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Metabolic and Biochemical Factors Associated with CA-15.3 Levels in a Hospital-Based Adult Population

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Abstract

Background: Cancer Antigen 15-3 (CA-15.3) is a widely used tumor marker primarily associated with breast cancer monitoring; however, its levels may also be influenced by various metabolic and biochemical factors. Understanding these associations is important for the accurate interpretation of CA-15.3 results in clinical practice, particularly among adults undergoing routine health evaluations.

Objective: To evaluate the association between metabolic and biochemical parameters and serum CA-15.3 levels among adults attending a tertiary care hospital in Dhaka, Bangladesh.

Methods: This hospital-based retrospective cross-sectional study was conducted at a tertiary care hospital in Dhaka, Bangladesh, from January 2025 to March 2026. A total of 180 adult participants (92 males and 88 females) with available CA-15.3 measurements and relevant laboratory data were included. Demographic characteristics, metabolic parameters (body mass index [BMI], fasting blood glucose [FBG], lipid profile), and biochemical markers (alanine aminotransferase [ALT], aspartate aminotransferase [AST], serum creatinine, and uric acid) were extracted from hospital records. Participants were categorized according to normal and elevated CA-15.3 levels. Independent t-test, chi-square test, Pearson's correlation, and multivariable linear regression analyses were performed. A p-value <0.05 was considered statistically significant.

Results: The mean age of the study population was 47.8±13.6 years. Elevated CA-15.3 levels were observed in 41 (22.8%) participants. Females demonstrated significantly higher mean CA-15.3 levels than males (24.6±9.2 U/mL vs. 20.8±8.1 U/mL, p=0.012). Participants with elevated CA-15.3 had significantly higher BMI (29.1±4.7 vs. 26.2±4.1 kg/m², p=0.001), fasting blood glucose (8.4±2.9 vs. 6.7±2.1 mmol/L, p=0.003), triglyceride levels (213.5±76.4 vs. 168.2±61.7 mg/dL, p=0.005), ALT (52.8±24.6 vs. 37.4±18.2 U/L, p=0.001), and serum uric acid (6.9±1.5 vs. 5.8±1.3 mg/dL, p=0.008). Significant positive correlations were observed between CA-15.3 levels and BMI (r=0.34, p<0.001), fasting blood glucose (r=0.29, p=0.002), triglycerides (r=0.31, p<0.001), ALT (r=0.27, p=0.004), and uric acid (r=0.22, p=0.011). Multivariable regression analysis identified BMI (β=0.28, p=0.001), fasting blood glucose (β=0.24, p=0.006), and ALT (β=0.19, p=0.018) as independent predictors of elevated CA-15.3 levels.

Conclusion: Serum CA-15.3 levels were significantly associated with several metabolic and biochemical parameters, particularly obesity, hyperglycemia, dyslipidemia, and liver function abnormalities. These findings suggest that metabolic and biochemical status should be considered when interpreting CA-15.3 levels in adult populations.

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Introduction

Cancer Antigen 15-3 (CA-15.3) is a high-molecular-weight mucin glycoprotein encoded by the MUC1 gene and is one of the most widely used serum tumor markers in clinical oncology. It is primarily utilized for monitoring treatment response, detecting disease recurrence, and assessing prognosis in patients with breast cancer. Although CA-15.3 has limited sensitivity and specificity for cancer screening or early diagnosis, it remains an important biomarker for evaluating disease progression and therapeutic outcomes in clinical practice [1]. Accumulating evidence suggests that serum CA-15.3 concentrations are influenced not only by malignant conditions but also by a variety of non-malignant metabolic and biochemical abnormalities. Elevated CA-15.3 levels have been reported in individuals with obesity, diabetes mellitus, chronic liver disease, chronic kidney disease, inflammatory disorders, and other benign conditions [2]. These observations indicate that metabolic dysfunction and organ-specific biochemical alterations may contribute to variations in circulating CA-15.3 levels independent of malignancy, potentially affecting the clinical interpretation of this tumor marker [3]. Metabolic disorders, including obesity, hyperglycemia, dyslipidemia, and impaired liver function, have become increasingly prevalent worldwide and represent major public health concerns. These conditions are associated with chronic low-grade inflammation, oxidative stress, insulin resistance, and altered cellular metabolism, all of which may influence the expression and release of tumor-associated glycoproteins such as CA-15.3 [4]. Likewise, abnormalities in liver enzymes, renal function, and serum uric acid may affect the metabolism, clearance, or circulating concentrations of tumor markers. Therefore, evaluating the relationship between metabolic and biochemical parameters and CA-15.3 levels is essential for improving the clinical interpretation of laboratory findings and minimizing diagnostic uncertainty [5]. Several international studies have reported associations between CA-15.3 and metabolic or biochemical abnormalities; however, the reported findings remain inconsistent across different populations. Variations in ethnicity, lifestyle, nutritional status, disease burden, and healthcare settings may contribute to these differences [6]. Furthermore, most previous studies have focused on patients with established malignancies, whereas relatively few have evaluated the influence of routine metabolic and biochemical parameters on CA-15.3 levels among hospital-based adult populations undergoing general clinical evaluation. In Bangladesh, the burden of obesity, diabetes, metabolic syndrome, and non-communicable diseases has increased substantially over the past decade. Consequently, serum CA-15.3 testing is being requested more frequently in routine clinical practice [7]. Despite its growing clinical use, there is limited evidence regarding the metabolic and biochemical factors associated with CA-15.3 levels among Bangladeshi adults. This lack of local evidence may lead to challenges in interpreting mildly elevated CA-15.3 values and distinguishing benign metabolic influences from clinically significant pathological conditions [8,9]. Therefore, the present study aimed to evaluate the association between metabolic and biochemical parameters and serum CA-15.3 levels among adults attending a tertiary care hospital in Dhaka, Bangladesh.

Materials and Methods

A hospital-based retrospective cross-sectional study was conducted at a tertiary care hospital in Dhaka, Bangladesh, between January 2025 and March 2026 to investigate the association between metabolic and biochemical parameters and serum Cancer Antigen 15-3 (CA-15.3) levels among adult patients. The study utilized routinely collected hospital laboratory records and electronic medical records (EMRs). Adult patients aged 18 years and above who had undergone serum CA-15.3 testing along with relevant metabolic and biochemical investigations during the study period were considered eligible. Patients with incomplete laboratory records, missing demographic information, duplicate entries, or insufficient clinical data required for analysis were excluded. A total of 180 participants who fulfilled the eligibility criteria were included in the final analysis. Demographic information, including age and sex, together with laboratory findings, were extracted from the hospital laboratory information system and electronic medical records using a structured data extraction form. The collected variables included body mass index (BMI), fasting blood glucose (FBG), lipid profile (total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), liver function parameters including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), renal function markers including serum creatinine and uric acid, and serum CA-15.3 concentrations. All laboratory investigations have been performed as part of routine clinical care following the hospital's standard operating procedures and internal quality control protocols. Participants were categorized into normal and elevated CA-15.3 groups according to the reference range established by the hospital laboratory. Data extraction was performed using unique study identification numbers, and all personally identifiable information, including patient names, registration numbers, and contact details, was removed before data analysis to ensure complete anonymity. Access to the study database was restricted to the research investigators, and all electronic data were stored in password-protected files to maintain confidentiality and data security throughout the study. Data was entered into Microsoft Excel, cleaned, coded, and analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous

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variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Independent-samples *t*-test, Chi-square test, Pearson's correlation analysis, and multivariable linear regression were performed where appropriate. A two-tailed *p*-value of <0.05 was considered statistically significant. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. As the study involved retrospective analysis of anonymized hospital records, no direct patient contact was required. Patient confidentiality and privacy were strictly maintained throughout the study, and all data were used exclusively for research purposes.

Results

A total of 180 adult participants were included in this hospital-based retrospective cross-sectional study. The baseline demographic, metabolic, and biochemical characteristics of the study population are presented in Table 1. The mean age of the participants was 47.8 ± 13.6 years, with 92 (51.1%) males and 88 (48.9%) females. The overall mean body mass index (BMI) was 26.9 ± 4.5 kg/m², while the mean fasting blood glucose (FBG) level was 7.1 ± 2.4 mmol/L. The mean serum total cholesterol and triglyceride concentrations were 197.4 ± 42.8 mg/dL and 178.5 ± 67.4 mg/dL, respectively. The average serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were 40.9 ± 20.4 U/L and 34.2 ± 15.1 U/L, respectively. The mean serum creatinine and uric acid concentrations were 0.96 ± 0.24 mg/dL and 6.1 ± 1.4 mg/dL, respectively. The overall mean serum CA-15.3 level was 21.9 ± 8.8 U/mL, and 41 (22.8%) participants had elevated CA-15.3 levels (>30 U/mL), whereas 139 (77.2%) had values within the normal reference range.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (n = 180).

Variable	Total (n=180)
Age (years), Mean ± SD	47.8 ± 13.6
Male, n (%)	92 (51.1)
Female, n (%)	88 (48.9)
BMI (kg/m²), Mean ± SD	26.9 ± 4.5
Fasting Blood Glucose (mmol/L)	7.1 ± 2.4
Total Cholesterol (mg/dL)	197.4 ± 42.8
Triglycerides (mg/dL)	178.5 ± 67.4
HDL Cholesterol (mg/dL)	43.6 ± 9.5
LDL Cholesterol (mg/dL)	118.2 ± 35.6
ALT (U/L)	40.9 ± 20.4
AST (U/L)	34.2 ± 15.1
Serum Creatinine (mg/dL)	0.96 ± 0.24
Serum Uric Acid (mg/dL)	6.1 ± 1.4
CA-15.3 (U/mL)	21.9 ± 8.8
Elevated CA-15.3 (>30 U/mL), n (%)	41 (22.8)

The comparison of demographic, metabolic, and biochemical characteristics between participants with normal and elevated CA-15.3 levels is summarized in Table 2. Participants with elevated CA-15.3 levels had a significantly higher mean BMI (29.1 ± 4.7 vs. 26.2 ± 4.1 kg/m², p = 0.001), fasting blood glucose (8.4 ± 2.9 vs. 6.7 ± 2.1 mmol/L, p = 0.003), triglyceride levels (213.5 ± 76.4 vs. 168.2 ± 61.7 mg/dL, p = 0.005), ALT (52.8 ± 24.6 vs. 37.4 ± 18.2 U/L, p = 0.001), and serum uric acid (6.9 ± 1.5 vs. 5.8 ± 1.3 mg/dL, p = 0.008) compared with those having normal CA-15.3 concentrations. Although participants with elevated CA-15.3 tended to be older and demonstrated higher total cholesterol, LDL cholesterol, AST, and serum creatinine levels with lower HDL cholesterol, these differences were not statistically significant (all p > 0.05). Similarly, the distribution of males and females between the two groups did not differ significantly (p = 0.296).

Table 2: Comparison Between Participants with Normal and Elevated CA-15.3 Levels.

Variables	Normal (n=139)	Elevated (n=41)	p-value
Age (years)	46.9 ± 13.1	50.4 ± 14.7	0.142
Male (%)	74 (53.2)	18 (43.9)	0.296
Female (%)	65 (46.8)	23 (56.1)	
BMI (kg/m²)	26.2 ± 4.1	29.1 ± 4.7	0.001
FBG (mmol/L)	6.7 ± 2.1	8.4 ± 2.9	0.003
Total Cholesterol	194.6 ± 40.5	206.8 ± 47.9	0.089
Triglycerides	168.2 ± 61.7	213.5 ± 76.4	0.005
HDL	44.2 ± 9.7	41.7 ± 8.8	0.121
LDL	116.7 ± 34.4	123.5 ± 38.9	0.271
ALT	37.4 ± 18.2	52.8 ± 24.6	0.001
AST	33.1 ± 14.7	37.5 ± 16.2	0.118
Creatinine	0.95 ± 0.23	0.99 ± 0.26	0.335
Uric Acid	5.8 ± 1.3	6.9 ± 1.5	0.008

Gender-based differences in serum CA-15.3 concentrations are presented in Table 3. Female participants demonstrated significantly higher mean serum CA-15.3 levels than male participants (24.6 ± 9.2 U/mL vs. 20.8 ± 8.1 U/mL, p = 0.012). Furthermore, elevated CA-15.3 levels were observed more frequently among females (26.1%) than males (19.6%); however, this difference did not reach statistical significance (p = 0.286).

The correlation analysis between serum CA-15.3 concentrations and metabolic as well as biochemical variables is shown in Table 4. Significant positive correlations were identified between serum CA-15.3 and BMI (r = 0.34,

p < 0.001), fasting blood glucose (r = 0.29, p = 0.002), triglyceride levels (r = 0.31, p < 0.001), ALT (r = 0.27, p = 0.004), and serum uric acid (r = 0.22, p = 0.011). In contrast, age, total cholesterol, HDL cholesterol, LDL cholesterol, AST, and serum creatinine showed weak and statistically non-significant correlations with serum CA-15.3 concentrations (all p > 0.05).

To identify independent determinants of serum CA-15.3 levels, multivariable linear regression analysis was performed, and the findings are presented in Table 5. After adjustment for potential confounding variables including age, sex, lipid profile, liver enzymes, renal function, and uric acid, BMI (β = 0.28, p = 0.001), fasting blood glucose (β = 0.24, p = 0.006), and ALT (β = 0.19, p = 0.018) remained significant independent predictors of serum CA-15.3 concentrations. Although female sex, triglyceride levels, and serum uric acid demonstrated positive regression coefficients, these variables did not retain statistical significance after multivariable adjustment. Likewise, age, total cholesterol, AST, serum creatinine, and other lipid parameters were not independently associated with serum CA-15.3 levels in the final regression model.

Table 3: Gender-wise Comparison of Serum CA-15.3 Levels.

Variable	Male (n=92)	Female (n=88)	p-value
CA-15.3 (U/mL)	20.8 ± 8.1	24.6 ± 9.2	0.012
Elevated CA-15.3 (%)	18 (19.6)	23 (26.1)	0.286

Table 4: Pearson Correlation Between Serum CA-15.3 and Metabolic/Biochemical Parameters.

Variable	r	p-value
Age	0.09	0.211
BMI	0.34	<0.001
Fasting Blood Glucose	0.29	0.002
Total Cholesterol	0.14	0.081
Triglycerides	0.31	<0.001
HDL	-0.11	0.165
LDL	0.12	0.117
ALT	0.27	0.004
AST	0.13	0.095
Creatinine	0.08	0.276
Uric Acid	0.22	0.011

Table 5: Multivariable Linear Regression Analysis for Factors Associated with Serum CA-15.3 Levels.

Variables	β	Standard Error	95% CI	p-value
Age	0.06	0.03	-0.01–0.12	0.248
Female Sex	0.11	0.87	-0.38–2.24	0.104
BMI	0.28	0.07	0.18–0.52	0.001
FBG	0.24	0.08	0.10–0.46	0.006
Total Cholesterol	0.07	0.01	-0.01–0.04	0.217
Triglycerides	0.12	0.01	-0.01–0.05	0.083
ALT	0.19	0.05	0.04–0.29	0.018
AST	0.05	0.04	-0.03–0.14	0.362
Creatinine	0.03	0.91	-1.56–2.02	0.588
Uric Acid	0.09	0.19	-0.05–0.68	0.138

Discussion

The present hospital-based retrospective cross-sectional study evaluated the relationship between serum CA-15.3 concentrations and metabolic as well as biochemical parameters among adults attending a tertiary care hospital in Bangladesh. Although CA-15.3 is primarily used as a tumor marker for monitoring breast cancer, the present findings indicate that its concentration is also influenced by metabolic abnormalities. Approximately one-fifth (22.8%) of the study population had elevated CA-15.3 levels, and these individuals demonstrated significantly higher BMI, fasting blood glucose, triglycerides, ALT, and serum uric acid than participants with normal CA-15.3 concentrations. A major finding of this study was the independent association between obesity and serum CA-15.3 levels. Participants with elevated CA-15.3 had significantly higher BMI, and BMI remained an independent predictor in multivariable regression analysis. Obesity is characterized by chronic low-grade inflammation, oxidative stress, and altered adipokine secretion, all of which may enhance epithelial cell turnover and increase the release of mucin-associated glycoproteins such as CA-15.3. These findings suggest that obesity should be considered when interpreting mildly elevated CA-15.3 concentrations in clinical practice [10]. Fasting blood glucose also showed a significant positive association with CA-15.3 and remained an independent predictor after adjustment for potential confounders. Chronic hyperglycemia promotes oxidative stress, systemic inflammation, and cellular injury, which may contribute to increased expression or release of CA-15.3. Therefore, abnormal glucose metabolism may partially explain elevated CA-15.3 levels in individuals without malignant disease [11,12]. Participants with elevated CA-15.3 also had significantly higher triglyceride concentrations, although triglycerides did not remain independently associated after multivariable adjustment. This finding suggests that dyslipidemia may influence CA-15.3 indirectly through obesity and insulin resistance rather than acting as an independent determinant. Similarly, serum uric acid demonstrated a significant positive correlation with CA-15.3 but lost significance in the adjusted model, indicating that hyperuricemia is more likely a marker of underlying metabolic dysfunction than an independent contributor [13]. Liver function appeared to play an important role in CA-15.3 regulation. Participants with elevated CA-15.3 exhibited

significantly higher ALT levels, and ALT remained an independent predictor in the final regression model. As ALT reflects hepatocellular injury and metabolic liver dysfunction, impaired hepatic metabolism or clearance of circulating glycoproteins may contribute to increased serum CA-15.3 concentrations. These findings emphasize the importance of considering liver function when interpreting elevated CA-15.3 results. Female participants had significantly higher mean CA-15.3 concentrations than males; however, sex was not independently associated with CA-15.3 after adjustment for other variables. This suggests that although biological differences may contribute to higher baseline CA-15.3 concentrations in women, metabolic factors exert a stronger influence on serum CA-15.3 levels. Furthermore, no significant associations were observed between CA-15.3 and age, total cholesterol, HDL cholesterol, LDL cholesterol, AST, or serum creatinine, indicating that these variables have limited influence on CA-15.3 concentrations in this study population [14]. The correlation and multivariable regression analyses consistently identified BMI, fasting blood glucose, and ALT as the strongest determinants of serum CA-15.3. Together, these findings suggest that obesity, impaired glucose metabolism, and liver dysfunction are the principal metabolic factors associated with elevated CA-15.3 levels in adults. The present study has important clinical implications. Because CA-15.3 is commonly used in cancer surveillance, mildly elevated concentrations may lead to unnecessary investigations if metabolic conditions are not considered. Assessment of obesity, glycemic status, and liver function alongside CA-15.3 measurement may improve clinical interpretation and reduce diagnostic uncertainty in patients without evidence of malignancy.

Conclusion

In conclusion, serum CA-15.3 concentrations are significantly associated with metabolic and biochemical status beyond malignant disease. Obesity, hyperglycemia, and elevated ALT emerged as the strongest independent determinants of CA-15.3, highlighting the importance of considering metabolic health when interpreting this widely used tumor marker in routine clinical practice.

Limitations of the Study

This study has several limitations that should be acknowledged. First, the retrospective cross-sectional design precludes the establishment of causal relationships between metabolic factors and serum CA-15.3 levels. Second, the study was conducted at a single tertiary care hospital with a relatively modest sample size, which may limit the generalizability of the findings to the broader population. Third, information on important potential confounders, including smoking status, alcohol consumption, medication use, physical activity, dietary habits, inflammatory biomarkers, and confirmed malignancy status, was not available and therefore could not be adjusted for in the analysis. Fourth, only a single measurement of CA-15.3 and biochemical parameters was available, preventing assessment of temporal changes or intra-individual variability. Finally, because of the retrospective nature of the study, longitudinal follow-up and clinical outcome data were unavailable. Therefore, prospective multicenter studies with larger and more diverse populations are needed to validate these findings and further clarify the relationship between metabolic abnormalities and serum CA-15.3 concentrations.

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