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STUDY OF THYROID DYSFUNCTION AMONG METABOLIC SYNDROME PATIENTS IN RURAL POPULATION OF CENTRAL INDIA

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Running Title: - Study of thyroid dysfunction among metabolic syndrome patients.

Conflict of Interest: NIL

ABSTRACT

Background: Thyroid dysfunction with metabolic syndrome is recognized risk of atherosclerotic and cardiovascular disease. This study is an effort to investigate the proposed association between these two disease entities and to identify the factors that increase the risk of this association.

Methods: A cross sectional study from a teaching hospital in Bhopal city of central India. Total80 patients with metabolic syndrome were included in this study. Metabolic syndrome patients required to fulfil NCEP-ATP III criteria and 80 patients without metabolic syndrome were allocated into the control group. The biochemical parameters like: Fasting Glucose, Lipid Profile, Thyroid Profile, Hs-CRP, FINS, HOMA-IR levels were determined for assessment of metabolic dysfunctions.

Results: Fasting blood sugar, Total cholesterol, LDL and TAG level of metabolic syndrome subjects are significantly increases compare than to control group. Abnormal thyroid functions were found in metabolic syndrome group compare to control group. Hs-CRP, FINS and HOMA-IR level of metabolic syndrome subjects are significantly increases compare than to control group.

Conclusion: Our study suggests that a slight increase in serum TSH might be a risk factor for metabolic syndrome. Therefore, the screening of thyroid level essential to reduce the severity of disease and further investigations are needed to evaluate the mechanism of this correlation.

Keywords: Thyroid hormone, Metabolic Syndrome, Hs-CRP, FINS and HOMA-IR level.

INTRODUCTION:-

Metabolic syndrome (MetS) is a group of risk factors and characterized by hypertension, atherogenic dyslipidemia, hyperglycemia, prothrombotic and proinflammatory conditions[1]. MetS is linked with an increased risk of atherosclerotic cardiovascular disease and type 2

diabetes[2]. It was also referred to as insulin resistance syndrome by some until 1999, when the WHO named it metabolic syndrome as there was not ample evidence to show that the entire its components were caused by insulin resistance[3]. Accordingly to Anchanla R study, hypertension is common in Indian urban population[4]. Among these hypertension patients, the prevalenceof other components of metabolic syndrome was: diabetes in 31.8%, impaired glucose tolerance in 17.9%, hypercholesterolemia in 38.8%, hypertryglyceridemia in 38%, abdominal obesity in 64.3% and general obesity in 40%[5]. A other Studies have reported that in Indian city population, age-adjusted prevalence of metabolic syndrome was 69.3% in men and87.7% in women[6].

Subclinical hypothyroidism (SCH) is defined as an asymptomatic condition with high serum thyroid stimulating hormone (TSH) levels and normal free thyroid hormone levels[4]. SCH has also been suggested as a risk factor for atherosclerotic cardiovascular disease, and metabolic disorders such as hyperlipidemia, hypertension, low grade inflammation and hypercoagulability may accompany this process[7–8]. Our study is an effort to investigate the proposed association between these two disease entities and to identify the factor that increase the risk of this association with this aim, the prevalence of SCH was investigated in patients with and without MetS and the relation between SCH and MetS parameters was evaluated.

MATERIALS AND METHODS: -

Total 160 patients were included in this study among consecutive patients attending the out patients clinics of MIMS Hospital, Bhopal. 80 MetS patients required to fulfil NCEP-ATP III MetS diagnostic criteria and 80 patients without MetS were allocated into the control group.

A diagnosis of MetS was made if at least three of the diagnostic criteria proposed by the American National Cholesterol Education Program Adult III Treatment Panel (NCEP-ATP III) were met [blood pressure ≥130/85 mmHg (or use of antihypertensive medication); fasting plasma glucose ≥110 mg/dl (or use of anti diabetic medication); fasting triglycerides ≥150 mg/dl; HDL cholesterol <40 mg/dl (men) or <50 mg/dl (women); and waist circumference >102 cm (men) or >88 cm (women)][9].

Patients with known diabetes or other endocrine disorders, patients receiving any medication that may alter thyroid functions or lipid levels, pregnant women, and patients with an abdominal mass or ascites, or severe liver, heart or renal failure were excluded.

At baseline, demographic data was collected and a detailed physical examination was done. Sitting blood pressure was measured in left arms after at least 10 minutes of rest with an appropriate mercury sphygmomanometer using the Phase I and Phase IV Koroskoff sounds. The waist circumference was measured at the plane between anterior superior iliac spines and lower costal margins at the narrowest part of the waistline while the patient was standing and during slight expiration. Body Mass Index (BMI) was calculated by using Quetlet index (weight/height^2-kg/m^2)[10].

Blood samples obtained following 12 hours of fasting were immediately centrifuged (3500 rpm) and the serum were separated. Fasting Glucose, total cholesterol, HDL cholesterol and triglyceride levels were determined by enzymatic methods. LDL cholesterol was determined by using Friedewald formula[11]. Serum TSH, Total T_3 and Total T_4 measurements were made with Roche Elecsys Modular Analytics E170 device by using electrochemiluminescence immunoassay “ECLIA” method.

Serum levels of Hs-CRP were measured using validated high sensitivity assay (Dade Behring N high sensitivity CRP assay, Marburg, Germany), with a coefficient of variation of 3.6%. Reference range < 3.0 mg/l.[12]

Statistical Methods:

Inter-group comparisons of quantitative variables were made by using student t test for parameters with normal distribution and Mann Whitney U test for parameters without normal distribution.

Analysis of variance (ANOVA) has been used to find the significance of studyparameters between three or more groups of patients, Student t test (two tailed,independent) was used to find the significance of study parameters on continuousscale between two groups (Inter group analysis) on metric parameters. Statistical software SPSS version 21 were (IBM corporation, SPSS inc. RM 1804, Quarry Bay, Hongkong) used for statistical calculation.

Ethics statement: The study was approved by the Ethical Committee of the Institute. Informed consent was obtained from each patient.

Table 1: Demographic characteristics of metabolic syndrome patients and control group.

S No	Parameters		Met S (n=80)	Control (N=80)	*P* Value
1	Age (year)		43.18±15.01	42.18±15.62	--
2	Gender (n, %)	Male	37, 46.25%	40, 50%	--
3		Female	43, 53.75%	40, 50%	--
4	Smoking (n, %)		25, 31.25%	21, 26.25%	--
5	Alcohol (n, %)		30, 37.5%	20, 25%	--
6	Diabetes(n, %)		42, 46.4%	--	--
7	Hypertension(n, %)		45, 51.2%	05, 3.2%	--
8	BMI (kg/m^2)		33.7±5.77	26.56±4.26	0.001
9	SBP (mmHg)		142.2±20.6	112.4±17.7	0.001
10	DBP (mmHg)		92.4±8.7	86.1±9.6	0.001
11	WC (cm)		97.8±9.4	86.1±9.6	0.001
12	Total Cholesterol (mg/dL)		216.2±45.4	184.6±39.1	0.001
13	LDL (mg/dL)		126.5±43.1	114.2±41.6	0.001
14	HDL (mg/dL)		41.2±10.7	48.4±11.2	0.001
15	TAG (mg/dL)		205.5±95.6	117.6±69.9	0.001
16	FBS (mg/dL)		111.6 ±12.1	94.3±8.7	0.001

(BMI = Basal Metabolic Rate, MetS = Metabolic Syndrome, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, WC = waist circumference , HDL = high density lipoprotein, LDL = low density lipoprotein , TAG = Triglyceride, FBS = fasting blood sugar)

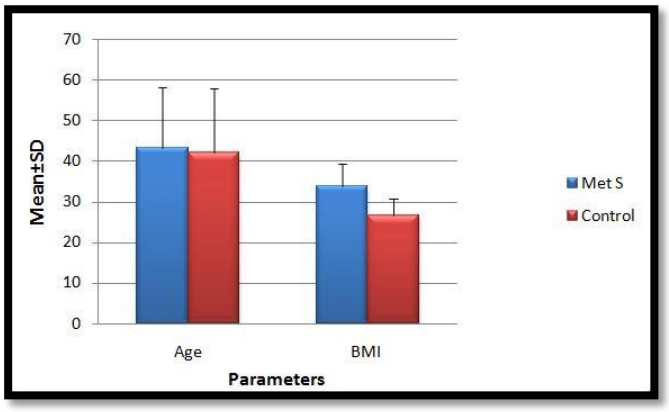


Figure 1a: Age and BMI of Metabolic syndrome patients and control group.

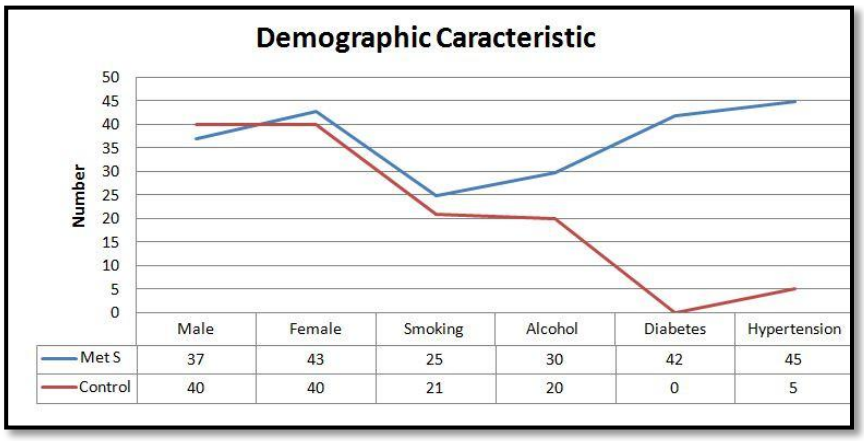
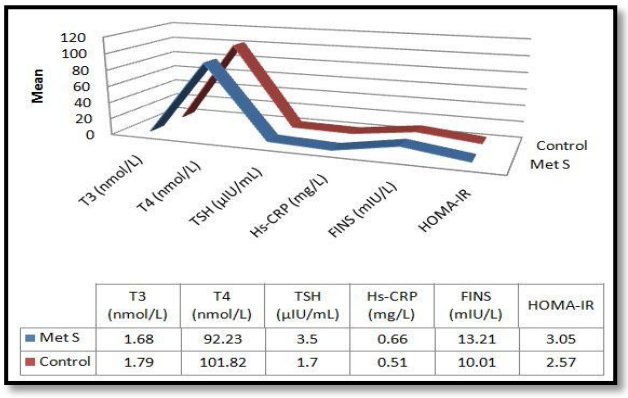


Figure 1b: Demographic Characteristics of Metabolic syndrome patients and control group.

Table 2 : Comparison of clinical variables in Metabolic syndrome patients and control group.

S No	Parameters	Met S (n=80)	Control (N=80)	*P* Value
1	T_3 (nmol/L)	1.68±0.38	1.79±0.36	0.062
2	T_4 (nmol/L)	92.23±22.67	101.82±23.71	0.001
3	TSH (µIU/mL)	3.5±2.7	1.7±1.4	0.001
4	Hs-CRP (mg/L)	0.66±0.31	0.51±0.28	0.001
5	FINS (mIU/L)	13.21±8.75	10.01±6.11	0.002
6	HOMA-IR	3.05±2.6	2.57±1.68	0.16

(TSH = thyroid stimulating hormone, Hs-CRP = high-sensitivity C-reactive protein, FINS = Fasting Insulin, HOMA-IR = Homeostatic model assessment- insulin resistance)



	T3 (nmol/L)	T4 (nmol/L)	TSH (µIU/mL)	Hs-CRP (mg/L)	FINS (mIU/L)	HOMA-IR
Met S	1.68	92.23	3.5	0.66	13.21	3.05
Control	1.79	101.82	1.7	0.51	10.01	2.57

Figure 2 : Comparison of clinical variables in Metabolic syndrome patients and control group.

Table 3 : Thyroid Status in Metabolic syndrome patients group.

S No	Thyroid status	Met S (no, %)
1	Euthyroid	60, 75%
2	Subclinical hypothyroidism	10, 12.5%
3	Overt hypothyroidism	08, 10%
4	Hyperthyroidism	02, 2.5%
	Total	80, 100%

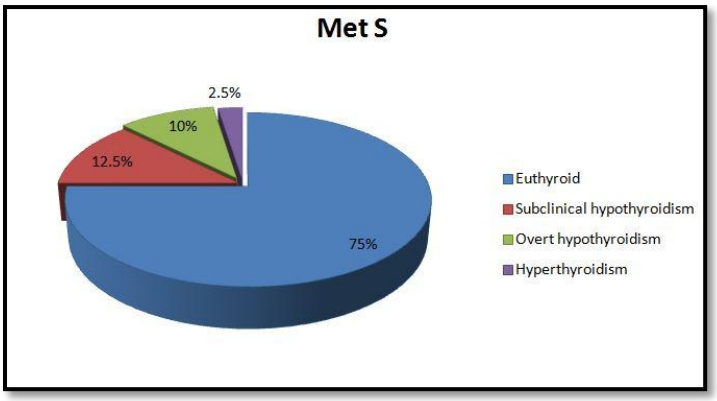
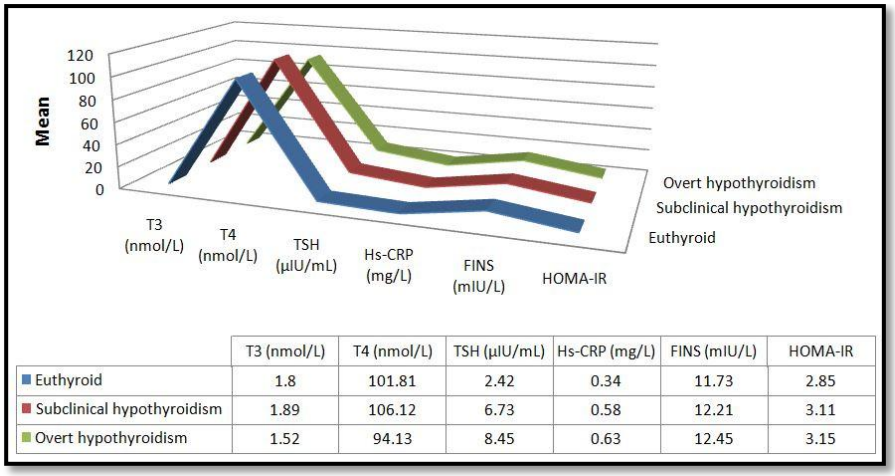


Figure 3 : Thyroid Status in Metabolic syndrome patients group.

Table 4: Comparison of Thyroid profile, Hs-CRP, Fasting Insulin and HOMA-IR in Metabolic syndrome patients.

	DIAGNOSIS METABOLIC SYNDROME PATIENTS			*P* Value
Parameters	**Euthyroid (60)**	**Subclinical hypothyroidism (10)**	**Overt hypothyroidism (08)**	
T_3 (nmol/L)	1.80±0.42	1.89±0.31	1.52±0.21	0.11
T_4 (nmol/L)	101.81±21.43	106.12±26.57	94.13±22.91	0.51
TSH (µIU/mL)	2.42±1.17	6.73±1.68	8.45±11.76	0.001
Hs-CRP (mg/L)	0.34±0.25	0.58±0.32	0.63±0.22	0.001
FINS (mIU/L)	11.73±5.11	12.21±6.01	12.45±5.83	0.91

HOMA-IR	2.85±1.83	3.11±1.78	3.15±1.56	0.84



	T3 (nmol/L)	T4 (nmol/L)	TSH (µIU/mL)	Hs-CRP (mg/L)	FINS (mIU/L)	HOMA-IR
Euthyroid	1.8	101.81	2.42	0.34	11.73	2.85
Subclinical hypothyroidism	1.89	106.12	6.73	0.58	12.21	3.11
Overt hypothyroidism	1.52	94.13	8.45	0.63	12.45	3.15

Figure 4: Comparison of Thyroid profile, Hs-CRP, Fasting Insulin and HOMA-IR in Metabolic syndrome patients.

RESULTS: -

Table 1: Total Eighty Met S subjects aged from 42 years to 60 years were enrolled (Figure 1a) and compared with age matched 80 healthy controls. Out of eighty MetSindividuals 37 (46.25 %) were males and 43 (53.75%) were females. Mean age of the MetS subjects was 43.18±15.01 with mean BMI 33.37±5.77 [Table 1]. Waist circumference of the Met S subjects was92.4±8.7 cm.

Met S group have 42 (46.4%) diabetic patients.Hypertension was the most commonly associated disease in the study population affecting 45 (51.2%) patients(Figure 1b).BMI, waist circumference (WC), SBP and DBP ofMetabolic syndromesubjects are significantly increases compare thanto control group respectively 33.7±5.77, 97.8±9.4, 142.2±20.6 and 92.4±8.7.

Fasting blood sugar, Total cholesterol, LDL and TAGlevel ofmetabolic syndromesubjects are significantly increases compare thanto control group respectively 111.6±12.1, 216±45.4, 126.5±43.1 and 205.5±95.6. HDL level of Met S group was significantly decreases compare thanto control group 41.2±10.7.

Table 2: Comparison of thyroid status of metabolic syndrome and control group. Abnormal thyroid functions were found in MetS group compare to control group, THS level of MetS group was significantly increases 3.5±2.7 and T4 level significantly decreases 92.23±22.67 compare to control group. However, T3 level of Met S group decreases non-significantly 1.68±0.38 compare to control group(Figure 2).

Hs-CRP, FINS and HOMA-IR level ofmetabolic syndromesubjects are significantly increases compare thanto control group respectively 0.66±0.3, 13.21±8.75 and 3.05±2.6.

Table 3: Show thyroid status of Met S group. Abnormal thyroidfunctions were found in 20 patients (25%) of Met S groupvsControl group. Subclinicalhypothyroidism was the most

common thyroid abnormality found in 10 patients (12.5%) of Met S group.Overt hypothyroidism was found in 08 patients (10%) andhyperthyroidismwas found in 02 patients (2.5%) of Met S group(Figure 3).

Table 4: Comparison of Thyroid profile, Hs-CRP, Fasting Insulin (FINS) and HOMA-IR were in metabolic syndrome patientsand its component. There was significant increase (p = 0.001) in TSHlevels between subclinical hypothyroid and Overt-hypothyroidism compare to euthyroid group.Hs-CRP level was significant increases (p = 0.001)between subclinical hypothyroid and Overt-hypothyroidismcompare toEuthyroid group. Other parameters T3, T4, FINS and HOMA-IR showed non-significant changes compare between subclinical hypothyroid, Overt-hypothyroidism and Euthyroid group. HOMA-IR and FINS level were increases in Overt-hypothyroidism compare to subclinical hypothyroidand Euthyroid group(Figure 4).

DISCUSSION:

Metabolic syndrome is a group of diseases, and it'sfocused on because it is a risk factor of thyroid disease, type 2 diabetesand cardiovascular diseases (CVD). The components ofmetabolic syndrome vary with different diagnostic criteria.The CDS diagnostic criteria for metabolic syndromecontain overweight/obesity, hyperglycemia,hypertension and dyslipidemia. Besides, metabolicsyndrome contains other metabolic dysfunction and diseases.Recent studies showed that thyroiddysfunction[13], even TSH within normal range[14]may be related to metabolic syndrome and its components and this is the clinical profile we scrutinize and discuss in our research.

A study indicated the level of insulin in Met Sgroup was obviously higher than thatin normal controls; however non-significant difference was found inHOMA-IR[15]. Asimilar study also indicatedthere was no correlation between and HOMA-IR, healso found FT4 correlated with insulin[11].Recently, Apublished a study conductedin Taiwan people, they found there was a significantincrease in a cluster of metabolic disease risk factors among people with hypothyroidism[16]. So more epidemiological studieswere needed to determine whether we should measureTSH in people with metabolic syndrome or not.

Our study found the level of TSH in metabolic syndromegroup was obviously higher than that in control group. So far,the majority studies believed metabolic syndrome is related toinsulin resistance, and central obesity in one cause ofinsulin resistance. Our study shows concordance with mentioned research and this is therapeutically judicious that we should payattention to the level of serum TSH in people with centralobesity apart from focusing on only insulin resistance.

The prevalence of subclinical hypothyroidismin normal population is about 12.5 %[17], most ofthe patients were women with mean age 43. Hypothyroidismis a main reason affecting blood lipid metabolism.

Inpatients with overt hypothyroidism, the LDL-C receptor'son hepatocytes was down regulated, so the clearanceof LDL-C was delayed, usually it is characterisedby high levels of serum cholesterol and LDL-C and lowlevel of HDL-C[18, 19]. Another study showed thelevels of TC, LDL-C and TG in hypothyroidgroup were elevated than in euthyroid group, but novariation was found in HDL-C level between the twogroups[20], also there was a study which found no differencesin the levels of total cholesterol, TG and HDL-C between hypothyroid group and euthyroid group[21].

Our study found the level of TG increased whilethe level of HDL-C decreased in MetSgroup. So this is reflected that our findings are in line with prior research although the results were different in differentstudies because of socio demographic variables,ethnic as well as other relevant clinical factors may play significant role , we could also show elevation of TSH insubclinical hypothyroidism may cause dyslipidemia.

A study showed that in euthyroid population, thecorrelation between TSH and blood lipid was regulatedby the insulin sensitivity, as a result, subjects with relativelyhigh TSH and insulin resistance had more possibilityfor dyslipidemia[22].Researchers still argued the relationship betweenserum TSH and blood pressure in subjects with subclinicalthyroid function and euthyroidism. Some researchersthought TSH positively correlated with SBP and/orDBP[23], while some other researchers did notget such results[24]. One study of Jayas Singh*et al* showed that when TSH was within normal range,there was no correlation between TSH and SBP andDBP. A studytook 728 healthy womenas subjects and found TSH positively correlated withSBP, with TSH increasing by 1mIU/L, SBP increased1.53mmHg, no correlation was found between TSHand DBP[22].

In subclinical hyperthyroidism subjects, we found TSH significantly increased with Hs-CRP and the risk of overweight/obesityincreased with TSH increasing, which was similar tosome other studies[25]. Some studies showedadipocytes and preadipocytes expressed TSH receptors,TSH binded with TSH receptors and induced preadipocytesto produce and release adipokines, some ofthem such as leptin played a very important role in theonset of metabolic syndrome and cardiovascular diseases[26]. Acute administration of TSH to thyroid patients caused endothelial dysfunctionand increased serum levels of C-reactive protein,TNF-α, several indices of oxidative stress and IL-6[27]. Perhaps TSH elevation stimulates the secretion ofinflammatory cytokines which leads to an increase inthe components of metabolic syndrome, but this is onlyour hypothesis and further investigations are needed toexplain the relationship between TSH elevation and theincrease of components of metabolic syndrome.

This study found the relationship between TSHand metabolic syndrome as well as its components inpeople with subclinical hyperthyroidism. Also, we saw the correlationbetween TSH and blood glucose level, maybe it was becausethe effect of thyroxine on blood glucose was strongerthan that of TSH[28]. Our recommendation is that those whoare MetS, whose TSH is over 10mIU/L and whoare thyroid autoantibodies positive should receive LT4replacement therapy. Recently, A studyused thyroid hormone analogue proteome in patientsreceiving treatment with statins and found it was associatedwith decreases in levels of atherogenic lipoproteinswithout adverse effects on heart and bone[29],maybe in the future this kind of drug

can be used inthe treatment of metabolic syndrome in order to lowerweight and control serum cholesterol without adverseeffects caused by LT4.

Our study suggests that a slight increase in serumTSH might be a risk factor for metabolic syndrome.Further investigations are needed to evaluate the mechanismof this correlation.

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Conflicts of interest - There are no conflicts of interest.

REFERENCES

1. Haffner SM. The metabolic syndrome: inflammation, diabetes mellitus, and cardiovascular disease. Am J Cardiol [Internet]. 2006;97(2A):3A-11A. Available from: http://dx.doi.org/10.1016/j.amjcard.2005.11.010

2. Wang C, Ye D, Xie Z, Huang X, Wang Z, Shangguan H, et al. Assessment of cardiovascular risk factors and their interactions in the risk of coronary heart disease in patients with type 2 diabetes with different weight levels, 2013-2018. Diabetes Metab Syndr Obes [Internet]. 2021;14:4253–62. Available from: http://dx.doi.org/10.2147/DMSO.S335017

3. Roberts CK, Hevener AL, Barnard RJ. Metabolic syndrome and insulin resistance: underlying causes and modification by exercise training. Compr Physiol [Internet]. 2013;3(1):1–58. Available from: http://dx.doi.org/10.1002/cphy.c110062

4. Anchala R, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, et al. Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. J Hypertens [Internet]. 2014;32(6):1170–7. Available from: http://dx.doi.org/10.1097/HJH.0000000000000146

5. Shantha GPS, Kumar AA, Jeyachandran V, Rajamanickam D, Rajkumar K, Salim S, et al. Association between primary hypothyroidism and metabolic syndrome and the role of C reactive protein: a cross-sectional study from South India. Thyroid Res [Internet]. 2009;2(1):2. Available from: http://dx.doi.org/10.1186/1756-6614-2-2

6. Surana SP, Shah DB, Gala K, Susheja S, Hoskote SS, Gill N, et al. Prevalence of metabolic syndrome in an urban Indian diabetic population using the NCEP ATP III guidelines. J Assoc Physicians India. 2008;56:865–8.

7. Kachhawa P, Sinha V. Assessment of thyroid dysfunction, dyslipidemia and oxidative stress in hypertensive end stage chronic renal disease patients in a teaching hospital in Western Uttar Pradesh. Asian J Med Sci [Internet]. 2019 Aug. 9 [cited 2021 Dec. 22];10(5):13-8. Available from: https://www.nepjol.info/index.php/AJMS/article/view/24688

8. Brienza C, Grandone A, Di Salvo G, Corona AM, Di Sessa A, Pascotto C, et al. Subclinical hypothyroidism and myocardial function in obese children. Nutr Metab Cardiovasc Dis [Internet]. 2013;23(9):898–902. Available from: http://dx.doi.org/10.1016/j.numecd.2012.04.006

9. Lorenzo C. The National Cholesterol Education Program-Adult Treatment Panel III, International Diabetes Federation, and World Health Organization definitions of the metabolic.

10. Ma W-Y, Yang C-Y, Shih S-R, Hsieh H-J, Hung CS, Chiu F-C, et al. Measurement of Waist Circumference: Midabdominal or iliac crest? Diabetes Care [Internet]. 2013;36(6):1660–6. Available from: http://dx.doi.org/10.2337/dc12-1452

11. Kannan S, Mahadevan S, Ramji B, Jayapaul M, Kumaravel V. LDL-cholesterol: Friedewald calculated versus direct measurement-study from a large Indian laboratory database. Indian J Endocrinol Metab [Internet]. 2014;18(4):502–4. Available from: http://dx.doi.org/10.4103/2230-8210.137496

12. Başkurt M, Aktürk F, Keskin K, Canbolat P, Karadag B, Kaya A, et al. Serum high-sensitivity C-reactive protein, amyloid associated protein and N-terminal proBNP levels do not predict reversible myocardial ischaemia. Cardiovasc J Afr [Internet]. 2011;22(2):85–9. Available from: http://dx.doi.org/10.5830/cvja-2010-041

13. Huang PL. A comprehensive definition for metabolic syndrome. Dis Model Mech [Internet]. 2009;2(5–6):231–7. Available from: http://dx.doi.org/10.1242/dmm.001180

14. Khatiwada S, Sah SK, Kc R, Baral N, Lamsal M. Thyroid dysfunction in metabolic syndrome patients and its relationship with components of metabolic syndrome. Clin Diabetes Endocrinol [Internet]. 2016;2(1):3. Available from: http://dx.doi.org/10.1186/s40842-016-0021-0

15. Srinivasa Nageswara Rao G, Prema G, Priya G, Arumugam SB, Kirthivasan V, Saibabu R, et al. Comparison between serum insulin levels and its resistance with biochemical, clinical and anthropometric parameters in South Indian children and adolescents. Indian J Clin Biochem [Internet]. 2011;26(1):22–7. Available from: http://dx.doi.org/10.1007/s12291-010-0069-z

16. Liu F-H, Hwang J-S, Kuo C-F, Ko Y-S, Chen S-T, Lin J-D. Subclinical hypothyroidism and metabolic risk factors association: A health examination-based study in northern Taiwan. Biomed J [Internet]. 2018;41(1):52–8. Available from: http://dx.doi.org/10.1016/j.bj.2018.02.002

17. Hennessey JV, Espaillat R. Diagnosis and management of subclinical hypothyroidism in elderly adults: A review of the literature. J Am Geriatr Soc [Internet]. 2015;63(8):1663–73. Available from: http://dx.doi.org/10.1111/jgs.13532

18. Havel RJ, Frost PH. The role of non-high-density lipoprotein-cholesterol in evaluation and treatment of lipid disorders. J Clin Endocrinol Metab [Internet]. 2000;85(6):2105–8. Available from: http://dx.doi.org/10.1210/jcem.85.6.6642-4

19. Davignon J, Genest J Jr. Genetics of lipoprotein disorders. Endocrinol Metab Clin North Am [Internet]. 1998;27(3):521–50. Available from: http://dx.doi.org/10.1016/s0889-8529(05)70024-4

20. Rizos CV, Elisaf MS, Liberopoulos EN. Effects of thyroid dysfunction on lipid profile. Open Cardiovasc Med J [Internet]. 2011;5(1):76–84. Available from: http://dx.doi.org/10.2174/1874192401105010076

21. Caraccio N. Lipoprotein profile in subclinical hypothyroidism: Response to levothyroxine replacement, a randomized placebo-controlled study. J Clin Endocrinol Metab [Internet]. 2002;87(4):1533–8. Available from: http://dx.doi.org/10.1210/jc.87.4.1533

22. Jayasingh IA, Puthuran P. Subclinical hypothyroidism and the risk of hypercholesterolemia. J Family Med Prim Care [Internet]. 2016;5(4):809–16. Available from: http://dx.doi.org/10.4103/2249-4863.201177

23. Bai M-F, Gao C-Y, Yang C-K, Wang X-P, Liu J, Qi D-T, et al. Effects of thyroid dysfunction on the severity of coronary artery lesions and its prognosis. J Cardiol [Internet]. 2014;64(6):496–500. Available from: http://dx.doi.org/10.1016/j.jjcc.2014.03.009

24. Khan S, Afsana F, Talukder SK, Ashrafuzzaman SM, Pathan F, Latif ZA. Presence and association of sub clinical hypothyroidism in subjects with metabolic syndrome. Diabetes Metab Syndr [Internet]. 2011;5(4):183–7. Available

from: http://dx.doi.org/10.1016/j.dsx.2010.12.006

25. Ghergherehchi R, Hazhir N. Thyroid hormonal status among children with obesity. Ther Adv Endocrinol Metab [Internet]. 2015;6(2):51–5. Available from: http://dx.doi.org/10.1177/2042018815571892

26. Janson A, Rawet H, Perbeck L, Marcus C. Presence of thyrotropin receptor in infant adipocytes. Pediatr Res [Internet]. 1998;43(4 Pt 1):555–8. Available from: http://dx.doi.org/10.1203/00006450-199804000-00021

27. Czarnywojtek A, Owecki M, Zgorzalewicz-Stachowiak M, Woliński K, Szczepanek-Parulska E, Budny B, et al. The role of serum C-reactive protein measured by high-sensitive method in thyroid disease. Arch Immunol Ther Exp (Warsz) [Internet]. 2014;62(6):501–9. Available from: http://dx.doi.org/10.1007/s00005-014-0282-1

28. Johnson JL. Diabetes control in thyroid disease. Diabetes Spectr [Internet]. 2006;19(3):148–53. Available from: http://dx.doi.org/10.2337/diaspect.19.3.148

29. Ladenson PW, Kristensen JD, Ridgway EC, Olsson AG, Carlsson B, Klein I, et al. Use of the thyroid hormone analogue eprotirome in statin-treated dyslipidemia. N Engl J Med [Internet]. 2010;362(10):906–16. Available from: http://dx.doi.org/10.1056/NEJMoa0905633