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Biochemical association of obesity, atherosclerosis risk related to infertility in hypothyroid reproductive age group of women.

Biochemistry

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ABSTRACT

Background: The journey for people who are facing infertility may also suffers unrecognized health problems; and having difficulties in obtaining services that usually are not included by health insurance policy

Material and methods: The study was carried out in biochemistry department of Geetanjali Medical College & Hospital, Udaipur, and Rajasthan after obtaining GMCH ethical committee permission. Patients attending gynecology (Infertility & IVF) on 300 subjects and controls. Biochemical parameters were estimated by Cobas e-411 and c-311.

Results: Increased level of CRP, AIP and BMI (Positive correlation) were found in hypothyroid subjects along with having complications in fertility in this age group of women.

Conclusion: This is an opportunity for infertile couples to understand the impact of body weight on their reproductive capacity and take steps, without expert advice, to improve their reproductive capacity.

KEYWORDS:

hypothyroidism, infertility, obesity, TSH.

Introduction: Hypothyroidism is the second most common condition that affects women of reproductive age. An elevated level of TSH with normal peripheral thyroid hormone concentration suggesting sub-clinical hypothyroidism has been consistently found in obese subjects. TSH production is also regulated by neurotransmitters and hormones that influence body weight such as neuropeptide Y and alfa-melanocyte-stimulating hormone related peptide, that innervate hypophysiotropic TRH neurons.[1]

Slender women experience different signs and symptoms from obese women. The initial sign of altered reproductive cycles is similar to that of obese women. However, as estrogen production decreases, slender women experience decreasing vaginal mucous secretions as well as decreased breast size. Eventually, slender women experience vaginal dryness and loss of sex drive. [2]

Again, women who experience these signs and symptoms associated with changes in body weight can make the correlation, evaluate and treat themselves. If they seek professional medical attention, their physician(s) should support their self-evaluation and encourage them to correct their weight problem.[3]

The journey for people who are facing infertility may also suffers unrecognized health problems; and having difficulties in obtaining services that usually are not included by health insurance policy.4 Success with physical requirements and high cost of medical facilities may results in unexpected adverse outcome on the quality and health of person and their children.[5]

Male and female both can feel symptoms of hormonal imbalance, but female absolutely appear to get the bigger contribute in the pie when it comes to hormonally driven indications. Hormones are responsible for asserting so many functions like frame of mind, fertility, sleep, sexual characteristics, and capacity to handle anxiety.[6]

Dyslipidemia generally involve high levels of triglycerides, total cholesterol (TC), low density lipoprotein (LDL) and a decreased level of HDL cholesterol in plasma.7 . Atherogenic index of plasma is a marker of plasma atherogenicity. it is calculated as log (TG / HDLc). 8 . People who are at higher risk of CAD have increased AIP. 9 Etherification rate of apo-B lipoprotein is represent close to the AIP Value. AIP indicate the delicate metabolic interactions in the lipoprotein complex. [10.]

A recent report from the Coronary Artery Risk Development in Young Adults (CARDIA) study shows that among non–surgically infertile women, African and American women had two time increase in probability of describing a record of infertility.11 Economic problem limit access to diagnosis, estimation, as well as treatment and may direct to selectively underestimating the incidence of infertility in the similar population groups.12 The purpose of this research work was to outline the reasons why infertility , obesity and risk of atherosclerosis are public health concern in hypothyroid reproductive age group of women.

Material and Methods

The study was carried out in Biochemistry department, Geetanjali Medical College & Hospital, Udaipur, Rajasthan after obtaining GMCH ethical committee permission. Patients attending gynecology (Infertility & IVF) and Medicine OPD and IPD of Geetanjali hospital associated with Geetanjali medical college, Udaipur were enrolled in this study. Based on the inclusion and exclusion criteria 300 individuals were included in the present study after obtaining informed consent.

Blood collection, separation and storage of sample: Unique ID number was given to each participant of the study and same ID was given on sample container. After obtaining informed consent from all patients and healthy control, 5 ml of venous blood was collected in a sterile plain bulb under all aseptic precautions. Blood was drawn from anticubital vein in plain vial . After samples collection, samples were centrifuged in REMI centrifuge at 3000 RPM for a period of 15 minutes at central laboratory of Geetanjali Hospital. Serum were separated after centrifugation. Estimation of biochemical parameters was by following methods - Total Cholesterol (TC) CHOD-Pap,AllainC.C.1974 Total Triglyceride (TG) trinder method, Bucolo,G.,1973, High density Lipoprotein (HDL) (Kaplan A.1984), Low density Lipoprotein (LDL) (Friedewald WT, Levy RI,1972), Very low density lipoprotein (VLDL) (by calculation), Atherogenic index of plasma (AIP) (Dobiasova & Frohlich, 2001), C- reactive protein (CRP) (Andersen H.C,1950), T3 (3,5,3'-triiodothyronine) (Wheeler Mh,1994), T4 (Thyroxine) (Wheeler Mh,1994), Thyroid stimulating Hormone (TSH), (Evered DC,1985)

Measurement of body mass index (BMI)

Body mass index was measured as weight in kilogram per square of height in meter (Kg/m2). The patients were categorized as follows: Severely thin <16.9, underweight 17–18.4, desirable weight 18.5–24.9, overweight 25–29.9 and obese when BMI was>30 Kg/m2.

Statically analysis: The data was analyzed by using standard statistical software.

Results:

In the present study table no- 1shows Distribution of subjects according to BMI along with figure 1. BMI status was shown in table-2 . table 3 shows distribution according to pregnancy and infertility . table 4,5 shows TSH and CRP level in subjects and controls , respectively. Table 5 shows one way Anova for subjects and control to

lipid profile and atherogenic risk, which was showed significantly in table.

Figure6,7,8,9,10,11 shows correlation between hypothyroidism and obesity, hypothyroidism and risk of atherosclerosis, respectively. All figures were showed a significant positive correlation between infertility, hypothyroidism, obesity and risk of cardiac diseases.

Table-1 Distribution according to BMI

BMI(Body Mass index) kg/m2	Age (years)	Number (n)	Percentage%
Normal (18.5-24.9)	20-28	98	64.47 %
	29-36	55	56.12%
Overweight	20-28	32	21.05%
	29-36	27	27.55%
Obese Class -I (30-	20-28	10	6.57%
	29-36	9	9.18%
Severely Obese Class-II (35-	20-28	8	5.26%
	29-36	5	5.10%
Morbid obese Class -III(>40)	20-28	4	2.63%
	29-36	2	2.04%

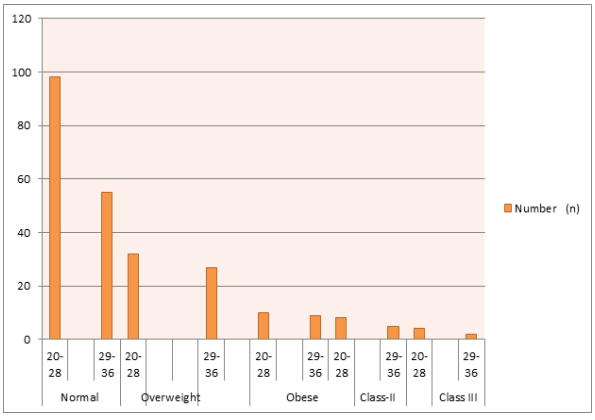

Figure -1 Distribution according to BMI

Table -2 BMI of subjects and control

Subjects	BMI(kg/m2) Mean± sd	BMI Control Mean± sd (Group C)	p-value
20-28 year (Group A)	24.65757 ± 5.754612 (n=151)	19.25± 4.23 (n=50)	A&C 0.0001 S
29-36 year (Group B)	25.17389 ± 5.035046 (n=98)	B&C 0.0001 S	
p-value(A& B)	0.4642 NS		

Table-3 Distribution according to normal pregnancy and infertility

Age (years)	Number (n)	Type of subjects	Number (n)	Percentage (%)
20-28	152	Normal hypothyroid pregnant women	91	60%
		Hypothyroid primary infertile women	45	30%
		Hypothyroid secondary infertile women	16	10%
29-36	98	Normal hypothyroid pregnant women	12	12%
		Hypothyroid primary infertile women	26	26%
		Hypothyroid secondary infertile women	60	62%

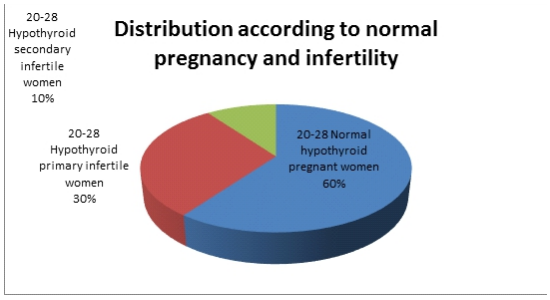

Figure 3 (A) : Distribution according to normal pregnancy and infertility(20-28 years)

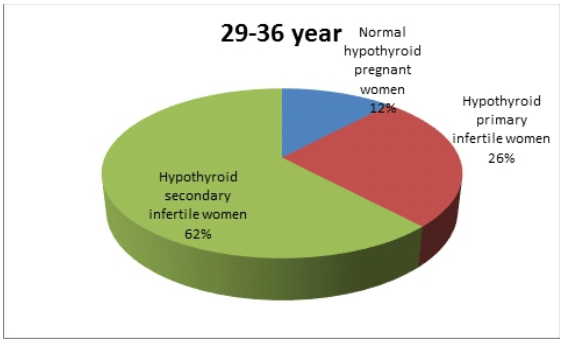

Figure3 (B) : Distribution according to normal pregnancy and infertility(29-36 years)

Table-4 Status of Thyroid Stimulating Hormone (TSH) level in Subjects and control

Subjects	20-28 years (n=152) Group A Mean ± Sd	29-36 years (n=98) Group B Mean ± Sd	Control (n=50) Group C Mean ± Sd	p-value A & C	p-value B &C	p-value A&B
Normal hypothyroid pregnant women	7.169230769± 1.257395218 (n= 91)	7.533333333± 1.364040344 (n=12)	2.788 ± 1.072778	0.0001 S	0.0001 S	0.0001 S
Hypothyroid primary infertile women	10.5866667± 3.76180566 (n=45)	16.5884615± 3.77140047 (n=26)		0.0001S	0.0001S	0.0001 S

Hypothyroid secondary infertile women	14.175± 1.819706 94 (n=16)	20.33167 ± 6.708899 (n= 60)		0.0001 S	0.0001 S	0.0001 S

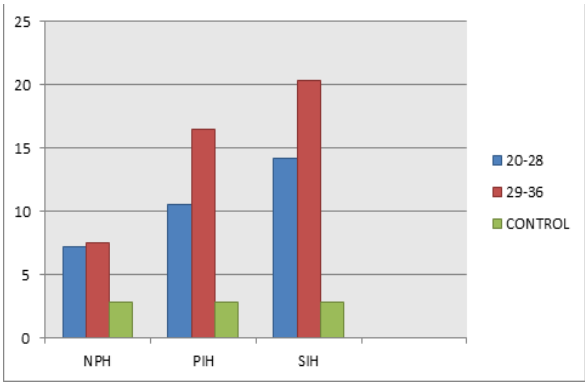

Figure- 4 status of thyroid stimulating hormone (TSH) level in subjects & control

Table-5

Subjects	20-28 years (n=152) Group A Mean ± Sd(mg/dl)	29-36 years (n=98) Group B Mean ± Sd(mg/dl)	Control (n=50) Group C Mean ± Sd(mg/dl)	p-value A & C	p-value B &C	p-value A&B
Normal hypothyroid pregnant women	8.382± 4.494931 (n= 91)	9.509375 ± 3.865036 (n=12)	5.9950980 4± 2.4922300 6	0.0007 S	0.0002 S	0.4113 NS
Hypothyroid primary infertile women	16.87467± 5.556672 (n=45)	19.17577 ± 4.824402 (n=26)		0.0001 S	0.0001 S	0.0824 NS
Hypothyroid secondary infertile women	22.00941± 4.02476 (n=16)	23.82567 ± 4.583004 (n= 60)		0.0001 S	0.0001 S	0.1520 NS

Status of C-reactive protein (CRP) in subjects

secondary infertile women	(n=16)	(n= 60)			

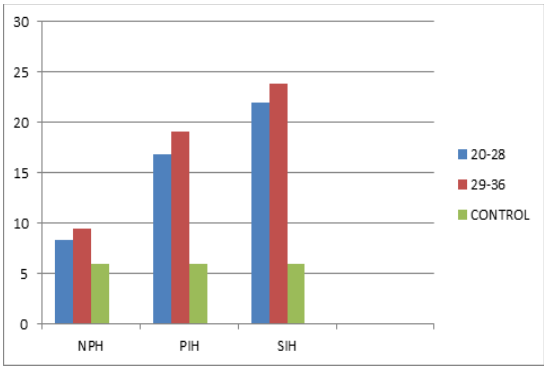

Figure- 5 Status of C-reactive protein (CRP) in subjects & control

Parameters	Mean ± SD(20-28 years)(n=152)	Mean ± SD(29-36years)(n=98)	Mean ± SD(control) (n=50)	SS	DF	F	MS	p-value
TC	198.54± 43.99	205.23 ± 44.64	152.58 ± 42.71	289,729.999	2	78.004	144,865.000	0.0001S
TG	166.17 ± 35.36	176.81 ± 51.56	113.81 ± 13.73	132,602.377	2	45.452	66,301.189	0.0002S
HDL	42.69 ± 13.05	40.97 ± 12.07	48.62 ± 4.62	9,948.193	2	166.685	4,974.096	0.0001S
LDL	111.63 ± 27.24	131.44 ± 23.44	68.58± 24.71	434,520.077	2	140.447	217,260.038	0.0001S
AIP	0.19± 0.15	0.28 ± 0.21	-0.02 ± 0.09	3.315	2	88.223	1.657	0.0001s

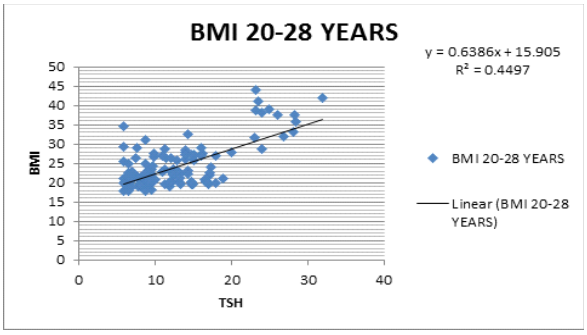

Figure-6 Correlations graph between BMI and TSH in age group 20-28 years

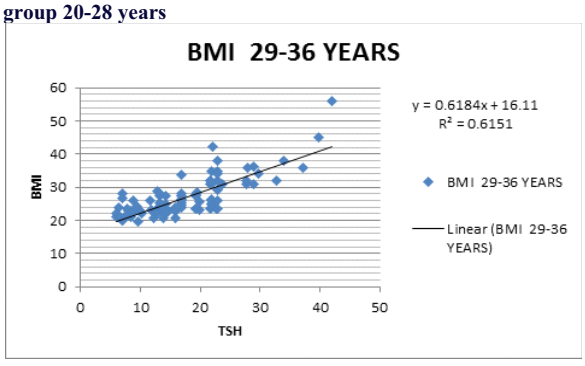

Figure -7 Correlations Graph between BMI and TSH in age group 29-36 years.

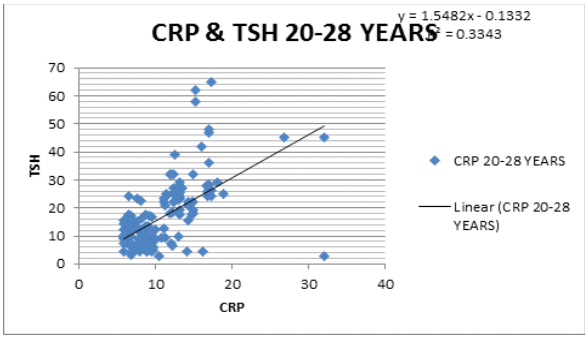

Figure -8 Correlations Between CRP and TSH in age group 20-28 years age.

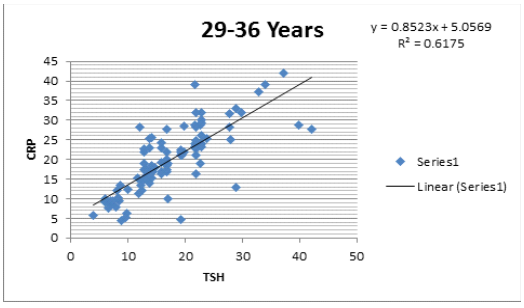

Figure -9 Correlations Between CRP and TSH in age group 29-36 years age.

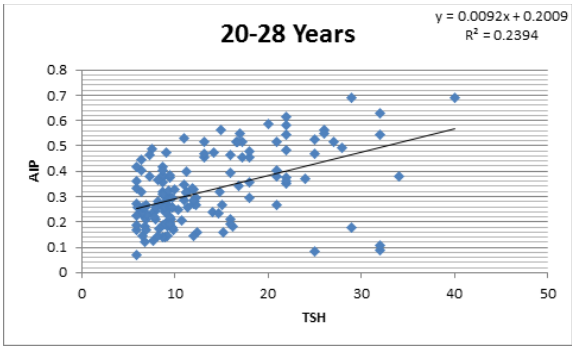

Figure -10 Correlations Between AIP and TSH in age group 20-28 years age.

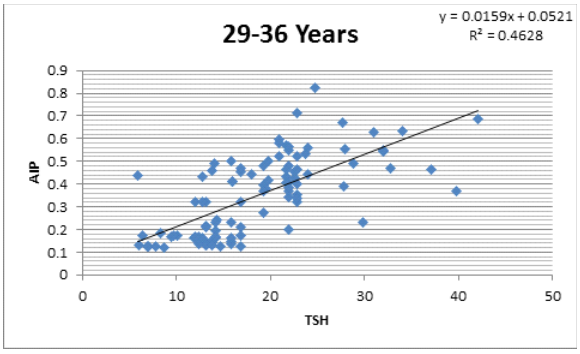

Figure -11 Correlations Between AIP and TSH in age group 29-36 years age.

Discussion:

The Present study "Biochemical association of CRP, IL-6,BMI and AIP in hypothyroid reproductive age group women with Gonadotrophin" has been done in Geetanjali medical college and hospital, Udaipur. We have been selected this topic because of " There is a great need for research into several issues regarding the complexity of infertility as well as related to pregnancy in hypothyroid women and their true negative late impact on woman's health. The real challenge will be after acquiring evidence based knowledge regarding the late consequences to adopt safe strategies in protecting woman's health during her all life."

Thyroid dysfunctions interfere with several aspects of reproduction along with pregnancy. Numerous articles have highlighted the involvement of hyperthyroidism and hypothyroidism with menstrual cycle disturbance, decreased fecundity and anovulatory cycle , increased morbidity in pregnancy.13 Problems associated in obese women include menstrual cycle disorders and decreased rate of Fertility. These are also related with obesity in the teenager and fertile periods, amplified perinatal abnormalities in obese women at the time of pregnancy or after pregnancy. Along with this increased incidence of cardiovascular diseases, ,cancer of the corpus uteri, and breast in obese women . 14 Butzow et al and Gurbuz were found in their study that in obese women found a positive (+ve) correlation between BMI and serum leptin level at the time of ovarian stimulation in IVF cycles.15 As well as found a negative correlation between increased concentration of serum leptin and number of oocyte retrieved. It showed that main source of leptin is adipose tissue. high concentration of leptin acting on ovarian level which suppresses ovarian response to gonadotropins 16.

Women with increases in BMI of one or more degrees between pregnancies are higher risk for pregnancy and complications in delivery for successive pregnancies. Women who's BMIs increased three times or more during pregnancies were twice risk as likely to have gestational diabetes in comparison to women with no change in BMI. Women who come into pregnancy overweight and obese maintain extra pregnancy weight gain. Obese Women are lose an average of 60 % of their weight gain even as normal women weight lose 80 %. Every year increased number of population, including kids and young people, is overweight and obese. The teenager girls in this increasing trend are the next generation of overweight as well as obese mothers. increase in overweight or obesity in adolescence today means a higher percentage of health problems, pregnancy complications in front of mothers or public health community in especially near future.17

Our study supports the hypothesis that hypothyroidism is associated with relatively increased inflammatory markers levels along with dyslipidemia in comparision to control group . this study was similar with the Christ-Crain,2003. 18 CRP levels rise rapidly in various pathological conditions and various inflammatory disorders e.g. overt hypothyroidism correlated with Ridker PM,2003, myocardial infarction correlated with Calorabo P,2012 and rheumatoid arthritis similar with Otterness IG.,1994.19,20,21

CRP is a sensible marker in inflammatory reactions. CRP level changed with gender and increase in age. Women at the time of parturition have elevated levels of CRP this is according to Wood WG,2000.22 CRP implements the innate immunity and protection against tissue damage by increase in phagocytosis, removing cells, damaged and dead organisms. Therefore, CRP through increasing redevelopment speed of damaged tissues leads in healing of these tissues. Although psychological stress causes rise in CRP, which can lead in a poor prognosis as well as pregnancy complications . our study was also similar with study of Coussons-Read ME,2007 . 23 De Maat MP, 2007 showed that CRP is a significant marker in inflammatory processes arises following hormonal stimulation . 24 This protein does not have diurnal alterations only administration of exogenous esterogen raises its level according to Störk S,,2008.25

Hypothyroidism is related with dyslipidaemia, therefore contributing to increase risk of atherosclerosis. Thyroid hormone affects the metabolism of TC and TG. The dilapidation of cholesterol is caused due to raise in hepatic LDL as well as in number of receptors or a stimulated LDL clearance. Therefore, TC or LDL levels are high in hypothyroidism. increase in LDL outcome in decreased exchange of cholesterol to bile acids . which lead to the down-regulation of LDL receptor. Increased levels of TG in hypothyroidism in due to decreased activity of enzyme lipoprotein lipase, consequential in a reduced clearance of TG rich lipoprotein, therefore representing decreased activity of hepatic lipase. The increase in LDL , TG depend on a decrease in oxidative capacity of fatty acids, that is shows a decrease of their catabolism these finding of our study were similar with the study of Shekhar R,2011 . 26

Dobiasova, M., and Frohlich, J,2001 showed The logarithmatically changed ratio of plasma TG and HDL-c strongly correlated with LDL-c particle size. 21It serve as an marker of atherogenic lipoprotein phenotype . AIP has higher predicted value for atherosclerosis according to Njajou, O., Kanaya,2009; Daniels,2008.22

Lipid profile is a group of biochemical tests. This is frequently used in diagnosing and treating lipid-related disorders according to Zoltan P, 2009 . 23 Normally, hyperlipidemias are significance to physician in perspective of risk factors for ischaemic heart disease or peripheral vascular disease this is similar to Parinita K,2012. 24,25 According to Burtis CA and Ashwood ER,1996 the initial step in diagnosis of cases of hyper- and hypolipoproteinaemias is to define lipoprotein pattern through chemical analysis of plasma levels of lipids and lipoproteins .25

According to Nwagha UI, 2010 Abundant facts have accumulated relating concentrations of lipids and their associated transporting lipoproteins with the incidence of atherosclerosis in common and CAD . 33 The strong relationship between the risk of CAD , higher level of LDL-c, lower level of HDL-C has been well recognized which was similar to Castelli WP,1988, Igweh JC,2005 .26

Conclusion: Despite the number of publications, both scientific publications and lay publications in the media, there is lack of knowledge about the relationship between body weight and infertility. This paper is an effort to further educate about this relationship so those couples contemplating pregnancy can assess their body weight as it pertains to their potential to conceive a pregnancy. This is an opportunity for infertile couples to understand the impact of body weight on their reproductive capacity and take steps, without expert advice, to improve their reproductive capacity.

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