Prevalence and Trends of Drinking Water Disinfection Byproducts-Related Cancers in Addis Ababa, Ethiopia

Nebiyou Tafesse¹, Massimiliano Porcelli², Sirak Robele Gari¹ and Argaw Ambelu¹

¹Ethiopian Institute of Water Resources, Addis Ababa University, Addis Ababa, Ethiopia. ²Quality, Health, Safety & Work Environment Department, Kuwait Institute for Scientific Research, Kuwait City, Kuwait.

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

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 (BrO₃⁻),...
chlorite (ClO$_2^-$), and chlorate (ClO$_3^-$). THMs are routinely treated as illustrative of DBPs in human health risk assessments. THMs are a class of DBPs that include chloroform (CHCl$_3$), bromodichloromethane (CHClBr$_2$), bromform (CHBr$_3$) and chlorodibromomethane (CHCIBr$_2$). Several epidemiological studies have discovered links between chlorination byproducts and increased cancer risks in the bladder, colon, blood, stomach, and rectum.

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. The MCL for TTHMs was reduced to 80 µg/L by the Stage 1 D-DBP Rule, 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. 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).

Studies have indicated that chlorinated water, particularly chlorinated surface water, has an elevated risk of GIT and UB cancers. 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. Data were collected on DBRCs cases using ICD-O (International classification of diseases for oncology)—31 codes (C15-16, C18-20, C64, C67) 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. 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 subcities (the largest administrative entity under Addis Ababa city) and woredas (the smallest administrative unit per subcity). 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.

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. The type of water source used per case is classified to a surrogate for comparing exposure versus non-exposure to DBPs. The type of water source used per case is classified as high or low. DBRCs cases and grouped by chlorination status.

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.
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). The data completeness and quality control were checked by the registry. The AACR uses the CanReg5 system for data entry, quality control, and management.

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.). To analyze the incidence rate, the total population of Addis Ababa projected for 2017 was used. Negative binomial regression was performed using STATA version 14.0 (Statistical Software: College Station, TX, USA) to analyze the incidence rate. Negative Binomial regression analysis was the best fit the model to use when modeling counts data. 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. 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).
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).

**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. However, inconclusive findings...
Environmental Health Insights

were reported from other studies. 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, however, contradictory findings were reported in other studies. 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, and other related studies are also in line with this study. The incidence of colorectal cancer (CRC) in this study was found to be 3.67/100,000 that was higher than a report from 2015 in Addis Ababa. However, the incidence of CRC in this study was also lower than from Sub-Saharan Africa (SSA) countries (4.04/100,000 population), 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.

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. However, the incidence of CRC in this study was also lower than from Sub-Saharan Africa (SSA) countries (4.04/100,000 population), 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.

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. However, the incidence of CRC in this study was also lower than from Sub-Saharan Africa (SSA) countries (4.04/100,000 population), 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.

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. However, the incidence of CRC in this study was also lower than from Sub-Saharan Africa (SSA) countries (4.04/100,000 population), 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.

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. However, the incidence of CRC in this study was also lower than from Sub-Saharan Africa (SSA) countries (4.04/100,000 population), 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.

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. However, the incidence of CRC in this study was also lower than from Sub-Saharan Africa (SSA) countries (4.04/100,000 population), 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.
Addis Ababa. Additionally, this study incidence of esophageal cancer was higher than a report from Senegal (0.97%) but this study result of EC was lower than Malawi (27%). This variation could be due to genetic polymorphisms and environmental factors, including drinking water chlorination byproducts.

Similarly, urology-based cancer called bladder incidence was observed to be 2.14, which was also slightly higher than the AACR report in 2015. Consistently, this work incidence of BC was comparable with the Eastern Africa report (ASR = 3.3); however, a systematic review by Adeloye et al 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. 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; however, there is only the same pattern of kidney cancer in the US in both sexes, but a higher incidence in males. GLOBOCAN (global cancer incidence) also showed a consistently higher incidence of kidney cancer among males, 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 \text{ 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. Other findings reported incidence of stomach cancer increased in Sub-Saharan Africa (SSA), including Ethiopia. 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.

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. 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. 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 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.

### 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.

Acknowledgements
We would like to thank the Addis Ababa Cancer Registry, Addis Ababa, Ethiopia, College of Health Sciences, Addis Ababa University, for giving us permission to conduct this study. We are also very grateful to the Addis Ababa Water and Sewerage Authority (AAWSA) for providing us with the water supply networks (Shape file) of Addis Ababa. We also duly acknowledge the American Cancer Society and Halle, United States of America.

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 (CNSIRB), Addis Ababa University. Written permission was obtained from AACR.

REFERENCES
1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136:E359-E386.
2. Fitzmaurice C, Dicker D, Pain A, et al. The global burden of cancer 2013. JAMA Oncol. 2015;1:505-527.
3. Fitzmaurice C, Allen C, Barber RM, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: a systematic analysis for the global burden of disease study. JAMA Oncol. 2017;3:524-548.
4. Sankaranarayanan R, Swaminathan R, Brenner H, et al. Regulation, formation, exposure, and treatment of disinfection by-products (DBPs) in drinking pool waters: a critical review. Environ Int. 2021;171:813-822.
5. Lee A, El-Dine W, Fergie J, et al. The epidemiology and possible mechanisms of disinfection by-products in drinking water. Philos Trans A Math Phys Eng Sci. 2009;367:4043-4076.
6. Kalanek Y, Rodriguez-Couto S, Zouali MA, Moosazadeh M, Mousavina-Sab S. Do disinfection byproducts in drinking water have an effect on human cancer risk worldwide? A meta-analysis. Environ Qual Manag. 2019;29:105-119.
7. Benmarhnia T, Delphi I, Schwarz L, Rodrigues MJ, Levallios P. Heterogeneity in the relationship between disinfection by-products in drinking water and cancer: A systematic review. Int J Environ Res Public Health. 2018;15:979.
8. Mazhar MA, Khan NA, Ahmed S, et al. Chlorination disinfection by-products in municipal drinking water – a review. J Clin Exp Prod. 2020;73:132159.
9. Yang L, Chen X, She Q, et al. Regulation, formation, exposure, and treatment of disinfection by-products (DBPs) in swimming pool waters: A critical review. Environ Int. 2018;121:1039-1057.
10. DeMarini DM. A review on the 40th anniversary of the first regulation of drinking water disinfection by-products. Environ Mol Mutagen. 2020;61:588-601.
11. Kumari M, Gupta SK. Occurrence and exposure to trihalomethanes in drinking water: a systematic review and meta-analysis. Expo Health. 2022;14:1-25.
12. Chen Z, Yang L, Li Z, et al. Application of biomarkers in the study of the health effects of disinfection by-products. Current Opinion in Environmental Science & Health. 2019;7:109-116.
13. Egwari L, Benson N, Effok W. Disinfection by-product-induced diseases and human health risk. In: Prasad MNV, ed. Disinfection by-Products in Drinking Water. Elsevier; 2020;185-204.
14. Cotruvo JA, Amato H. National trends of bladder cancer and trihalomethanes in drinking water: a review and multicountry ecological study. Deep-Res. 2015;4:453-450.
15. Srivastav AL, Kaur T. Factors affecting the formation of disinfection by-products in drinking water: human health risk. In: Prasad MNV, ed. Disinfection By-Products in Drinking Water. Elsevier; 2020;185-204.
16. Righi E, Bechtold P, Tortorici D, et al. Trihalomethanes, chlorite, chloride in drinking water and risk of congenital anomalies: a population-based case-control study in Northern Italy. Environ Res. 2012;116:66-73.
17. Babsi AA, Alavi N, Hassani G, Yousefian F, Shirmardi M, Atari L. Occurrence and related risk assessment of trihalomethanes in drinking water, Ahvaz, Iran. P preenviron Environ Biol. 2015;24:4807-4815.
18. Padih RK, Subramanian S, Mohanty AK, Satpathy KK. Monitoring chlorine residual and trihalomethanes in the chlorinated seawater effluent of a nuclear power plant. Environ Monit Assess. 2019;191:471.
19. Zhong Y, Gan W, Du Y, et al. Disinfection byproducts and their toxicity in wastewater effluents treated by the mixing oxidant of ClO3/Cl2. Water Res. 2019;152:471-481.
20. Gilchrist ES, Healy DA, Morris VN, Glennon JD. A review of oxyhalide disinfection by-products determination in water by ion chromatography and ion chromatography-mass spectrometry. Anal Chim Acta. 2016;942:12-22.
21. Huang J, Liu Y, Song X, et al. Bromine incorporation into five DBP classes upon chlorination of water with extremely low SUVA values. Sci Total Environ. 2017;590-591:720-728.
22. Zhou X, Zheng L, Chen S, et al. Factors influencing DBPs occurrence in tap water of Jinhua region in Zhejiang Province, China. Environ Sci Total. 2019;171:813-822.
23. Padih RK, Satpathy KK, Subramanian S. Impact of groundwater surface storage on chlorination and disinfection by-product formation. J Water Health. 2015;13:838-847.
24. Ibrahim MBM, Radwan EK, Mousry AS, Bedair AH. Humic substances as precursors for trihalomethanes yields upon chlorination. Desalination Water Treat. 2016;57:26494-26500.
25. Righi E, Fantuzzi G, Predieri G, Aggazzotti G. Bromate, chlorite, chlorate, halocarbon disinfection by-products in drinking water and ion chromatography-mass spectrometry. Anal Chim Acta. 2014;813:23-29.
26. Michalski R. Inorganic oxyhalide by-products in drinking water and ion chromatographic determination methods. Pol J Environ Sci. 2005;14:257-268.
27. Padih RK, Subramanian S, Satpathy KK. Formation, distribution, and speciation of DBPs (THMs, HAA5, ClO3-, and ClO4-) during treatment of different source water with chlorine and chlorite. Chemosphere. 2019;218:540-550.
28. Mishasha EI, Radwan EK, Ibrahim MBM, Hegazy TA, Ibrahim MS. Multi-exposure human health risks assessment of trihalomethanes in drinking water of Egypt. Environ Res. 2017;120:2643.
29. Pan S, An W, Li H, Su M, Zhang J, Yang M. Cancer risk assessment on trihalomethanes and halocarbon acids in drinking water of China using disability-adjusted life-years. J Hazard Mater. 2014;280:288-294.
30. Siddique A, Saied S, Mumtaz M, Hussain MM, Khwaja HA. Multipathways human health risk assessment of trihalomethanes exposure through drinking water. Environ Toxicol. 2015;116:129-136.
35. Xia Y. Disinfection Byproducts in Drinking Water: Formation, Analysis, and Control. CRC press; 2003.
36. Chowdhury S, Chowdhury JR, Mazumder MAJ, Al-Suwaiyan MS. Predicting risk and loss of disability-adjusted life years (DALY) from selected disinfection byproducts in multiple water supply sources in Saudi Arabia. Sci Total Environ. 2017;602:737-746.
37. Central Statistical Agency of Ethiopia. Drinking Water Quality in Ethiopia Results from the 2016 Ethiopia Socioeconomic Survey. Central Statistical Agency of Ethiopia; 2017.
38. Villanueva CM, Cordier S, Salas LA, Levallois P. Overview of disinfection by-products and associated health effects. Curr Environ Health Rep. 2015;2:107-115.
39. Garner E, Zhu N, Strom L, Edwards M, Pruden A. A human exposure framework for guiding risk management and holistic assessment of recycled water quality. Environ Sci Water Res Technol. 2016;2:580-598.
40. Zainal Ariffin O, Nor Saleha I. Chlorination by-products in drinking water: a review and roadmap for research. Mutat Res Rev Mutat Res. 2016;739:1-19.
41. Xie Y. Tafesse et al. Chlorination by-products in drinking water and risk of bladder cancer - A population-based cohort study. Water Res. 2022;141:118202.
42. Ackerson NOB, Killinger AH, Liberatore HK, et al. Impact of chlorine exposure time on disinfection byproduct formation in the presence of isopamidol and natural organic matter during chlorination. J Environ Sci. 2019;78:204-214.
43. Helte E, Sæve-Sidherhug M, Uge H, Full K, Larsson SC, Aksesson A. Chlorination by-products in drinking water and risk of bladder cancer - A population-based cohort study. Water Res. 2022;141:118202.
44. Menraa S, Halbe Y, Charafeddine M, Saifl O, Mukherji D, Shamseddine A. The unveiling of a new risk factor associated with bladder cancer in Lebanon. BMC Public Health. 2019;19:116-124.
45. Flatén TP. Chlorination of drinking water and cancer incidence in Norway. Int J Epidemiol. 1992;21:6-15.
46. Chen AIARo. Chlorinated drinking water-chlorination by-products; some other halogenated compounds; cobalt and cobalt compounds. International Agency for Research on Cancer (IARC) Working Group, Lyon, 12-19 June 1990. IARC Monogr Eval Carcinog Risks Hum. 1991;52:1-544.
47. Irabor DO. Emergence of colorectal cancer in West Africa: accepting the inevitable. Niger Med J Niger Med Assoc. 2017;58:87-91.
48. Benson NU, Akinotukun OA, Adeleko AE. Disinfection byproducts in drinking water and evaluation of potential health risks of long-term exposure in Nigeria. J Environ Public Health. 2017;2017:7535797.
49. Doci R, Gennari L, Bignami P, Montalto F, Moretto A, Bozzetti F. One hundred patients with hepatic metastases from colorectal cancer treated by resection: analysis of prognostic determinants. Br J Surg. 1991;78:797-801.
50. Jen J, Powell SM, Papadopoulos N, et al. Molecular determinants of dysplasia in colorectal lesions. Cancer Res. 1994;54:5523-5526.
51. Gatta G, Capoccia R, Sant M, et al. Understanding variations in survival for colorectal cancer in Europe: a EUROCARC high resolution study. Gut. 2013;62:753-758.
52. Macharia LW, Mureithi MW, Anzala O. Cancer in Kenya: types and infection-attributable. Data from the adult population of two National referral hospitals (2008-2012). AIDS Open Research. 2019;1:25.
53. Diaz D, Bassent M, Noluey-BN, et al. Endoscopic features of esophageal cancer in Dakar, Senegal: study of 76 observations. Med Thap. 2011;71:286-288.
54. Wolf LL, Ibrahim R, Miao C, Muyco A, Hosseinipour MC, Shores C. Esophageastroduodenoscopy in a public referral hospital in Lilingonge, Malawi: spectrum of disease and associated risk factors. World J Surg. 2012;36:1074-1082.
55. Hendriks D, Parker MI. Oesophageal cancer in Africa. JUIMB Life. 2002;53:263-268.
56. Wong MCS, Fung FDH, Leung C, Cheung WWL, Goggins WB, Ng CF. The global epidemiology of bladder cancer: a jointpoint regression analysis of its incidence and mortality trends and projection. Sci Rep. 2018;8:1129.
57. Adedoyin A. Harhan MO, Ayedola AO, et al. Estimate of the incidence of bladder cancer in Africa: a systematic review and Bayesian meta-analysis. Int J Urol. 2019;26:102-112.
58. Katalambula IK, Ntwenyenje FE, Ngoma T, et al. Pattern and distribution of colorectal cancer in Tanzania: a retrospective chart audit at two national hospitals. J Cancer Epidemiol. 2016;2016:3769829.
59. Morris CR, Lara LN Jr, Purikhe-Patel A, Kizer KW. Kidney cancer incidence in California: end of the trend? Kidney Cancer. 2017;1:71-81.
60. Mohamedin M, Pakrad R, Towhidi F, Makhsossi BR, Ahmadz A, Salehiniya H. Incidence and mortality of kidney cancer and its relationship with HDI (Human Development Index) in the world in 2012. Clayton Med. 2017;2017:286-293.
61. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66:683-691.
62. Malhotra GK, Yanala U, Ravipati A, Follett M, Vijayakumar M, Are C. Global trends in esophageal cancer. J Surg Oncol. 2017;115:564-579.
63. Wong MC, Goggins WB, Yip BH, et al. Incidence and mortality of kidney cancer: temporal patterns and global trends in 39 countries. Scientific Rep. 2017;7(1):15699.