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Original Article

Assessment of Serum Creatinine, Uric Acid, and Blood Urea Nitrogen Levels among Untreated Cervical Cancer Patients Attending Wolaita Sodo University Comprehensive Specialized Hospital: A Case-Control Study

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Abstract

Background: Cervical cancer (CC) is a major public health issue associated with metabolic and biochemical alterations that may influence disease progression and the clinical management of patients. Serum biomarkers such as creatinine (Cr), uric acid (UA), and blood urea nitrogen (BUN) can reflect changes in renal function and cellular metabolism in individuals affected by cancer. Therefore, this study aimed to assess the Cr, UA, and BUN levels among untreated CC patients.

Methods: A case–control study was conducted involving 32 untreated CC patients and 32 controls without a history of cancer, matched for key demographic characteristics such as age. Potential confounding variables were considered during both participant selection and statistical analysis. Independent-samples t-test was used to compare mean values of continuous variables between the two groups. Correlations between variables were assessed using Pearson's correlation for continuous variables and Spearman's rank correlation for ordinal variables. A p-value of < 0.05 with a 95% confidence interval was considered statistically significant in all analyses.

Result: Results: Comparative analysis between the untreated CC cases and controls revealed significantly higher levels of Cr, UA, and BUN in the case group ($P < 0.01$). In addition, a significant positive correlation was observed between Cr, UA, and BUN levels and disease stage ($P < 0.01$), indicating a progressive increase in these biochemical markers with advancing disease.

Conclusions: Elevated levels of Cr, UA, and BUN were observed in patients with untreated CC, and these biomarkers were significantly associated with advancing disease stage. These findings suggest that routine assessment of renal function and metabolic markers may be clinically valuable in monitoring and management of untreated CC patients.

Key words: Cervical cancer, Serum creatinine, Uric acid, and Blood urea nitrogen

Introduction

The complicated set of disorders known as cancer is defined by the unchecked proliferation of abnormal cells that cause masses and spread throughout the body. There are various kinds of malignancies, and instead of dying and dividing into new, aberrant cells, cancer cells always keep growing, dividing, and re-dividing (1). CC is among the most prevalent forms of carcinoma among women in developing nations worldwide. It starts with the cervix, where aberrant cervix cells begin to proliferate out of control and develop tumors (2).

The primary cause of CC is infection with human papillomavirus (HPV), with high-risk strains like HPV-16 and HPV-18 being closely associated with development of precancerous lesions and invasive disease (3, 4). However, most HPV infections are transient and resolve spontaneously; not all infections progress into cancer. Persistent infection, along with other host and environmental variables, affects the development of CC (5, 6).

Cervical cancer has systemic effect on numerous organs, including the liver and kidneys, this can result in problems and cell metabolic dysfunction (7). According to recent studies, in the early phases of their diseases, more than 25% of CC patients had renal problems and elevated oxidative stress. BUN, Cr, and UA abnormalities in CC patients have a detrimental impact on their overall survival, quality of life, and response to treatment (8). According to several reports, CC is one of the leading causes of disease and death in women worldwide. Furthermore, there are notable effects on the financial burden of CC in high-incidence countries, as well as on the mental, reproductive, and physical health of patients, the challenges associated with treatment, and the resulting doubts over its effectiveness (9). Taken together, new scientific findings that have been converted into innovative treatment approaches have transformed the medical field and made cancer curable in many cancer types, including CC (10).

However, survival rates have shown limited improvement over the past few decades, despite all the advancements achieved in surgical and non-surgical treatment approaches for CC, with the exception of cases where the illness was identified and treated early (11). The scientific community has recently proposed theories regarding the underlying mechanism of metabolic changes and their connection to cancer pathogenesis in an effort to find effective strategies to combat cancer (12). Through intricate, genetically controlled reprogramming of many metabolic pathways, cancer cells are able to maintain their elevated energy demands, which are necessary to support their unique malignant characteristics (13).

Tumor development and invasion are known to be significantly influenced by changes in particular metabolic pathways, such as aerobic glycolysis or fatty acid oxidation, which have been examined in relation to some of these mechanisms (14). Also, it has been noted that many cancer forms exhibit dysregulation of anabolic and catabolic processes. These findings were associated with tumor growth and carcinogenesis (13). In this sense, assessing metabolic byproducts that are regularly used to monitor liver and kidney function, such as serum Cr, UA or BUN, may provide crucial information about the pathophysiology of cancer.

The kidney is responsible for excretion of UA; a byproduct of purine metabolism derived from endogenous sources or dietary intake of guanine

and adenine (15). Because UA is involved in oxidative stress and metabolic regulation and has been investigated in relation to various cancers (16). Cr is a commonly used marker of renal function and has been evaluated in cancer patients, while BUN indicates both renal function and protein metabolism (17).

In CC, renal impairment may occur due to metabolic alterations or tumor-related complications such as urinary tract blockage (18). However, most existing evidence on Cr, UA, and BUN is derived from studies focused on other chronic diseases. Notably, few studies have concurrently evaluated Cr, UA, and BUN in relation to cancer, and data are particularly limited among Ethiopian patients with untreated CC. Therefore, the aim of this study is to assess Cr, UA, and BUN levels among untreated CC patients.

Methods and materials

Study area

The study was conducted at Wolaita Sodo University Comprehensive Specialized Hospital (WSUCSH), a renowned teaching and referral facility under the management of Wolaita Sodo University. It is the principal facility for clinical and preclinical training in health and health-related subjects and is located in Sodo City, Wolaita Zone, in Southern Ethiopia. The hospital has several specialty clinics that serve a variety of patient needs, one of which is devoted to offering care to patients with various cancers.

Study design and period

A case-control study was conducted from June to September 2024.

Population and eligibility criteria

The study population consisted of untreated CC patients aged 18 years and above who attended WSUCSH and fulfilled the eligibility criteria during the data collection period.

For the case group, inclusion criteria included all untreated CC patients aged 18–70 years attending the cancer center during the study period. The exclusion criteria included patients older than 70 years, individuals with mental illness, and those with chronic comorbid conditions that may influence biochemical parameters, particularly renal and hepatic diseases. Patients with a history of prior cancer treatment, and unwilling or unable to provide reliable information were excluded.

Control group were apparently healthy, age-matched individuals with no previous history or clinical evidence of cancer. Their health status was confirmed through medical history review and clinical assessment at the time of recruitment to reduce the likelihood of including undiagnosed malignancy. Individuals with any history or clinical signs suggestive of chronic illness or underlying diseases were excluded. In particular, participants with renal disease or other significant chronic metabolic disorders were not eligible, in order to reduce potential confounding effects on Cr, UA, and BUN levels.

Sample size and sampling technique

The sample size was determined using the two-population proportion formula for case–control study. Due to the limited availability of locally generated evidence in Ethiopia on the association between CC and biological renal function markers (Cr, UA, and BUN, the calculation was based on findings from previous published comparable case–control studies conducted in Ethiopia and other similar settings, which applied OpenEpi (Kelsey and Fleiss methods) for sample size estimation and reported odds ratios ranging from 2.0 to 4.0 with exposure proportions among controls between 20% and 60% (19, 20).

Using a 95% confidence level, 80% statistical power, a case -to-control ratio of 1:1, an assumed odd of 3.5–4.0 (representing a large effect size consistent with biochemical differences expected between cancer patients and controls), and a population of exposure among controls (P_0) of 20, the minimum required sample size was calculated using OpenEpi software (Version 3.01). The initial computation yielded a total sample size of 58 participants, comprising 29 cases and 29 controls. After adding a 10% contingency to account for potential no-response and incomplete data, the final sample size was adjusted to be 64 participants, consisting of 32 cases and 32 controls.

Data collection tools and procedures

Socio-demographic and clinical data were collected from untreated CC patients and apparently healthy individuals through structured interviews and anthropometric assessments conducted by trained clinical nurses. Participants provided information on sociodemographic characteristics and risk factors, while clinical data such as cancer stage and duration were extracted from the medical records of CC patients. Blood pressure was measured using a mercury-based sphygmomanometer after participants had rested for at least 10 minutes; if systolic blood pressure (SBP) was ≥140 mmHg and diastolic blood pressure (DBP) was ≥ 90 mmHg, a second measurement was taken after one minute, and the average was recorded. Anthropometric measurements followed WHO guidelines; height measured to the nearest 0.5 cm using a stadiometer and converted to meters for Body Mass Index (BMI) calculation, and weight was recorded to the nearest 0.1 kg using a calibrated balance while participants in light clothing. BMI was then calculated as weight (kg) divided by height (m^2).

Blood Sample collection and processing

A total of 5 mL venous blood was collected from the antecubital vein using aseptic techniques and appropriate sterile needles. After clotting for 20–30 minutes, the blood samples were centrifuged at 3000 rpm to separate the serum. The obtained serum was aliquoted and stored in a deep freezer until analysis.

Cr, UA, and BUN levels were analyzed using a semi-automated biochemistry analyzer (Dirui Industrial, Changchun, China). To ensure accuracy and reliability, the analyzer was calibrated prior to analysis in accordance with the manufacturer's instructions. Internal quality control was performed using commercially prepared normal and pathological control sera, and all laboratory procedures were conducted following standard operating procedures to maintain consistency, minimize analytical error, and ensure the validity of the results.

Data management and analysis

After cleaning and checking the data for completeness, laboratory and questionnaire data were coded and entered into SPSS version 25 for analysis. Sociodemographic characteristics were summarized using descriptive statistics. The distribution of continuous variables was assessed using the Shapiro–Wilk normality test and visual inspection of histograms. Normally distributed continuous variables were presented as mean ± standard deviation and compared using the independent samples Student's t-test or one-way ANOVA, as appropriate. Correlations between variables were assessed using Pearson's for continuous variables and Spearman rank correlation for ordinal variables. A P-value of <0.05 was considered statistically significant.

Results

Socio-demographic characteristics

The study included 64 participants who fulfilled all inclusion requirements, 32 of whom were in the case group and 32 of whom were in the control group. The participants ranged in age

from 23 to 62 years. There was no statistically significant difference in the mean ages of the untreated CC cases and the control groups. Among untreated CC patients, 25 (78.1%) were rural areas, while 7 (21.9%) urban residents. Regarding educational status 23 (71.9%) were illiterate, 8 (25%) had education up to high school learned, and 1 (3.1%) had diploma or above. In terms of maternal status, 1 (3.1%) was single, 28 (87.5%) were married, and 3 (6.3%) were divorced. Concerning the socioeconomic status, 19 (59.4%) belonged to the low category, 12 (37.8%) to the middle category, and 1 (3.1%) to the high category.

Similarly, among the controls, 19 (59.4%) were from rural residents and 13 (40.6%) were from urban. Educational status showed that 10 (31.3%) were illiterate, 18 (56.3%) had education up to high school, and 4 (12.3%) had a diploma or above. Most controls, 24 (75.0%) were married, while 2 (6.3%) were single and 6 (18.8%) were divorced. Regarding socioeconomic status, 16 (50.0%) were in the low category, 13 (40.6%) were in middle, and 3 (9.4%) in high category (Table 1).

Although the two groups were comparable in terms of age, differences were observed in other socio-demographic variables such as residence and educational status. These disparities may act as potential confounders in the observed associations. Since the matching was performed only for age, residual confounding from other socio-demographic factors cannot be ruled out, and this should be considered when interpreting the study results.

The behavioral and clinical characteristics of the study participants are summarized in Table 2. Most participants had no history of alcohol consumption, including 23 (71.8%) of the cases and 28 (87.5%) of the controls. Similarly, oral contraceptive use was relatively similar between the two groups with 17 (53.1%) of the cases and 16 (50.0%) of the controls reporting no use. Most participants reported having only one sexual partner, accounting for 22 (68.8%) of the cases and 24 (75%) of the controls.

Table 1: Socio-demographic characteristics of untreated CC patients and controls at WSUCSH, 2024

Variables	Categories	Cases, n (%)	Controls, n (%)
Residence	Rural	25 (78.1)	19 (59.4)
	Urban	7 (21.9)	13 (40.6)
Educational status	Illiterate	23 (71.9)	10 (31.3)
	Up to high school	8 (25.0)	18 (56.3)
	Diploma and above	1 (3.1)	4 (12.5)
Marital status	Single	1 (3.1)	2 (6.3)
	Married	28 (87.5)	24 (75.0)
	Divorced	3 (9.4)	6 (18.8)
Socioeconomic status	Low	19 (59.4)	16 (50.0)
	Middle	12 (37.5)	13 (40.6)
	High	1 (3.1)	3 (9.4)

Regarding BMI, the majority of participants were within the normal weight range (18.5–24.9 kg/m²), comprising 22 (75%) of cases and 23 (71.9%) of controls. Smoking was rare in both groups, with nearly all participant being non-smokers. In terms of clinical characteristics, among untreated CC cases, the majority were diagnosed at Stage II CC, 18 (56.3%) of the cases, followed by Stage III, 6 (18.8%), Stage I with 5 (15.6%), and Stage IV, 3 (9.4%).

Biochemical parameters

The comparison of Cr, UA, and BUN levels between untreated CC cases and controls is presented in Table 3.

Table 2: Behavioral and clinical characteristics of untreated CC patients and controls at WSUCSH, 2024

Variables	Categories	Cases, n (%)	Controls, n (%)
Oral contraceptive use	Yes	15 (46.9)	16 (50.0)
	No	17 (53.1)	16 (50.0)
Number of sexual Partners	Only one	22 (68.8)	24 (75.0)
	More than two	10 (31.3)	8 (25.0%)
Alcohol consumption	Non-drinker	23 (71.8)	28 (87.5)
	Non-habitual	9 (28.1)	4 (12.5)
Smoking status	Non-smoker	32 (96.9)	32 (100.0)
	Non-habitual smoker	0 (0.0)	0 (0.0)
BMI	Under weight	9 (28.1)	8 (25.0)
	Normal	22(68.8%)	23 (71.9)
	Overweight	1 (3.1%)	1 (3.1)
Disease stage	Stage (I)	5 (15.6)	0 (0.0)
	Stage (II)	18 (56.3)	0 (0.0)
	Stage (III)	6 (18.8)	0 (0.0)
	Stage (IV)	3 (9.4)	0 (0.0)

Prior to statistical analysis, the assumption of independent samples t-test was carefully evaluated. The normality of the data for Cr, UA, and BUN, was evaluated using the Kolmogorov–Smirnov and Shapiro–Wilk tests. The results confirmed that all variables were normally distributed in both groups ($P > 0.05$), confirming that the assumption of normality was satisfied and appropriate for parametric testing.

Following confirmation of assumptions, the mean values of biochemical parameters between the two groups were compared using the independent samples Student's t-test. The analysis showed statistically significant differences in all measured parameters. The mean Cr level was significantly higher in case group (0.85 ± 0.1 mg/dL) compared to the control group (0.71 ± 0.03 mg/dL) ($P < 0.01$). Similarly, the mean UA levels were elevated among cases (5.6 ± 1.1 mg/dl) relative to controls (4.87 ± 0.7 mg/dL) ($P < 0.01$). In addition, BUN levels were also significantly increased in untreated CC (21.23 ± 1.3 mg/dL) compared to the controls (18.9 ± 0.7 mg/dl), ($P < 0.01$) (Table 3).

Table 3: Comparison of Cr, UA, and BUN levels between CC patients and controls at WSUCSH, 2024

Parameters	Cases (n = 32) Mean ± SD	Controls (n =32) Mean ± SD	P-value
Cr (mg/dL)	0.85 ± 0.1	0.71 ± 0.03	< 0.001
UA (mg/dL)	5.6 ± 1.1	4.87 ± 0.7	0.001
BUN (mg/dL)	21.23 ± 1.3	18.9 ±0.7	< 0.001

Note: values are presented as mean ± standard deviation (SD). Statistical significance was considered at $P < 0.05$.

Building on initial findings, further analysis was conducted to explore how the disease progression influences Cr, UA, and BUN levels. A one-way ANOVA was performed to determine whether there were statistically significant in the mean values of Cr, UA, and BUN across CC stages (Stage I, II, III, and IV). The results indicated a statistically significant increase in Cr levels with advancing cancer stage ($P < 0.05$). Similarly, UA levels increased progressively with disease advancement, reaching statistical significance ($P \leq 0.05$). Furthermore, BUN levels also showed a significant increase trend across

the stages ($P \leq 0.05$) (Table 4). Given the small sample sizes in same stage groups, particularly Stage I, a non-parametric Kruskal–Wallis test was additionally performed as a sensitivity. The findings were consistent with those obtained from the one–ANOVA, supporting the robustness of the observed stage-related differences. Overall, the findings suggest that progressive biochemical alterations in renal and metabolic markers may be associated with the advancement of CC

Table 4: One-way ANOVA showing the effect of cancer stages on Cr, UA and BUN levels among untreated CC patients at WSUCSH, 2024

Parameters	Stage I (n = 5) Mean ± SD	Stage II (n = 18) Mean ± SD	Stage III (n = 6) Mean ± SD	Stage IV (n = 3) Mean ± SD	P- value
Cr (mg/dL)	0.81 ± 0.11	0.89 ± 0.05	0.91 ± 0.017	0.99 ± 0.00	0.023
UA (mg/dL)	5.2 ±0.97	6.31 ± 1.1	6.4 ± 1.1	6.61 ± 0.35	0.049
BUN (mg/dL)	20.69 ± 1.59	21.74 ± 0.30	22.3 ±0.29	22.7 ± 0.21	0.022

Note: values are presented as mean ± standard deviation (SD). P-values were obtained using one-way ANOVA. A Kruskal–Wallis sensitivity analysis yielded consistent results. Statistical significance was considered at $P < 0.05$.

The association between baseline characteristics (age, BMI, and socioeconomic status) and biochemical parameters (Cr, UA, and BUN) was assessed using Pearson correlation analysis, while the association between socioeconomic status and disease status with Cr, UA, and BUN was evaluated using Sparman rank correlation, as summarized in Table 5. Socioeconomic status was treated as an ordinal variable, and disease stage was also considered ordinal; both were appropriately coded prior to analysis.

Normality of continuous variables was assessed before conducting statistical tests. For comparisons involving more than two groups, one-way ANOVA was applied when assumptions of normality and homogeneity of variance were satisfied; otherwise, the Kruskal–Wallis test was used.

In the case group, a strong positive and statistically significant correlation was observed between disease stage and all biochemical parameters, including Cr, UA, and BUN ($P < 0.01$). As expected, disease stage was not applicable in the control group. A moderate positive correlation was found between age and Cr, UA, and BUN n both groups, although these association were not statistically significant ($p > 0.05$). BMI showed a weak Positive correlation with all three biochemical parameters. In contrast, socioeconomic status showed a moderate negative correlation with Cr, UA and BUN levels in both groups, though these relationships were also not statistically significant ($p > 0.05$) (Table 5).

Discussion

Assessing Cr, UA, and BUN levels in untreated CC patients may provide useful information on potential metabolic alterations associated with the disease. The findings of this study indicate differences in Cr, UA, and BUN levels between cases and controls. However, due to the case–control design, these findings reflect associations rather than causal relationships. A plausible clinical explanation for altered renal function

markers in untreated CC patients is obstructive uropathy. Advance CC may lead to ureteric obstruction through tumor invasion or external compression, resulting in impaired urine drainage, hydronephrosis, and progressive renal function. This mechanism may contribute to elevated levels of Cr and BUN observed in affected patients and should be considered when interpreting renal biochemical changes in this population.

Table 5: Correlation between baseline characteristics and biochemical markers among untreated CC cases and controls at WSUCSH, 2024

Group	Variables	Age (Pearson) (r, P)	BMI (Pearson) (r, P)	Socioeconomic status (Spearman) (r, P)	Disease Stage (Spearman) (r, P)
Cases (n = 32)	Cr	0.429	0.120	-0.418	0.515**
		0.068	0.508	0.071	0.003
	UA	0.518	0.160	-0.507	0.488**
		0.056	0.632	0.058	0.005
	BUN	0.417	0.270	-0.484	0.482**
		0.072	0.230	0.065	0.005
Controls (n = 32)	Cr	0.393	0.110	-0.413	–
		0.076	0.540	0.092	–
	UA	0.325	0.258	-0.347	–
		0.12	0.632	0.096	–
	BUN	0.365	0.486	-0.431	–
		0.082	0.061	0.068	–

Note: values are presented as correlation coefficient (r) and P-value. Pearson correlation was used for continuous variables (age and BMI), while Spearman rank correlation was applied for ordinal variables (socioeconomic status and disease status). ** represents statistical significance at $P < 0.01$, and (–) indicates not applicable or not analyzed.

In the present study, the majority of untreated CC patients lived in rural areas, had low socioeconomic status, and lacked literacy. The result coincided with previous studies conducted in Ethiopia and Asia (21, 22). One of the major challenges in the implementation Ethiopia's cancer control strategy is the limited availability of adequate public health information. Previous studies have shown that women with low socioeconomic and educational status tend to have limited awareness of CC and its preventive measures, which may contribute to in adequate screening and poor gynecological practices (23).

Cr, a widely used biomarker for assessing kidney function, is an endogenous end product of creatine metabolism, which plays a crucial role in cellular energy production. In cancer patients,

creatine metabolism may become dysregulated due to the high energy demands of rapidly proliferating tumor cells, leading to increased creatine utilization and elevated Cr production as metabolic waste product (18, 24). Recent evidence suggests that disruptions in creatine metabolism may contribute to cancer initiation and progression. Furthermore, prolonged oxidative stress and inflammation may promote a microenvironment favorable for tumor development and progression (25).

According to the recent studies, low-grade inflammation, characterized by increased production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, may contribute to renal dysfunction. These inflammatory mediators can reduce nitric oxide production, bioavailability and impair renal hemodynamics, which may partly explain the elevated Cr levels observed in cancer patients (26, 27).

In the present study, untreated CC patients exhibited significantly higher Cr levels, with concentrations steadily increased as the disease advanced. This elevation in Cr may be attributed to cancer- related renal impairment, persistent inflammatory responses, and metabolic adaptations that enhance ATP production to meet the increased energy demands of rapidly proliferating tumor cells. These metabolic alterations may contribute to elevated Cr levels observed among untreated CC patients. Our findings are consistent with previous studies involving both cancer patients and animal models (28, 29). Furthermore, the results are in agreement with recent evidence demonstrating that chronic low-grade inflammation in cancer is associated with systemic organ dysfunction, including renal injury observed in mice colon cancer (24, 30).

However, a contradictory finding has been reported in studies conducted at St. Thomas's Hospital and Medical School in London, where lower Cr levels were observed among cancer patients. Similarly, other studies have documented reduced Cr levels in patients with lung cancer (31, 32). These inconsistencies may be may be attributed to differences in sample size, study population characteristics, lifestyle factors, and genetic variations among the participants.

UA is the final product of purine metabolism, and it is primarily excreted through the kidneys (15). Moreover, several studies suggested that elevated UA levels may enhance ROS production, oxidative stress, and inflammatory response, thereby exerting pro-oxidant effects (33, 34). In cancer, altered purine metabolism supports the rapid proliferation of malignant cells by increasing nucleotide synthesis required for DNA and RNA replication. Consequently, enhanced purine turnover and accelerated cellular proliferation contribute to increased UA production (35, 36). Dysregulated purine metabolism has been implicated in the pathogenesis of several malignancies, including breast and colon cancer (16, 37).

In current study, untreated CC patients demonstrated significantly elevated UA levels, which progressively increased with advancing disease stage. This finding may be explained by increased purine synthesis and altered purine metabolic pathways in cancer cells to meet the high nucleotide demand associated with rapid tumor growth and replication. Elevated UA levels in untreated CC patients may therefore reflect increased tumor burden, enhanced metabolic activity, and disease progression. In addition, underlying renal dysfunction and physiological stress may further contribute to impaired UA clearance and accumulation (33, 34).

The present findings are consistent with previous studies malignancies, although the clinical significance of UA appears to differ according to cancer type. Increased UA concentrations have been associated with disease progression in

hepatocellular carcinoma (38). Similarly, higher UA concentrations have been observed in patients with advanced or metabolic melanoma (39). In pancreatic and breast cancers, elevated UA has been linked to increased metastasis and reduced survival rates (35). These observations suggest that pathological role and prognostic significance of UA may be cancer- specific, potentially reflecting differences in tumor metabolism, oxidative stress, and proliferative activity. Therefore, elevated UA levels in CC patients may indicate increased tumor burden and more advanced disease severity.

Conversely, some studies have reported lower UA levels in certain cancers. A recent study published in Indian Journal of Dental Research demonstrated reduced UA concentrations among patients with oral cancer that patients with oral cancer have lower levels of UA. In the human body, UA may serve as a powerful antioxidant and a scavenger of free radicals (40). However, it plays a complicated and seemingly cancer-type-dependent role in the initiation and spread of cancer. In certain situations, UA may have a beneficial antioxidant effect by minimizing DNA damage and lowering oxidative stress. On the other hand, raised UA levels may indicate accelerated tumor cell turnover, inflammation, and enhanced nucleic acid breakdown in various malignancies, which is linked to the advancement of the disease. The heterogeneity in UA levels seen across various cancer types, including CC, where elevated UA concentrations may be more indicative of tumor load and metabolic activity rather than a strictly protective impact, may be explained by this dual and context-dependent role. Contrasting with high UA, which may be linked to a risk of other cancer types, low UA may be linked to a risk of oral cancer.

BUN is a metabolic by product formed during the breakdown of proteins and amino acids in the liver. Following production, urea is transported through the blood stream to the kidney, where filtered and excreted in urine (41). Because the kidneys are primarily responsible for removing urea from circulation, BUN levels are commonly used as an indicator renal function. Previous studies have suggested that various metabolic alterations are associated with cancer development and progression (42).

The changes in metabolism are crucial features that distinguish malignant cells and their systemic implications on the host. Frequently, these changes include disturbances in nitrogen metabolism, which might result in increased BUN levels (17). A significant amount of metabolic reprogramming is frequently done by cancer cells in order to meet the energy requirements of rapid expansion, survival, and proliferation, leading to increased BUN levels (43). Glutamate metabolism dysregulation is a major cause of the altered nitrogen balance and high BUN levels in cancer cells (44). Studies have shown that glutamine metabolism is disrupted in tumors, particularly those in the pancreas and liver (45, 46).

A possible mechanism for high BUN in CC could be the increasing glutamine metabolism. Glutaminase is an enzyme that changes glutamine into glutamate in cancer cells. α-ketoglutarate, a crucial step in the tricarboxylic acid cycle, can be produced by further metabolizing this glutamate. A key component of energy generation, α-ketoglutarate supplies the carbon required to synthesize crucial components, including lipids and nucleotides, which are critical for the fast development and division of cancer cells. Higher nitrogen turnover may result from tumor cells enhanced metabolic activity, which could explain elevated BUN levels (1).

The untreated CC patient in our study had a higher BUN. Additionally, we determined that BUN levels steadily elevated as the disease progressed. The cancer within causes the dysregulation of glutamine metabolism to meet

the energy demands of rapid growth, survival, and proliferation, which may explain the high BUN levels in untreated CC cases. This hypothesis, which links high BUN levels to the progression and spread of CC, suggests that renal dysfunction and metabolic alteration contribute to the capacity of cancer cells to continue rapid proliferation, survival, and spread (47).

Our findings are in support of the idea that gastrointestinal cancers, such as colorectal and pancreatic tumors, have spread and frequently result in elevated protein catabolism, which boosts BUN levels (43, 46, 47). However, a study presented in the Journal of Clinical Medicine revealed that patients with oral squamous cell carcinoma had lower BUN and no appreciable difference in their Cr and UA levels (48). These results may be explained by variations in sample size, lifestyle, understanding of risk factors, and genetic factors.Although serum Cr, UA, and BUN were significantly higher than in the cases than controls, most values remained with in normal ranges, suggesting early or subclinical changes rather than overt renal dysfunction. These differences may reflect tumor-related metabolic activities and altered renal handling (49, 50).

In the present study, age, BMI, and socioeconomic status were considered potentially influencing Cr, UA, and BUN levels among the participants. In both the case and control groups, age showed a positive correlation with Cr, UA, and BUN levels. Age-related patterns observed in both groups support the comparability and homogeneity of the study population. Previous studies conducted among healthy individuals have also demonstrated that CR, UA, and BUN levels progressively increase with advancing age, with noticeable changes occurring across successive decades of life. These findings are consistent with the gradual decline in renal function commonly associated with aging (51, 52). In our study groups, Cr, UA, and BUN levels were inversely correlated with socioeconomic status both the case and control groups. These findings are consistent with previous studies that found socioeconomic status to be a key determinant of Cr, UA, and BUN levels, with lower socioeconomic backgrounds having higher levels of Cr, UA, and BUN. There may be a number of contributing factors, such as restricted access to wholesome food, safe housing, and suitable medical care (53, 54).

In contrast, the association between BMI and the Cr, UA, and BUN levels was weak both study groups, suggesting that BMI may not have a substantial impact on Cr, UA, and BUN levels in the present study population (55). Furthermore, the case group in our study showed a strong positive correlation between their BUN, UA, and Cr levels and their disease condition. This relationship may indicate underlying renal impairment could serve as a sign of further systemic involvement. In our study, there are several limitations that should be considered when interpreting the findings. The relatively small sample size, which was constrained by the limited number of eligible untreated CC patients during the study period, may limit the generalizability of the results. In addition, important potential confounding factors such as dietary habits, hydration status, and HIV infection were not directly assessed due to resource and time limitations.

Although strict inclusion and exclusion criteria were applied, the possibility of undiagnosed subclinical conditions, such as early renal impairment or partial urinary tract obstruction, could not be completely ruled out. In addition, laboratory-based screening was not performed for control participant to further exclude subclinical and undiagnosed renal or metabolic abnormalities; therefore, some apparently healthy controls may have had underlying conditions that could influence biochemical parameters such as Cr, UA, and BUN, potentially introducing residual confounding.

Furthermore, the study was conducted in a single institution, which may limit the applicability of the findings to other settings with different patient populations and healthcare conditions. Despite these limitations, the study provides important baseline evidence on biochemical alterations among untreated CC patients in the study area.

Conclusion

The present study demonstrated that serum levels of Cr, UA, and BUN levels were higher in untreated CC patients compared to healthy controls. These biochemical differences suggest a potential association between CC status and alterations in renal and metabolic function. In addition, Cr, UA, and BUN levels showed an association with tumor stage and grade, indicating that more advanced disease may be accompanied by greater changes in these biochemical markers. However, due to the case-control design of the study, causal relationships cannot be established.

These findings highlight the potential usefulness of monitoring renal and metabolic biomarkers in untreated CC patients, while further longitudinal studies are needed to clarify temporal relationships and underlying clinical mechanisms. We recommend that the study parameters such as Cr, UA, and BUN, should be considered in the initial evaluation of CC patients prior to treatment initiation. Early monitoring of these biochemical parameters may assist in the early detection of subclinical renal impairment and support timely clinical decision-making.

In addition, further large-scale, multicenter studies are recommended to confirm these findings and to explore the influence of additional factors such as dietary habits, hydration status, HIV infection, and other comorbid conditions on biochemical parameters in CC patients.

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Ethical considerations

The protocol was approved by the Hawassa University Collage Medicine and Health Sciences Institutional Review Board (Reference Number IRB/269/2024), in accordance with the Declaration of Helsinki and local ethical guidelines. Informed written consent was also obtained from each study participant before the actual data collection.

Data availability statement

Data will be available from corresponding author upon request

Conflicts of interest

The authors hereby declare that they have no conflict of interests regarding this paper.

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