Study of Correlation of Raised Crp Levels in Premenopausal and Postmenopausal Females with Hypothyroidism: Raised Crp Levels in Hypothyroidism

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ABSTRACT

Objective: To evaluate the correlation of raised CRP levels in premenopausal and postmenopausal females with hypothyroidism and to assess the future risk of adverse coronary events amongst them.

Methodology: This was a prospective,observational,cross-sectional,analytical study,conducted in department of cardiology and medicine,Gandhi medical college,Hamidia hospital,Bhopal from October 2013 to October 2014.Patients having hypothyroidism were subjected to this study.Age matched controls were selected randomly.Purpose of this study was explained and informed consent was obtained.

Results: Percentage of raised CRP levels in hypothyroid premenopausal females was 13.3% and in hypothyroid postmenopausal females was 24.4%.CRP levels were raised only in 3.3% of premenopausal control group and in 10% of postmenopausal control group.

Conclusion: This study showed that there is strong association of raised CRP levels with hypothyroidism in both premenopausal and postmenopausal females.

Keywords: Crp, Hypothyroidism.

I. INTRODUCTION

CRP is called as C-reactive protein, is an inflammatory marker, produced by hepatocytes and is an acute phase reactant. Despite its name it is found to be elevated in both acute and chronic inflammation. More than 30 epidemiological studies have been done so far for association of raised CRP levels and adverse coronary events, but very few studies have shown importance of raised CRP levels in hypothyroidism and none have evaluated raised CRP levels in premenopausal and postmenopausal females with hypothyroidism. It has been found that population with raised CRP levels is associated with high risk of adverse coronary events. Adverse coronary events in our study are described as acute onset of myocardial infarction, unstable/stable angina, stroke, transient is chemic attack, congestive heart failure. There is an increased evidence of raised CRP levels and its association with recurrent episodes of cardiovascular morbidity in patients with established cardiovascular disease and in patients without any history of cardiovascular disease but having other conventional risk factors for cardiovascular disease.[1]studies have shown that CRP levels were found to be raised in postmenopausal females taking hormone replacement therapy,in middle aged males,females having high body mass index,high subcutaneous and visceral fat.A strong negative predictor was found to be high density lipoprotein for CRP.Despite of extensive studies on raised CRP levels and its association with adverse coronary events as described above,it lacks specificity for cardiovascular diseases but its role in development of atherosclerosis and plaque's rupture in atherosclerosed vessels is strong and it is a systemic as well as local inflammatory marker in the development of atherosclerosis.

Hypothyroidism is defined as raised TSH levels above the reference value (0.4-5.5micro international unit per millilitre) with or without decrease in free T4 levels.Patients with only raised TSH values and clinical symptoms of hypothyroid are considered to have subclinical hypothyroidism and included in our study.

II. METHODOLOGY

The study was conducted in department of cardiology band medicine, Gandhi medical college, Hamidia hospital, Bhopal from October 2013 to September 2014.It was a prospective- observational, cross sectional, analytical study on 90 premenopausal females with hypothyroidism and 90 postmenopausal females with hypothyroidism and 90 premenopausal and 90 postmenopausal females of age matched control groups from hospital staff and opd's,

without having hypothyroism and other conventional risk factors for cardiovascular diseases like DM2, Hypertension, hyperlipedemia and high body mass index and other systemic illnesses. Purpose of study was explained to study group and control group and informed consent was obtained.

III.   INCLUSION CRITERIA

(1) Patients diagnosed with hypothyroidism based on reference TSH values (0.4-5.5micro international unit per millilitre) and symptoms of hypothyroidism, on the basis of history, clinical examinations and investigations.

(2) Females are divided into 2 main groups of premenopausal and postmenopausal groups.Menopause is defined as permanent cessation of menstrual cycle for continuous period of 12 months due to loss of follicular activities of ovaries without any evidence of pathology leading to amenorrhea.

IV.   EXCLUSION CRITERIA

(1) Age less than 30 years

 (2) Females on oral contraceptives,hormone replacement therapy

(3) Patients with history of ischemic heart disease

(4) Patients taking steroids

(5) Patients with other systemic medical illnesses like liver diseases, renal failure, connective tissue diseases, rheumatoid arthritis.

Demographic determinants (age), personal habits (smoking, alcohol consumption, tobacco chewing), physical examinations and anthropometric measurements were recorded.

Blood samples were taken for biochemical investigations, CD-ECHO, Tread mill test if no

contraindication), ultrasonography of abdomen were carried out for each case and control group.

Diagnostic criteria for hypothyroidism is taken as TSH values more than reference level(0.4-5.5 micro international unit per millilitre) and CRP levels are termed qualitatively as positive or negative.

V.   RESULTS

Mean age of cases in premenopausal group was 38.83 with standard deviation of 4.856 years. Agewise distribution of patients showed that maximum number of hypothyroid premenopausal females belong to 35 to 40 years age group.

Premenopausa

	High CRP	%	Normal CRP	%	Total
Cases	12	13.3	78	86.7	90
Controls	3	3.3	87	96.7	90
Total	15	8.3	165	91.7	180

Chi square 4.6

p= 0.031

Mean age of cases in post menopausal group was 51.54 with standard deviation of 4.812 years. Agewise distribution of patients showed that maximum number of hypothyroid postmenopausal females belong to 45 to 55 years of age group.

Postmenopausal

	High CRP	%	Normal CRP	%	Total
Cases	22	24.4	68	75.6	90
Controls	9	10.0	81	90.0	90
Total	31	17.2	149	82.8	180

Cases n=180

PRE/POST MENOPAUSAL		AGE	BMI	SBP	DBP	TC	LDL	TG	HDL	VLDL	LVEF
POST MENOPAUSAL (n-80)	Mean	51.54	27.823353	126.25	80.06	201.65	82.590	149.16	38.81	26.107937	61.43
	Std. Deviation	4.812	3.7531870	13.648	11.048	53.058	21.4608	44.805	5.781	7.3555619	2.740
	Minimum	39	21.2585	110	62	116	46.0	69	24	13.8000	48
	Maximum	62	34.6260	160	110	302	124.0	288	48	44.0000	66
	Range	23	13.3675	50	48	186	78.0	219	24	30.2000	18

		AGE	BMI	SBP	DBP	TC	LDL	TG	HDL	VLDL	LVEF
PRE MENOPAUSAL (n-80)	Mean	38.83	26.678161	120.45	77.13	206.00	75.808	161.62	38.58	27.850000	62.78
	Std. Deviation	4.856	3.1726284	12.554	6.915	49.984	19.4160	30.492	5.660	7.4950739	3.48
	Minimum	28	18.0802	100	62	118	45.0	98	20	15.0000	48
	Maximum	48	32.8889	154	96	296	118.0	215	48	52.0000	70
	Range	20	14.8087	54	34	178	73.0	117	28	37.0000	22
Total	Mean	44.59	27.197205	123.08	78.46	204.03	78.882	155.97	38.68	27.060432	61.54
	Std. Deviation	7.972	3.4823053	13.332	9.109	51.257	20.5739	38.026	5.695	7.4562552	3.01
	Minimum	28	18.0802	100	62	116	45.0	69	20	13.8000	48
	Maximum	62	34.6260	160	110	302	124.0	288	48	52.0000	70
	Range	34	16.5458	60	48	186	79.0	219	28	38.2000	22

Cases n=180

Variables		AGE	BMI	SBP	DBP	TC	LDL	TG	HDL	VLDL	LVEF
Diabetic	Mean	47.04	28.649800	125.60	79.81	209.32	80.264	160.96	38.19	27.317333	61.000
	± SD	7.926	2.8021854	13.942	10.199	51.423	20.2599	160.96	5.642	7.7445774	3.500
	Minimum	32	20.5457	100	62	116	45.0	69	20	13.8000	48
	Maximum	62	34.6260	160	110	302	124.0	215	48	52.0000	70
	Range	30	14.0803	60	48	186	79.0	146	28	38.2000	22
Non diabetic	Mean	41.72	25.494945	120.13	76.88	197.83	77.263	150.13	39.27	26.759375	62.000
	± SD	7.063	3.4472895	12.026	7.405	50.761	20.9791	38.468	5.747	7.1525935	3.750
	Minimum	28	18.0802	100	68	116	45.0	69	20	13.8000	48
	Maximum	55	32.8731	154	100	296	124.0	288	48	52.0000	70
	Range	27	14.7929	54	32	180	79.0	219	28	38.2000	22
Total	Mean	44.59	27.197205	123.08	78.46	204.03	78.882	155.97	38.68	27.060432	61.000
	± SD	7.972	3.4823053	13.332	9.109	51.257	20.5739	38.026	5.695	7.4562552	3.643
	Minimum	28	18.0802	100	62	116	45.0	69	20	13.8000	48
	Maximum	62	34.6260	160	110	302	124.0	288	48	52.0000	70
	Range	34	16.5458	60	48	186	79.0	219	28	38.2000	22

Premenopausal

	DM2 present	%	NO DM	%	Total
Cases	33	36.7	57	63.3	90
Controls	15	16.7	75	83.3	90
Total	48	26.7	132	73.3	180

p-0.004
Chi square 8.2

Postmenopausal

	DM2 present	%	NO DM	%	Total
Case	42	46.7	48	53.3	90
Controls	20	22.2	70	77.8	90
Total	62	34.4	118	65.6	180

Chi square 4.6
P=0.032

A. *Results of regression analysis*

Post menopausal group

Dyslipidemia	High CRP	% High CRP	Normal CR	% Normal CRP	Total
YES	19	36.5	33	63.5	52
NO	3	7.9	35	92.1	38
Total	22	24.4	68	75.6	90

p=0.004   Significant

Pre menopausal group

Dyslipidemia	High CRP	% High CRP	Normal CR	% Normal CRP	Total
YES	11	22.4	38	77.6	49
NO	1	2.4	40	97.6	41
Total	12	13.3	78	86.7	90

p=0.013 Significant

Post menopausal group

BMI	High CRP	% High CRP	Normal CRP	% Normal CRP	Total
HIGH BMI	19	38.0	31	16.7	50
Normal BMI	3	7.5	37	76.5	40
Total	22	24.4	68	65.1	90

p=0.0019   Significant

Pre menopausal group

BMI	High CRP	% High CRP	Normal CRP	% Normal CRP	Total
HIGH BMI	11	18.6	48	16.7	59
Normal BMI	1	3.2	30	76.5	31
Total	12	13.3	78	65.1	90

p=0.085   Not significant

Post menopausal group

HTN	High CRP	% High CRP	Normal CRP	% Normal CRP	Total
YES	14	35.9	25	64.1	39
NO	8	15.7	43	84.3	51
Total	22	24.4	68	75.6	90

p=0.049   Significant

Pre menopausal group

HTN	High CRP	% High CRP	Normal CRP	% Normal CRP	Total
YES	10	24.4	31	75.6	41
NO	2	4.1	47	95.9	49
Total	12	13.3	78	86.7	90

p=0.12   Significant

Incidence of fatty liver and high bmi in our study groups:

Pre menopausal group

	Fatty liver present	%	Normal liver	%	Total
Cases	14	15.6	76	84.4	90
Controls	4	4.4	86	95.6	90
Total	18	10.0	162	90.0	180

Chi square   5
p=   0.025

Postmenopausal

	Fatty liver present	%	Normal liver	%	Total
Cases	27	30.0	63	70.0	90
Controls	11	12.2	79	87.8	90
Total	38	21.1	142	78.9	180

Chi square 7.5
p= 0.006

Premenopausal

	High BMI	%	Normal BMI	%	Total
Cases	59	65.6	31	34.4	90
Controls	42	46.7	48	53.3	90
Total	101	56.1	79	43.9	180

Chi square 5.7

p= 0.01

Postmenopausal

	High BMI	%	Normal BMI	%	Total
Cases	50	55.6	40	44.4	90
Controls	35	38.9	55	61.1	90
Total	85	47.2	95	52.8	180

Chi square 4.3

p= 0.03

VI. DISCUSSION

Total number of hypothyroid premenopausal females with raise CRP levels are 12 and 13.3% .Total number of euthyroid females from control group with raised CRP levels are 3 and 3.3%.

Total number of hypothyroid postmenopausal females with raised CRP are 22 and 24.4%,whereas euthyroid postmenopausal females from control group are 9 and 10%.As shown in above tables p value for premenopausal females with hypothyroidism is 0.031 which is significant and in post menopausal females with hypothyroidism is 0.01 which is also significant.

Postmenopausal females with hypothyroidism with DM 2 are 42 and 46.7% with p value 0.032and in premenopausal females with hypothyroidism with DM 2 are 33 and 36.7% with p value 0.004.

IT is significantly found that the raised CRP levels are present in our study group along with the DM 2.After regression analysis BMI ,Hypertension and dyslipidemia are significantly responsible in post menopausal group for raised CRP levels.Many of the premenopausal group in early 30's had presented with metabolic syndrome along with the hypothyroidism which is responsible for the raise CRP levels amongst them and their risk for developing adverse coronary events as mentioned above , in future.So this group is particularly important for long term.

VII. CONCLUSION

Above findings have suggested that there should be active interventions to screen pre and postmenopausal females for raised CRP levels in hypothyroidism to prevent future risk of adverse coronary events.In significant number of premenopausal and postmenopausal females with hypothyroidism DM2 is present which is again an independent risk factor for both raised CRP levels and adverse coronary events.However further studies need to be conducted and follow up of these cases are required to look for adverse coronary events.Above tables have also includes body mass index,systolic and diastolic blood pressures,lipid profiles with left ventricular ejection fractions.

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