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Inflammatory markers and lipid profile based on age in asymptomatic individuals with or without family history of type 2 diabetes mellitus

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Abstract
Introduction: Although there was a weak positive link between inflammatory indicators and serum lipid levels, assessing both of these parameters combined may aid in the early detection and treatment of people who are at high risk for metabolic disorders like type 2 diabetes mellitus and other cardio vascular diseases.
Materials and Methods: This experiment was carried out at the Department of Biochemistry research lab in India. The sample size was determined to be N=100 based on a 0.56 connection between visceral fat composition and oxidative stress and inflammation. The study included students and apparently healthy cases between the ages of 18 and 30 who followed DM patients in (n = 50). Individuals taking any medications for a health condition that precludes them from performing sub-maximal exercise, as well as those who participate in regular physical activity, yoga, or other biofeedback, were excluded from the study. Age and gender matched ostensibly healthy persons with no family history of diabetes were recruited for the control group (n = 50).
Results: Significant difference was noted in the inflammatory markers & the lipid profile parameters except for the HDL. In individual with type 2 diabetes, worsening dyslipidemia and inflammation over time raises concerns about the early onset of atherosclerosis. In the absence of glycemic control, insulin treatment is of poor effect. Efforts to improve glycemic control are required.
Conclusion: Lipid profile of an individual is associated to obesity, inflammation, vascular function, and diabetes. Appropriate lifestyle adjustments may be performed to lower the inflammatory markers and metabolic disorders. A greater understanding of the causes of inflammatory markers and lipid profile aid in the development of specialized therapeutic approaches for treatment of type 2 diabetes mellitus.
Keywords: Inflammatory markers, lipid profile, type 2 diabetes mellitus

Introduction

Inflammation is the body's natural defense system. However, in chronic conditions such as diabetes mellitus, hypertension, asthmaand so on, this protective system becomes a critical component in the progression of illness. The loss of cell mass in Type 2 diabetes mellitus is also linked to glucose toxicity, which is mitigated by IL-1-induced apoptosis. Numerous investigations have emphasized the importance of the fiery component in the pathophysiology of Diabetes mellitus.
Inflammation is described as a protective mechanism in which the body produces a large

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number of inflammatory proteins. Excessive synthesis of inflammatory proteins causes tissue damage in inflammatory diseases and atherosclerosis [1-3]. When glycated end products bind to their receptors, they cause NFk gene expression to spike, resulting in the activation of the inflammatory cascade. The cholinergic efferent pathway that secretes acetylcholine blocks inflammation and when the acetylcholine receptor binds to 7nAchR, it inhibits NFk and stops the inflammatory cascade[4].

TNF-and IL-6 are important inflammatory indicators that show how visceral fat and inflammation are linked [5]. TNF-and IL-6 increase lipolysis and free fatty acid release, resulting in increased hepatic glucose production and IR [6]. TNF-levels are higher in people who have larger adipocytes [7]. In adipocytes and muscle, TNF-promotes serine phosphorylation of IRS-1, which inhibits insulin receptor tyrosine kinase function [8]. According to Indulekha*et al*., the inflammatory markers hsCRP, TNF- and individuals had high levels of IL-6. Several studies revealed metabolic issues associated with T2 DM heritage, including pulse expansion and other DM features [9,10].

Inflammatory proteins elicited by stimuli, such as infection or invaders, stimulate the vagus nerve, which reduces inflammation indicators and improves chronic inflammatory illnesses [11-13]. The treatment of an acetylcholine receptor agonist lowered the generation of TNF-, IL-6, and other interleukins in Wang's experiments [14]. The "cholinergic anti-inflammatory route" refers to the link between the parasympathetic system and inflammatory proteins or immunological organs [11]. Furthermore, no parasympathetic efferent to the immune system has been discovered in experimental trials.

As a result, it's clear that the parasympathetic nervous system's anti-inflammatory component is regulated in tandem with the sympathetic nervous system [15]. Nor-epinephrine inhibits TNF production via beta-adrenergic receptors, according to *in vitro* tests [16]. *In vitro* investigations have also shown that sympathetic activation by intracranial injection of cytokines[17] has a stimulatory effect [15], i.e., increased nor-epinephrine turnover in the spleen. The effect of the sympathetic nervous system on inflammatory proteins is thus demonstrated. The studies based on human subjects confirmed the inverse association between LF, HF spectral power and SDNN and direct association of resting HR with inflammatory markers IL-6 and CRP, even after having adjusted for confounding factors [18]. The amount of nor-epinephrine was raised in an experimental model after sympathetic nerve stimulation and the formation of cytotoxic hydroxyl free radicals was increased in the rat myocardium as a result [19,20]. The sympathetic system appears to cause oxidative stress through the auto-oxidation of catecholamines in the extracellular fluid [21,22]. In human research, an inverse relationship between impaired autonomic function and oxidative stress [23] has been discovered.

To our knowledge, no solid evidence exists about the association between inflammatory markers, lipid profile and age relevance of type 2 diabetes mellitus in first-degree relatives (cases). As a result, the researchers investigated the link between inflammatory markers as well as lipid profile according to age distribution and its relevance, in healthy persons with and without a family history of Type 2 diabetes.

Materials and Methods

After getting clearance from the institutional ethics committee, study participants were provided written and informed consent. Experiments were carried out at the Department of Biochemistry research lab in India. The sample size was determined to be N=100 based on a 0.56 connection between visceral fat composition and oxidative stress and inflammation.The study included students and apparently healthy cases between the ages of 18 and 30 who followed DM patients in (n = 50). Individuals taking any medications for a health condition that precludes them from performing sub-maximal exercise, as well as those who participate in regular physical activity, yoga, or other biofeedback, were excluded from the study. Age and gender matched ostensibly healthy persons with no family history of diabetes were recruited for the control group (n = 50).

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Participants were advised to acquire enough sleep the night before recording and to abstain from caffeinated beverages, exercise, alcohol, and nicotine for 24 hours. Participants were asked to report to the Department of Biochemistry in the morning after fasting overnight. A fasting venous blood sample (5 mL) was obtained from the median cubital vein as soon as they arrived at the lab for biochemical assessment of lipid profile, inflammatory markers. Total cholesterol (TC) was determined using colorimetric and enzymatic methods with cholesterol oxidase peroxidase by utilising a Diagnostic kit. The kit used to do the test is from the Auto Span company. For lipid profile testing, the ERBA CHEM 5 X Model is employed.
hs CRP kit measures the Human High Sensitivity C-Reactive Protein using an enzyme-linked immunosorbent assay based on Biotin double antibody sandwich technology (hs-CRP). The kit used to conduct the test is from the R & D SYSTEM firm. For his CRP test, he uses the Alere Reader AM 2100 Model.
A TNF alphaspecific antibody has been precoated on the microtiter plate included in the Ray Biotech made the test kit that was used.

Results

In table 1, depicts the age distribution, mean, standard deviation of Inflammatory Markers among individuals with or without family background of type 2 diabetes mellitus.

Table 1: Age distribution of inflammatory markers levels among the study population

Parameters	Age Distribution	Controls without family historyof type 2diabetes			Cases with family history of type 2 diabetes			p-value
		N	Mean	Std.Deviation	N	Mean	Std.Deviation	
TNF alpha (pg/ml)	18-21 Years	38	120.00	50.66	29	275.00	74.31	0.001
	22-25 Years	12	145.50	52.89	21	296.63	80.41	0.075
IL 6 (pg/ml)	18-21 Years	38	4.96	1.01	29	13.28	1.11	0.538
	22-25 Years	12	4.51	1.08	21	13.83	1.44	0.558
hsCRP (ng/ml)	18-21 Years	38	3051.20	528.29	29	9377.20	2105.32	0.000
	22-25 Years	12	2834.40	462.68	21	9025.00	3048.21	0.000

Table 2: Age distribution of Lipid profile among the study population

Parameters	Age Distribution	Controls without family history of type 2 diabetes			Cases with family history of type 2 diabetes			P value
		N	Mean	Std.Deviation	N	Mean	Std.Deviation	
TC (mg/dl)	18-21 Years	38	163.26	23.81	29	209.34	14.85	0.001
	22-25 Years	12	177.42	27.98	21	211.29	16.61	0.010
HDL (mg/dl)	18-21 Years	38	40.87	6.20	29	39.35	5.56	0.167
	22-25 Years	12	43.97	6.93	21	40.87	6.22	0.173
TGL (mg/dl)	18-21 Years	38	123.44	18.87	29	144.07	9.96	0.000
	22-25 Years	12	130.08	20.03	21	147.48	16.70	0.147
LDL (mg/dl)	18-21 Years	38	97.71	16.87	29	141.60	16.24	0.650
	22-25 Years	12	107.43	19.54	21	140.92	18.80	0.841
VLDL (mg/dl)	18-21 Years	38	24.68	3.77	29	28.74	2.02	0.000
	22-25 Years	12	26.02	4.01	21	29.49	3.34	0.147

In table 2 depicts the age distribution, mean, standard deviation of LIPID PROFILE among individuals with or without family background of type 2 diabetes mellitus

Discussion

TNF alpha in 18- 21 year olds in the control group (120.00±50.66 pg/ml) and the case group (275.0±50.66 pg/ml). TNF alpha 22-25 years in control (145.50±52.89 pg/ml) and case group

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(296.63±80.41 pg/ml) had a statistically significant difference (p<0.001), whereas TNF alpha 22-25 years in control (145.50 ±52.89 pg/ml) and case group (296.63±80.41 pg/ml) had a statistically insignificant difference (p=0.075 TNF alpha levels were found to be higher in diabetics in a Southern Karnataka population, according to Rama Hotamisligil GS *et al*. [24] In a similar study, Saghizadeh M *et al*. found a difference in TNF alpha between the case and control groups [25].

The inflammatory cytokine tumour necrosis factor (TNF) is one molecule that has gotten a lot of attention. Although the mechanism by which TNFa exerts these divergent outcomes in NOD mice is unknown, it has been shown to have a favourable or negative effect on the progression to diabetes [26].

Early and more aggressive infiltration of the islets with immune cells, as well as an increase in the presentation of islet antigen in situ in the islets by islet infiltrating antigen presenting cells to T cells, are linked to rapid development to diabetes. TNF can boost presentation of islet antigen to both effector CD4 and CD8± T cells in adoptive transfer studies, however further research in TNFNOD animals defective in either CD4± or CD8 * T cells revealed that diabetes progression is dependent on CD8± T cells, with CD4± T cells playing a minor role. The evidence from TNFNOD mice discussed in this review suggests new routes by which inflammatory stimuli can cause inflammation autoimmune and recommends innovative ways in the development of therapeutic medicines that don't destroy cells [27].

In the Case Group, IL-6 levels increased by 13.28 ± 1.11 pg/ml compared to the control group's 4.96 ± 1.01 pg/ml (p=0.001), while in the 22-25-year group, IL-6 levels increased by 13.83 ± 1.44 pg/ml compared to the control group's 4.51 ± 1.08 pg/ml (p=0.075). In diabetic patients with coronary heart disease, E Pradhan AD *et al*. from Pondicherry discovered a significant rise in IL-6 levels (15.73 ± 0.93 pg/ml) compared to healthy controls (3.07 ± 0.01 pg/ml). [28]

hsCRP in 18-21 years in the Case Group increased by 9377.20 ± 2105.32 ng/ml compared to control group 3051.20 ± 528.29 ng/ml (p=0.0001), whereas hsCRP in 22-25 years increased by 9025.0 ± 3048.21 ng/ml compared to control group 2834.40 ± 462.68 ng/ml (p=0.0001). The increase in hsCRP in the case group was 6230.12 ng/ml. Increased inflammatory markers in Diabetes were reported by Volanakis JE Ahmed from Mauritius, as evidenced by an elevated CRP level [29]. In a similar study, Black S *et al*.found a difference in CRP levels between the case and control groups [30]. According to Gewurz H *et al*.study, there is no difference in CRP levels between the case and control groups [31].

In the Case Group, total cholesterol (TC) increased from 18 to 21 years old. Total cholesterol (TC) in 22-25 years in Case Group showed an increase in Mean 211.29 ± 16.61 mg/dl compared to control group 177.42 ± 27.98 mg/dl (p=0.001) and Total cholesterol (TC) in 22-25 years in Case Group showed an increase in Mean 211.29 ± 16.61 mg/dl compared to control group 163.26 ± 23.81 mg/dl (p=0.001). HDL levels in 18-21 year old. The case group had a lower mean of 39.35±5.56 mg/dl than the control group, which had a mean of 40.87±5.56 mg/dl. 6.20 mg/dl (p=0.167) and HDL in 22-25 years in the Case Group decreased to 40.87±6.22 mg/dl compared to 43.97 ± 6.93 mg/dl in the Control Group (p=0.173).

TGL levels in 18-21 year olds in the Case Group increased by 144.07±9.96 mg/dl compared to 123.44 ± 18.87 mg/dl in the Control Group (p0.0001), ± 16.70 mg/dl compared to 130.08± 20.03 mg/dl in the Control Group (p0.0001). dl (p=0.0147); dl (p=0.0147); dl (p=0.0 LDL levels in 18-21 year olds in the Case Group increased to 141.60±16.24 mg/dl, compared to 141.60 ± 16.24 mg/dl in the Control Group. Similar LDL in 22-25 years in the Case Group showed an increase in Mean 140.92 ± 18.80 mg/dl compared to 107.43 ± 19.54 mg/dl in the control group (p=0.841). VLDL in the Case Group increased by 28.74 ± 2.02 mg/dl compared to the control group's 24.68 ± 3.77 mg/dl (p0.0001), and VLDL in the Case Group increased by 29.49 ± 3.34 mg/dl compared to the control group's 26.02 ± 4.01 mg/dl (p0.0001). A comparable study by Sahu S *et al*.found that a prediabetes group had considerably high lipid levels, except for HDL [32].

Conclusion

A mix of metabolic, inflammatory and cardiovascular processes are likely to explain the therapeutic effects. To determine the most effective intervention(s) for specific advantages, further mechanistic study is required. Weight loss appears to have a significant impact on inflammatory markers. Lipid profile of an individual is associated to obesity, inflammation, vascular function, and diabetes. Appropriate lifestyle adjustments (e.g., exercise training, nutritional therapy) may be performed to lower the inflammatory markers and metabolic disorders. A greater understanding of the causes of inflammatory markers and lipid profile aid in the development of specialized therapeutic approaches for treatment of type 2 diabetes mellitus.

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