

Risk of Cardiovascular Diseases and Inflammation in Hypothyroid Infertile Women

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ABSTRACT

Object: Day by day increasing number of evidence shows a higher risk of cardiovascular diseases in infertile women. It's associated with conditions like thyroid dysfunction and obesity. The aim of our study was to evaluate whether there any relationship exists between CVD and hypothyroid infertile women.

Material & Methods: 75 patients with 75 healthy controlled were enrolled for this study. CVD and inflammation markers like, interleukin-6, CRP, lipid profile were assessed by cobas-6000 and Elisa Methods.

Results: TC, TG, LDL, IL-6 and CRP higher and HDL level were lower in patients in comparisons to control.

Conclusion: our study suggested a positive relationship between hypothyroid infertile women and risk of CVD.

Key words: CVD, inflammation, hypothyroid, lipid profile.

INTRODUCTION

In a woman's life most important moment comes when she bears and delivers a child. But unfortunately all the women are not fortunate enough in this regard, and therefore, do not conceive and bear a child. In India where, usually, having kids is compulsory in conditions of family cheerfulness and numerous people still think about infertility as a "woman's problem". This problem develops crucial social existence. ^[1] The journey for people who are facing infertility may also suffer unrecognized health problems. ^[2] 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. Elevated IL-6 is usually marked in the altered cytokine profiles feature of

unexplained infertility, frequent spontaneous abortion, preeclampsia and preterm delivery. ^[3]

Cardiovascular disease is the most important cause of death in most developed nations for both male and female. The main key factor for the increase of cardiovascular complain is dyslipidemia, which may be coupled with complain like diabetes mellitus and obesity. Dyslipidemia generally involve high levels of triglycerides, total cholesterol (TC), LDL and a decreased level of HDL cholesterol in plasma. ^[4-8]

CRP may be vigorously linked with the atherosclerotic process. Endothelial dysfunction characteristically precedes development of atherosclerotic lesions. CRP collects in fatty streaks as well as fibrous plaques of the atherosclerotic vessel wall,

suggestive of a local inflammatory event. Two other inflammatory markers, interleukin-6 or myeloperoxidase, have been newly proposed as important intermediates of coronary artery disease. [9,10] But there is lack of literature relevant to infertility and hypothyroid infertile women in southern part of Rajasthan, so we have planned this study. The aim of our study was to evaluate whether there any relationship exists between CVD and hypothyroid infertile women.

METHODS

Present study was carried out in department of Biochemistry Geetanjali Medical College & Hospital, Udaipur, and Rajasthan after obtaining GMCH ethical committee permission. 75 Patients along with 75 healthy controls attending gynecology department (Infertility & IVF) and Medicine OPD and IPD of Geetanjali hospital associated with Geetanjali medical college, Udaipur were enrolled in this study. Patients between 20-36 years hypothyroid women were divided into following two groups depending upon their age.

Group I. Hypothyroid between age group 20-28 years.

Group II. Hypothyroid between age group 29-36 years

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 antecubital 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. Serums were separated after centrifugation. Serum was kept frozen at -20°C (for IL-6) until assayed. While analyzed for the following parameters:- Lipid profile (TC, TG, HDL, LDL, VLDL), CRP and IL-6. Lipid Profile Done by Cobas -6000 Fully automated Analyzer.

[11] CRP- it was estimated by turbidimetric immunoassay method at 546 nm by ERBA CHEM 5 PLUS V2 semi auto analyzer. [12]

Estimation of serum T₃, T₄, TSH : It was done by electrochemiluminescence immunoassay “ECLIA method in Roche Cobas e-411 along with quality control sera for accurate result. [13] Estimation of Serum Interleukin -6 done by ELISA Method. [14]

Statically Analysis: Statistic analysis used Student t- test and one way Anova by using software Graph-pad 8.0 version.

RESULTS

In our study we have found the levels of serum TSH in healthy control and infertile hypothyroid patients were 2.78±1.07 and 10.58± 3.76 respectively in 20-28, 16.53 ±3.77, respectively in 29-36 years of age group. Serum T₃ in healthy control and infertile hypothyroid patients were 1.25±0.36 and 0.40± 0.08 respectively in 20-28 years and 0.34 ±0.09, respectively in 29-36 years of age group. Serum T₄ in healthy control and infertile hypothyroid patients were 10.07±2.53 and 3.34± 0.95, respectively in 20-28 years and 3.14 ±1.08, respectively in 29-36 years of age group. (Table-1)

The levels of serum CRP in healthy control and infertile hypothyroid patients were 5.99±2.49 and 16.87±5.55, respectively in 20-28 years of age group and 19.17±4.82, respectively in 29-36 years of age group. The levels of serum IL-6 in healthy control and infertile hypothyroid patients were 1.16±1.56 and 12.42± 2.13, respectively in 20-28 years of age group and 18.13±0.90, respectively in 29-36 years of age group. (Table-1)

The levels of serum TC in healthy control and infertile hypothyroid patients were 152.58±42.71 and 200.88 ± 52.44, respectively in 20-28 years and 213.61±46.02, respectively in 29-36 years of age group. The levels of serum TG in healthy control and infertile hypothyroid patients were 113.81±13.73 and 170.81± 45.60, respectively in 20-28 years and 180.08 ± 65.32, respectively in 29-36 years

of age group. The levels of serum HDL in healthy control and infertile hypothyroid patients were 48.62± 4.68 and 45.57±12.98, respectively in 20-28 years and 41.24 ± 12.64, respectively in 29-36 years of age group. The levels of serum LDL in healthy control and infertile hypothyroid patients were 68.58± 24.71 and 124.66±23.70,

respectively in 20-28 years and 133.80 ± 21.89, respectively in 29-36 years of age group. Table-3, figure-1,2 shows a strong positive correlation between hypothyroid infertile women and inflammation with risk of CVD.

Table-1 Thyroid profile and inflammatory markers in hypothyroid infertile women and controls

Parameters	Control(n=75) Mean± SD	Patients (n=75) Mean± SD	p-value
T ₃ (20-28 years)	1.25±0.36	0.40± 0.08	<0.0001S*
(29-36 years)		0.34 ±0.09	
T ₄ (20-28 years)	10.07±2.53	3.34± 0.95	<0.0001S*
(29-36 years)		3.14 ±1.08	
TSH(20-28 years)	2.78±1.07	10.58± 3.76	<0.0001S*
(29-36 years)		16.53 ±3.77	
CRP(20-28 years)	5.99 ±2.49	16.87± 5.55	<0.0001S*
(29-36 years)		19.17±4.82	
IL-6(20-28 years)	1.16±1.56	12.42± 2.13	<0.0001S*
(29-36 years)		18.13±0.90	

*- Significant

Table-2 lipid profile in hypothyroid infertile women and controls

Parameters	Control (n=75) Mean± SD	Patients (n=75) Mean± SD	p-value
TC(20-28 years)	152.58±42.71	200.88 ± 52.44	<0.0001S*
(29-36 years)		213.61±46.02	
TG(20-28 years)	113.81±13.73	170.81±45.60	<0.0001S*
(29-36 years)		180.08 ± 65.32	
HDL(20-28 years)	48.62± 4.68	45.57±12.98	<0.0001S*
(29-36 years)		41.24 ± 12.64	
LDL(20-28 years)	68.58± 24.71	124.66±23.70	<0.0001S*
(29-36 years)		21.89	

*Significant

Table-3 (correlation between hypothyroid infertile and inflammation with risk of CVD)

PARAMETER	Mean ± Sd	r value
TSH	10.63± 2.25	0.53
IL-6	12.35± 2.80	
CRP	15.75± 4.68	

Showing a strong positive correlation between risk of CVD and hypothyroidism in infertile hypothyroid women

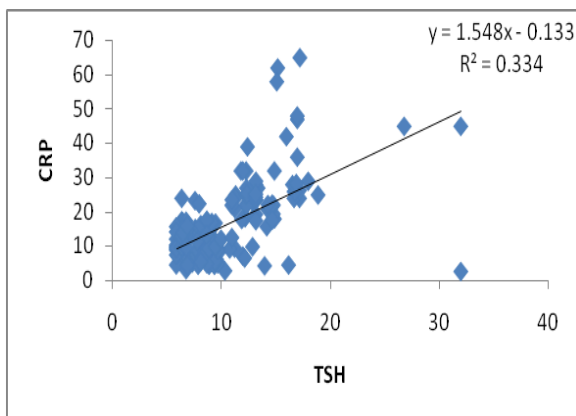


Figure-1CRP and TSH in hypothyroid infertile women (positive correlation)

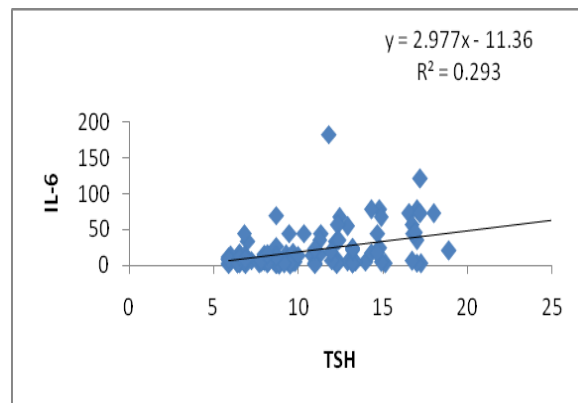


Figure-2 IL-6 and hypothyroid infertile women (positive correlation)

DISCUSSION

Infertile couples may transfer their irritation toward others, like family or friends. Unfortunately, irritation exhibited toward family may chase away those who are in rightist perspective to provide emotional support for infertile couple. One partner may besides become very irritated by other if they intellect that he or she does

not think about the same degree of emotional pain and have same powerful desire to overcome to infertility. In addition to, psychological stressors can directly stimulate transient increases in pro inflammatory cytokines, [15,16] and chronic stressors have been associated to continued overproduction of IL-6. In our study we have found higher level of IL-6 in patients, (Table-1) our these finding were supported with Steptoe, 2007. While regular physical activity is linked with lower range of IL-6 as well as other pro inflammatory cytokines. Acute exercise rapidly promotes production or release of IL-6 from skeletal muscles. IL-6 is released during physical activity inhibits production of TNF α and it can induce production of IL-10, single mechanism implicit in exercise's anti-inflammatory function. [17] In this study we have found higher level of CRP in patients in comparisons to control. Our finding were (Table-1) similar to Ridker PM, 2003. CRP is a sensible marker in inflammatory reactions. CRP level changed with gender and increase in age. CRP levels rise rapidly in various pathological conditions and various inflammatory disorders e.g. overt hypothyroidism, [18] myocardial infarction [19] and rheumatoid arthritis. [20] CRP is an efficient tool for diagnosis of risk of cardiac diseases. [17-20] Activity of CRP is stimulated by a specific cytokine; interleukin-6, which is an important as well as well established marker for inflammation. [17] Hypothyroidism could encourage chronic subclinical inflammation which raises Interleukin-6 levels resulting to raised level of CRP. Raised level of CRP could increase risk of atherosclerosis directly. [18-20]

Hypothyroidism has a deleterious impact on pregnancy. [21] This statement in support to our study with the finding of complications in pregnancy in hypothyroidism. (Table-1) In present study there were reported higher TC, TG, HDL (Table-2) in patients similar to study of Nwagha, 2010. Abundant facts have accumulated relating concentrations of lipids and their associated transporting

lipoproteins with the incidence of atherosclerosis in common and coronary artery disease. [22] The strong relationship between the risk of CAD, high of LDL-C levels, low HDL-C levels has been well recognized. [23,24] Still massive contributions of TG to cardiovascular risk have been underestimated. [22] The ratio of TG to HDL-C was a strong predictor of myocardial infarction. [25]

Our study is correlated with the other study. According to that highly significant decrease in HDL-C in hypothyroid patients were found as compared to controls. [26] LDL-C level was found low in hypothyroid subjects as compared to controls. [27] Hypothyroid patients had higher levels of oxidised LDL. Because in hypothyroidism LDL oxidation process is delayed. [27] So in our study we have found higher risk of CVD in these infertile hypothyroid Women. We had a strong positive correlation between inflammation and CVD risk in Hypothyroid infertile women (Table-3, Figure1,2) *Limitation of this study:* this was area wise study, less number of data were enrolled for the study.

CONCLUSION

There is a great need to aware people for hypothyroidism and infertility, so they can be prevented for future cardiac risk.

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