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RESEARCH ARTICLE

CORRELATION OF PROLACTIN AND THYROID STIMULATING HORMONE LEVEL IN INFERTILE WOMEN.

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Abstract

High Prolactin levels interferes with normal Hypothalamo Pituitary Ovarian axis resulting in menstrual abnormalities , disturbances in ovulation, imbalance in hormone secretion and reduce the chances for conception. Hence this study was undertaken to include estimation of serum Prolactin while treating infertile patients. Hypothyroidism also contributes to anovulatory cycles in reproductive age group.

Introduction:-

Prolactin plays a major role in fertility and conception. High Prolactin level known as Hyperprolactinemia has been identified as a possible cause of infertility in women. High PRL levels can interfere with ovulation causing hormone imbalance, irregular menstruation, anovulation which reduces the chance of becoming pregnant and cause low progesterone levels also. Too much or too little of a certain hormone interferes with natural regular menstrual cycle. Hence it is very essential to keep them in complete balance while trying to conceive. FSH,LH,PRL & Thyroid Hormones are essential for the development of ova & needs to be investigated in cases of infertility. Men having high PRL suffer from Azoospermia, decreased libido and erectile dysfunction.

Aim & objectives:-

1. To evaluate and compare the level of Prolactin in BMI matched middle aged infertile women and parous groups.
2. To evaluate and compare the level of TSH in BMI matched middle aged infertile women and parous women.
3. To investigate the impact of serum prolactin on Thyroid hormone levels in infertile women.

Materals and methods:-

After getting Ethical Committee approval, informed written consent were obtained from patients.
It is a cross sectional study involving patients attending OPD for Infertility in the Department of Obstetrics and Gynaecology, Government Rajaji Hospital attached to Madurai Medical College, Madurai.

Study group:- consists of 30 infertile women attending Out patient Department of Obstetric and Gynaecology, Government Rajaji Hospital attached to Madurai Medical College, Madurai.
Control group:- consists of normal , fertile parous women with (regular menstrual cycles)attending OPD of both Gynaec and Endocrinology OPD, GRH,MDU.
Serum Prolactin & TSH were measured by enzyme immune assay on Elisa reader from venous blood collected around 8.30 a.m.to 9.30a.m.

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Review of literature:-

Arguments has raged for years about the existence of a purely prolactational hormone in the human**. Shearman & Turtle** 1970 emphasised the existence of Prolactin distinct from Growth Hormone.

Peake et al; 1969 studied Prolactin secreting cells to be different from those secreting Human Growth Hormone HGH. (1)

An acceptable concept is that there is no specific Prolactin releasing factor in the Hypothalamus but a specific inhibiting factor (PIF) is present.

Prolactin secreting cells are called as Lactotroph cells which constitute about 15-25 % of functioning anterior pituitary cells. Prolactin is also said to be secreted by various immune cells, lymphocytes (NK cells) , the brain and lining of uterus.

Two cell forms expressing Prolactin gene forms are present- Large PRL secretory granules (250-800 nm) are evenly distributed & 200-350 nm sized smaller granules are sparsely populated.

History:-

The **New York Times** on December 3, 1937 indicated Prolactin as the 'key to peace in the world '
Prof. C.R. Stockard proposed ' higher forms of life ' were governed by a 'glandocrazy ' especially Prolactin having an absolute control over functioning of individual from conception to death.

Structure:- The human PRL gene is located in chromosome 6 (2). PRL is a 199 amino acid polypeptide containing three intramolecular disulphide bonds. It circulates in blood in various sizes- monomeric PRL (little PRL;23 kd) , dimeric PRL (big PRL; 48-56 kd) and polymeric forms (bib,big PRL > 100 kd) (3).

Normal values for Prolactin are;
Males; 2-18 ng/ ml. (Ganong-5 ng/ml)
Non pregnant females; 2-29 ng/ml.(Ganong 8 ng/ml)
Pregnant females; 10-209 ng/ml.
The new units are pmol/l and to convert , multiply by 44. This means the normal level is less than 700 pmol/l or m IU//L Half life ranges from 26-47 minutes.

Regulation of secretion:-

- PRL secretion is under the inhibitory control of Dopamine , produced by the tubero infundibular (TIDA) cells and by the hypothalamic tubero hypophyseal dopaminergic system. (4,5)
- Dopamine released from the Hypothalamus suppresses PRL synthesis and release by the pituitary gland. It acts as 'Hypothalamic brake set' causing PRL secretion only when the brake is released.
- Dopamine reaches the lactotrophs through hypothalamo pituitary portal system and inhibits PRL secretion by binding with D2 receptors on pituitary lactotrophs. PRL by negative feedback controls its release by increasing Tyrosine hydroxylase activity in the TIDA neurons.
- PRL is down regulated by Dopamine and upregulated by Oestrogen.
- PRL secretion is inhibited by Endothelin-1, Transforming GF β1 and Calcitonin.
- Thyroid releasing hormone and Gonadotropin releasing hormone increases PRL secretion.
- FGF and Epidermal GF induce PRL synthesis and secretion.
- VIP stimulates PRL synthesis by cAMP .
- Oxytocin helps in its release.
- Estrogen stimulates PRL gene transcription and secretion explaining women having higher PRL levels. Women with regular menstrual cycles have a higher pulse frequency than postmenopausal women and men. (6)
- Galanin acts as a PRL releasing factor.
- Serotonin mediates nocturnal PRL secretion.
- Stimulation of the nipple , Exercise, Surgical and Psychological stress leads to Hypothalamic activation and PRL release. (10)
- Plasma PRL rises during onset of sleep and persists throughout sleep and lowest between 10 am and noon. It is also increased during pregnancy reaching a peak at the time of parturition.(11)

- PRL receptor gene is a member of cytokine receptor super family. It induces protein tyrosine phosphorylation and activates JAK 2 kinase and STATS 1 to 5 (7)

PRL effects on Reproductive function.:-

Prolactin also called as Luteotropic Hormone is a hormone released by Anterior Pituitary gland that plays a role in fertility. PRL acts by inhibiting Follicle stimulating hormone (FSH) and Gonadotropin Releasing Hormone (GnRH) , the hormones that trigger ovulation and allow eggs to develop and mature.

High Prolactin levels inhibit secretion of FSH causing hypo-estrogenism with ovarian dysfunction, menstrual abnormalities, suppression of ovulation and trouble getting pregnant in married women.Some women with hyperprolactinemia may have hypothyroidism characterized by low levels of serum thyroxine (14)& decreased negative feedback on hypothalamo pituitary thyroid axis. This results in increased secretion & release of TRH which acts on thyrotropes & lactotropes causing a significant rise in the levels of both TSH & Prolactin.A modest raise in PRL levels 20-40 ng/ml interferes with endometrial proliferation, ovarian follicular growth and development, reducing reproductive potential.(8)

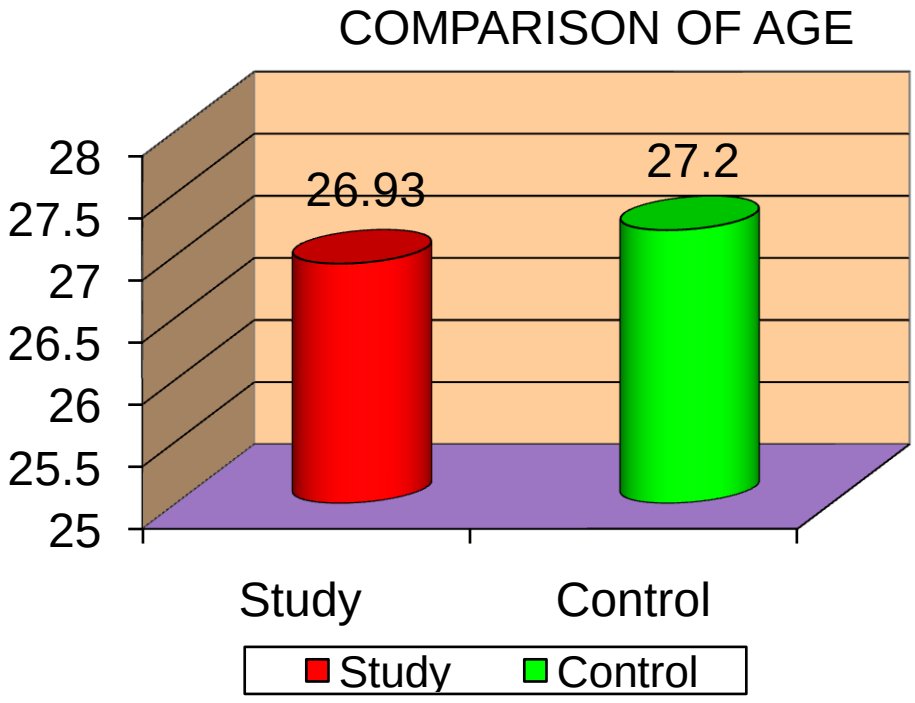
It reduces central FSH, LH levels. Decreases granulosa cells and oestradiol levels resulting in short luteal phase and finally amenorrhea. Fig 8-22 page 204 in Williams.

PRL secretion:-

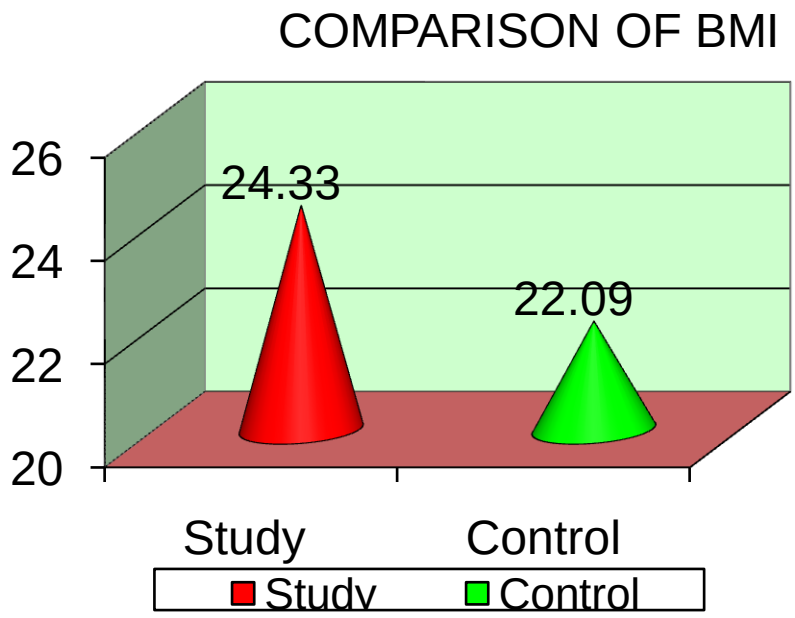
The release of prolactin is suppressed by Dopamine in the brain and any reduction in Dopamine will raise PRL and hinder the secretion and release of FSH and LH which result in menstrual dysfunction and disrupt ovulation . Hence it is very essential to get all hormones in balance to increase the chances of becoming pregnant.

The calculated production rate of PRL ranges from 200-536 µg/ day/ m2 and the metabolic clearance rate ranges from 40-71 ml/ min/m2 (9).

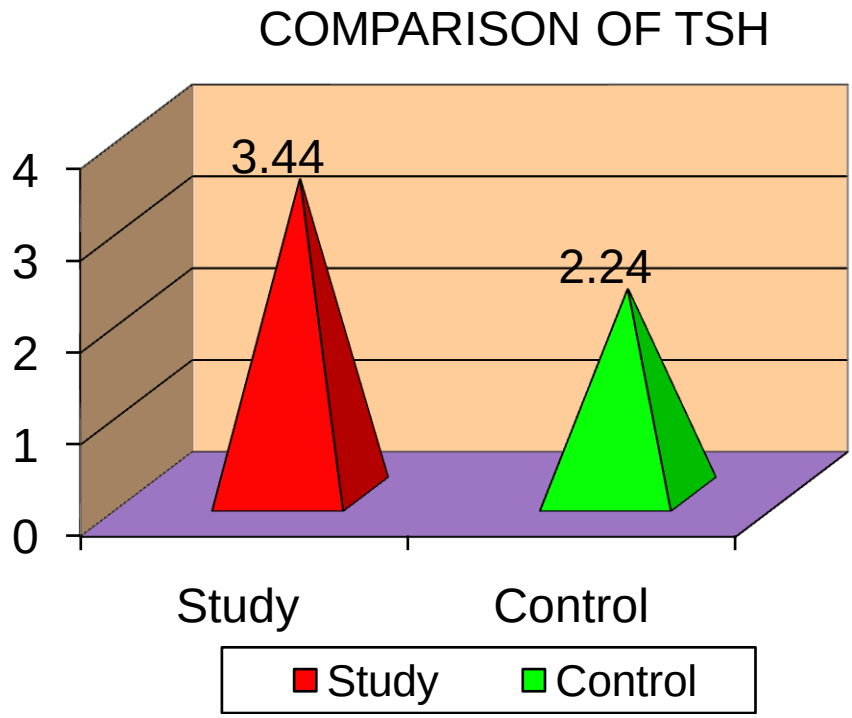
Observation:-



While analyzing the age in years in infertile with parous group, the mean age for the study group is 26.93 with standard deviation 4.94 and for control , it is 27.2 with SD 3.69. P value is 0.814 -not significant.

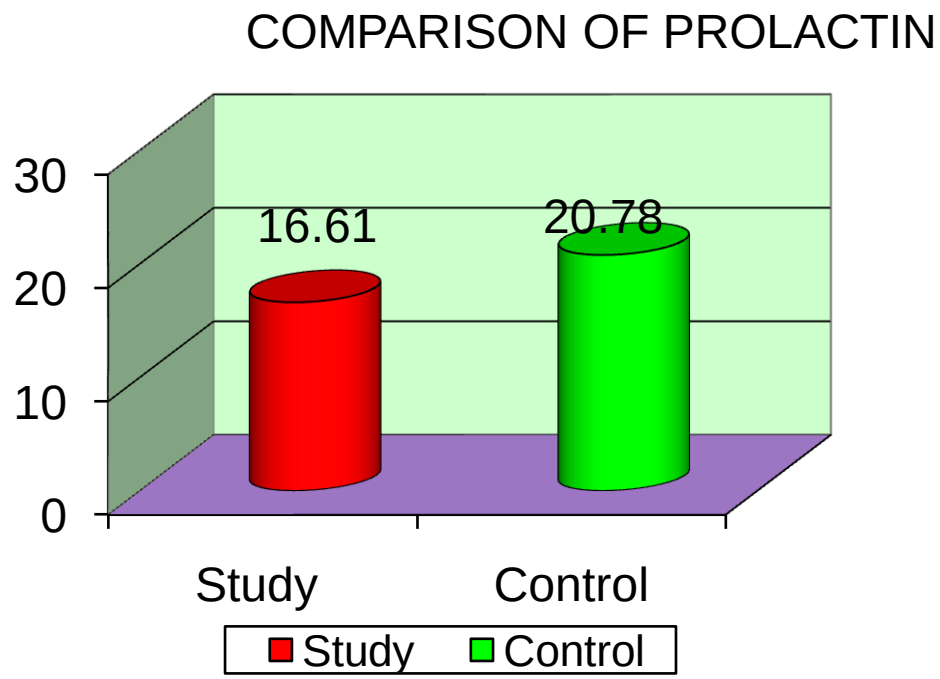


On comparing BMI in infertile with parous group, the mean BMI for the study group is 24.33 (SD 4.97) and for control , it is 22.09 (SD 2.77) .P value is 0.035 ie., significant.



On reviewing TSH levels, the mean TSH level for the study group is 3.44 (SD 1.96) and for control , it is 2.24(SD 1.11) the P value is 0.005 ie., significant.

On comparing Prolactin levels, the mean Prolactin level for the study group is 16.61(SD 15.38) and for control , it is 20.78(SD 15.73) the P value is 0.302 ie., not significant.



Discussion:-

Elevated Prolactin a common problem encountered in reproductive failures (15). It causes sexual dysfunction through a short loop feedback effect on gonodotropin pulsatility (12) presumably inhibiting GnRH (13) release. Numerous interactions of thyroid hormones with female reproductive system have led to ovulatory dysfunction in women with hypothyroidism. Hyperprolactinemia due to increased TRH production and altered GnRH pulsatile release results in delayed LH response and Corpus luteal insufficiency. Hypothyroidism is one of the causes for ovulatory failure. Hence this study is taken to find out the role of prolactin & its possible comparison with serum TSH levels in female infertility.

Conclusion:-

Not being able to conceive is heart breaking and may be little frustrating. When ovaries do not release eggs, the chance of getting pregnant is questionable. That is why healthy ovaries and a healthy uterus are vital to conception and carrying to fullterm.

Every hormone has a purpose and follows its own pattern, increasing or decreasing at different points throughout the cycle to produce a predictable and regular chain of events.

Too much Prolactin paves a major road block while trying conception. Incidental high levels of TSH in these patients emphasise the screening of TSH levels in infertility work outs.
Just figure out the causes for high PRL levels, treat it ,for a woman to be a happy and proud mother.

Administration of Thyroxine is beneficial to subclinical thyroid individuals as it normalizes prolactin and LH levels, corrects menstrual abnormalities and increases conception.

By eating a good balanced diet with plenty of vegetables and fresh fruits which contains Lycopenes, the hormone levels are balanced and the high PRL levels are also reduced. Lowering PRL helps ovaries perform the job they are intended for; uterus is also ready to receive the conceptus and carry the baby to term.

Proforma:-

Name Age Sex

Occupation

Inclusion criteria:- women with H/O anxious to conceive (infertility) in the age group of 15-40 years were selected for the study.

Exclusion criteria:-

H/O sternuous exercise / stress
H/O lack of sleep
H/O frequent analgesic intake
H/O anti depressant usage
H/O taking anti thyroid drugs
H/O PCOD
H/O visual disturbances
H/O thiazide diuretic intake
H/O taking anti hypertensives like Emdopa and Verapamil
H/O using cimetidine
H/O liver disease, kidney disease,shingles
H/O pituitary or sellar tumours.

Bibliography:-

1. Human Reproductive Physiology-Rodney P.Sherman P-49-52.
2. Owerbach D, Rutter W J, Cooke NE,et al. PRL gene. Science 1981; 212;815-816.
3. Sinha Y N. Structural variants of PRL; occurrence and physiological significance. Endocri. Rev 1995; 16; 354-369.
4. Kline JB , Clevenger CV. Identification and characterization of the Prolactin binding protein in human serum and milk. J Biol. Chem 2001; 276; 24760-24766.
5. Liu J W ,Ben Jonathan N . Prolactin releasing activity of neuro hypophyseal hormones; structure and functional relationship. Endocrinology 1994;134;114-118.
6. Katznelson L, Riskind PN et al- PRL pulsatile characteristics in postmenopausal women. J Clini. Endocrinol. Metab. 1998; 83;761-764.
7. Gao J, Hughes JP et al. Interactions among Janus kinases and PRL receptors. Mol Endocrinology 1996;10; 847-856.
8. Geoffrey Sher Aug,24. Significance of raised blood prolactin in women undergoing infertility treatment.
9. Cooper DS ,Ridgway EC, Kliman B et al. Metabolic clearance and production rates of prolactinin man. J Clin Invest 1979;64; 1669-1680.
10. Ganong's review of Medical Physiology-25th edition.p331-333.
11. Sassin JF, Frantz ag, WeitzmanED, KapenS, Human PRL -24 Hours pattern during sleep.Science 1972;177; 1205-1207.
12. Saunder SE, Frager M, Case GA et al. Abnormal pattern of LH secretion in women with hyperprolactinemia and amenorrhea. J Clini. Endocrina. Metabolism.1984; 59; 941-948.
13. Milenkovik et al. Inhibition of GnRH release by PRL GT1 neuronal cell lines through PRL receptors. Proc Natl Acad Sci USA1994; 91;1244-1247.
14. Avasti Kumkum. Hyperprolactinemia & its correlation with hypothyroidism in infertile women. J Obstet Gynaecol India,2006;56;68-71.
15. Choudhary SD, Goswami A. Hyperprolactinemia & reproductive Disorders –A profile from Northeast. J Assoc.Physicians India 1995;43;617-8.