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HYPOTHYROIDISM;

AS A CAUSE OF DYSLIPIDEMIA IN YOUNG PREDISPOSES TO INCREASED RISK OF CARDIOVASCULAR DISEASE.

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ABSTRACT… Cardiovascular diseases (CVDs) are the number one cause of death globally: more people die annually from CVDs than from any other cause. An estimated 17.5 million people died from CVDs in 2012, representing 31% of all global deaths. Although CVDs are uncommon entity in young patients, it constitutes significant health problem due to its dyslipidemia cases and devastating effects on active life style of young patients, it is therefore important to identify diseases in young that are associated with or a cause of dyslipidemia[1]. Hypothyroidism is an important cause of dyslipidemia in young that can significantly increase the risk of CVDs[2]. **Objectives:** This study is designed "to determine frequency of dyslipidemia in young hypothyroid patients". **Place and duration of Study:** Study conducted at Medical OPD JPMC, Karachi (outpatient) in six months duration from 25th May 2009 to 24th November 2009. **Patients and Methods:** Study is performed on 100 newly diagnosed cases of primary hypothyroidism between ages 25 to 55 years, non-smokers, having no previous history of Ischemic Heart Disease (IHD) or family history of premature CVD, diabetes mellitus (DM), hepatic or renal disease, not on drugs which could alter serum lipids. Selected case undergone 14 hours fasting lipid profile check. **Results:** Out of 100 hypothyroid cases, 91% had dyslipidemia which was directly proportional to severity of hypothyroidism. Out of 100 hypothyroid cases, 95 (95%) were of young age group i-e from 25-49 years, and all of them were dyslipidemic, while 05 (5%) hypothyroid patients were of age group more than 50 years and none of them had dyslipidemia. (0.00%) and this distribution of dyslipidemic in young hypothyroid patients is statistically significant (p value 0.031) **Conclusion:** Hypothyroidism is associated with high frequency of dyslipidemia in young patients which significantly predisposes them to risks of CVDs.

Key words: Primary Hypothyroidism, thyroid hormones, lipoproteins, Dyslipidemia, Cardiovascular diseases (CVDs), Levothyroxine therapy.

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INTRODUCTION

CVDs are the number one cause of death globally: more people die annually from CVDs than from any other cause. An estimated 17.5 million people died from CVDs in 2012, representing 31% of all global deaths. Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke. Over three quarters of CVD deaths take place in low- and middle-income countries. Although cardiovascular diseases are an uncommon entity in young patients, it constitutes a significant health problem due to its dyslipidemia cases and devastating effects on the active lifestyle of young patients. The frequency of Myocardial infarction (MI) in younger subjects is normally low; however, over the years, a rising trend has been observed in the number of young patients presenting with MI. Most cardiovascular diseases can be prevented by early identification and management of modify-able risk factors like Smoking, Dyslipidemia, Hypertension, Syndrome X and hyper-homocystinemia. Dyslipidemia is one of the major and an independent risk factor for coronary heart disease and commonly coexist with other major risk factors. It is defined as elevation of plasma cholesterol, Total Cholesterol (TC), Low Density Lipoproteins (LDL), triglycerides (TGs) and a low levels of high-density lipoproteins (HDL) that contributes to the development of atherosclerosis.[1] Among the most important causes of secondary dyslipidemia is hypothyroidism because Thyroid function

significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors, thus influencing overall CVD risk. Hypothyroidism is a common metabolic disorder in the general population. Indeed, data from the third National Health and Nutrition Examination Survey (NHANES III) showed a 4.6% prevalence of hypothyroidism in the general population.[2] According to one estimate, 15/1000 females and 01/1000 males are affected worldwide[3] In Pakistan thyroid diseases are common and incidence of hypothyroidism is twice that of hyperthyroidism, but exact data is not available. No age is immune for hypothyroidism, however autoimmune phenomena and iodine deficiency are important causes of hypothyroidism in young. Hypothyroidism associated dyslipidemia presents as raised TC, LDL-C, Apo-lipoprotein (A and B), TGs and low levels of HDL-C thus associated with cardiovascular morbidity and mortality.

Thyroid hormones can influence HDL metabolism by increasing cholesteryl ester transfer protein (CETP) activity, which exchanges cholesteryl esters from HDL_2 to the very low density lipoproteins (VLDL) and TGs to the opposite direction. In addition, thyroid hormones stimulate the lipoprotein lipase (LPL), which catabolizes the TG-rich lipoproteins, and the hepatic lipase (HL), which hydrolyzes HDL_2 to HDL_3 and contributes to the conversion of intermediate-density lipoproteins (IDL) to LDL and in turn LDL to small dense LDL (sdLDL). Another effect of T_3 is the up-regulation of Apo lipoprotein AV (ApoAV), which plays a major role in TG regulation. Indeed, increased levels of ApoAV have been associated with decreased levels of TGs. which is negatively affected in hypothyroidism.[4] Hypothyroidism effects CVDs risks by other means like: insulin resistance[5], arterial hypertension, vascular stiffness, raised uric acid and phosphate levels, Hyperhomocystinemia, Syndrome X, raised BMI, endothelial dysfunction[6] and increase oxidative damage to vessels. As primary hypothyroidism equally affects young with female preponderance, it is therefore important to diagnose these case and treat with thyroid replacement therapy especially in overt cases. This will revert thyroid related dyslipidemia and thus significantly reduce risk of CVDs.

Study Design
Cross Sectional Study.

Setting
Patients attending Medical OPD, JPMC Karachi.

Duration of Study
Six months from 25th May 2009 to 24th November 2009.

Sample Size
Medical OPD received 8-10 patients of thyroid disease daily. On average 1500 patients reported for thyroid related complaints in six months duration from 25-5-2009 to 25-11-2009 out of which 280 patients were newly diagnosed cases of primary Hypothyroidism. 100 patients fulfilling Inclusion and exclusion criteria selected for study.

Sample Technique
Non – probaliliting purposive

Inclusion Criteria
1. All newly diagnosed, untreated cases of primary hypothyroidism.
2. Both young and old patients were included in study, however extremes of ages were avoided. Minimum age 25 years and maximum age was 55.

Exclusion Criteria
1. All patients with secondary hypothyroidism (low levels of both TSH and FT3 and FT4)
2. All patients with diabetes mellitus.
3. All patients with nephritotic syndrome.
4. All patients with pre-existing CVDs and family history of premature CVDs.
5. All patients with three months history of use of pharmacological agents as levothyroxine, B- blockers, anabolic steroids, diuretics, oral contraceptives and statins.

Data Collection Procedure
Newly diagnosed, untreated but registered cases of primary hypothyroidism fulfilling inclusion

exclusion criteria included in study. Diagnostic criteria of primary hypothyroidism was taken as TSH level >4.05mIU/L, and FT4 level <0.89 mIU/L, according to values recommended by laboratory of Atomic Energy Centre, JPMC, by using Kit of IMMUNOTECH BACKMAN COULTER COMPANY. Diabetes mellitus was excluded out by checking fasting sugar as per American Diabetic Association (ADA) criteria. Nephrotic syndrome was excluded on basis of negative history and examination and 24 hour urinary protein loss in suspected cases. IHD and family history of premature coronary heart disease was excluded on basis of history and ECG findings. All the cases were non- smokers. In all selected cases 14 hours fasting lipid profile including TC, LDL-C, HDL-C and TGs checked in mg/dl of serum. Informed consent was taken from all patients and Information regarding variables were collected on proformas.

Data Analysis Procedure

The filled on proforma were converted into database on SPSS number 10. For description purpose variables were divided into categories. Hypothyroidism divided into mild, moderate and severe groups, on basis of TSH in mIU/L as: mild (4.05-13), moderate (14-24) and severe (>24). Serum. TC, LDL-C, HDL-C and TGs levels were classified into desirable, near optimal, borderline, high and very high levels according to the classification given by National Cholesterol Education Program, adult Panel III (NCEP ATP III) (Table-I).

Patients were labeled as dyslipidemia who's two or more than two values of lipid profile were raised (above desirable or near optimal values). The total dyslipidemia was presented by theirs frequencies and percentages and with 95% confidence interval. Total no of patients (including both dyslipidemic and non-dyslipidemic) were distributed in 06 age groups (minimum age 25 and maximum 55 years) Ages of dyslipidemic patients were presented as frequencies and percentages and Mean + SD. P-value and Chi-square test were applied to achieve the objective of study. In all statistical analysis, only P-value < 0.05 considered as significant.

RESULTS

In our study, patients selected according to inclusion and exclusion criteria. Total number of patients was 100. Frequency of Dyslipidemia was calculated in all patients and association of dyslipidemia with severity of hypothyroidism were also established. Ages of total no of patients were divided into 06 groups. Minimum age of patient was 25 and maximum age was 55.

Out of 100 cases 91 (91%) cases had dyslipidemia (Table-II) as per classification given by NCEP ATP III. As risk of cardiovascular disease is directly proportional to raised levels of above lipids. Thus above results support the hypothesis that hypothyroidism is associated with higher degree of dyslipidemia, which makes hypothyroidism a strong risk factor for CVDs. In addition, strong association of dyslipidemia with severity of hypothyroidism were also seen. (Table-II)

All the dyslipidemia patients were categorized into various age group and strikingly it's seen that out of 100 hypothyroid cases, 95 (95%) were of young age group < 50 years, and 91 of them (95.78%) were dyslipidemic, while 05 (5%) hypothyroid patients were of age group more than 50 years and none of them had dyslipidemia. (0.00%) and this distribution of dyslipidemic in young hypothyroid patients is statistically significant (p value 0.031) (Table-III).

Classification of lipids	TC mg%	LDL-C mg%	HDL-C mg%	TGs mg%
Desirable	<200	<100	>60	<150
Near optimal	-	100-129	Higher value is better	-
Borderline high	200-239	130-159	-	150-199
High	240 and above	160-189	59-40	200-499
Very high	-	190 and above	<40 major risk factor	500 and above

Table-I. Ncep atp III
Classification of TC, LDL-C, HDL-C and TGs (mg/dl)

Hypothyroidism	Total no of case	Dyslipidemia Case
Mild	24	18(75.0%)
Moderate	25	22 (88.0%)
Severe	51	51 (100%)
Total	100	91 (91%)

Table-II. Distribution of dyslipidemia in hypothyroid patients
P-value= 0.002 Chi-square test=12.82

Age in groups(years)	Total no of patients	Dyslipidemia cases with percentage
<30	10	10 (100%)
30-34	16	16 (100%)
35-39	18	18 (100%)
40-44	25	25 (100%)
45-49	26	22 (84.61%)
50 and >50	05	0 (0.00%)
Total	**100**	**91 (91%)**

Table-III. Distribution of dyslipidemia according to age
P value- 0.031

DISCUSSION

Although cardiovascular diseases are an uncommon entity in young patients, it constitutes a significant health problem due to its dyslipidemia cases and devastating effects on the active lifestyle of young patients. In addition, these patients have different risk factors, clinical presentations and prognoses as compared to older patients. The frequency of Myocardial infarction (MI) in younger subjects is normally low; however, over the years, a rising trend has been observed in the number of young patients presenting with MI. Heart diseases are rising in Asian Indians 5-10 years earlier than in other populations around the world.[8] As opposed to what was previously thought, adolescent patients with MI do not have a significantly high prevalence of normal coronaries in comparison to older patients; perhaps, the severity of coronary artery disease is comparable in both the young and old populations. Important behavioral risk factors that have been reported in young include unhealthy diet, physical inactivity, tobacco use, endocrine abnormalities like hypothyroidism, connective tissues diseases, elevated plasma homocysteine level, hypovitaminosis D and E, pregnancy and the consumption of processed meat. Hypothyroidism which affects both young and old is an important cause of dyslipidemia.

In our study It was observed that out 100 hypothyroid patients, 91 (91%) had dyslipidemia which is statistically significant. This is in accordance with available literature.

Another striking association that favors available literature i-e severity of dyslipidemia was directly proportional to the severity of hypothyroidism, as frequency of dyslipidemia in Mild hypothyroid cases was 75%, in Moderate was 88% and in Severe was 100%.

Objective of study was to determine frequency of Dyslipidemia in young hypothyroid cases. It's observed that out of 100 hypothyroid patients, 95 were young (age group <50 years) and out of these 95 young hypothyroid patients 91 (95.78%) had dyslipidemia, while out of 100, 05 (5%) hypothyroid patients were old (ages 50 years and above) and none of them suffers from dyslipidemia. (0.00%). It means irrespective of severity of hypothyroidism, all the young hypothyroid patients had dyslipidemia and this distribution of dyslipidemia in young hypothyroid patients is statistically significant. (P-value 0.031). Limitation of our study was, that majority of older hypothyroid patients were already on anti dyslipidemic therapy that's why there were not included in study and only 5 patients of age >50 were enrolled in study.

Though this pattern of age distribution is little different from available literature according to which dyslipidemia affects older patients as well, but due to limitations in our study we need to conduct more studies, in relatively larger sample size. In addition more variables need to study like BMI, smoking, Alcohol use, Dietary habits, Physical inactivity and endocrinopathies in young that may influence lipid metabolism. Simultaneously we need to improve our understanding regarding mechanisms through which thyroid hormones can affect lipid pathways in young. Prospective studies can also be performed to check weather

Hypothyroid patients if remain untreated develop more Cardiovascular events in future or not, but it has its ethical limitations i-e to keep patients away from treatment, despite of establishment of diagnosis of overt hypothyroidism and health hazards associated with it.

Here it is important to highlight that dyslipidemia associated with hypothyroidism is essentially cure able and replacement therapy with Levothyroxine significantly reverts lipid abnormalities in short duration.[9] Levothyroxine not only corrects lipoprotein levels but improves all the other mechanisms which are associated with CVDs like; insulin resistance, arterial hypertension, vascular stiffness, raised uric acid and phosphate levels, Hyperhomocystinemia, Syndrome X, endothelial dysfunction and oxidative distress.

It is therefore strongly recommended that;

1. All the patients especially young suffering from CVDs should be checked for dyslipidemia and hypothyroidism.
2. All the patients specially young suffering from Dyslipidemia must be looked for Hypothyroidism
3. All the patients especially young suffering from Hypothyroidism must be investigated for lipid abnormalities and other CVDs risks.
4. Early diagnosis and prompt treatment of all hypothyroid patients with thyroid replacement therapy (levothyroxine) as it reverts lipid abnormalities and significantly reduce risk of CVDs.
4. There is a need to do more studies in larger population to identify various mechanism through which hypothyroidism increases risk of CVDs

CONCLUSION

Hypothyroidism is an important risk factor for CVDs through its strong association with Dyslipidemia in young age. CVDs that manifests at a younger age can have devastating consequences for an individual, the family, and society. Prevention of these CVDs in young people is possible by early diagnosis and prompt treatment of hypothyroidism with Levothyroxine (Thyroid replacement therapy) in this way thyroid related dyslipidemia may be corrected and thus overall risk of CVDs will be reduced. In addition, we need to improve our understanding regarding various mechanisms through which thyroid hormones can affect lipid pathways in young by conducting more studies.

REFERENCES

1. Singapore Med J. 2012 Jul; 53(7):498. **The rising trend of myocardial infarction in young patients in Pakistan.** Saleem MD, Mulla J, Tahir F.

2. Int J Cardiol. 2016 Jul 1; 214:299-300. doi: 10.1016/j.ijcard.2016.03.217. Epub 2016 Apr 6. **Left ventricular diastolic dysfunction in young patients with subclinical hypothyroidism: To screen or not to screen?** To treat or not to treat? Zuin M[1], Scaranello F[2], Rigatelli G[3], Picariello C[1], Roncon L[4].

3. J CollPhyscianSurg Pak 2001; 11: 676-8. **Clinical presentation of primary hypothyroidism,** Ahmed B, Hussain T, Memon AR, Solangi GA.

4. J Trop Med. 2016; 2016:7073894. doi: 10.1155/2016/7073894. Epub 2016 Jun 22. **Atherogenic Risk Assessment among Persons Living in Rural Uganda.** Wekesa C[1], Asiki G[1], Kasamba I[1], Waswa L[1], Reynolds SJ[2], Nsubuga RN[1], Newton R[1], Kamali A

5. J Indian Med Assoc. 2013 May; 111(5):324-6, 329. **Insulin resistance and hypothyroidism: a complex relationship in non-alcoholic fatty liver disease.** Misra S, Singh B.

6. Kardiol Pol. 2015; 73(5):337-43. doi: 10.5603/KP.a2014.0241. Epub 2015 Jan 7. **Particularities of endothelial dysfunction in hypothyroid patients.** Tudoran M[1], Tudoran C.

7. J Clin Endocrinol Metab. 2013 Jun; 98(6):2256-66. doi: 10.1210/jc.2012-3818. Epub 2013 Apr 4. **Is subclinical hypothyroidism a cardiovascular risk factor in the elderly?** Pasqualetti G[1], Tognini S, Polini A, Caraccio N, Monzani F.

8. Vasc Health Risk Manag. 2005; 1(3):217-25. **Premature coronary artery disease in Indians and its associated risk factors.** Sharma M[1], Ganguly NK.

9. Int J Cardiol. 2016 Jul 1; 214:299-300. doi: 10.1016/j.ijcard.2016.03.217. **Epub 2016 Apr 6. Left ventricular diastolic dysfunction in young patients with subclinical hypothyroidism: To screen or not to screen? To treat or not to treat?** Zuin M[1], Scaranello F[2], Rigatelli G[3], Picariello C[1], Roncon L[4].

PREVIOUS RELATED STUDY

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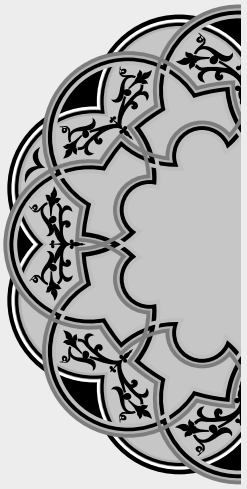

"If you judge people,
you have no time to love them."

Mother Teresa

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Shafat Khatoon	Intellectual concept and design of study, data collection, interpretation, analysis, discussion and recommendations	
2	Aijaz Ahmed	Concept, Data collection, analysis	
3	Nighat Jabeen	Discussion	
4	Erum Rehman	Data analysis	