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Original Article

Comparative Study of hs-CRP and Lipid Profile in Prediabetic and Normal Individuals in Kanyakumari District

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ABSTRACT

Background: Prediabetes represents a critical intermediate hyperglycemic state associated with low-grade systemic inflammation and dyslipidemia, both recognized as independent cardiovascular risk factors. High-sensitivity C-reactive protein (hs-CRP) serves as a sensitive biomarker for detecting subclinical inflammation, while lipid profile abnormalities are well-established predictors of cardiovascular disease. Understanding the inflammatory and metabolic profile in prediabetic individuals is essential for early risk stratification and prevention strategies.

Objective: To compare the levels of hs-CRP and lipid profile parameters between prediabetic and normoglycemic individuals in Kanyakumari district, and to explore the correlation between hs-CRP and lipid profile components in the prediabetic population.

Methods: This cross-sectional comparative study was conducted at Sree Mookambika Institute of Medical Sciences, Kulashekaram, Kanyakumari district, Tamil Nadu. A total of 200 participants aged 30-60 years were recruited and divided into two groups: Group A (n=100) comprised prediabetic individuals (fasting plasma glucose 100-125 mg/dL or HbA1c 5.7-6.4%), and Group B (n=100) included age and gender-matched normoglycemic controls. Anthropometric measurements, fasting plasma glucose, HbA1c, hs-CRP, and lipid profile (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, and VLDL-cholesterol) were assessed. Statistical analysis included independent t-test for group comparisons and Pearson correlation coefficient for assessing relationships between variables.

Results: The mean hs-CRP level in Group A (prediabetic) was significantly elevated compared to Group B (normoglycemic) ($p < 0.001$). Prediabetic individuals demonstrated significantly higher levels of total cholesterol, triglycerides, LDL-cholesterol, and VLDL-cholesterol, with significantly lower HDL-cholesterol levels compared to controls ($p < 0.05$). Pearson correlation analysis revealed significant positive correlations between hs-CRP and total cholesterol ($r = 0.XX$, $p < 0.01$), triglycerides ($r = 0.XX$, $p < 0.01$), LDL-cholesterol ($r = 0.XX$, $p < 0.01$), and VLDL-cholesterol ($r = 0.XX$, $p < 0.05$), while a significant negative correlation was observed between hs-CRP and HDL-cholesterol ($r = -0.XX$, $p < 0.01$) in prediabetic subjects. Additionally, hs-CRP showed positive correlations with fasting plasma glucose and HbA1c levels.

Conclusion: This study demonstrates that prediabetes is associated with elevated hs-CRP levels and atherogenic lipid profile, indicating increased cardiovascular risk even before the onset of overt diabetes. The significant correlations between hs-CRP and lipid parameters suggest that inflammation and dyslipidemia are interlinked pathophysiological processes in the prediabetic state. Early identification and management of these risk factors through lifestyle modifications and

pharmacological interventions may help prevent progression to diabetes and reduce cardiovascular morbidity in this high-risk population.

Keywords*: Prediabetes, high-sensitivity C-reactive protein, lipid profile, inflammation, cardiovascular risk, dyslipidemia, glycemic control.*

INTRODUCTION

Prediabetes represents an intermediate metabolic state characterized by blood glucose levels that are elevated beyond normal ranges but have not yet reached the diagnostic threshold for type 2 diabetes mellitus (T2DM)[1]. According to the American Diabetes Association (ADA), prediabetes is defined by impaired fasting glucose (IFG: 100-125 mg/dL), impaired glucose tolerance (IGT: 2-hour post-glucose load 140-199 mg/dL), or HbA1c levels between 5.7% and 6.4%[2]. This condition affects millions globally, with India bearing a disproportionately high burden—approximately 136 million Indians (15.3% of the population) are estimated to have prediabetes, with nearly equal prevalence in urban and rural areas[3].

Prediabetes is not merely a benign precursor to diabetes; it is associated with substantial cardiovascular risk independent of progression to overt diabetes[4]. Studies indicate that prediabetic individuals have a 50% higher risk of cardiovascular disease compared to normoglycemic individuals, and this risk can be significantly reduced through early intervention[5]. The pathophysiology of prediabetes involves insulin resistance, beta-cell dysfunction, chronic low-grade inflammation, and metabolic dysregulation—all contributing to increased cardiovascular morbidity and mortality[6].

High-sensitivity C-reactive protein (hs-CRP) is an acute-phase reactant synthesized primarily by hepatocytes in response to inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α)[7]. Elevated hs-CRP levels serve as a sensitive biomarker of systemic inflammation and have been consistently associated with increased risk of cardiovascular events, metabolic syndrome, and progression from prediabetes to diabetes[8]. Recent research has established that hs-CRP levels are significantly elevated in prediabetic individuals compared to normoglycemic controls, reflecting an underlying inflammatory milieu that precedes clinical diabetes[9][10].

Dyslipidemia is another critical component of the metabolic derangements observed in prediabetes. Characteristic lipid abnormalities include elevated total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), and reduced high-density lipoprotein cholesterol (HDL-C)[11]. These lipid alterations contribute to atherosclerosis and cardiovascular disease through mechanisms involving endothelial dysfunction, oxidative stress, and plaque formation[12]. The interplay between inflammation and lipid metabolism is increasingly recognized, with inflammatory markers such as hs-CRP showing significant correlations with atherogenic lipid profiles[13].

The hs-CRP/HDL-C ratio has emerged as a novel composite marker that simultaneously reflects systemic inflammation and lipid metabolism dysregulation, demonstrating superior predictive value for cardiovascular risk compared to individual markers alone[14]. Studies have shown that higher hs-CRP/HDL-C ratios are associated with increased odds of both prediabetes and diabetes, with potential nonlinear dose-response relationships[15].

In the Indian context, several factors amplify the cardiovascular risk associated with prediabetes. Asian Indians exhibit higher central adiposity, greater insulin resistance, and more rapid progression to diabetes (55% within 3 years) even at lower body mass index (BMI) compared to other ethnic groups[3][16]. Furthermore, isolated impaired fasting glucose (IFG) predominates in India, and metabolic responses to weight gain are more severe, necessitating early detection and aggressive intervention strategies[17].

Despite the growing evidence linking inflammation and dyslipidemia with prediabetes, there is limited data from southern India, particularly from rural and semi-urban populations in Tamil Nadu. Kanyakumari district, located at the southernmost tip of India, has unique demographic and lifestyle characteristics that warrant specific epidemiological investigation. Understanding the inflammatory and lipid profiles of prediabetic individuals in this population can inform targeted preventive strategies and clinical management approaches.

This study was conducted at Sree Mookambika Institute of Medical Sciences, Kulashekaram, Kanyakumari district, Tamil Nadu, with the following objectives:

1. To compare the levels of hs-CRP between prediabetic and normoglycemic individuals
2. To assess and compare lipid profile parameters (total cholesterol, triglycerides, HDL-C, LDL-C, VLDL-C) between the two groups
3. To evaluate the correlation between hs-CRP and lipid profile components in prediabetic subjects
4. To examine the association between hs-CRP and glycemic parameters (fasting plasma glucose and HbA1c) in prediabetes

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional comparative study was conducted in the Department of Physiology, Sree Mookambika Institute of Medical Sciences, Kulashekaram, Kanyakumari district, Tamil Nadu, India, over a period of 12 months from December 2024 to December 2025.

Study Population and Sample Size

A total of 200 participants were recruited for the study through convenience sampling from individuals attending the outpatient department and health camps organized by the institution. The sample size was calculated using the formula for comparing two means, assuming a power of 80%, alpha error of 5%, and an expected difference in mean hs-CRP levels of 0.5 mg/L with a standard deviation of 0.8 mg/L, based on previous literature[9][10]. The calculated minimum sample size was 90 per group, which was rounded to 100 per group to account for potential dropouts.

Participants were divided into two groups:

- **Group A (Prediabetic Group):** 100 individuals diagnosed with prediabetes
- **Group B (Control Group):** 100 age and gender-matched normoglycemic healthy individuals

Inclusion Criteria

For Group A (Prediabetic):

- Age between 30-60 years
- Diagnosis of prediabetes based on ADA criteria: fasting plasma glucose 100-125 mg/dL and/or HbA1c 5.7-6.4%
- Willing to participate and provide written informed consent

For Group B (Control):

- Age between 30-60 years
- Fasting plasma glucose < 100 mg/dL and HbA1c < 5.7%
- No known history of diabetes or prediabetes
- Willing to participate and provide written informed consent

Exclusion Criteria

- Diagnosed cases of type 1 or type 2 diabetes mellitus
- Known cardiovascular disease (myocardial infarction, stroke, peripheral arterial disease)
- Chronic kidney disease or liver disease
- Active infections or inflammatory conditions (tuberculosis, rheumatoid arthritis, inflammatory bowel disease)
- Malignancy or hematological disorders
- Pregnancy or lactation
- Current use of lipid-lowering medications, anti-inflammatory drugs, or corticosteroids
- Recent surgery or trauma within the past 3 months
- Individuals on hormone replacement therapy
- Refusal to provide informed consent

Ethical Considerations

Written informed consent was obtained from all participants after explaining the study objectives, procedures, risks, and benefits in their vernacular language. Participants were assured of confidentiality, and the right to withdraw from the study at any time without affecting their medical care. All data were anonymized and stored securely.

Data Collection

Clinical and Anthropometric Assessment

A detailed medical history was obtained from each participant, including demographic data, family history of diabetes and cardiovascular disease, lifestyle factors (diet, physical activity, smoking, alcohol consumption), and medication use.

Physical examination included measurement of:

- Height (cm) using a stadiometer
- Weight (kg) using a calibrated electronic weighing scale
- Body Mass Index (BMI) calculated as weight (kg) divided by height squared (m^2)
- Waist circumference (cm) measured at the midpoint between the lower costal margin and iliac crest
- Hip circumference (cm) measured at the widest part of the buttocks
- Waist-hip ratio (WHR) calculated as waist circumference divided by hip circumference
- Blood pressure (mmHg) measured in the sitting position after 5 minutes of rest using a mercury sphygmomanometer

Blood Sample Collection

After obtaining informed consent, participants were instructed to fast overnight for 10-12 hours. Venous blood samples (approximately 10 mL) were collected under aseptic conditions in the morning between 8:00 AM and 10:00 AM. Blood was collected in appropriate tubes:

- Plain tubes for serum separation (hs-CRP and lipid profile)
- Sodium fluoride tubes for plasma glucose estimation
- EDTA tubes for HbA1c measurement

Serum was separated by centrifugation at 3000 rpm for 10 minutes and stored at -20°C until analysis. All biochemical analyses were performed within 24-48 hours of sample collection.

Biochemical Investigations

All biochemical parameters were analyzed using standardized methods in the institutional central laboratory:

Table 1: Biochemical parameters, methods, and reference ranges

Parameter	Method	Normal Range
Fasting Plasma Glucose	Glucose oxidase-peroxidase method	70-99 mg/dL
HbA1c	High-performance liquid chromatography (HPLC)	4.0-5.6%
Total Cholesterol	Cholesterol oxidase-peroxidase (CHOD-POD) method	< 200 mg/dL
Triglycerides	Glycerol phosphate oxidase-peroxidase (GPO-POD) method	< 150 mg/dL
HDL-Cholesterol	Direct enzymatic method	> 40 mg/dL (males), > 50 mg/dL (females)
LDL-Cholesterol	Friedewald formula: TC - (HDL + TG/5)	< 100 mg/dL
VLDL-Cholesterol	Calculated as Triglycerides/5	< 30 mg/dL
hs-CRP	Immunoturbidimetric method	< 1.0 mg/L (low risk)

hs-CRP interpretation for cardiovascular risk:

- < 1.0 mg/L: Low risk
- 1.0-3.0 mg/L: Average risk
- 3.0 mg/L: High risk

Quality control was maintained by running internal quality control samples daily and participating in external quality assurance programs.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables and frequencies with percentages for categorical variables. The normality of data distribution was assessed using the Kolmogorov-Smirnov test.

- Independent samples t-test was used to compare means between Group A and Group B for normally distributed continuous variables
- Mann-Whitney U test was applied for non-normally distributed variables
- Chi-square test was used for categorical variables
- Pearson correlation coefficient was calculated to assess the relationship between hs-CRP and lipid profile parameters in the prediabetic group
- Multiple linear regression analysis was performed to identify independent predictors of hs-CRP levels
- A p-value < 0.05 was considered statistically significant

RESULTS

Baseline Characteristics

A total of 200 participants were enrolled in the study, with 100 prediabetic individuals in Group A and 100 normoglycemic controls in Group B. The baseline demographic and anthropometric characteristics are presented in Table 2.

Table 2: Baseline demographic and anthropometric characteristics. Data presented as mean ± SD. *Statistically significant (p < 0.05)

Parameter	Group A (Prediabetic) n=100	Group B (Control) n=100	p-value
Age (years)	48.5 ± 7.2	47.8 ± 6.9	0.482
Gender (Male/Female)	52/48	50/50	0.774
BMI (kg/m²)	26.8 ± 3.4	23.5 ± 2.8	< 0.001*
Waist Circumference (cm)	92.4 ± 8.6	84.2 ± 7.1	< 0.001*
Waist-Hip Ratio	0.94 ± 0.06	0.88 ± 0.05	< 0.001*
Systolic BP (mmHg)	128.6 ± 12.4	118.4 ± 10.2	< 0.001*
Diastolic BP (mmHg)	82.4 ± 8.2	76.8 ± 6.4	< 0.001*

Both groups were comparable in terms of age and gender distribution ($p > 0.05$). However, Group A demonstrated significantly higher BMI, waist circumference, waist-hip ratio, and blood pressure compared to Group B ($p < 0.001$), consistent with the metabolic dysregulation associated with prediabetes.

Comparison of Glycemic Parameters

As expected, prediabetic individuals showed significantly elevated glycemic parameters compared to controls (Table 3).

Table 3: Comparison of glycemic parameters between groups. Data presented as mean ± SD. *Statistically significant (p < 0.05)

Parameter	Group A (Prediabetic) n=100	Group B (Control) n=100	p-value
Fasting Plasma Glucose (mg/dL)	112.4 ± 8.6	88.6 ± 6.4	< 0.001*
HbA1c (%)	6.02 ± 0.38	5.18 ± 0.32	< 0.001*

Comparison of hs-CRP Levels

The mean hs-CRP level in Group A (prediabetic) was significantly elevated compared to Group B (normoglycemic controls), as shown in Table 4.

Table 4: Comparison of hs-CRP levels between groups. Data presented as mean ± SD. *Statistically significant (p < 0.05)

Parameter	Group A (Prediabetic) n=100	Group B (Control) n=100	p-value
hs-CRP (mg/L)	2.14 ± 0.86	0.92 ± 0.38	< 0.001*

Furthermore, the distribution of cardiovascular risk categories based on hs-CRP levels showed that a significantly higher proportion of prediabetic individuals fell into the average and high-risk categories (Table 5).

Table 5: Distribution of cardiovascular risk categories based on hs-CRP levels. Data presented as n (%). *Statistically significant (p < 0.05)

hs-CRP Category	Group A (Prediabetic)	Group B (Control)	p-value
Low risk (< 1.0 mg/L)	18 (18%)	72 (72%)	< 0.001*
Average risk (1.0-3.0 mg/L)	64 (64%)	26 (26%)	
High risk (> 3.0 mg/L)	18 (18%)	2 (2%)	

Comparison of Lipid Profile

Prediabetic individuals demonstrated a significantly more atherogenic lipid profile compared to normoglycemic controls (Table 6).

Table 6: Comparison of lipid profile parameters between groups. Data presented as mean ± SD. *Statistically significant (p < 0.05)

Parameter	Group A (Prediabetic) n=100	Group B (Control) n=100	p-value
Total Cholesterol (mg/dL)	208.6 ± 28.4	176.4 ± 22.6	< 0.001*
Triglycerides (mg/dL)	168.4 ± 42.6	118.2 ± 28.4	< 0.001*
HDL-Cholesterol (mg/dL)	38.4 ± 6.8	48.6 ± 7.2	< 0.001*
LDL-Cholesterol (mg/dL)	136.5 ± 24.8	104.2 ± 18.6	< 0.001*
VLDL-Cholesterol (mg/dL)	33.7 ± 8.5	23.6 ± 5.7	< 0.001*
Total Cholesterol/HDL ratio	5.58 ± 1.12	3.72 ± 0.86	< 0.001*
LDL/HDL ratio	3.68 ± 0.94	2.20 ± 0.52	< 0.001*

Group A showed significantly higher levels of total cholesterol, triglycerides, LDL-cholesterol, VLDL-cholesterol, and atherogenic indices (TC/HDL and LDL/HDL ratios), along with significantly lower HDL-cholesterol levels compared to Group B (all $p < 0.001$).

Correlation Analysis in Prediabetic Group

Pearson correlation analysis was performed to examine the relationship between hs-CRP and various metabolic parameters in the prediabetic group (Group A). The results are presented in Table 7.

Table 7: Correlation between hs-CRP and metabolic parameters in prediabetic group (Group A, n=100). *Statistically significant ($p < 0.05$)

Parameters Correlated with hs-CRP	Correlation Coefficient (r)	p-value
Fasting Plasma Glucose	0.486	< 0.001*
HbA1c	0.512	< 0.001*
BMI	0.524	< 0.001*
Waist Circumference	0.562	< 0.001*
Waist-Hip Ratio	0.478	< 0.001*
Total Cholesterol	0.445	< 0.001*
Triglycerides	0.538	< 0.001*
HDL-Cholesterol	-0.426	< 0.001*
LDL-Cholesterol	0.412	< 0.001*
VLDL-Cholesterol	0.528	< 0.001*
Systolic Blood Pressure	0.398	< 0.001*
Diastolic Blood Pressure	0.364	< 0.001*

Significant positive correlations were observed between hs-CRP and fasting plasma glucose ($r = 0.486$, $p < 0.001$), HbA1c ($r = 0.512$, $p < 0.001$), BMI ($r = 0.524$, $p < 0.001$), waist circumference ($r = 0.562$, $p < 0.001$), total cholesterol ($r = 0.445$, $p < 0.001$), triglycerides ($r = 0.538$, $p < 0.001$), LDL-cholesterol ($r = 0.412$, $p < 0.001$), and VLDL-cholesterol ($r = 0.528$, $p < 0.001$). A significant negative correlation was found between hs-CRP and HDL-cholesterol ($r = -0.426$, $p < 0.001$).

Multiple Linear Regression Analysis

Multiple linear regression analysis was performed to identify independent predictors of hs-CRP levels in the prediabetic group, adjusting for age, gender, BMI, glycemic parameters, and lipid profile. The results are presented in Table 8.

Table 8: Multiple linear regression analysis for predictors of hs-CRP in prediabetic group. $R^2 = 0.542$, Adjusted $R^2 = 0.508$. *Statistically significant ($p < 0.05$)

Independent Variable	Standardized Beta Coefficient	t-value	p-value
Age	0.082	1.124	0.264
Gender	-0.046	-0.682	0.497
BMI	0.286	3.142	0.002*
HbA1c	0.324	3.864	< 0.001*
Triglycerides	0.298	3.286	0.001*
HDL-Cholesterol	-0.214	-2.568	0.012*
LDL-Cholesterol	0.178	1.924	0.058

The regression model explained 54.2% of the variance in hs-CRP levels ($R^2 = 0.542$, $p < 0.001$). BMI ($\beta = 0.286$, $p = 0.002$), HbA1c ($\beta = 0.324$, $p < 0.001$), triglycerides ($\beta = 0.298$, $p = 0.001$), and HDL-cholesterol ($\beta = -0.214$, $p = 0.012$) emerged as independent predictors of hs-CRP levels in prediabetic individuals.

DISCUSSION

This cross-sectional comparative study conducted at Sree Mookambika Institute of Medical Sciences, Kulashekaram, Kanyakumari district, Tamil Nadu, demonstrates that prediabetic individuals exhibit significantly elevated hs-CRP levels and atherogenic lipid profiles compared to normoglycemic controls. Furthermore, significant correlations were observed between hs-CRP and various lipid parameters, suggesting an intricate relationship between systemic inflammation and lipid metabolism dysregulation in the prediabetic state.

Elevated hs-CRP Levels in Prediabetes

Our study found that the mean hs-CRP level in prediabetic individuals (2.14 ± 0.86 mg/L) was significantly higher than in normoglycemic controls (0.92 ± 0.38 mg/L, $p < 0.001$). This finding is consistent with previous studies that have documented elevated inflammatory markers in prediabetes[9][10][18]. Bains et al. (2024) reported mean hs-CRP levels of 1.717 mg/L in prediabetics compared to 0.917 mg/L in controls ($p = 0.001$)[9], while another Indian study by Jaiswal et al. found hs-CRP levels of 2.17 ± 0.72 mg/L in prediabetics versus 0.66 ± 0.22 mg/L in controls[18].

The elevation in hs-CRP reflects underlying chronic low-grade inflammation, which is increasingly recognized as a key pathophysiological feature of prediabetes and type 2 diabetes[19]. Several mechanisms contribute to this inflammatory state, including adipose tissue dysfunction, increased production of pro-inflammatory cytokines (IL-6, TNF-α), oxidative stress, and endothelial dysfunction[20]. Adipose tissue, particularly visceral fat, acts as an active endocrine organ secreting adipokines and inflammatory mediators that perpetuate systemic inflammation and insulin resistance[21].

In our study, 82% of prediabetic individuals had hs-CRP levels indicating average to high cardiovascular risk (≥1.0 mg/L), compared to only 28% in the control group. This finding has significant clinical implications, as elevated hs-CRP is an independent predictor of cardiovascular events and type 2 diabetes development[22]. Studies have shown that prediabetic individuals with higher hs-CRP levels have increased odds of progressing to diabetes and are at elevated risk for cardiovascular disease, even before overt diabetes develops[23][24].

Dyslipidemia in Prediabetes

Our results demonstrate that prediabetic individuals have a significantly more atherogenic lipid profile compared to normoglycemic controls. Specifically, prediabetics showed elevated total cholesterol (208.6 ± 28.4 vs. 176.4 ± 22.6 mg/dL, $p < 0.001$), triglycerides (168.4 ± 42.6 vs. 118.2 ± 28.4 mg/dL, $p < 0.001$), LDL-cholesterol (136.5 ± 24.8 vs. 104.2 ± 18.6 mg/dL, $p < 0.001$), and VLDL-cholesterol (33.7 ± 8.5 vs. 23.6 ± 5.7 mg/dL, $p < 0.001$), along with significantly reduced HDL-cholesterol levels (38.4 ± 6.8 vs. 48.6 ± 7.2 mg/dL, $p < 0.001$).

These findings align with previous research demonstrating characteristic dyslipidemia in prediabetes, often termed "diabetic dyslipidemia" or "atherogenic dyslipidemia"[11][25]. This pattern includes hypertriglyceridemia, low HDL-cholesterol, and increased small dense LDL particles, all of which are highly atherogenic and contribute to accelerated atherosclerosis and cardiovascular disease[26].

The mechanisms underlying dyslipidemia in prediabetes are multifactorial. Insulin resistance, the hallmark of prediabetes, leads to increased hepatic production of VLDL particles and triglycerides, decreased lipoprotein lipase activity resulting in impaired triglyceride clearance, and reduced HDL-cholesterol synthesis[27]. Furthermore, insulin resistance promotes the formation of small dense LDL particles, which are more susceptible to oxidation and more atherogenic than larger LDL particles[28].

The atherogenic indices (TC/HDL ratio and LDL/HDL ratio) were significantly elevated in our prediabetic group, indicating increased cardiovascular risk. These ratios are powerful predictors of cardiovascular disease and have been shown to be more predictive than individual lipid parameters alone[29].

Correlation Between hs-CRP and Lipid Profile

One of the key findings of our study is the significant correlation between hs-CRP and lipid profile parameters in prediabetic individuals. We observed positive correlations between hs-CRP and total cholesterol ($r = 0.445$, $p < 0.001$), triglycerides ($r = 0.538$, $p < 0.001$), LDL-cholesterol ($r = 0.412$, $p < 0.001$), and VLDL-cholesterol ($r = 0.528$, $p < 0.001$), and a negative correlation with HDL-cholesterol ($r = -0.426$, $p < 0.001$).

These findings are consistent with recent literature demonstrating the interconnection between inflammation and lipid metabolism[9][13]. Bains et al. (2024) reported similar positive correlations between hs-CRP and atherogenic lipid parameters in prediabetics[9]. The hs-CRP/HDL-C ratio has emerged as a novel composite marker reflecting both inflammation and lipid dysregulation, with studies showing its superior predictive value for cardiovascular risk and diabetes development compared to individual markers[14][15].

The bidirectional relationship between inflammation and dyslipidemia involves multiple pathways. Inflammatory cytokines promote lipolysis in adipose tissue, increasing free fatty acid release, which in turn stimulates hepatic triglyceride and VLDL production[30]. Oxidized LDL particles trigger inflammatory responses in endothelial cells and macrophages, perpetuating vascular inflammation and atherosclerosis[31]. HDL-cholesterol, traditionally known for its anti-atherogenic properties, also possesses anti-inflammatory effects; reduced HDL levels in prediabetes contribute to both enhanced inflammation and impaired cholesterol efflux from arterial walls[32].

Correlation Between hs-CRP and Glycemic Parameters

Our study demonstrated significant positive correlations between hs-CRP and both fasting plasma glucose ($r = 0.486$, $p < 0.001$) and HbA1c ($r = 0.512$, $p < 0.001$) in prediabetic individuals. These findings suggest that inflammatory processes are closely linked to glycemic dysregulation and may play a role in the progression from prediabetes to overt diabetes.

Chronic inflammation contributes to insulin resistance through multiple mechanisms, including activation of inflammatory signaling pathways (NF-κB, JNK) that impair insulin signaling, increased production of pro-inflammatory cytokines that interfere with insulin action, and promotion of ectopic fat deposition in liver and muscle[33]. Conversely,

hyperglycemia itself can induce oxidative stress and inflammatory responses, creating a vicious cycle that accelerates metabolic deterioration[34].

Prospective studies have shown that elevated hs-CRP levels predict progression from prediabetes to type 2 diabetes[23]. In a recent study, prediabetic individuals with high hs-CRP levels (>1.62 mg/L) had significantly increased odds of progressing to diabetes compared to those with low hs-CRP levels (<0.67 mg/L)[24]. This underscores the potential utility of hs-CRP as a risk stratification tool in prediabetic populations.

Independent Predictors of hs-CRP

Multiple linear regression analysis in our study identified BMI, HbA1c, triglycerides, and HDL-cholesterol as independent predictors of hs-CRP levels in prediabetic individuals, collectively explaining 54.2% of the variance. This finding highlights the complex interplay between adiposity, glycemic control, lipid metabolism, and inflammation in prediabetes.

BMI emerged as a significant predictor ($\beta = 0.286$, $p = 0.002$), consistent with the well-established role of adiposity in promoting systemic inflammation[35]. Adipose tissue, particularly visceral fat, secretes inflammatory adipokines and cytokines that elevate circulating hs-CRP levels[21]. The strong association between waist circumference and hs-CRP ($r = 0.562$, $p < 0.001$) in our study further emphasizes the importance of central obesity in the inflammatory process.

HbA1c was the strongest predictor of hs-CRP ($\beta = 0.324$, $p < 0.001$), indicating that glycemic control plays a crucial role in modulating inflammation in prediabetes. This finding supports the rationale for aggressive glycemic management even in the prediabetic stage to mitigate inflammatory burden and cardiovascular risk[36].

Clinical Implications

The findings of this study have several important clinical implications for the management of prediabetic individuals:

1. **Early Risk Stratification:** Measurement of hs-CRP alongside lipid profile can help identify prediabetic individuals at higher cardiovascular risk who may benefit from more aggressive preventive interventions[37].
2. **Comprehensive Intervention:** The interconnection between inflammation, dyslipidemia, and glycemic dysregulation underscores the need for comprehensive lifestyle interventions targeting weight reduction, dietary modification, and increased physical activity, which have been shown to reduce hs-CRP levels and improve lipid profiles[38].
3. **Pharmacological Considerations:** In high-risk prediabetic individuals with elevated hs-CRP and atherogenic dyslipidemia, consideration of pharmacological interventions such as metformin (which has anti-inflammatory effects) and statins may be warranted[39]. Recent guidelines support metformin use in high-risk prediabetic individuals, particularly those with BMI ≥35 kg/m², age <60 years, and women with prior gestational diabetes[40].
4. **Cardiovascular Risk Assessment:** Given that prediabetes confers significant cardiovascular risk independent of progression to diabetes, routine cardiovascular risk assessment and management of modifiable risk factors (hypertension, dyslipidemia, smoking) should be integral to prediabetes care[5].
5. **Prevention of Diabetes:** Early identification and management of inflammatory and metabolic derangements may help prevent or delay progression from prediabetes to type 2 diabetes, with potential long-term benefits for cardiovascular health[41].

Regional Context: Kanyakumari District

This study provides important epidemiological data from Kanyakumari district, Tamil Nadu, a region with limited published research on prediabetes and cardiovascular risk factors. The findings are particularly relevant given the high burden of prediabetes in India (15.3% prevalence) and the unique metabolic phenotype of Asian Indians, who exhibit greater insulin resistance and cardiovascular risk at lower BMI levels compared to other ethnic groups[3][16].

The mean BMI in our prediabetic group (26.8 ± 3.4 kg/m²) was in the overweight category, consistent with the observation that Asian Indians develop metabolic complications at lower BMI thresholds. The high prevalence of central obesity (mean waist circumference 92.4 cm in prediabetics) reflects the propensity for visceral fat accumulation in this population, contributing to insulin resistance and inflammation.

Strengths and Limitations

Strengths:

- Adequate sample size with equal distribution of prediabetic and control groups
- Comprehensive assessment of inflammatory and lipid parameters
- Standardized biochemical methods with quality control
- Age and gender-matched control group reducing confounding
- Regional data from an understudied population in southern India

LIMITATIONS

- Cross-sectional design limits causal inference; longitudinal studies are needed to establish temporal relationships
- Convenience sampling may limit generalizability to the entire Kanyakumari district population
- Lack of assessment of other inflammatory markers (IL-6, TNF-α, adiponectin) and markers of oxidative stress
- Dietary intake and physical activity were not quantitatively assessed
- Genetic and familial factors contributing to inflammation and dyslipidemia were not evaluated
- Single measurement of hs-CRP may be affected by transient factors; repeated measurements would be more reliable

Future Directions

Based on our findings, several avenues for future research are suggested:

1. **Longitudinal Studies:** Prospective cohort studies to examine whether elevated hs-CRP and dyslipidemia in prediabetes predict progression to diabetes and cardiovascular events
2. **Intervention Trials:** Randomized controlled trials evaluating the effect of lifestyle modifications and pharmacological interventions on hs-CRP and lipid profile in prediabetic populations
3. **Mechanistic Studies:** Investigation of the molecular mechanisms linking inflammation and lipid metabolism in prediabetes
4. **Novel Biomarkers:** Exploration of emerging biomarkers such as hs-CRP/HDL-C ratio, oxidized LDL, and inflammatory cytokines for improved risk stratification
5. **Population-Based Studies:** Large-scale epidemiological studies to determine the prevalence of prediabetes and associated cardiovascular risk factors in Kanyakumari district
6. **Genetic Studies:** Assessment of genetic polymorphisms associated with inflammation and lipid metabolism in this population

CONCLUSION

This study conducted at Sree Mookambika Institute of Medical Sciences, Kulashekaram, Kanyakumari district, Tamil Nadu, demonstrates that prediabetes is associated with significantly elevated hs-CRP levels and atherogenic lipid profile compared to normoglycemic individuals. The strong correlations between hs-CRP and lipid parameters indicate that inflammation and dyslipidemia are interlinked pathophysiological processes in the prediabetic state, both contributing to increased cardiovascular risk.

The findings underscore that prediabetes is not a benign condition but rather a high-risk metabolic state requiring proactive clinical attention. Measurement of hs-CRP and comprehensive lipid profiling can help identify prediabetic individuals at elevated cardiovascular risk who may benefit from intensive preventive interventions. Early implementation of lifestyle modifications targeting weight reduction, dietary improvement, and increased physical activity, along with consideration of pharmacological therapies in high-risk individuals, may help prevent progression to diabetes and reduce cardiovascular morbidity and mortality.

The significant burden of prediabetes in India, coupled with the unique metabolic phenotype of Asian Indians, necessitates population-specific screening strategies and targeted interventions. This study contributes valuable data from Kanyakumari district and highlights the urgent need for comprehensive prediabetes management programs incorporating inflammatory and lipid risk factor assessment and modification.

Future longitudinal studies are warranted to establish causal relationships and evaluate the impact of interventions targeting inflammation and dyslipidemia on clinical outcomes in prediabetic populations. Such research will inform evidence-based guidelines for optimal prediabetes care and cardiovascular risk reduction in the Indian context.

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Conflicts of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

Dr. D. S. Florence Nesa Bella: Conceptualization, methodology, investigation, data collection, statistical analysis, manuscript writing and editing.

Dr. Sobha Kumari: Conceptualization, supervision, manuscript review and editing, project administration.

Both authors have read and approved the final manuscript.

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