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ORIGINAL RESEARCH ARTICLE

Comprehensive serum profiling in colorectal cancer: Evidence from a South Indian case–control study

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Abstract

Colorectal cancer (CRC) has been associated with metabolic and inflammatory dysregulation, particularly in lipid and glucose metabolism. This study investigates the role of serum lipids and biochemical markers as potential biomarkers for CRC in the South Indian population. A case–control observational study was conducted involving 65 CRC patients and 65 age- and sex-matched healthy controls. Participants were selected based on strict inclusion and exclusion criteria, ensuring the elimination of confounding factors such as other malignancies or chronic conditions. Blood samples were analyzed for lipid profiles, high-sensitivity C-reactive protein (hs-CRP), and other biochemical parameters using enzyme immunoassay kits. Statistical analyses were performed to evaluate differences between groups, with a $p<0.05$ considered statistically significant. Significant elevations in total cholesterol (TC), low-density lipoprotein (LDL), and the TC/high-density lipoprotein (HDL) and LDL/HDL ratios were observed in CRC patients compared to controls. The observed high hs-CRP levels indicate the heightened inflammatory state in CRC. The levels of triglycerides, HDL, and very-LDL showed no significant differences, although trends of elevated uric acid and urea levels in CRC patients were noted. Blood glucose levels were significantly higher in CRC patients, suggesting possible disruptions in glucose metabolism. Liver and renal function markers remained within comparable ranges across both groups. The study highlights dysregulated lipid and glucose metabolism and increased inflammatory markers in CRC patients from the South Indian population. Elevated LDL, TC, and hs-CRP may serve as potential biomarkers for early detection and risk assessment in CRC. These findings highlight the importance of monitoring lipid and glucose profiles in CRC patients and pave the way for further research into their role in CRC pathogenesis and progression.

Keywords: Cholesterol biomarkers; Colorectal cancer; Inflammatory markers; Lipid profile; Metabolic dysregulation

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1. Introduction

Serum markers are powerful indicators that may provide deep insights into the metabolic and inflammatory processes associated with colorectal cancer (CRC).[1,2] While elevated levels of certain lipid fractions – such as high-density lipoprotein (HDL) and low-density lipoprotein (LDL) – have already been linked to CRC, there is a vast array of other serum markers that could enrich our understanding.[3-6] Markers such as very-LDL (VLDL), high-sensitivity C-reactive protein (hs-CRP), uric acid, urea, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine (CREA), and blood sugar levels are critically involved in regulating cellular functions, including proliferation, inflammation, and apoptosis processes, which are often disrupted in CRC.[7-10] Through comprehensive analysis of these serum markers, this study aims to identify new and clinically relevant biomarkers that may support CRC risk assessment, early diagnosis, and therapeutic decision-making. Notably, this study focuses on the South Indian population, a group that has been underrepresented in CRC biomarker research. The limited regional data may stem from an insufficient understanding of how population-specific factors influence CRC risk and progression. By examining the serum marker profiles within this demographic, the study seeks to provide new insights that could refine early detection strategies, enhance risk assessment models, and support the development of population-tailored prevention approaches.

2. Materials and methods

2.1. Ethical permission and consent to participate

The study was conducted in accordance with established ethical standards and guidelines. Ethical approval was obtained from the Institutional Ethics Committee of Bharathiar University (Ethical reference no. BUHEC-006/2018). Written informed consent was obtained from all participants before their inclusion in the study. Participants were fully informed about the purpose, procedures, and any potential risks involved, and their participation was entirely voluntary. Confidentiality of personal and medical information was strictly maintained, with all data anonymized before analysis.

2.2. Characteristics of patients and collection of blood samples

In this case–control observational study, 65 CRC patients were recruited from clinical settings. Inclusion criteria required participants to be adults (≥18 years) with a confirmed histopathological diagnosis of CRC and no prior chemotherapy, radiotherapy, or cancer-related surgery. Exclusion criteria included a history of other malignancies, metastatic disease, chronic conditions (e.g., inflammatory bowel disease and autoimmune disorders), and significant exposure to carcinogens (e.g., chemicals or ionizing radiation).

For comparing the features of CRC with healthy individuals, the control group comprised 65 healthy individuals matched to cases by age and sex. Inclusion criteria required adults (≥18 years) with no personal or family history of malignancies, systemic illnesses, or chronic diseases. Exclusion criteria included significant exposure to carcinogens, recent infections or surgeries, and chronic conditions (e.g., inflammatory bowel disease or autoimmune disorders). All control participants provided informed consent.

Blood samples were collected from CRC patients at various hospitals in South India following their diagnosis, whereas control blood samples were obtained voluntarily from healthy individuals through venipuncture. The blood was drawn into two sterile tubes: one without anticoagulant and one containing ethylenediaminetetraacetic acid. Serum and plasma were separated accordingly and analyzed for several biochemical parameters, including TC, triglycerides (TG), HDL, LDL, VLDL, hs-CRP, uric acid, urea, CREA, AST, ALT, and blood sugar levels. The results were then compared with those of the control group. All blood samples were stored at room temperature for up to 24 h before processing to maintain sample integrity. Lipid profiles were quantified in the serum using enzyme immunoassay kits (Sigma-Aldrich, United States), according to reference values listed in Table 1.

2.3. Statistical analysis

The collected data were initially subjected to descriptive analysis, using frequency methods to summarize the dataset, along with measures of central tendency (mean) and variability (standard deviation). Subsequently, inferential statistical tests (*t*-test) were employed to determine significant differences between groups (https://www.graphpad.com/quickcalcs/ttest1/), with a $p<0.05$ considered statistically significant. These analyses facilitated the identification of meaningful patterns and differences within the data. A graphical representation of the analytical methodology is provided in Figure 1.

3. Results

All participants in this study were recruited consecutively, with control subjects carefully age matched to CRC patients within a ±2-year age range to minimize age-related biases. The clinical characteristics of CRC patients (test group) and healthy individuals (controls) were systematically

Table 1. Lipid profiles quantified using enzyme immunoassay kits (with reference values)

Biochemical parameter	Principle	Reference value	References
TC	The TC assay kit measures TC levels in serum and plasma samples. Sample absorbance is compared against a known concentration of a cholesterol standard using a 96-well colorimetric plate reader.	≤200 mg/dL	11
TG	TG quantification kit is a simple colorimetric assay designed to quantitatively measure TG concentrations in plasma, serum, and cell lysates, utilizing a 96-well microtiter plate format.	≤100 mg/dL	11
HDL	HDL assay kit measures HDL in serum or plasma samples. The kit provides reagents for separating HDL from other lipoproteins prior to cholesterol measurement. Quantification is performed by comparing sample fluorescence to a known cholesterol standard using a 96-well fluorometric plate reader.	40 – 59 mg/dL	11
LDL	LDL assay kit is a simple fluorometric assay designed to measure LDL levels in plasma or serum samples using a 96-well microtiter plate format.	100 – 129 mg/dL	11
VLDL	VLDL assay kit is a simple fluorometric assay designed to measure VLDL levels in plasma or serum samples using a 96-well microtiter plate format.	2 – 30 mg/dL	11
High-sensitivity CRP	Human high-sensitivity CRP ELISA kit is an enzyme immunoassay kit developed for the detection and quantitation of human high-sensitivity CRP in plasma, serum, or other biological fluid samples. The kit has a detection sensitivity of 1ng/mL and provides sufficient reagents to perform up to 96 assays.	≤3.0mg/L	12
Uric acid	The uric acid assay kit is a sensitive, quantitative fluorometric assay used to measure uric acid concentrations. The fluorescence values are proportional to the concentration of uric acid or uricase, depending on the target of the assay.	3.4 – 7.0 mg/dL	13
Urea	Urea assay kit measures urea levels in serum and plasma samples. Sample absorbance is compared to a known urea standard using a 96-well microtiter plate format and a standard 96-well spectrophotometric plate reader.	7 – 20 mg/dL	14
CREA	CREA assay kit measures CREA levels in blood samples. Samples are incubated for 30 min with a reaction reagent that changes color from yellow to bright orange upon formation of the CREA – picrate complex. Absorbance is measured using a standard 96-well spectrophotometric plate reader.	0.6 – 1.2 mg/dL	15
AST	AST assay kit provides a simple colorimetric method to measure AST activity in blood samples. The assay involves the transfer of an amino group from aspartate to ketoglutarate, producing glutamate, which is detected colorimetrically.	10 – 40 U/L	16
ALT	ALT assay kit provides a direct measurement of ALT activity via the conversion of alanine and α-ketoglutaric acid to pyruvic acid and glutamic acid at pH 7.4 and 37°C. Enzymatic activity is quantified by measuring optical density at 505 nm.	7 – 56 U/L	17
Blood glucose	Sugar assay kit measures sugar levels in biological samples. Glucose is oxidized by glucose oxidase into D-gluconic acid and hydrogen peroxide. The hydrogen peroxide is detected with a highly specific colorimetric probe. Sample absorbance is compared to a known sugar standard using a 96-well microtiter plate format.	≤100 mg/dL	18

Abbreviations: ALT: Alanine transaminase; AST: Aspartate aminotransferase; CREA: Creatinine; CRP: C-reactive protein; ELISA: Enzyme-linked immunosorbent assay; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; TC: Total cholesterol; TG: Triglycerides; VLDL: Very-low-density lipoprotein.

documented. Participants were categorized into two age groups: Group I (≤50 years) and Group II (>50 years), with 24 participants (36.92%) in Group I and 41 participants (63.08%) in Group II.

The test group was further categorized into four groups according to Dukes' staging: Stage A (n = 8, 12.31%), stage B (n = 14, 21.54%), stage C (n = 25, 38.46%), and stage D (n = 18, 27.69%). Based on tumor location, CRC patients were grouped as follows: Ascending colon (n = 10, 15.39%), transverse colon (n = 4, 6.15%), descending colon (n = 9, 13.85%), sigmoid colon (n = 17, 26.15%), and rectal cancer (n = 25, 38.46%).

Tumor grade classification divides the test group into well-differentiated (n = 21, 32.31%), moderately differentiated (n = 25, 38.46%), and poorly differentiated tumors (n = 19, 29.23%). Based on clinical history, participants were classified as having sporadic (n = 47, 72.31%), hereditary (n = 12, 18.46%), or familial (n = 6, 9.23%). In addition, the presence of metastasis was used to categorize patients into metastatic (n = 20, 30.77%)

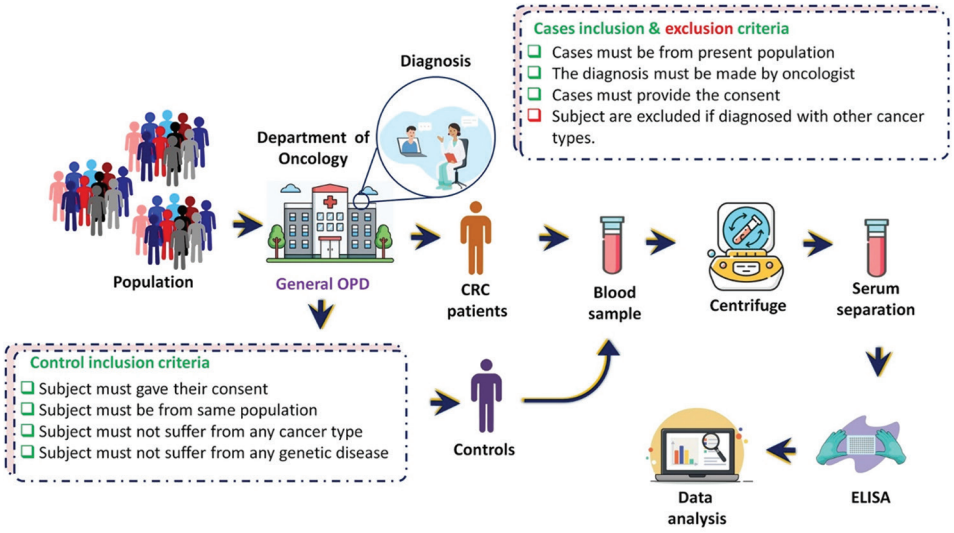

Figure 1. Schematic representation of the methodology employed in the present case-control study
Abbreviations: CRC: Colorectal cancer; ELISA: Enzyme-linked immunosorbent assay; OPD: Outpatient department.

and non-metastatic (n = 45, 69.23%) groups. Notably, all participants were male, ensuring gender uniformity and reducing variability related to gender-specific biochemical and metabolic differences.

A comprehensive assessment of biochemical markers provides valuable insights into CRC-associated metabolic disturbances. This study evaluated TC, TG, HDL, LDL, VLDL, hs-CRP, uric acid, urea, CREA, AST, ALT, and blood sugar levels in CRC patients and healthy controls. Key findings reveal significantly higher levels of TC, LDL, TC/HDL ratio, LDL/HDL ratio, and hs-CRP in CRC patients compared to healthy controls (Table 2), indicating pronounced lipid metabolism dysregulation and heightened systemic inflammation – factors potentially contributing to tumorigenesis and cancer progression.

Moreover, CRC patients exhibit significantly elevated blood sugar levels, suggesting glucose metabolism disruptions that may exacerbate disease severity (Table 2). Although TG, HDL, and VLDL levels demonstrate no significant differences, the observed trends of elevated uric acid and urea levels in CRC patients suggest possible links between metabolic byproducts and cancer development, warranting further investigation (Table 2). Liver function markers (e.g., AST and ALT) and renal function markers (e.g., CREA) remain comparable between the groups, indicating minimal hepatic or renal dysfunction in this cohort. The differences in biochemical markers between CRC patients and controls may provide valuable insights into the metabolic and physiological changes associated with CRC (Figure 2). These results not only illuminate the metabolic and inflammatory changes associated with CRC but also highlight the importance of monitoring lipid and glucose profiles in affected individuals. These findings could inform early detection strategies, support targeted interventions, and ultimately improve patient outcomes in CRC management.

4. Discussion

Serum markers are pivotal in understanding the metabolic and inflammatory changes associated with CRC.[19] Examining the levels of various serum components can help identify potential indicators of CRC risk, progression, and prognosis within specific populations.[20] These markers – including lipid fractions, inflammatory proteins, and metabolic byproducts – play critical roles in cellular processes such as proliferation, inflammation, and apoptosis. Investigating these serum markers offers valuable insights into CRC treatment development and could lead to improved risk assessment and early detection strategies, particularly in the South Indian population.[21,22]

The present study demonstrates that increased TG levels are significantly associated with an elevated risk of CRC (Figure 2A). This finding aligns with previous research, which has shown a positive correlation between TG and glucose levels and increased CRC risk.[23] In addition, the study reveals that serum TC, TG and LDL levels are higher in CRC patients compared to healthy controls. Interestingly, these markers are notably lower in patients diagnosed at an early stage, suggesting that abnormal TG and HDL levels may serve as significant risk factors and potential biomarkers for CRC.[24,25] Serum lipids, including LDL and HDL, have been established as CRC biomarkers, with high

Table 2. Serum levels between colorectal cancer patients and controls

No.	Parameter	CRC		CTL		Significance testing		
		Mean	SD	Mean	SD	*t*-test	*p*-value	Interpretation
1	TC	206.42	41.8	176.73	33.18	4.485	<0.0001	Significantly elevated TC levels in CRC patients
2	TG	178.4	86.22	158.49	78.04	1.3803	0.1699	No significant differences in TG levels.
3	HDL	36.68	6.72	38.49	6.09	1.6091	0.1101	HDL levels are lower in CRC patients, but the difference is not statistically significant.
4	LDL	134	37.5	106.6	28.59	5.5687	<0.0001	Significantly elevated LDL levels in CRC patients
5	VLDL	35.72	17.28	31.65	14.7	1.4464	0.1505	No significant differences in VLDL levels.
6	TC/HDL	5.75	1.24	4.63	0.96	5.758	<0.0001	Elevated TC/HDL ratio in CRC patients.
7	LDL/HDL	3.77	1.09	2.8	0.83	5.7082	<0.0001	Significantly elevated LDL/HDL ratio.
8	TG/HDL	4.84	2.33	4.19	2.08	1.677	0.095	TG/HDL ratio is higher in CRC patients, but the difference is not statistically significant.
9	CRP	1.7	0.87	1.3	0.91	2.56	0.0116	Elevated CRP levels in CRC patients.
10	Uric Acid	5.65	1.36	5.34	1.45	1.25	0.211	No significant differences in uric acid levels.
11	Urea	27.96	8.74	25.09	9.65	1.777	0.0779	Slightly higher urea levels in CRC patients, but the difference is not statistically significant.
12	AST	25.95	6.01	26.52	9.6	0.405	0.685	No significant differences in AST levels.
13	ALT	28.14	6.89	28.89	12.69	0.418	0.6761	No significant differences in ALT levels.
14	CREA	1.05	0.21	1.08	0.3	0.6605	0.5101	No significant differences in CREA levels.
15	AST/ALT	0.89	0.15	0.92	0.28	0.4478	0.7614	No significant differences in AST/ALT ratios.
16	Sugar	129.56	37.22	114.23	38.14	2.319	0.022	Higher blood sugar levels in CRC patients.

Abbreviations: ALT: Alanine transaminase; AST: Aspartate aminotransferase; CRC: Colorectal cancer; CREA: Creatinine; CRP: C-reactive protein; CTL: Control; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SD: Standard deviation; TC: Total cholesterol; TG: Triglycerides; VLDL: Very-low-density lipoprotein.

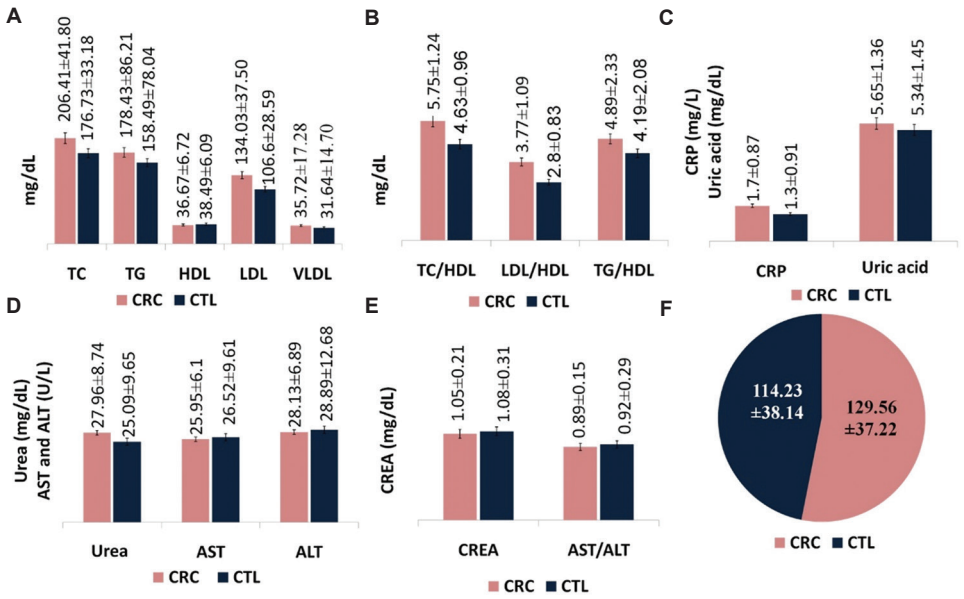

Figure 2. Comparative analysis of biochemical parameters in CRC patients and healthy CTLs: (A) Serum levels of TC, TG, HDL, LFL, and VLDL; (B) Lipid ratio indices: TC/HDL, LDL/HDL, and TG/HDL ratios; (C) Inflammatory and metabolic markers: CRP and uric acid; (D) Renal and hepatic function markers: urea, AST, and ALT; (E) CREA and AST/ALT ratio; and (F) Mean blood glucose levels

Abbreviations: ALT: Alanine transaminase; AST: Aspartate aminotransferase; CRC: Colorectal cancer; CREA: Creatinine; CRP: C-reactive protein; CTL: Control; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; TC: Total cholesterol; TG: Triglycerides; VLDL: Very-low-density lipoprotein.

TC, LDL, TG and low HDL levels being well-recognized risk profiles (Figure 2B). Recent studies have also reported that low serum lipid levels are positively associated with cancer incidence and mortality, particularly in CRC.[26,27]

Furthermore, the relationship between VLDL and CRC has been explored, with findings suggesting that high HDL levels are inversely related to VLDL. Elevated VLDL levels have been linked to an increased risk of colorectal adenomas in CRC patients. The relationship between LDL and VLDL has been well documented in studies of lipoprotein metabolism.[28] In addition to the lipid profile, the study identifies CRP as a potential CRC marker (Figure 2C). Elevated CRP levels are associated with inflammatory symptoms and responses in CRC, highlighting its potential utility in enhancing risk stratification within prediction models. However, the clinical significance of CRP compared to conventional risk factors warrants further investigation and validation in diverse populations.[2,29]

Blood sugar also shows significantly higher levels in CRC patients compared to controls (Figure 2F). This finding aligns with a recent study reporting that high sugar intake is positively associated with an increased risk of CRC among men with a history of smoking.[30,31] Conversely, the risk of CRC was found to be reduced among male smokers with lower sugar intake.[32,33] This highlights the potential role of sugar metabolism in CRC risk, particularly among populations with specific lifestyle factors such as smoking.

Furthermore, the difference between various markers such as uric acid, urea, AST, ALT, and CREA shows no significant differences (Figure 2D and E). Several studies suggest that high urate levels – the dominant monosodium form of uric acid at physiological pH – may be associated with increased premature cancer mortality in both genders.[34,35] AST plays a vital role in the metabolism of amino acids in the liver, serves as a biochemical marker of liver damage, and may increase the risk of CRC.[36] The increased AST levels may result from the progression of liver damage, as intracellular AST is released when hepatic parenchymal cells are injured, thereby increasing the risk of CRC.[37,38] A similar study reported a significant difference between CRC patients with and without liver metastasis.[39] The study reported that the levels of ALT and AST were significantly higher in CRC patients with liver metastasis than in those without liver metastasis. Another important marker observed in previous studies was CREA, a key parameter for assessing renal function. In normal individuals, the excretion of CREA is dependent on lean body mass, and its plasma concentration serves as a reliable indicator of nephrotoxicity. Interestingly, the present study shows slightly lower mean CREA levels in CRC patients compared to healthy controls (Figure 2E). This finding contradicts previous research, which suggested that elevated plasma CREA levels are a significant risk factor for CRC.[40]

4.1. Strength, limitation, and future perspective

This study possesses several strengths that enhance its significance. It focuses on a South Indian population, offering unique regional insights into metabolic and inflammatory biomarkers in CRC patients – a relatively understudied demographic. The comprehensive analysis of diverse parameters – including lipid profiles, glucose metabolism, and inflammatory markers – provides a holistic understanding of metabolic dysregulation in CRC. Furthermore, the findings hold clinical relevance by contributing actionable insights for early diagnosis and risk stratification, potentially facilitating the development of population-specific preventive strategies.

Despite its strengths, the study has certain limitations. The relatively small sample size limits the generalizability of the findings across diverse South Indian subpopulations. Furthermore, unaccounted confounding factors such as dietary habits, physical activity, and genetic predispositions may influence the observed associations. Future research should involve multi-center studies in diverse South Indian populations and longitudinal tracking of metabolic and inflammatory markers to establish causation. Investigating the mechanisms linking lipid dysregulation, glucose metabolism, and inflammation to CRC could offer new insights into prevention and treatment strategies. Combining these biomarkers with genetic profiling may improve risk prediction and advance personalized CRC management.

5. Conclusion

This study highlights significant metabolic and inflammatory alterations in CRC patients from the South Indian population. Elevated levels of TC, LDL, and hs-CRP, alongside dysregulated glucose metabolism, suggest their potential as biomarkers for CRC risk assessment and early detection. These findings underscore the importance of integrating lipid and glucose profile monitoring into routine diagnostic and preventive strategies for CRC. Further research is warranted to explore the mechanistic links between these metabolic changes and CRC progression, which could provide new insights into the development of targeted therapeutic interventions, improving patient outcomes.

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Conflict of interest

The authors declare that they have no competing interest.

Author contributions

Conceptualization: Mohd Younis, Vijaya Anand
Formal analysis: Ashma Gupta, Parvinder Kumar
Investigation: Mohd Younis
Methodology: Mohd Younis, Vijaya Anand
Visualization: Ashma Gupta, Parvinder Kumar
Writing – original draft: Mohd Younis
Writing – review & editing: Amrit Sudershan, Arizoo Hamid, Vijaya Anand

Ethics approval and consent to participate

The study was conducted in accordance with established ethical standards and guidelines. Ethical approval was obtained from the Institutional Ethics Committee of Bharathiar University (Ethical reference no. BUHEC-006/2018). Written informed consent was obtained from all participants before their inclusion in the study. Participants were fully informed about the purpose, procedures, and any potential risks involved, and their participation was entirely voluntary. Confidentiality of personal and medical information was strictly maintained, with all data anonymized before analysis.

Consent for publication

Informed consent was obtained from all participants, ensuring their voluntary participation and understanding of the study's purpose, procedures, and any potential risks involved. Participants were assured of the confidentiality of their personal and medical information, with all data being anonymized for analysis. Participants consented to the publication of their data.

Availability of data

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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