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INFLUENCE OF INFLAMMATORY MARKER INTERLEUKIN-4 ON ATHEROGENIC INDICES IN HEALTHY INDIVIDUALS

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Abstract

Background: Interleukin-4 (IL-4), an inflammatory marker, is associated with the development of atherosclerosis which is a chronic inflammatory condition that progresses into cardiovascular disease (CVD). It poses a higher risk of earlier onset at a younger age, elevated fatality rates, and more premature deaths. The prevalence of CVD among Indians is high (27%), with risk factors including altered lipid profiles, genetic inheritance, obesity, and a sedentary lifestyle. The ratios of low-density lipoprotein cholesterol/high-density lipoprotein cholesterol (LDLC/HDLC) and total cholesterol/high-density lipoprotein cholesterol (TC/HDLC), also known as the atherogenic or Castelli index, are better indicators of CVD risk than individual parameters. Correlating IL-4 with atherogenic indices may help identify underlying causes and serve as a marker of onset of metabolic diseases at younger age. **Aim:** To investigate the correlation between IL-4 and atherogenic indices (TC/HDLC; LDLC/HDLC) in young adults, **Material and Methods**: A sample size of 100 individuals was tested for IL-4 using an ELISA. The atherogenic indices, including TC, HDLC, and LDLC, were measured using a semi-automated analyzer through spectrophotometry (Vitros 5600). **Results**: Interleukin-4 is positively correlating with atherogenic indices. **Conclusion:** This study found significant variations in serum IL-4 levels among genders and obese/non-obese individuals, with higher levels observed in obese subjects. Positive associations were identified between serum IL-4 and the atherogenic index TC/HDLC, as well as between TC/HDLC and LDLC/HDLC.

Keywords: Interleukin-4, Atherogenic İndices, Cardiovascular Diseases.

INTRODUCTION

Atherosclerosis is a chronic inflammatory condition that slowly progresses into CVD and is characterised by the build-up of lipids and immune cells within the artery wall (1). Cardiovascular disease is an epidemic among Indians, with a prevalence of 27% (2). It carries the risk of an earlier onset at a younger age, elevated case fatality rates, and a higher number of premature deaths (3). The changed lipid profile is the main contributing component (4). Chronic inflammation has also been connected to lipid metabolic dysregulation (5-7). The TC/HDLC Ratio known as atherogenic or Castelli index and the ratio of LDLC/HDLC, are better markers of CVD than individual measurements. The categories of risk and desired levels for atherogenic indices categorized by gender are given in Table 1 (8,9).

Table 1: Risk and desired levels for atherogenic indices (8-10)

Atherogenic Indices	Primary prevention			
	Risk level		Target	
	Men	Women	Men	Women
TC/HDL-C	>5.0	>4.5	<4.5	<4.0
LDL-C/HDL-C	>3.5	>3.0	<3.0	<2.5

Atherosclerosis exhibit elevated levels of serum IL- 4 (11). By preventing adipogenesis and increase in lipolysis, IL-4 contributes to the metabolism of lipids. IL-4 may be useful in the management of metabolic disorders and obesity. Additionally, IL-4 has been linked to increased insulin sensitivity, decreased fat buildup, enhanced glucose tolerance and abdominal obesity (12-14). It has been found to be an indicator of CVD in chronic kidney disease (CKD) patients (15). From 1.1 pg/ml to 35 pg/ml, the IL-4 assay ranges (16). There is paucity of data regarding serum IL-4 levels and its correlation with atherogenic index. Though, previous studies discovered inflammatory markers such as IL-6, 8, 18 & Tumor Necrosis Factor (TNF) -alpha, are elevated in individuals with higher risk of developing CVD (17-19). Therefore, the key question is whether there is correlation between IL- 4 and CVD in young adults.

MATERIALS AND METHODS

This study was completed at Sharda University in Greater Noida, Uttar Pradesh, in the Department of Biochemistry after receiving approval from the Institutional Ethical Committee. 100 individuals who seemed to be in good health made up the study's cross-sectional sample. In accordance with how the WHO classifies young adults (18–24 years), subjects were separated into groups based on gender (male & female) and obesity (obese & non-obese) (20). The WHO Asia Pacific and Misra A., et al. guidelines classify a BMI of 25.O or more as obese for the Indian population (21,22).

Inclusion Criteria:

Apparently healthy young adults aged 18-24 years.

Exclusion Criteria:

The research excluded participants who had a history of using medications like statins, those with chronic disorders including thyroid and renal disease, and those who were pregnant.

Biochemical Measurements:

Serum samples were taken and preserved at -20°C. To detect serum IL-4 levels ELISA was used. Using a semi-automated analyzer (Vitros 5600), spectrophotometry was used to assess the atherogenic indices, including TC, HDLC, and LDLC.

Statistical Analysis:

Using SPSS version 22, statistical analysis was performed on the acquired data. The data were analysed using independent t-tests and Pearson correlation coefficients.

RESULT

According to the data analysis, 22% of men and 28% of women had an atherogenic index that was greater than desired cutoff. Men and women, as well as obese and non-obese individuals, had significantly different mean serum IL-4 levels ($p < 0.05$) (Tables 2 and 3). In addition, it was shown that obese and non-obese people had

significantly different TC/HDLC ratios. In comparison to non-obese individuals, obese had serum IL-4 levels that were more than thrice higher (7 pg/ml) (Table no. 3). Karl Pearson's correlation of the data revealed a significant positive connection between serum IL-4 and the atherogenic index TC/HDLC, with an r-value of 0.470. Additionally, a positive association was identified between TC/HDLC and LDLC/HDLC, with an r value of 0.774 (Table 4).

Table 2: Group statistics on basis of Gender (including range, mean, Standard mean of error, Standard Deviation and p value using independent t test)

Parameters	Group Statistics on basis of Gender					
	Groups	N (no. of samples)	Mean	Std. Deviation	Std. Error Mean	Significance One-Sided p
IL-4 (pg/ml)	Male	50	5.0512	2.83946	0.40156	<.001
	Female	50	2.8362	2.59839	0.36747	
TC/HDLC	Male	50	3.8388	1.76167	0.24914	0.085
	Female	50	3.3008	1.29775	0.18353	
LDLC/HDLC	Male	50	1.7154	1.45174	0.20531	0.431
	Female	50	1.514	1.06511	0.15063	

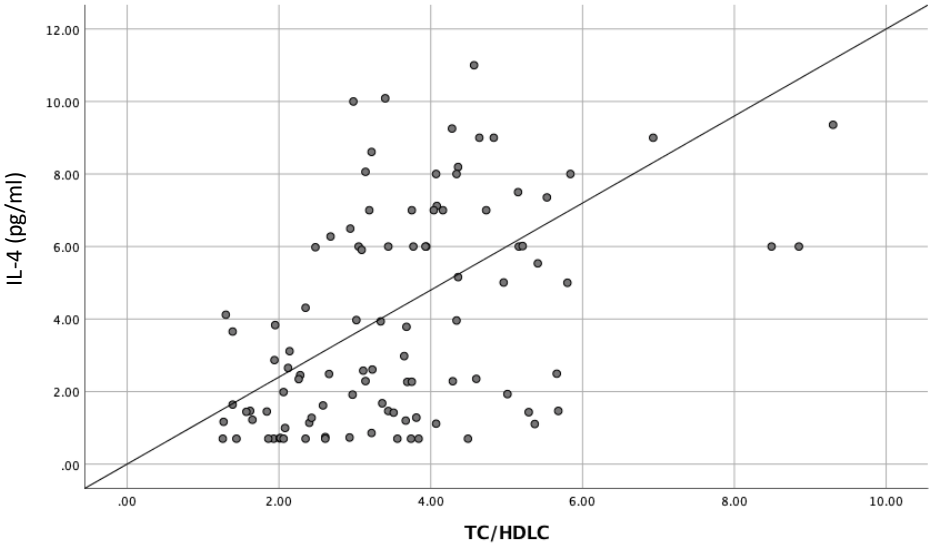
Table 3: Group statistics on basis of Obesity (including range, mean, Standard mean of error, Standard Deviation and p value using independent t test)

Parameters	Group Statistics on basis of obesity					
	Groups	N (no. of samples)	Mean	Std. Deviation	Std. Error Mean	Significance One-Sided p
IL-4 (pg/ml)	Non-obese	63	1.9797	1.30278	0.16413	<.001
	Obese	37	7.2878	1.55058	0.25491	
TC/HDLC	Non-obese	63	2.9214	1.14679	0.14448	<.001
	Obese	37	4.6738	1.56979	0.25807	
LDLC/HDLC	Non-obese	63	1.4884	1.00501	0.12662	0.196
	Obese	37	1.8297	1.62047	0.2664	

Table 4: Karl Pearson's correlation

Correlations				
		IL-4 (pg/ml)	TC/HDLC	LDLC/HDLC
IL-4 (pg/ml)	Pearson Correlation	1	.470**	0.087
	Sig. (2-tailed)		0	0.388
	N	100	100	100
TC/HDLC	Pearson Correlation	.470**	1	.774**
	Sig. (2-tailed)	0		0
	N	100	100	100
LDLC/HDLC	Pearson Correlation	0.087	.774**	1
	Sig. (2-tailed)	0.388	0	
	N	100	100	100
** Correlation is significant at the 0.01 level (2-tailed).				
* Correlation is significant at the 0.05 level (2-tailed).				

Graph 1: Scatter dot plot; IL-4 verses TC/HDLC



DISCUSSION

This research examines the correlation between IL-4 and atherogenic indices in young adults. In the younger population, there has been a noticeable rise in the incidence of CVD, potentially due to factors like physical inactivity and substance abuse especially in urban areas. This trend contrasts with the declining rates of CVD observed in individuals aged 50 years and older (23). In the present study among healthy subjects between 18-24 years age, 22% of males and 28% of females exhibit atherogenic risk as per Table 1. The atherogenic index is an indicator of CVD risk when TC/HDLC > 5 in males and > 4.5 in females, as discussed by Millan J et al. in 2009 (8).

Cardiovascular disease is significantly influenced by atherosclerosis, a chronic inflammatory illness characterised by the accumulation of lipids and immune cells in the walls of the arteries (1). Risk factors for CVD include hypertension, abnormal lipid profiles, genetic predisposition, obesity, and a sedentary lifestyle (3,4). The abnormalities in lipoprotein levels, such as high levels of LDLC and low levels of HDLC, are highlighted in development of CVD (5-7). The atherogenic indices are more accurate CVD indicator than individual lipid profile parameters and were found to be higher in obese individuals (8,9).

Similarly, in this study, there was a substantial difference in the TC/HDLC ratio between obese and non-obese, suggesting that obese are more susceptible to CVD compared to non-obese. Additionally, obese have serum IL-4 levels more than thrice than those of non-obese subjects. Interleukin 4, besides its inflammatory functions, also has metabolic role. Under physiological condition, IL-4 has been linked to improved glucose tolerance, reduced lipid accumulation, and beneficial effects on insulin sensitivity (12).

IL-4 elevates cAMP levels and in turn increases the translocation of hormone sensitive lipase and thereby promotes breakdown of fats (lipolysis) and inhibition lipogenesis. Shiau M.-Y, et al. in their research postulated that IL-4 may not be adequate on its own to maintain energy homeostasis once insulin resistance has developed (13). Studies showed IL-4 presence in atherosclerotic lesions, elevated serum levels in type

2 diabetes mellitus and Abdominal obesity, which may explain its limitation in regulatory functions (11-14). Gu L. and associates in 2020, discovered a notable positive link between IL-4 and the atherogenic index and postulated that elevated serum IL-4 levels could potentially serve as a valuable tool for clinicians in predicting early CVD risk in patients with CKD.

Likewise, this study identified a significant correlation between serum IL-4 and the atherogenic index TC/HDLC, as well as between TC/HDLC and LDLC/HDLC in apparently healthy adults. These findings suggest a potential role for IL-4 in the development of CVD in young individuals.

Examining the correlation between IL-4 and atherogenic indices could assist in the discovery of root causes and potentially serve as an indicator for the early onset of CVD in younger individuals. Further research is required with larger population size to support this hypothesis and to better understand the underlying association between IL-4 and CVD.

CONCLUSION

These findings contribute to our understanding of the role of IL-4 and atherogenic indices in lipid metabolism and CVD development. It suggests that IL-4 is positively correlated with atherogenic indices and may have therapeutic implications for obesity and metabolic diseases. The study also reveals gender differences in IL-4 levels and higher atherogenic indices in obese individuals, indicating their increased susceptibility to CVD.

Lımıtatıons of Study

A longitudinal study could be conducted on a broader geographic scale with a larger population.

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