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ABSTRACT

BACKGROUND: Disinfection byproducts (DBPs) from chlorinated drinking water have been linked to an increased risk of cancer in the bladder, stomach, colon, and rectum. No studies showed the independent trends and prevalence of these cancers in Ethiopia. Therefore, this study aimed to determine the prevalence and trends of disinfection byproducts-related cancers in Addis Ababa, Ethiopia.

METHODS: Data were collected from the Addis Ababa Cancer Registry. Spatial data sets were produced and classified into households receiving chlorinated surface water and less chlorinated groundwater. The Cochran-Armitage trend test was used to evaluate whether there was a disinfection byproducts-related cancers (DBRCs) trend among communities receiving chlorinated water. Negative binomial regression was used to analyze the incidence rate.

RESULTS: A total of 11,438 cancer cases were registered between 2012 and 2016, and DBRCs accounted for approximately 17%. The majority of the total cancer cases were female; 7,706 (67%). The prevalence of DBRCs was found to be higher in communities supplied with chlorinated water. From 2012 to 2016, the trend of colon cancer increased ($\beta = 10.3$, *P* value = .034); however, esophageal cancer decreased ($\beta = -6.5$, *P* value = .018). Approximately 56% of colorectal cancer patients and 53% of stomach cancer patients are known to be using chlorinated surface water for drinking regularly. In addition, approximately 57.1% and 54% of kidney and bladder cancer patients, respectively, used chlorinated surface water.

CONCLUSION: The prevalence of DBRCs in this study was found to be high. The colon cancer trend increased substantially from 2012 to 2016. The prevalence of DBRCs was higher in communities supplied with chlorinated surface water. Similarly, the prevalence of DBRCs was higher among males than females. Further study is required to validate the association between DBRCs and water chlorination.

KEYWORDS: Cancers, chlorination, disinfection byproducts, drinking water, trihalomethanes, Ethiopia

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Background

Cancer is becoming a serious issue in every country. It is the world's second most likely cause of death.[1] Cancer incidence has increased in most countries in relation to the growing and aging population and the emergence of potential risk factors, such as smoking, obesity, an unhealthy diet and lifetime exposure to chlorination byproducts in drinking water.[2,3] Survival from cancer is relatively low in Sub-Saharan African (SSA) countries, and its health burden has been rising. In SSA, the cancer's health burden is estimated to show an 85% increase by 2030.[4] The DBRCs in this study include gastrointestinal tract (GIT)-related cancers, namely, colon, rectal, stomach, and esophagus and urology-based (UB) cancers (kidney and bladder cancers). The GIT and UB are the cancer sites that are most often associated with the use of chlorinated water or with the quantity of chlorination disinfection byproducts in the water-supply network.[5-16]

Drinking water disinfection is an essential process for protecting public health and providing safe drinking water because it eliminates pathogenic organisms.[17] Chlorine (gaseous or hypochlorite salt solutions), chloramines, ozone, chlorine dioxide, and UV irradiation have all been used as disinfectants.[18] Although other technologies and resources have been utilized, chlorine is a frequently used and effective disinfectant.[19,20] However, several undesired inorganic and organic disinfection byproducts (DBPs) are produced when a disinfectant reacts with natural organic matter (NOM) and anthropogenic organics, including halides in raw water.[18,21,22]

DBP formation is highly reliant on the composition and concentration of NOM, which can be broadly divided into 2 fractions of hydrophobic (humic) and hydrophilic (nonhumic) substances.[23]

The type, occurrence, and levels of these DBPs depend on both the disinfectant used and the characteristics of the source water.[24-27] The most common organic DBPs include trihalomethanes (THMs), haloacetic acids, haloacetonitriles, halo ketones (HKN), and emerging organic DBPs.[28] Organic DBPs have attracted the attention of researchers due to their frequent discovery and harmful effects.[29] The hazardous inorganic DBPs, also known as oxy halide DBPs, include bromates (BrO_3^-), chlorite (ClO_2^-), and chlorate (ClO_3^-).[21,30,31] THMs are routinely treated as illustrative of DBPs in human health risk assessments.[32] THMs are a class of DBPs that include chloroform ($CHCl_3$), bromodichloromethane ($CHCl_2Br$), bromoform ($CHBr_3$) and chlorodibromomethane ($CHClBr_2$). Several epidemiological studies have discovered links between chlorination byproducts and increased cancer risks in the bladder, colon, blood, stomach, and rectum.[33,34]

THMs were regulated by the USEPA (the United States Environmental Protection Agency) shortly after their discovery in disinfected drinking water, with total trihalomethanes (TTHMs) having a maximum contaminant limit (MCL) of 100 μg/L.[35] The MCL for TTHMs was reduced to 80 μg/L by the Stage 1 D-DBP Rule,[36] while the MCLs for haloacetic acids (HAAs), bromate, and chlorite were set at 60, 10, and 1000 μg/L, respectively.

Water treatment utilities in Ethiopia employ chlorine to disinfect water for public distribution.[37] However, Ethiopian drinking water utilities, particularly in Addis Ababa, have not measured DBPs in drinking water. Furthermore, Ethiopia's drinking water distribution systems lack a DBP monitoring and control mechanism. As a result, given the paucity of historical data on the levels of DBPs, estimations of past exposure have been dependent on prior information about the water sources (ground and surface water sources).[38]

Studies have indicated that chlorinated water, particularly chlorinated surface water, has an elevated risk of GIT and UB cancers.[39,40] No studies showed the independent trends and prevalence of these cancers in Ethiopia in general and in Addis Ababa in particular. Therefore, this study aimed to show the trend and prevalence of DBRCs in Addis Ababa, Ethiopia.

Methods

Study design and population

A retrospective record review using the Addis Ababa Cancer Registry (AACR) was conducted in Addis Ababa, Ethiopia. According to the Central Statistical Agency's (CSA) 2013 population prediction for 2017, Addis Ababa had a population of 3,434,000 people, with 47% male and 53% female.[41] Data were collected on DBRCs cases using ICD-O (International classification of diseases for oncology)—31 codes (C15-16, C18-20, C64, C67)[42] for incidence in Addis Ababa between 2012 and 2016. All DBRCs cases of both sex and age groups were targeted for this study. The AACR collects data on cancer cases submitted by 3 public hospitals and 12 private facilities (the only cancer treatment centers) in Addis Ababa, Ethiopia.[43] All methods were performed in accordance with relevant guidelines and regulations.

Inclusion criteria

Cancer patients diagnosed, followed and living in Addis Ababa (with a complete residential address) were included.

Data collection and organization

The data about DBRCs cancer cases included in this study were the patient's age, sex, address, and cancer type with topology, morphology and diagnosis date. Geocoding of administrative units, road lines, and geographical databases were used to establish the locations of cancer cases. Administrative unit data sets comprise administrative boundaries as areas and allocation centers as points for sub cities (the largest administrative entity under Addis Ababa city) and woredas (the smallest administrative unit per sub-city). To investigate the association between water source type (chlorination status) and cancer cases, various types of spatial data sets were created and classified accordingly. To analyze the crude incidence rate, the projected population of Addis Ababa for 2017 was used. The center recorded 1,894 DBRCs from 2012 to 2016.

Water type identification

Different types of spatial data sets were collected and categorized to investigate the association between water source type (chlorination status) and cancer cases. The water supply network of DBRCs was discovered using GIS (Geographic Information System) data from the Addis Ababa Water and Sewerage Authority (AAWSA) water supply network (Figure 1). Addis Ababa's water supply system consists of 13 subsystems. Surface water sources (highly chlorinated) are located in the city's western and eastern quadrants. Groundwater sources (less chlorinated) are present in the southern and various stages of Addis Ababa.[44]

Geocoding was performed on 1,894 cancer patients using their address information to identify the type of water source ingested (surface water [highly chlorinated] or groundwater [less chlorinated]) (Figure 1). Cancer cases with incomplete address information were excluded. Following the distribution network of water sources, each residence was classified as highly chlorinated or less chlorinated. During the categorization process, AAWSA hydraulic engineers assisted us in determining the type of water the households received for some households whose water sources appeared difficult to distinguish. Finally, all cancer cases (Figures 2 and 3) were classified using Addis Ababa's water supply system (Figure 1).

Operational Definitions highly chlorinated and less chlorinated water supply. Consumption of surface water (highly chlorinated) and groundwater (less chlorinated) was used as an acceptable surrogate for comparing exposure versus non-exposure to DBPs.[45] The type of water source used per case is classified using the water supply networks of Addis Ababa. The linkage of individual residential addresses with their water supplies permitted improved measures of exposure.[46]

Disinfection byproducts-related cancers (DBRCs): GIT cancers, namely, colorectal, esophageal, stomach and urological

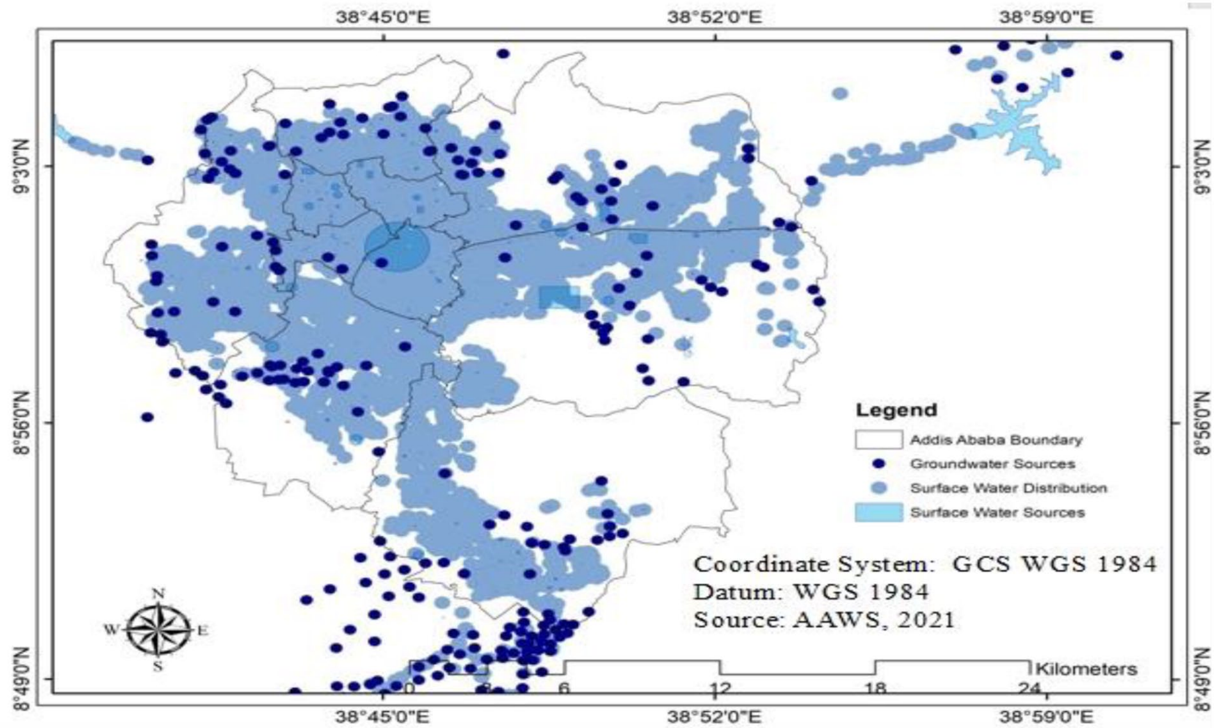

Figure 1. Addis Ababa water supply network, Addis Ababa, Ethiopia, 2021.

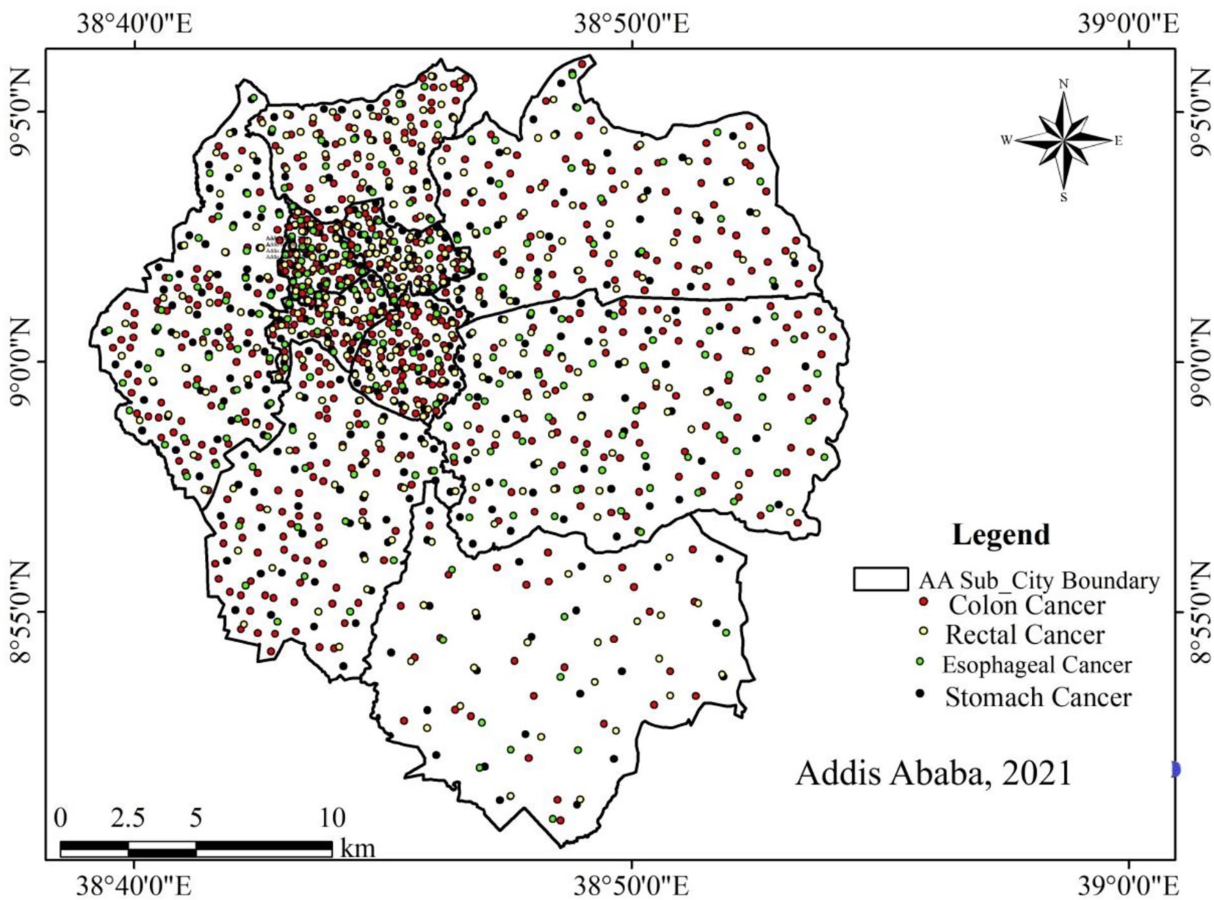

Figure 2. GIT-Disinfection byproducts-related cancers in Addis Ababa, 2021.

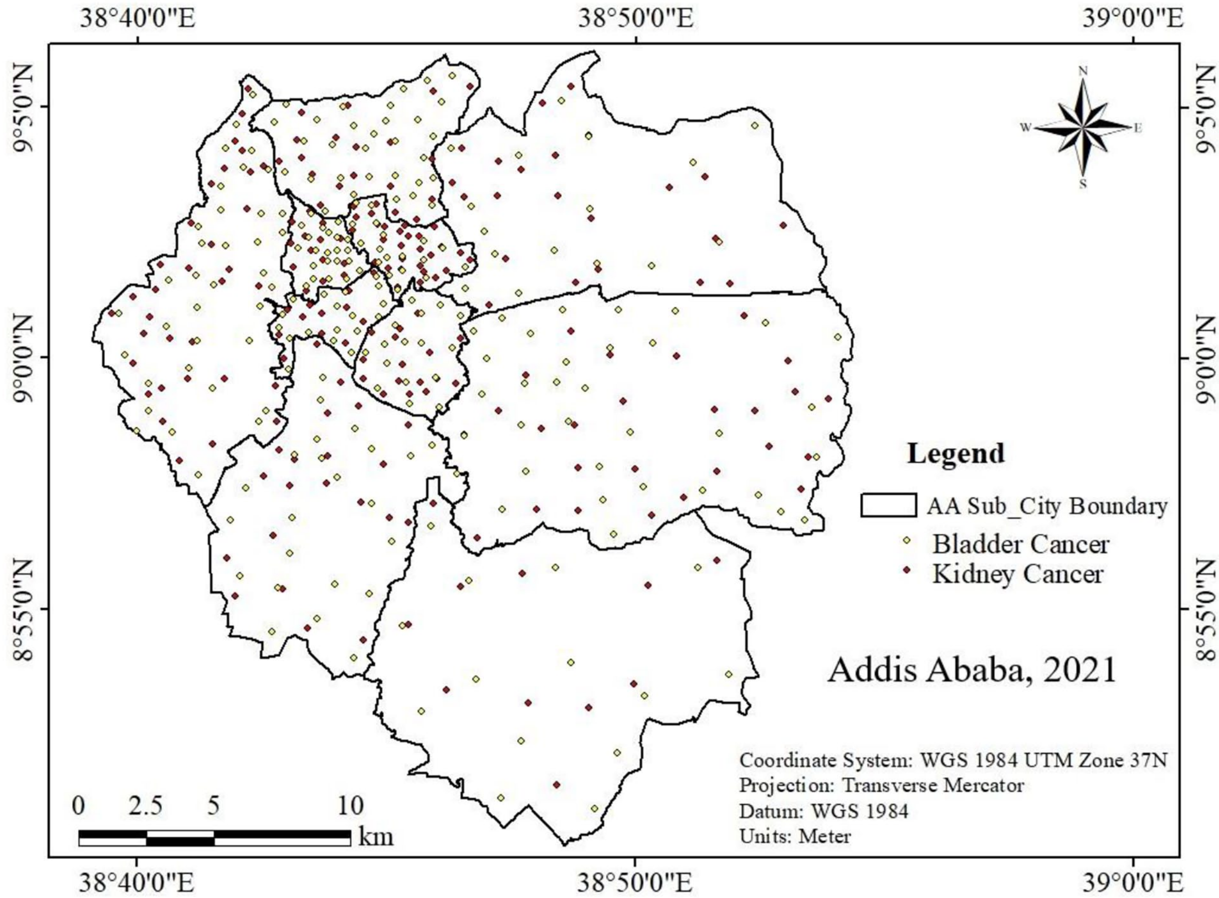

Figure 3. UT cancers, Disinfection byproducts-related cancers in Addis Ababa, 2021.

cancers (kidney and bladder cancers), were included in this study.

Data management and quality assurance

Digestive organ- and urinary tract-related cancers were the focus of this study based on the International Classification of Disease for Oncology, third edition (ICD-O-32 latest).[47] The data completeness and quality control were checked by the registry. The AACR uses the CanReg5 system for data entry, quality control, and management.[48]

Data analysis

Frequency, tables, charts, and graphs were used to present the data. Descriptive statistics was performed using SPSS version 20(IBM SPSS Statistics, Version 20.0. Armonk, NY: IBM Corp).[49] To analyze the incidence rate, the total population of Addis Ababa projected for 2017 was used.[50] Negative binomial regression was performed using STATA version 14.0 (Statistical Software: College Station, TX, USA)[51] to analyze the incidence rate. Negative Binomial regression analysis was the best fit the model to use when modeling counts data.[52] The negative binomial regression model fits the data better and accounted for overdispersion better than the Poisson regression model, which assumed the mean and variance were the same.[53] In addition, the residual deviance by the degree of freedom or the quotient is greater than one. Trend Analysis was done using the Cochran-Armitage trend test.

Results

Sociodemographic characteristics of GIT cancer patients

The total number of cancer cases observed during the study period was 11,438. This study focuses on GIT-based cancers (GBCs) (colon, rectal, stomach, and esophageal cancers), which accounted for 13% of the total, while urology-based cancers (kidney and bladder cancers) accounted for approximately 4% of the total. Of the 11,438 cancer cases registered by AACR, the majority were females (67%). The numbers of colon and rectal cancers in this study among males were 298 (50.4%) and 174 (54.5%), respectively. The percentages of stomach and esophageal cancers among males were 179 (51.3%) and 85 (41.7%), respectively. The highest number of colon, rectal and stomach cancer cases occurred in the age groups of 35 to 54 years; however, esophageal cancer was more prevalent from 55 to 74 years (Table 1).

Table 1. Sociodemographic characteristics of GIT cancers from 2012 to 2016, Addis Ababa, Ethiopia, 2021.

VARIABLES	RECTAL CANCER	(%)	COLON CANCER	(%)	STOMACH CANCER	(%)	ESOPHAGUS CANCER	(%)
Sex								
Male	174	54.5	298	50.4	179	51.3	85	41.7
Female	145	45.5	293	49.6	170	48.7	119	58.3
Total	319	100	591	100	349	100	204	100
Age								
15-34	76	23.6	88	14.9	44	12.6	13	6.4
35-54	137	43.1	234	39.6	151	43.3	64	31.4
55-74	91	28.6	232	39.3	127	36.4	112	54.9
75-94	15	4.7	37	6.3	27	7.7	15	7.4
Total	319	100	591	100	349	100	204	100

Table 2. Sociodemographic characteristics of urology based cancer patients from 2012 to 2016, Addis Ababa, Ethiopia, 2021.

VARIABLES	KIDNEY CANCER	(%)	BLADDER CANCER	(%)
Sex				
Male	101	49.8	158	69.3
Female	102	50.2	70	30.7
Total	203	100	228	100
Age				
15-34	29	14.3	13	4.9
35-54	88	43.3	69	30.5
55-74	65	32.0	116	51.3
75-94	21	10.3	30	13.3
Total	203	100	228	100

Sociodemographic characteristics of urology based cancers (UBCs) patients

Kidney cancer was more prevalent in the age group 35 to 54 years, while the burden was almost the same for males and females. The number of bladder cancer cases among males was 158 (69.3%), and the greatest percentage occurred in the 55- to 74-year-old age group (Table 2).

Incidence of gastrointestinal and urology-related cancers

The aim was to test whether the incidence of DBRCs increased or decreased. The incidence rates of colorectal cancer and stomach cancer were 6.1 and 2.59, respectively. The incidence of esophageal cancer was 1.46 (Table 3).

Trend test of GIT- and urology-based cancers in Addis Ababa, Ethiopia

The aim was to test whether the population increase over the year is considered. In this regard, the regression analysis showed that only colon cancer significantly increased from the baseline year 2012 to 2016. However, esophageal cancer significantly decreased from the baseline year 2012 to 2016 (Table 4). Both rectal and stomach cancers did not significantly increase from the baseline year 2012 to 2016. Similarly, kidney and bladder cancers did not significantly increase (Figures 4 and 5)

Correlation of DBRCs with sociodemographic characteristics

The correlation of DBRCs with years and age showed variable results for both GIT and UB cancers in Addis Ababa. Stomach cancer was the only cancer correlated with the follow-up years (Table 5).

Proportion of consumption of highly chlorinated surface and less chlorinated groundwater in Addis Ababa, Ethiopia

Approximately 56% and 53% of the colorectal and stomach cancer patients, respectively, used chlorinated surface water. Approximately 63% of the esophageal cancer patients used chlorinated surface water. In addition, approximately 57.1% and 54% of the kidney and bladder cancer patients, respectively, used chlorinated surface water (Table 6).

Discussion

The proportion of chlorinated surface water utilization by the GIT cancer patients in this study was high. Other related studies reported similar findings.[54-56] However, inconclusive findings

Table 3. Incidence rate of GIT- and urology-based cancer from 2012 to 2016, Addis Ababa, Ethiopia, 2021.

TYPE OF CANCER	NAME OF THE CANCER, ICD CLASSIFICATION	>NUMBER	INCIDENCE RATE WITH 95% CI (CONFIDENCE INTERVAL)
GBCs	Colon, C18-19	591	2.99 (2.39, 3.58)
	Rectal, C 20	319	3.11 (2.59, 3.61)
	Colo-rectal, C18-20	910	3.67 (3.16,4.18)
	Stomach, C16	349	2.59 (2.19,3.01)
	Esophagus, C 15	204	1.46 (0.40, 2.51)
UBCs	Kidney, C64	203	2.14 (1.55, 2.73)
	Bladder, C67	228	2.30 (1.72, 2.89)

Abbreviation: ICD, International classification of diseases.

Table 4. Trend test of GIT and urology cancers in Addis Ababa from 2012 to 2016, Addis Ababa, Ethiopia, 2021.

VARIABLE	REGRESSION COEFFICIENT	*P* VALUE	95% CI
Colon	10.3	.034	1.49-19.10
Rectal	11.9	.064	1.31-25.10
Stomach	10.5	.079	2.26-23.26
Esophagus	–6.5	.018	–10.85-(–2.14)
Kidney cancer	3.8	.095	1.23-8.83
Bladder cancer	3.1	.509	10.00-16.21

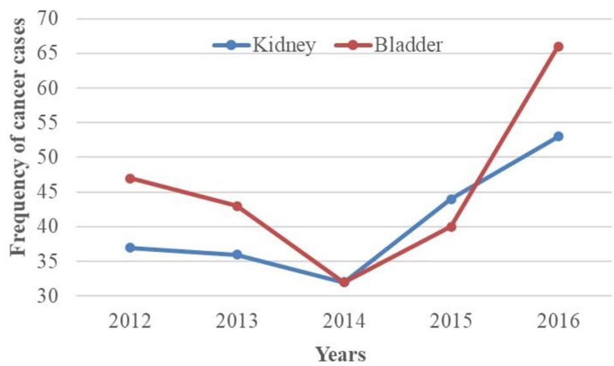

Figure 5. Trends of urology-based cancers from 2012 to 2016, Addis Ababa, Ethiopia, 2021.

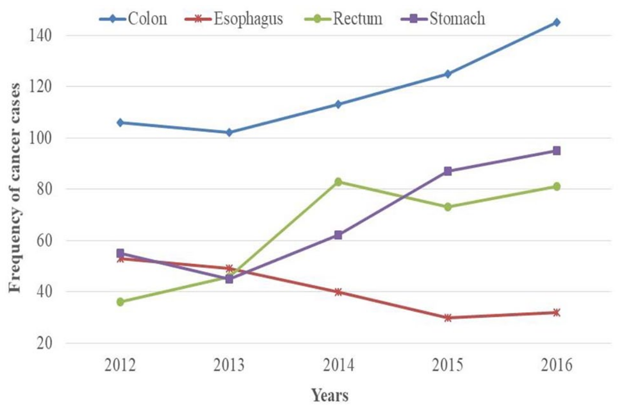

Figure 4. Trend of GIT cancers Addis Ababa, 2012 to 2016, Addis Ababa, Ethiopia, 2021.

were reported from other studies.[57-60] This variability could be due to differences in exposure assessment.

Similarly, a high proportion of urology-based cancer (kidney and bladder) patients used chlorinated surface water. Similar observations were reported in different parts of the world[58,61]; however, contradictory findings were reported in other studies.[56,62-64] In general, the prevalence of DBRCs is higher in communities supplied with chlorinated surface water than in those supplied with less chlorinated groundwater. Another study conducted in Norway showed that chlorination was associated with a 20 to 40% increase in colorectal cancer rates,[65] and other related studies are also in line with this study.[55,57,66]

The crude incidence rate of colo-rectal cancer (CRC) in this study was found to be 3.67/100,000 that was higher than a report from 2015 in Addis Ababa.[43] However, the incidence of CRC in this study was also lower than from Sub-Saharan Africa (SSA) countries (4.04/100,000 population),[67] middle east and northern Africa in 2016 (8.2/100,000 population) and in Kenya for the period 2013 to 2017 registry (9.1/100,000 population). The dissimilarity between countries might be due to lifestyles, nutritional behavior, increasing incidence of obesity, screening activities and lifetime exposure to the drinking water chlorination byproducts.[68-71]

The incidence of stomach cancer in this study was 2.59/100,000 population, which was slightly higher than a report from 2015 in Addis Ababa[43]; however, this study incidence was lower than a related report from Kenya, which was 5.2/100,000.[72] With regard to esophageal cancer, its incidence was 1.46, which was higher than a report from 2012 to 2015 in

Table 5. Correlation of DBRCs with sociodemographic characteristics, Addis Ababa, Ethiopia, 2021.

VARIABLES	PEARSON CORRELATION COEFFICIENTS	SIGNIFICANCE
	Colon cancer	
Years*	0.066	0.110
Age	0.001	0.984
	Stomach cancer	
Years	0.113	0.003*
Age	0.38	0.318
	Esophagus cancer	
Years	0.123	0.083
Age	0.37	0.595
	Rectal cancer	
Years	0.561	0.761
Age	0.934	0.643
	Kidney	
Years	0.621	0.543
Age	0.341	0.222
	Bladder	
Years	0.234	0.432
Age	0.310	0.212

*Years include from 2012 to 2016.

Addis Ababa.[43] Additionally, this study incidence of esophageal cancer was higher than a report from Sénégal (0.97%)[73]; however, this study result of EC was lower than Malawi (27%).[74] This variation could be due to genetic polymorphisms and environmental factors, including drinking water chlorination byproducts.[75]

Similarly, urology-based cancer called bladder incidence was observed to be 2.14, which was also slightly higher than the AACR report in 2015.[43] Consistently, this work incidence of BC was comparable with the Eastern Africa report (ASR = 3.3)[76]; however, a systematic review by Adeloye et al[77] in 2019 showed a higher pooled incidence of bladder cancer (8.8) in Africa, where North Africa is the highest. The GBD (global burden of diseases) also estimated an overall incidence of bladder cancer at 5.3 per 100 000.[1] This could be because more than 50% of the bladder cancer patients in this study used chlorinated surface water and were likely to be exposed to disinfection byproducts in drinking water.

The percentages of kidney and colon cancer cases were almost the same in both sexes, a similar finding reported only for colon cancer in Tanzania[78]; however, there is only the same pattern of kidney cancer in the US in both sexes, but a higher incidence in males.[79] GLOBOCAN (global cancer incidence) also showed a consistently higher incidence of kidney cancer among males,[80] possibly because both sexes are at equal exposure to potential environmental factors, including drinking water chlorination.

The trends of colon cancer were rising in this study from baseline 2012 until 2016 (Cochran-Armitage trend test (*P* value, $P < .000$). These findings were in line with a global study that indicated that CRC incidence is still rising rapidly in many low-income and middle-income countries.[81] Other findings reported incidence of stomach cancer increased in Sub-Saharan Africa (SSA), including Ethiopia.[82] However, the incidence of esophageal cancer showed a decreasing trend, even though a contrary study reported that Africa, including Ethiopia, is expected to surpass the incidence of Europe.[82]

In the same context, the incidence of kidney cancer showed a rising trend in this study. Another population-based study also highlighted that the temporal trends of kidney cancer are increased.[83] Similarly, bladder cancer incidence showed an increasing trend, and a consistent study also showed a growing incidence of bladder cancer in Africa in recent years.[77] This study tried to show the incidence of DBRCs with their water supply types (surface and groundwater sources) and warranted further studies to explore its association with drinking water disinfection byproducts (Trihalomethanes) in Addis Ababa, Ethiopia.

Conclusion

The prevalence of DBRCs in this study was found to be high. The colon cancer trend increased substantially from 2012 to 2016. The prevalence of DBRCs was higher in

Table 6. Proportion of chlorinated surface water and less chlorinated groundwater consumed by patients in Addis Ababa, Ethiopia, 2021.

NAME OF CANCER	CONSUMPTION OF HIGHLY CHLORINATED WATER WITH 95% CI	CONSUMPTION OF LESS CHLORINATED WATER WITH 95% CI
Colorectal	513, 56.4 (53.0-59.6)	397, 43.6 (40.4-47.0)
Stomach	187, 53.6 (48.1-58.7)	162, 46.4 (41.3-51.9)
Esophagus	128, 62.7 (55.9-69.9)	76, 37.3 (30.4-44.1)
Kidney	116, 57.1 (49.8-63.5)	87, 42.9 (36.5-50.2)
Bladder	123, 53.9 (46.9-60.5)	105, 46.1 (39.5-53.1)
	1067	827

communities supplied with chlorinated surface water. Similarly, the prevalence of DBRCs was higher among males than females. The prevalence of DBRCs was higher among the 35 to 54 age category than others. Further study is required to validate the association between DBRCs and the chlorination of water.

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Author Contributions

NT conceived the study and was involved in the study design, reviewed the article, analyzed, reported the writing, and drafted and revised it. MP, SR, and AA contributed to data analysis, report writing, drafted and revised the manuscript, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Availability of Data and Materials

The data sets generated for this analysis are available from the corresponding author upon reasonable request.

Consent for Publication

This manuscript does not contain any personal identification.

Ethics Approval and Consent to Participate

Ethical approval was obtained from the College of Natural and Computational Science Institutional Review Board (CNS-IRB), Addis Ababa University. Written permission was obtained from AACR.

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