	PRIMARY	2 YEARS	0.56	15	22	HYPOTHYROID	T.ELTROXIN100 mcg	NORMAL	NORMAL
5	ANANDHI 32	32	5318	PRIMARY	5 YEARS	7.1	29	27	HYPOTHYROID	T.ETROXIN 25 MCG	NORMAL	NORMAL
6	VIMALA	33	6189	PRIMARY	4 YEARS	3	26	35	HYPOTHYROID	T.ELTROXIN 25 MCG	NORMAL	NORMAL
7	DILSATH	24	4774	PRIMARY	4 YEARS	2.9	22	24	-	-	NORMAL	NORMAL
8	LAKSHMI	23	4839	PRIMARY	5 YEARS	3.4	25	25	-	-	NORMAL	NORMAL
9	MYTHILI	24	3831	PRIMARY	5 YEARS	4	28.32	28	-	-	NORMAL	NORMAL
10	MEGALAVTHY	22	3960	PRIMARY	6 YEARS	2.11	19	23	-	-	NORMAL	NORMAL

S.NO.	NAME	AGE	OP/IP NO	TYPE OF INFERTILITY	DURATION OF MARRIAGE	TSH	PROLACTIN	BMI	COMORBIDITIES	TREATMENT	HSG	SEMEN ANALYSIS
11	REVATHY	33	3596	PRIMARY	8 YEARS	1.92	17	24	-	-	NORMAL	NORMAL
12	AYESHA	27	1885	PRIMARY	6 YEARS	2	20	25	-	-	NORMAL	NORMAL
13	NISHA	24	3355	SECONDARY	4 YEARS	2.93	25	26	-	-	NORMAL	NORMAL
14	RADHIKA	27	1949	PRIMARY	2 YEARS	0.42	17	24	-	-	NORMAL	NORMAL
15	BHARATHI	27	1142	PRIMARY	10 YEARS	1	19	22	-	-	NORMAL	NORMAL
16	SOUNDARYA	22	652	SECONDARY	3 YEARS	0.672	21	24	-	-	NORMAL	NORMAL
17	ANBUKARASI	26	1992	PRIMARY	5 YEARS	2.59	22	25	-	-	NORMAL	NORMAL
18	ZEENATH	25	847	PRIMARY	2 YEARS	3.93	25.13	27	-	-	NORMAL	NORMAL
19	PAVITHRA	22	10557	PRIMARY	5 YEARS	1.9	17	25	-	-	NORMAL	NORMAL
20	JOTHI	27	7597	SECONDARY	7 YEARS	4.74	23.1	28	-	-	NORMAL	NORMAL
21	INDHUMATHY	29	10449	SECONDARY	5 YEARS	1.54	9.43	20		-	NORMAL	NORMAL
22	ZEENATH	28	10325	PRIMARY	3 YEARS	2.4	14.47	31.61		-	NORMAL	NORMAL

S.NO.	NAME	AGE	OP/IP NO	TYPE OF INFERTILITY	DURATION OF MARRIAGE	TSH	PROLACTIN	BMI	COMORBIDITIES	TREATMENT	HSG	SEMEN ANALYSIS
23	DIVYA	26	3580	SECONDARY	5 YEARS	3	14.6	26		-	NORMAL	NORMAL
24	RAJALAKSHMI	26	3290	PRIMARY	5 YEARS	1.22	12.17	21		-	NORMAL	NORMAL
25	RAMYA	31	3199	PRIMARY	4 YEARS	1.57	16.5	22		-	NORMAL	NORMAL
26	DHANAKOTTI	25	3140	PRIMARY	3 YEARS	2.47	5.38	22		-	NORMAL	NORMAL
27	NANDINI	22	3229	PRIMARY	4 YEARS	1.6	6.8	19		-	NORMAL	NORMAL
28	KANAGA	27	3099	PRIMARY	5 YEARS	0.32	6.68	19		-	NORMAL	NORMAL
29	RAMYA	30	1190	PRIMARY	3 YEARS	3.86	39	29		-	NORMAL	NORMAL
30	KALAISELVI	34	1290	SECONDARY	8 YEARS	5.04	23	28		-	NORMAL	NORMAL
31	HEMAVATHY	24	1919	PRIMARY	3 YEARS	3.2	14.89	23		-	NORMAL	NORMAL
32	LAVANYA	25	1339	PRIMARY	5 YEARS	1.13	3.67	25		-	NORMAL	NORMAL
33	JEYANTHI	30	1980	PRIMARY	6 YEARS	1.52	8.68	20.13		-	NORMAL	NORMAL
34	NANDINI	25	1920	PRIMARY	4 YEARS	1.15	7.4	21.1		-	NORMAL	NORMAL

S.NO.	NAME	AGE	OP/IP NO	TYPE OF INFERTILITY	DURATION OF MARRIAGE	TSH	PROLACTIN	BMI	COMORBIDITIES	TREATMENT	HSG	SEMEN ANALYSIS
35	SARASWATHY	31	3149	SECONDARY	6 YEARS	11.1	80.17	30		-	NORMAL	NORMAL
36	VIJAYADARSHINI	23	607	PRIMARY	2 YEARS	5.46	26.51	28		-	NORMAL	NORMAL
37	PRASANNA	25	694	PRIMARY	4 YEARS	14.95	41.83	32		-	NORMAL	NORMAL
38	AMUL	34	1289	SECONDARY	10 YEARS	40	94	34		-	NORMAL	NORMAL
39	GEETA	22	1490	PRIMARY	2 YEARS	5.45	16.32	29		-	NORMAL	NORMAL
40	ARTHI	20	1432	PRIMARY	2 YEARS	12.13	45.86	33		-	NORMAL	NORMAL
41	JAYA	35		PRIMARY	9 YEARS	8.64	22	27		-	NORMAL	NORMAL
42	DEVAKI	35		PRIMARY	7 YEARS	8.44	31.8	28		-	NORMAL	NORMAL
43	KANCHANA	33		PRIMARY	6 YEARS	9.44	24	30		-	NORMAL	NORMAL
44	RAJALAKSHMI	34		PRIMARY	7 YEARS	6.74	28	29		-	NORMAL	NORMAL
45	SANGEETHA	21		PRIMARY	7 YEARS	13.44	35.2	28		-	NORMAL	NORMAL
46	SHEEBA	23	265746	PRIMARY	2 YEARS	10.9	43.5	33		-	NORMAL	NORMAL

S.NO.	NAME	AGE	OP/IP NO	TYPE OF INFERTILITY	DURATION OF MARRIAGE	TSH	PROLACTIN	BMI	COMORBIDITIES	TREATMENT	HSG	SEMEN ANALYSIS
47	MANIMOZHI	23	250283	SECONDARY	5 YEARS	2.6	15	22		-	NORMAL	NORMAL
48	AYESHA	27	239645	PRIMARY	6 YEARS	2	10	21		-	NORMAL	NORMAL
49	RAJESWARI	30	260436	PRIMARY	10 YEARS	1.9	10	22		-	NORMAL	NORMAL
50	SANDHYA	21	264767	SECONDARY	3 YEARS	1.9	12	24		-	NORMAL	NORMAL
51	LAVANYA	33	231502	PRIMARY	2 YEARS	4.4	22	27		-	NORMAL	NORMAL
52	KALIDA	25	206417	SECONDARY	6 YEARS	4.9	27	30		-	NORMAL	NORMAL
53	VARALAKSHMI	25	262667	PRIMARY	6 YEARS	4	25	27		-	NORMAL	NORMAL
54	MAHAZA BEE	26	264507	PRIMARY	12 YEARS	2.5	19	21		-	NORMAL	NORMAL
55	PRABHAVATHY	24	256082	SECONDARY	3 YEARS	6.4	26	29		-	NORMAL	NORMAL
56	AYESHA	27	239645	PRIMARY	6 YEARS	2	22	24		-	NORMAL	NORMAL
57	LAKSHMI	29	261848	PRIMARY	2 YEARS	1	22	23		-	NORMAL	NORMAL

S.NO.	NAME	AGE	OP/IP NO	TYPE OF INFERTILITY	DURATION OF MARRIAGE	TSH	PROLACTIN	BMI	COMORBIDITIES	TREATMENT	HSG	SEMEN ANALYSIS
58	VANITHA	32	257134	PRIMARY	4 YEARS	2	20	24		-	NORMAL	NORMAL
59	VINOSI	23	258408	SECONDARY	4 YEARS	1.9	17	23		-	NORMAL	NORMAL
60	REBEKHA	32	260745	PRIMARY	4 YEARS	2.6	25.5	29		-	NORMAL	NORMAL
61	MANIMOZHI	23	250289	SECONDARY-	4 YEARS	2.41	22	28		-	NORMAL	NORMAL
62	ROJA	23	258760	PRIMARY	3 YEARS	2.9	25	29	-	-	NORMAL	NORMAL
63	MEENAKSHI	26	263743	PRIMARY	4 YEARS	3.167	25.9	31	-	-	NORMAL	NORMAL
64	GAYATHRI	23	264062	PRIMARY	3 YEARS	2	18	22	-	-	NORMAL	NORMAL
65	KANIMOZHI	27	251066	SECONDARY	7 YEARS	5	26	30	-	-	NORMAL	NORMAL
66	SHANTHI	28	263845	PRIMARY	7 YEARS	1	7.9	22	-	-	NORMAL	NORMAL
67	AYESHA	22	264003	PRIMARY	4 YEARS	2.1	19	25	-	-	NORMAL	NORMAL
68	CHITRA	35	1149	PRIMARY	3 YEARS	2.7	22	24	-	-	NORMAL	NORMAL
69	SANDHIYA	26	264893	PRIMARY	4 YEARS	4.56	25.9	32	-	-	NORMAL	NORMAL

S.NO.	NAME	AGE	OP/IP NO	TYPE OF INFERTILITY	DURATION OF MARRIAGE	TSH	PROLACTIN	BMI	COMORBIDITIES	TREATMENT	HSG	SEMEN ANALYSIS
70	LAKSHMI	29	261848	PRIMARY	3 YEARS	2.4	19	26	-	-	NORMAL	NORMAL
71	KUMARI	27	269142	SECONDARY	5 YEARS	1.9	22	24	-	-	NORMAL	NORMAL
72	DOWLATH	27	241045	SECONDARY	7 YEARS	1.5	16	27	-	-	NORMAL	NORMAL
73	MAHESWARI	32	241049	SECONDARY	6 YEARS	2	19	29	-	-	NORMAL	NORMAL
74	VIJAYALAKSHMI	30	241066	PRIMARY	5 YEARS	2.7	20	30	-	-	NORMAL	NORMAL
75	SAVITHRI	34	286705	PRIMARY	5 YEARS	0.9	6.3	22	-	-	NORMAL	NORMAL
76	SANGEETHA	22	788277	PRIMARY	2 YEARS	5.9	25	26	-	-	NORMAL	NORMAL
77	PAVITHRA	29	240446	PRIMARY	8 YEARS	3.5	12.9	27	-	-	NORMAL	NORMAL
78	KOWSALYA	28	234072	PRIMARY	6 YEARS	0.7	9.9	32	-	-	NORMAL	NORMAL
79	GIRIJA	28	288575	SECONDARY	8 YEARS	10.1	29	33	-	-	NORMAL	NORMAL
80	KARTIGA	24	240288	PRIMARY	5 YEARS	2.9	24	30	-	-	NORMAL	NORMAL

S.NO.	NAME	AGE	OP/IP NO	TYPE OF INFERTILITY	DURATION OF MARRIAGE	TSH	PROLACTIN	BMI	COMORBIDITIES	TREATMENT	HSG	SEMEN ANALYSIS
81	PAVITHRA	22	28834	PRIMARY	5 YEARS	2.8	17	26	-	-	NORMAL	NORMAL
82	SUSHEELA	32	31284	PRIMARY	12 YEARS	5	25	29	-	-	NORMAL	NORMAL
83	JARINA	20	28773	PRIMARY	2 YEARS	2	18	25	-	-	NORMAL	NORMAL
84	SUDHA	28	50121	PRIMARY	4 YEARS	1.5	16	27	-	-	NORMAL	NORMAL
85	PAVITHRA	20	240446	PRIMARY	2 YEARS	2	5.9	24	-	-	NORMAL	NORMAL
86	JANAKI	23	262828	PRIMARY	3 YEARS	0.9	5.8	22	-	-	NORMAL	NORMAL
87	SUMATHI	35	262806	PRIMARY	5 YEARS	1.2	15	24	-	-	NORMAL	NORMAL
88	LAKSHMI	23	2797	PRIMARY	2 YEARS	2.4	14	26	-	-	NORMAL	NORMAL
89	LINGESWARI	25	262847	PRIMARY	4 YEARS	1.2	21	29	-	-	NORMAL	NORMAL
90	CATHERINE	33	258120	SECONDARY	5 YEARS	2	13	22	-	-	NORMAL	NORMAL
91	SRILAKSHMI	30	246975	PRIMARY	8 YEARS	6.9	27	30	-	-	NORMAL	NORMAL
92	PRABHAVATHY	24	256082	PRIMARY	3 YEARS	1.2	15	27	-	-	NORMAL	NORMAL
93	LOGESWARI	20	259547	PRIMARY	4 YEARS	1.8	14	25	-	-	NORMAL	NORMAL

S.NO.	NAME	AGE	OP/IP NO	TYPE OF INFERTILITY	DURATION OF MARRIAGE	TSH	PROLACTIN	BMI	COMORBIDITIES	TREATMENT	HSG	SEMEN ANALYSIS
94	PADMAVATHY	22	260093	SECONDARY	5 YEARS	2.9	26	29	-	-	NORMAL	NORMAL
95	MANIMEGALAI	23	2809	PRIMARY	4 YEARS	3.4	26	30	-	-	NORMAL	NORMAL
96	ASWINI	25	262898	PRIMARY	2 YEARS	1.9	21	26	-	-	NORMAL	NORMAL
97	AMULU	20	254344	PRIMARY	2 YEARS	0.5	4.5	21	-	-	NORMAL	NORMAL
98	HEMAVATHY	35	180219	SECONDARY	6 YEARS	3.5	25	28	-	-	NORMAL	NORMAL
99	PAVITHRA	22	24446	PRIMARY	2 YEARS	9.56	30	33	-	-	NORMAL	NORMAL
100	NISHANTHI	28	247900	SECONDARY	4 YEARS	7.3	27	31	-	-	NORMAL	NORMAL