DOCTORAL THESIS

DRINKING WATER CHLORINATION BYPRODUCTS AND CANCER RISKS IN ADDIS ABABA, ETHIOPIA

By

Nebiyou Tafesse (BSc, MSc)

Addis Ababa, Ethiopia
June, 2023

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DOCTORAL THESIS SUBMITTED TO THE SCHOOL OF GRADUATE STUDIES OF ADDIS ABABA UNIVERSITY, ETHIOPIAN INSTITUTE OF WATER RESOURCES IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PhD) IN WATER AND PUBLIC HEALTH

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June 2023

Addis Ababa, Ethiopia

DISSERTATION APPROVAL ADDIS ABABA UNIVERSITY

ETHIOPIAN INSTITUTE OF WATER RESOURCES

SUPERVISORS' SUBMISSION APPROVAL

DRINKING WATER CHLORINATION BYRPODUCTS AND CANCER RISKS IN ADDIS ABABA, ETHIOPIA

By Nebiyou Tafesse

Nebiyou Tafesse Layke has submitted this Dissertation of Drinking Water Chlorination Byproducts and Cancer Risks in Addis Ababa, Ethiopia. With my approval.

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EXECUTIVE SUMMARY

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 previous evidence showed the independent trends and prevalence of these cancers in association with DBPs in Ethiopia. Therefore, the study aimed to determine the prevalence and trends of disinfection byproducts related cancers (DBRCs) in Addis Ababa, Ethiopia. Close scrutiny of the published studies showed that this is the first study conducted indicating the association between drinking water source, chlorinated water and colorectal cancer (CRC) in Ethiopia. The present investigation is also the first study in assessing the trihalomethanes level and lifetime cancer risks in the drinking water supply in Addis Ababa, Ethiopia.

Methods: A retrospective record review using the Addis Ababa Cancer Registry (AACR) was conducted in Addis Ababa, Ethiopia. The AACR collects data on cancer cases submitted by three public hospitals and twelve private facilities (the only cancer treatment centers) in Addis Ababa, Ethiopia. Spatial data sets were produced and classified into households receiving chlorinated surface water and unchlorinated groundwater. The Cochran-Armitage trend test was used to evaluate whether there was a disinfection byproduct-related cancers (DBRCs) trend among communities receiving chlorinated water. Negative binomial regression was used to analyze the incidence rate. A facility-based matched case control study was conducted in Tikur Anbessa Specialized Hospital (TASH) involving 224 cases and 448 population controls from June 2020 to May 2021. A multivariable conditional logistic regression was used to identify risk factors of CRC. Stratified analysis was used to detect confounding factors and effect modification.

A cross-sectional study design was used to collect water samples in the water supply networks of Addis Ababa, Ethiopia. One hundred twenty (120) drinking water samples were collected from 21 sampling points in Addis Ababa, Ethiopia. The three sampling areas were Legedadi, Gefersa and groundwater sources. The United States Environmental Protection Agency (USEPA) protocol and practice for sample collection and handling were followed. The trihalomethanes (THMs) were separated by a DB-5 capillary column and detected by GC-ECD (gas chromatography-electron capture detector). Spectrophotometric and Insitu methods were used for physicochemical parameters. Canonical Correspondence Analysis (CCA) or Redundancy Analysis (RDA) was used for data analysis of trihalomethanes and environmental variables using CANOCO 4.5. Cancer and non-cancer risks of THMs via inhalation, ingestion and dermal contact routes have also determined.

Results: A total of 11,438 cancer cases were registered between 2012 and 2016, and DBRCs accounted for approximately 17%. The majority of the cases were females; 7,706 (67%). The prevalence of DBRCs was found to be higher in communities supplied with chlorinated water. Approximately 56% of colorectal cancer patients and 53% of stomach cancer patients are known to be using chlorinated surface water for drinking regularly. Of 214 colorectal cancer (CRC) cases, 148 (69.2%) used chlorinated water whereas out of 428 controls 161 (37.6%) used chlorinated water. In the final regression model, drinking chlorinated surface water (adjusted matched odds ratio (adjusted mOR) = 2.6;(95% CI: [1.7‒4.0]), history of swimming (adjusted mOR= 2.4; 95% CI: [1.4‒4.1]), years at the place of current residence (adjusted mOR=1.5; (95% CI: [1.1‒2.2]), hot tap water use for showering (adjusted mOR; 3.8= (95% CI: [2.5‒5.9]) were significantly associated with CRC.

The mean concentration of total trihalomethanes in drinking water in Addis Ababa was 76.3 µg/L. The concentration of chloroform in the drinking water supply in Addis Ababa, Ethiopia, ranged between 4.03-79.4µg/L. The results of the average THM concentration followed the order TCM (Trichloromethane) >BDCM(Bromodichloromethane) > DBCM (Dibromochloromethane) > TBM (Tribromomethane). The mean total THMs in the Gefersa and legedadi water supply systems were 77.4µg/L and 69.66µg/L respectively. The lowest THMs concentration was recorded in the groundwater supply system (15.5µg/L). The residual chlorine, phosphates, UV absorbance at 254 nm, and combined chlorine had positive correlations with THMs formation. However, electron conductivity had negative correlation with THMs formation. The cancer risk study discovered that among the examined routes, ingestion causes the greatest risk. The lifetime cancer risk by chloroform contributes the highest (72%) of the total risk, followed by BDCM (14%), DBCM (10%) and bromoform (4%).

Conclusions: The prevalence of DBRCs in this study was found to be high. The colon cancer trends increased substantially in Addis Ababa, Ethiopia. Drinking chlorinated water for extended years is a significant risk factor for CRC in Addis Ababa, Ethiopia. In addition, hot tap water use for showering, and swimming history are risk factors for CRC. Surface water supply networks have higher level total THMs than groundwater supply. The residual chlorine, UV absorbance, phosphate and hardness as calcium, and electron conductivity were found to be the main predictors determining the abundance and distribution of trihalomethanes. The cancer risk study discovered that among the examined routes, ingestion causes the greatest risk. The monitoring and regulation of the THMs is required on a regular basis to analyses trends and guide the water treatment and distribution system.

DECLARATION

I declare that the PhD Thesis entitled "**DRINKING WATER CHLORINATION BYRPODUCTS AND CANCER RISKS IN ADDIS ABABA, ETHIOPIA"** submitted by myself is an independent work carried out by me at Ethiopian Institute of Water Resources, Addis Ababa University, Addis Ababa, Ethiopia under supervision of Prof. Dr. Argaw Ambelu and Dr Sirak Robele Gari, and it has not been submitted anywhere else for any other degree, or diploma or title.

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Addis Ababa, Ethiopia

June , 2023

ACKNOWLEDGMENTS

First and foremost, I humbly bow before 'The Almighty God' for his immense blessings which showered on me the strength and wisdom to reach this milestone in my life. Words fall short in expressing my profound gratitude to my principal advisor and Co-advisor, Prof. Dr. Argaw Ambelu and Dr. Sirak Robele from Ethiopian Institute of Water Resources, Addis Ababa University for overall guidance of this work. I am so grateful for their dexterous guidance, motivation, constant encouragement, intellectual support, constructive criticism and above all the freedom they gave me during my doctoral studies.

I am also very grateful to Prof. Dr. Daniel A. Enquobahrie from the School of Public Health, Washington University, USA, for procurement and Shipment of certified reference materials. I would like to thank Ethiopian Institute of Water Resources, Addis Ababa University and College of Medicine and Health Sciences, Kotebe University of Education for providing a chance as student with such long journey research work. I would like to extend my appreciation to staffs of Ethiopian Institute of Water Resources for their full support extended to me during the course of my study and thesis work.

I would like to thank Dr. Zewdu Shewangezaw from College of Medicine and Health Sciences, Kotebe University of Education for the special support given throughout the work of these studies. I would like to thank Armauer Hanson Research Institute (AHRI) for procurement and importing certified reference materials and solvents from Aldrich Company, Germany. I would like to thank Addis Ababa Cancer Registry, American Cancer Society and Halle, United States of America and Tikur Anbessa Specialized Hospital (TASH) for providing the data and allowing us to conduct the matched case control study respectively. I would like also to extend the deepest appreciations to the data collectors and supervisors involved in this study.

The Ethiopian Agricultural Authority (EAA) and staffs of physicochemical laboratory services division duly acknowledged for their cooperation in providing the facilities to achieve the results. At this moment, I wish to acknowledge all scientists and technical staff of physicochemical laboratory for their kind co-operation during analysis of THMs. I also thank Addis Ababa Water and Sewerage Authority for providing us the shape file of water supply networks of Addis Ababa, Ethiopia. I would also like to extend my honest thanks to all the technicians from AAWSA for helping me during physicochemical analysis of the water samples. I want to express many thanks to Dr. Massimiliano Porcelli, Dr. R. K. Padhi, and Prof. Dr. Janvier Gasana for their unreserved support throughout the work of these studies.

I am grateful to Dr Asmamaw Malede from School of Public Health, Wollo University from Department of Environmental Studies who showed me an insight about Sat Scan and ArcGIS program and their continued support in all matters I needed. I am also indebted to my colleagues for their encouragement and support during the period of data entry, data analysis, writing and editing my thesis. I would like to offer special Thanks to Dr. Birhanu Teshome and Dr. Aynalem Abrha, although no longer with us, continues to inspire me the critical support given in all areas of My PhD work.

At this juncture, I owe my deep sense of gratitude to my family members Numhamin, Beemnet, Arsema, Natanem, Mehadot, Hirut, Fantu and Fantish for their whole-hearted support and pray to achieve this goal. Words fall short in expressing my heartfelt appreciation and forever satisfying to Hiwot Akalu, my beloved wife, Sosina H/Mariam, my beloved mother, who are always a source of constant support and stimulation. Without their love, care, appreciation, affection, and inspiration this thesis would never be realized.

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LIST OF ABBREVIATIONS

AACR	**A**ddis **A**baba **C**ancer **R**egistry
AAWSA	Addis Ababa Water and Sewerage Authority
AmOR	**A**djusted **M**atched **O**dds Ratio,
BDCM	**B**romodichloromethane
BMI	**B**ody **M**ass **I**ndex
CCA	**C**anonical **C**orrespondence **A**nalysis
CDI	**C**hronic **D**aily **I**ntake
CRC	Colorectal cancer
CSA	**C**entral **S**tatistical **A**gency
CSF	**C**ancer **S**lope **F**actor
DBCM	Dibromochloromethane
DBPs	**D**isinfection By-products
DBRCs	**D**isinfection **B**y-products **R**elated **C**ancers
EAA	**Et**hiopian **A**griculture **A**uthority
EC	electron conductivity
ECD	**E**lectron capture detector
GC-ECD	**G**as **C**hromatography **E**lectron **C**apture **D**etector
GIT	**G**astro-**I**ntestinal tract
GITD	Gastro-Intestinal Tract Diseases
HAAs	**H**aloacetic **A**cids
HKN	**Halo K**etones
ICD-O	**I**nternational **C**lassification of **D**isease for **O**ncology
ICD-O	International Classification of Disease for Oncology
IQR	Interquartile Range
LCR	Life Cancer Risk
LOD	**L**imit of **D**etection

LOQ	**L**imit of **Q**uantification
MAC	**M**aximum allowable concentrations
MCL	**M**aximum contaminant limit
MDL	**M**inimum **D**etection **L**imit
MH	Mantel–Haenszel
NOM	**N**atural **Or**ganic **M**atter
NOS	**N**ot otherwise specified
RDA	**R**edundancy **A**nalysis
SPSS	**S**tatistical **P**ackage for **S**ocial **S**ciences
SPWs	**S**wimming **P**ool **W**aters
SSA	**S**ub-**S**aharan **A**frica
TASH	Tikur Anbessa Specialized Hospital
TBM	Tribromomethane
TCM	Trichloromethane
TDS	total dissolved solids
THMs	**T**rihalomethanes
UBC	**U**rology **B**ased **C**ancer
UmOR	Unadjusted Matched Odds Ratio
USEPA	**U**nited **S**tates **E**nvironmental **P**rotection **A**gency

Chapter1 : Introduction

1.1. Background

Although CDC estimates that each year 1 in 44 people gets sick from waterborne diseases in the United States. The growth of water purification in the last decades has authorized cities in the industrialized countries to be mostly without of waterborne diseases (Bond et al., 2012, Weiner, 2008, Singh, 2020, Wittler, 2023). However, it was discovered in 1974 that water disinfectants themselves engage in interactions with naturally occurring organic materials (NOM) (Weiner, 2008, Ghernaout, 2018) forming unintended disinfection byproducts (DBPs) in water that are harmful to human health (Wang et al., 2015) Trihalomethanes (THMs) DBPs (Richardson and Plewa, 2020, Plewa and Wagner, 2015).

Disinfection of water is the critical public health progress of the last century as a result millions of people get quality drinking water daily from their public water systems. However, chemical disinfection has also concern for the public health due to the potential cause for cancer and developmental effects (Schwarzenbach et al., 2010a). In the early 1970s scientists first became aware of disinfection byproducts (DBPs) and most developed countries established guidelines to control DBPs and minimize consumer exposure (Howe et al., 2012).

DBPs are a complex mixture of hundreds of which almost the entire population of developed countries is exposed through ingestion, inhalation, or skin absorption while consuming or using municipal tap water and swimming in pools (Hebert et al., 2010, Richardson et al., 2007). Trihalomethanes (THMs) and haloacetic acids (HAAs) are the DBP classes that are generated at the highest amounts following chlorination, and chlorine is the most often used disinfectant in the world. The type and concentrations of DBPs found in municipal water are also influenced by raw water properties, such as the presence of natural organic matter, and the state of the distribution system (Villanueva et al., 2015, Charisiadis et al., 2015).

Recently exposure assessment improved using individual exposure measures as well as routinely collected water system THM measurements. Different countries have regulated total THM levels with various maximum containment levels (MCLs) ranges from 30 μg/L (in Austria, Belgium and Italy), 80 μg /L in US and WHO also set 200 μg /L for chloroform or 100 μg /L for bromoform (Kristiana et al., 2012). Addis Ababa obtains its water supply from both surface water and ground water sources. Chlorine and its compounds are the most commonly used disinfectants in Ethiopia both at large scale and small scale or household level (Adebo, 2016). As long as chlorine is being used for water treatment, there is no doubt this process will produces THMs. No research work on THMs is available in Addis Ababa, Ethiopia.

1.2. Statement of the problem

There is growing concern over the effects of disinfection byproducts of chlorination on human health (Li and Mitch, 2018). Early studies investigated links between disinfection byproducts of chlorination and increased risk of certain cancers such as bladder, rectal, stomach, and colon cancer (Morris et al., 1992). Similarly national institute of cancer (NCI) also indicated that THMs are carcinogenic leading to the public health concern (Villanueva et al., 2006b). Other studies also showed that there is an association between DBPs and adverse pregnancy outcomes including spontaneous abortion, low birth weight (LBW), small-for-gestational-age (SGA), still birth, and preterm delivery (Grellier et al., 2010, Grazuleviciene et al., 2011). Similarly epidemiologic report showed that cancer is an increasing public health burden for Ethiopia and Sub-Saharan Africa at large (Torre et al., 2015). Indeed, by the year 2030, cancer and other non-communicable diseases may overtake some infectious diseases as leading causes of death in the African region (Ngwa et al., 2022). Currently cancer accounts for about six percent of all deaths in Ethiopia (Duncan et al., 2019).

More recent studies have focused on the possible effects of disinfection byproducts of chlorination on certain reproductive outcomes, including low birth weight, stillbirth, spontaneous abortion, and congenital abnormalities. The results from these studies have been mixed (Reif et al., 1996). Since the discovery of chloroform as a chlorination by-product in drinking water in the early 1970s, disinfection by-products (DBPs) have raised public health concerns (Rook, 1974). The two most common groups of DBPs found in waters treated with free chlorine are trihalomethanes (THMs) and haloacetic acids (HAAs). Some DBPs from these two categories are probable carcinogenic in humans (Singer, 1994).

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(Xie, 2003). The MCL for TTHMs was reduced to 80 μg/L by the Stage 1 D-DBP Rule (Chowdhury et al., 2020b), while the MCLs for haloacetic acids (HAAs), bromate, and chlorite were set at 60, 10, and 1000 μg/L, respectively. Although the maximum acceptable concentrations (MACs) for TTHM and HAAs are 100 μg/L and 80 μg/L, respectively, and more DBP species are controlled in Canada (Canada, 2017) , the standards are similar to those in the United States. The South African National Standards has set the maximum contaminant levels (MCLs) for total THMs in drinking tap water at 300 μg/L(Mashau et al., 2021) .

Drinking water utilities in Ethiopia, particularly in Addis Ababa, have not measured DBPs. There is also no monitoring and controlling scheme of DBPs in drinking water distribution systems in Ethiopia. In addition, the water utilities in Ethiopia did not set the maximum allowed concentrations (MAC) of disinfection byproducts for total THMs and other DBPs. 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)(Villanueva et al., 2015).

Studies have indicated that chlorinated water, particularly chlorinated surface water, has an elevated risk of GIT (gastrointestinal tract) and UB(urology based) cancers (Garner et al., 2016, Cragle, 1984). Several case-control studies on exposure to chlorination by-products reported positive findings for colon and rectal cancers but the interpretation was limited (Oliver, 2017, Lawrence et al., 1984, Parbery, 2016). Case-control studies of cases related with drinking water chlorination have the potential to overcome the limitations of the early studies, but relatively few have been conducted (Water, 2013, Cragle, 1984, Rahman et al., 2010). No studies showed the independent trends and prevalence of these cancers in association with DBPs in Ethiopia in general and in Addis Ababa in particular. Moreover, there is no available study on the association between disinfection byproducts (DBPs) in chlorinated drinking water and colorectal cancer (CRC) in Ethiopia. Therefore, this study aimed to determine Prevalence, effects of drinking chlorinated water, the concentration of THMs and cancer risks in Addis Ababa, Ethiopia.

1.3. Significance of the study

- Drinking water that is free of contaminants is critical to one's health. Although microbiological contamination remains the leading cause of water-related morbidity and mortality worldwide, chemicals in water supplies can also cause disease, and evidence of the human health effects for many of them is limited or nonexistent (Garcıa-Villanova et al., 1997, Garcia-Villanova et al., 1997, Govorova et al., 2018).
- In developed countries, evaluating chlorinated disinfection by products in drinking water is a common task, but in developing countries, particularly in Africa including Ethiopia, the focus is on controlling water-related microbial morbidity and mortality by treating water with chlorine. However, problems caused by chlorinated disinfection by products have received little attention.
- THMs is the proxy indicator of drinking water disinfection byproducts and health risks from disinfection byproducts (THMs) are one of the issues that need to be investigated further in the field of water treatment (Ghernaout and Elboughdiri, 2020). THMs can be exposed to and absorbed through drinking, contact with the skin, or inhalation (Thiriat et al., 2009). THMs are known to cause numerous organ damage, even at low levels of exposure making systemic toxicants. They're also classified as possible or known human carcinogens (Nadali et al., 2019, Humans et al., 1994).
- Despite recent studies and organizations (WHO, USEPA, National Cancer Institute) indicated the potential risks of such products, Ethiopia has yet to conduct a study on the subject. Also, no DBPs guidelines have been established. Because health risk studies in Europe may not accurately reflect the risk in Ethiopia due to variations in THM concentrations and exposure status, it appears necessary to conduct this study.
- On the other hand, as the prevalence of non-communicable diseases, particularly cancer epidemiology, increases in Ethiopia, the most commonly cited factors for cancer

occurrence are nutritional lifestyle and other infectious diseases (Shiferaw et al., 2018). However, drinking water chlorination byproducts (THMs) not investigated in the study area and require special attention and more rigorous research. Furthermore, there has been no research on THMs in both large-scale and small-scale water treatment systems.

- Concerns about chlorine disinfection in drinking water by products known as trihalomethanes, as well as their link to a variety of diseases, have prompted the translation of evidence-based research into national policy to be a top priority.
- Delays in establishing a maximum allowable concentration (MAC) to protect human health have increased the burden of disease and resulted in significant and avoidable deaths. Trihalomethanes in drinking water have no current MAC in Ethiopia.
- Although Ethiopia is working to improve the quality and quantity of drinking water, it provides a compelling example of environmental health policy shortcomings.
- The findings of this study showed factors that aid policy change in Ethiopia in terms of THMs in drinking water and chlorine treatment, as well as action steps for designing continuous monitoring and thus protecting population health. Therefore, this study could be used as baseline for further research and to design an integrated project through considering the concentration of THMs and associated factors in Addis Ababa.

1.4. Research Questions

The following research questions were answered by this dissertation

- What is the prevalence of Drinking water disinfection byproducts related cancers (DBRCs) in Addis Ababa, Ethiopia?
- What are the trends of DBRCs in Addis Ababa, Ethiopia?
- What is the effect of chlorinated water towards colorectal cancers in Addis Ababa, Ethiopia?
- What is the concentration of drinking water disinfection byproducts (Trihalomethanes) in Addis Ababa?
- What is the level of Trihalomethanes related cancers and non–cancers risk in Addis Ababa, Ethiopia

1.5. Hypothesis

- Higher prevalence of drinking water disinfection byproducts related cancers are expected in the residents of Addis Ababa
- Increasing trends of DBRCs is expected in the residents of Addis Ababa
- Significant association between chlorination of water and colorectal cancers are expected.
- Drinking water may be contaminated with trihalomethanes. A health risk for consumers is expected.

1.6. Objectives of the Study

1.6.1. General Objective

The main objective of this thesis was to investigate Drinking water chlorination byproducts and cancer risks in Addis Ababa, Ethiopia

1.6.2. Specific Objectives

- To Determine the prevalence of Disinfection byproduct related cancers in Addis Ababa, Ethiopia (Paper one)
- To assess the trends of Disinfection byproduct related cancers in Addis Ababa, Ethiopia (Paper one)
- To investigate the relationship between Drinking Water Source, Chlorinated Water and Colorectal cancers in Addis Ababa, Ethiopia (Paper Two)
- To find out the concentration of Trihalomethanes in Drinking water supply networks in Addis Ababa, Ethiopia (Paper Three)
- To estimate Cancer Risks of Trihalomethanes concentration in Drinking water supply though multiple routes in Addis Ababa, Ethiopia (Paper IV)

1.7. Scope of the work

Concern over the effects of chlorination's disinfection byproducts on human health is growing. The drinking water chlorination byproducts are represented by trihalomethanes. Early studies examined the potential link between elevated cancer risk and disinfection byproducts of chlorination. An epidemiological study revealed that cancer is a growing public health burden for Sub-Saharan Africa and Ethiopia in particular. This dissertation was divided in to four phases (Fig. 2.2). **Phase I** involves determination of the prevalence and trends of disinfection byproducts-related cancers in Addis Ababa, Ethiopia. Disinfection byproducts (DBPs) from chlorinated drinking water have been linked to an increased risk of cancer in the bladder, stomach, colon, and rectum. A retrospective record review using the Addis Ababa Cancer Registry (AACR) was conducted in Addis Ababa, Ethiopia. Spatial data sets were produced and classified into households receiving chlorinated surface water and less chlorinated groundwater.

Phase II embodies the relation between chlorine based DBPs in drinking water and Colorectal cancers in Addis Ababa, Ethiopia. No study conducted on the association between disinfection byproducts (DBPs) in chlorinated drinking water and colorectal cancer (CRC) in Ethiopia. A facility based matched case control study was conducted in Tikur Anbessa Specialized Hospital (TASH) involving 224 cases and 448 population controls from June 2020 to May 2021. Cases were matched with controls by residence, age, and sex using frequency and individual matching. Geocoding of cases, health facility, and georeferencing of controls were carried out.

Phase III: Deals with Trihalomethanes and physicochemical quality of drinking water in Addis Ababa, Ethiopia. A cross-sectional study design was conducted in the water supply networks of Addis Ababa, Ethiopia. One hundred twenty (120) drinking water samples were collected from 21 sampling points in Addis Ababa, Ethiopia. The THMs were separated by an Agilent 122-5032 - GC Column DB-5 capillary column and detected by an electron capture detector (ECD).

Phase IV: Exposure and carcinogenic risk assessment of trihalomethanes (THMs) from water supply consumers in Addis Ababa, Ethiopia. This was done though modeling of the THMs concentration in drinking water through ingestion, dermal contact, and inhalation in Addis Ababa, Ethiopia. In addition, non-cancer risk assessment was evaluated by calculating the hazard index (HI) of THMs.

1.8. Thesis Organization

This dissertation entitled with "drinking water chlorination Byproducts and Cancer risks in Addis Ababa, Ethiopia" organized in eight chapters: **Chapter 1** consists of drinking water chlorination byproducts and epidemiology of cancers. The limitations of early studies and gaps of the study area have been elucidated. The statement of the problem, research questions, objectives, scope of the work and thesis organization were presented in this chapter. **Chapter 2** depicts summary of the literature review verifies and support the framework of the study. It critically analyzes the DBPs formation, the chlorine dilemma, regulation and guidelines of DBPs, related studies on DBPs, consumption of chlorinated surface water, formation of Trihalomethanes, epidemiology of cancers and factors associated with colorectal cancers. In addition, the conceptual framework of the study presented in this chapter.

Chapter 3 discusses the prevalence and trends of drinking water disinfection byproducts-related cancers in Addis Ababa, Ethiopia. It mainly focuses on determination of disinfection byproducts-related cancers using Addis Ababa cancer registry.

Chapter 4 deals with drinking water source, chlorinated water, and colorectal cancer: a matched case-control study in Ethiopia: It summarizes the relationships of chlorinated surface water and less chlorinated groundwater with risk of colorectal cancers. It consists of results and discussion of the drinking water chlorinated disinfection byproducts and colorectal cancers. It also highlighted the key factors associated with colorectal cancers.

Chapter 5: Pinpoint Trihalomethanes and physicochemical quality of drinking water in Addis Ababa, Ethiopia. It also depicts the physicochemical and related factors of Trihalomethanes formation in Addis Ababa, Ethiopia. The method verification and validation procedure of THMs determinations also emphasized in this chapter. **Chapter 6:** presents Exposure and carcinogenic risk assessment of trihalomethanes (THMs) from water supply consumers in Addis Ababa, Ethiopia. This chapter focuses on cancer and non-cancer risks of THMs though ingestion, dermal contact and inhalation.

Chapter 7: states general discussion and their implications. The factors affecting THMs formation are discussed. The most common routes of exposure, trihalomethane and risk of cancer are concluded. Under this chapter the strengths and limitations of the study depicted. In this, the novelty and the limitations of the study elaborated. **Chapter 8:** Conclusion, Recommendation and Future Prospect. The overall conclusion, recommendations and future prospect was presented in this chapter. The future work area is depicted to enhance monitoring and regulation of THMs.

Chapter2 : Literature Review

2.1. DBP formation mechanism

2.1.1. Disinfectants

2.1.2. Disinfectants and their aqueous chemistry

The most often utilized disinfection method for drinking water (DW) treatment is chlorination (Afifi and Blatchley III, 2015, Blatchley III and Cheng, 2010). The most common chlorine-based disinfectants are chlorine gas (Cl_2), sodium hypochlorite (NaClO), and calcium hypochlorite (Ca (ClO_2). These disinfectants are hydrolyzed and/or dissociated, yielding hypochlorous acid (HClO) and hypochlorite ion (ClO^-) as active components for disinfection (Eqs. (1)– (4)) (Richardson and Plewa, 2020). The pH and temperature of the equilibrium between HClO and ClO are both important.

$Cl_2 + H_2O \rightarrow HClO + H^+ + Cl^-$ (1)

$NaClO \rightarrow Na+ + ClO$ (2)

$Ca (ClO)_2 \rightarrow 2Ca^+ + 2ClO^-$ (3)

$ClO + H_2O \rightarrow HClO + OH$ (4)

Bromine-based disinfectants are utilized in pools under particular conditions, such as spas. Liquid bromine, which has a hydrolysis pattern similar to that of chlorine gas, is used to maintain swimming pool waters (SPWs), particularly hot tubs (Eq. (5)). Since the early 1900s, some European countries have been exploiting seawater as a source of SPWs (Parinet et al., 2012). Bromide ions, which have a concentration of 70 mg/L in seawater, can be oxidized by HClO to generate HBrO, which has a prominent role in disinfection (Eq. (6)) (Borges et al., 2005, Von Gunten and Oliveras, 1998). According to Parinet et al (Parinet et al., 2012), the synthesis of more harmful Br- DBPs (e.g., bromoform, tribromoacetic acid, and tribromoacetic acid) in seawater pools was significant. Bromine, with a lower vapor pressure, overcomes the unstable feature of chlorine at high temperatures. such as spas and hot tubs (Ghernaout, 2018). However, bromine-based sunlight quickly depletes disinfectants. However, bromine-based disinfectants decrease quickly under sunshine, making them unsuitable for outdoor pools and spas (Water Aid Organization, 2006).

$Br_2 + H_2O \rightarrow HBrO + H^+ + Br^-$ (5)

$HClO + Br \rightarrow HBrO + Cl^-$ (6)

2.2. The Chlorine Dilemma

Safe drinking water has been made possible through chlorine disinfection, although this practice is not without risk: Chlorine combines with organic matter in the environment to inactivate waterborne infections as well as create a number of harmful disinfection byproducts (DBPs) (Sedlak and von Gunten, 2011). Shortly after DBPs like chloroform were found in drinking water that had been chlorinated in the middle of the 1970s, regulatory criteria for DBPs were created in the US (DeMarini, 2020). Over the past ten years, the operation of water treatment systems has undergone significant adjustments as a result of the finding of a possible association between DBPs and an increase in miscarriage, neutral tube defects and bladder cancer rates (Hrudey, 2009). Recently, many drinking-water and wastewater treatment plants have stopped using chlorine disinfection due to these worries and the dangers of storing chlorine gas (Nozaic, 2004) (Fig. 2.1).

The principal precursors of DBPs, natural organic matter, can be removed from drinking water systems more efficiently by physical-chemical treatment procedures such as improved coagulation and activated carbon filtration (Jacangelo et al., 1995, Ibrahim and Aziz, 2014). Although these methods are efficient and have no known health hazards, they are typically the most expensive technique to reduce DBP formation. As a result, numerous utilities all around the world have chosen the less expensive strategy of employing chloramine. By adding too much ammonia to water before adding chlorine, this less reactive form of chlorine is created. The creation of a distinct set of hazardous DBPs has been one unforeseen effect of this change. Most significantly, the reaction between chloramines and organic nitrogen-containing molecules results in the production of cancer-causing nitrosamines such N-nitrosodimethylamine (NDMA) (Mazhar et al., 2020, McKenna, 2020). The move from chlorine to chloramine has been linked to higher amounts of lead recently found in drinking water and human blood in Washington, DC, and other cities, in addition to producing cancer-causing nitrosamines (Hrudey, 2009).

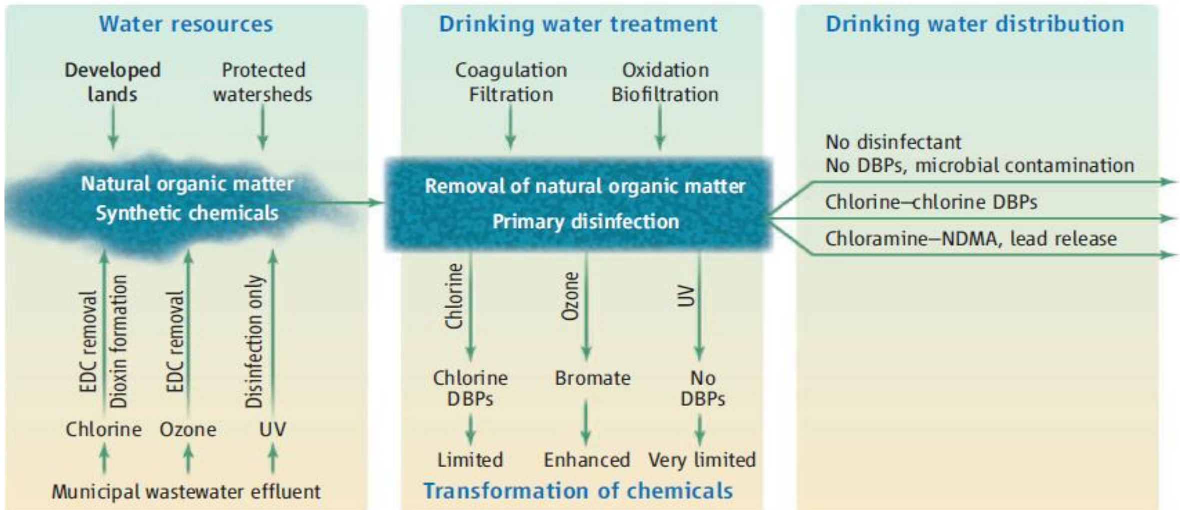


Figure 2.1: A schematic of water purification processes for drinking water and municipal wastewater. EDCs= endocrine-disrupting compounds, NDMA =N-nitrosodimethylamine, UV= ultraviolet (Sedlak and von Gunten, 2011)

2.3. Regulations and guidelines of DBPs

THMs, HAAs, haloacetonitriles (HANs), bromate, chlorate and chlorite, nitrosodimethylamine (NDMA), cyanogen chloride, and 2, 4, 6-trichlorophenol have all been subject to regulations and guidelines for DBPs in Drinking waters (DWs) (Table 2.1). THMs were originally controlled by the US EPA in 1979, with an MCL of 100 µg/L in DWs (Cotruvo, 1981). In 1998, the MCL for THMs was reduced to 80 µg/L, while HAA5 (the sum of chloro-, bromo-, dichloro-, dibromo-, and trichloroacetic acids) was controlled for the first time at 60 µg/L (EPA, 1998). Apart from the four THM and five HAA compounds controlled by the US EPA, the MCLs for bromate and chlorite are 10 and 1000 µg/L, respectively. In contrast, the European Union regulates only THMs (100 µg/L) and bromate (10 µg/L) (Hoekstra et al., 2008).

The World Health Organization (Edition, 2011) establishes guideline values for 15 individual DBPs in DWs. The WHO guidelines additionally include NDMA (0.1 µg/L), cyanogen chloride (70 µg/L), 2,4,6 trichlorophenol (200 µg/L), bromate (10 µg/L), chlorate (700 µg/L), chlorite (700 μg/L), and two individual HANs, dibromo acetonitrile (70 μg/L) and dichloroacetonitrile (20 μg/L). In different countries, the DW quality standard is mostly based on the WHO guidelines (Strogen et al., 2016). Table 2.1 includes DBP recommendations for Australian and Canadian DW quality.

Table 2.1 : DBP regulations and guidelines in drinking water

DBPs	**U.S.EPA (EPA, 1998)**	**WHO (Edition , 2011)**	**Singapore (Strogen et al., 2016)**	**European Union (Hoekstra et al., 2008)**	**Australia (NHMRC, 2011)**	**Canada (Dunn et al., 2014)**
	MCL[a] (μg/L)					
THMs[b]	80	–	–	100	250	100
Chloroform	70	300	300	–	–	–
Bromodichloromethane	0	60	60	–	–	–
Chlorodibromomethane	60	100	100	–	–	–
Bromoform	0	100	100	–	–	–
HAA_5[c]	60	–	–	–	–	80
Dichloroacetic acid	0	50	50	–	–	–
Trichloroacetic acid	20	200	200	–	100	–
Monochloroacetic acid	70	20	20	–	100	–
HANs	–	–	–	–	150	–
Dibromo acetonitrile	–	70	70	–	–	–
Dichloroacetonitrile	–	20	20	–	–	–
Bromate	10	10	10	10	20	10
Chlorate	–	700	700	–	–	1000
Chlorite	1000	700	700	–	800	1000
N-nitrosodimethylamine	–	–	–	–	0.1	0.04
Cyanogen chloride	–	700	70	–	80	–
2,4,6-Trichlorophenold[d]	–	200	200	–	20	5

Notes: a MCL means maximum contaminant level. b THMs refer to the summation of chloroform, bromodichloromethane, chlorodibromomethane, and bromoform. c HAA5 refers to the summation of chloro-, bromo-, dichloro-, dibromo-, and trichloroacetic acids. d 2, 4, 6-Trichlorophenol was not detected in swimming pool waters.

Trichloroisocyanuric acid (TCCA), dichloroisocyanuric acid (DCCA), and Bromochlorodimethylhydantoin (BCDMH) are the most common organic disinfectants (Table 2). Because of their role as chlorine stabilizers, TCCA and DCCA are commonly utilized in outdoor pools, particularly those exposed to direct sunshine (Yang et al., 2016, Zwiener et al., 2007). Because the former has significantly lower maximum absorption wavelengths, the bound forms of chlorine in TCCA, namely, monochloroisocyanurate ions (HClCy) and dichloroisocyanurate ions (Cl2Cy), are more stable during solar exposure than HClO and ClO (Wojtowicz, 1996). According to Askins (2013), the inclusion of cyanuric acid decreased chlorine decomposition during natural sunshine exposure. BCDMH is occasionally used to disinfect SPW (Lourencetti et al., 2012, Richardson and Plewa, 2020). It outperforms NaClO in terms of fecal coliform killing efficiency (Moffa et al., 2006). However, HBrO, the highly reactive disinfection ingredient in BCDMH, is unable to meet the criterion for continuous disinfection (Yang et al., 2016).

Table 2.2: Disinfectant classifications

Groups	**Disinfectants**
Chlorine based disinfectants	Chlorine gas
	Sodium hypochlorite
	Calcium hypochlorite
Bromine based disinfectants	Bromine liquid
	Sodium bromide hypochlorite
Organic based disinfectants	Bromochlorodimethylhydantoin (BCDMH)
	Trichloroisocyanuric acid (TCCA)
	Trichloroisocyanuric acid (DCCA)

2.4. Related studies on THMs in drinking water

A study conducted in southern Mauritius Riviera du Poste and Mont Blanc treatment plants trihalomethanes (THMs) was determined using a gas chromatograph linked with an electron capture detector (GC-ECD) and found a total THM concentration of 20.3 mg/L with a range of 13.0 mg/L to 24.8 mg/L (Uppeegadoo et al., 1999). A similar related study conducted in Hamadan and Tuyserkan cities, western Iran, also determined using gas chromatography equipped with mass spectrometry (GC–MS) and found that the mean concentrations of total THMs in the summer and winter were 42.75 and 17.75 µg/L, respectively, below the WHO and Iranian standards (Nadali et al., 2019). Another epidemiological study conducted in the United Kingdom also found the THM concentration using a gas chromatograph linked with an electron capture detector (GC-ECD), and the measured annual zone means for total THM (TTHM) were less than half the statutory concentration, at approximately 46 µg/l (Keegan et al., 2001). A similar related study conducted in Nigeria in drinking water investigated the levels of THM using a gas chromatograph linked with an electron capture detector (GC-ECD) and found THMs ranging from 43.69 to 95.94 µg/L (Benson et al., 2017).

2.5. Drinking Water Disinfection Byproducts

Although water disinfection is critical for lowering pathogens in the public water supply, disinfection byproducts (DBPs), such as trihalomethanes (THMs), can be generated when chlorine and other disinfectants react with naturally occurring organic matter and inorganic compounds in the water (Ashley et al., 2005, Ashley et al., 2019, Yang et al., 2018). DBPs have been discovered in drinking waters (DWs) since the early 1970s, with over 600 DBPs documented in the last 40 years (DeMarini, 2020). Trihalomethanes (THMs) were the first DBP group identified in DWs in 1974(Tak and Kumar, 2017) and have been linked to diseases such as bladder and colon cancer, asthma, eye and mucous membrane irritation, and reproductive function (Ratajczak and Piotrowska, 2019, Yang et al., 2018, Goodman and Hays, 2008).

Chlorination has been used for water disinfection since the nineteenth century, and it is still the most extensively utilized technology in the water sector (Schreiber, 1981). The overall THM concentration in chlorinated drinking water (sum of $CHCl_3$, $CHCl_2Br$, $CHClBr_2$ and $CHBr_3$) can range from tens to hundreds of μg/l (McGuire, 1989, McGuire and Meadow, 1988). The discovery that trihalomethanes (THMs) such as chloroform ($CHCl_3$, bromodichloromethane ($CHCl_2Br$), chlorodibromomethane ($CHClBr_2$), and bromoform (HBr_3) are formed during water chlorination has prompted extensive research into the occurrence of these chemicals and their potential adverse health effects.

Five years later, the US EPA restricted THMs in DWs to a maximum contaminant limit (MCL) of 100 μg/L (Cotruvo, 1981). THM MCL was reduced to 80 μg/L in 1998(EPA, 1998). At the same time, haloacetic acids (HAAs), another common class of DBPs, were regulated with an MCL of 60 μg/L for the total chloro-, bromo-, dichloro-, dibromo-, and trichloroacetic acids. THMs and HAAs account for approximately 25% of all halogenated DBPs (Krasner et al., 2006), with chloroform, bromodichloromethane, dichloroacetic acid, and trichloroacetic acid classified as pollutants probably carcinogenic to humans (Group 2B) by the International Agency for Research on Cancer (Grosse et al., 2019). Some new DBPs, which are not yet controlled, have the potential to be more harmful than THMs and HAAs, such as halo nitromethanes (HNMs), haloamides, and iodo-DBPs (Richardson et al., 2007)

2.6. Consumption of surface water and chlorination by-products (Trihalomethanes)

Most of the identified studies used consumption of surface water as an indirect measure of exposure to chlorination by-products. Unchlorinated natural waters do not contain significant amounts of chlorinated hydrocarbons. Consequently, the comparison of consumers of chlorinated water with consumers of unchlorinated water provided an acceptable surrogate for comparing exposure Vs non- exposure to chlorination by-products, groundwater tends to be less heavily chlorinated, and in the case of private wells the water is often unchlorinated. In addition, groundwater contains less organic matter than does surface water. Organic matter combines with chlorine to form chlorination by-products. Measurements of chlorination by-products in the drinking water supply (Cantor, 1983) have shown that chlorinated surface water contains much higher levels of these by-products than does chlorinated groundwater (medians of 50.7 and 0.8 ppb, respectively) even when the surface water is drawn from protected reservoirs. For these reasons, consumption of surface water Vs groundwater was also used as a surrogate for exposure to chlorination byproducts (Morris et al., 1993).

2.7. Factors associated with THMs formation

The creation of statistical models for DBPs is becoming increasingly regarded as a methodological foundation for predicting DBP formation. Such models assist water utility management in making decisions, such as establishing disinfectant dose, contact time, pH adjustment, and so on, to limit the development of DBPs while maintaining the required disinfectant residual (Tsitsifli and Kanakoudis, 2018). These models can also be used to determine the best sites for boosters to maintain the necessary amounts of disinfection residuals while reducing the production of DBPs. Using such models; optimal water sample points for water quality control can be discovered. When chlorine is employed as a disinfectant, complex mixes of disinfection byproducts (DBPs) are generated in drinking water, among which trihalomethanes (THMs) are discovered (Kampioti and Stephanou, 2002, Richardson et al., 2007). THM concentrations are affected by organic matter type and concentration, pH, temperature, chlorine dose, chlorine contact time, and halide content (Table 2.3) (Uyak et al., 2007, Laflamme, 2018). The literature indicates that pH and temperature are related to THM production, but pH effects vary for different DBPs (Sadiq and Rodriguez, 2004).

Because microorganisms multiply as temperatures rise, a larger disinfectant dose is used throughout the summer, resulting in high DBP concentrations. DBP production is influenced by the factors affecting disinfection efficiency as well as the requirements to preserve disinfectant residuals (vicious cycle). Several investigations (Abokifa et al., 2016) found that THM concentrations in WDNs (water distribution networks) are higher than those in storage tanks. This is also attributable to the presence of organic matter in the biofilms seen on the walls of water pipelines. Another factor influencing DBP development is organic materials in water (Table 2.3)

Table 2.3: Disinfection-by-product (DBP) predictive model parameters (based on (Sadiq and Rodriguez, 2004)

Parameters		Units
Br	Bromide ion	mg/L
Cl_2	Initial chlorine concentration	mg/L
pH	Ph	
T	Temperature	°C
NVTOC	Non-volatile organic carbon	mg/L
TOC	Total organic carbon	mg/L
D	Chlorine dose	mg/L
T	Reaction time	Hrs
UV	UV absorbance at 254 nm	cm^{-1}
TTHMo	Initial total THM concentration	cm^{-1}
Flu	fluorescence %	%
Co	Residual chlorine at the treatment plant after chlorination	mg/L
A	Parameter depending on location which chloroform is predicted	
€	Random error	
Ch-a	Chlorophyll-a	mg/m^3
DOC	Dissolved organic carbon	mg/L

2.8. Epidemiology of Cancers

Cancer is becoming a serious issue in every country. It is the world's second most likely cause of death (Ferlay et al., 2015). 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

(Fitzmaurice et al., 2015, Fitzmaurice et al., 2017). Survival from cancer is relatively low in Sub-Saharan African (SSA) countries, and its health burden has been rising. In SSA, cancer's health burden is estimated to show an 85% increase by 2030(Sankaranarayanan et al., 2010). 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 (Koivusalo and Vartiainen, 1997, Nieuwenhuijsen et al., 2009, Kalankesh et al., 2019, Benmarhnia et al., 2018, Mazhar et al., 2020, Yang et al., 2018, DeMarini, 2020, Kumari and Gupta, 2022, Chen et al., 2019, Egwari et al., 2020, Cotruvo and Amato, 2019, Srivastav and Kaur, 2020).

2.9. Colorectal Cancers

Colorectal cancer is a major cause of morbidity and mortality throughout the world (WHO, 2002). It accounts for over 9% of all cancer incidence (Fund and Research, 2007, Haggar and Boushey, 2009). It is the third most common cancer worldwide and the fourth most common cause of death (Fund and Research, 2007). It affects men and women almost equally, with just over 1 million new cases recorded in 2002, the most recent year for which international estimates are available (WHO, 2002), (Field and Lipton, 2007, Parkin et al., 2005). Colorectal cancer represents nearly 10% of global cancer incidence, with increasing rates over the last decades (Villanueva et al., 2017). However, part of the burden of disease remains unexplained by the abovementioned risk factors. Human and animal studies suggest that carcinogens in drinking water may be associated with colorectal cancer risk (Villanueva et al., 2017). 2002

2.10. Factors Associated with Colorectal Cancers

2.10.1. Sociodemographic Characteristics and Colorectal Cancers

A study conducted in tertiary hospital in Oman over five years of follow-up showed that males were found to have a higher prevalence of CRC than females (13.3 vs. 10.5), and the CRC prevalence increased with age, rising from 2.8 in those under 40 to 26.5 in those 70 and older (Alsumait et al., 2020). Other related study done on Florida Cancer Data System (FCDS) indicated that depicted that when compared to those aged 50 and older, those under the age of 50 were significantly more likely to have advanced stage CRC (Moore et al., 2018).

2.10.2. DBP exposure and colorectal cancer

Animal studies have suggested an association between DBP exposure and colorectal cancer. Preneoplastic lesions have been produced in the intestines of rodents administered DBPs via drinking water in chronic bioassays (Narotsky et al., 2015, Mcdorman et al., 2003). However, some studies have shown that chloroform may inhibit gastrointestinal carcinogenicity in rodents (Daniel et al., 1989, Daniel et al., 1991). Human epidemiological evidence is mixed. Case–control (Bove et al., 2007, Cragle et al., 1985, Hildesheim et al., 1998, King et al., 2000, YOUNG et al., 1987) studies including incident cases of colorectal cancer and quantitative estimates of exposure to DBPs such as trihalomethanes or related surrogates have produced contradictory results. Three studies reported positive associations with colon cancer (Cragle et al., 1985, Doyle et al., 1997, King et al., 2000) and three studies reported null associations (Hildesheim et al., 1998, Koivusalo et al., 1997). The inconsistency of human epidemiological evidence might be partly attributable to exposure misclassification, including a lack of evaluation of different routes of exposure and uncontrolled confounders.

A study conducted on the lifetime cancer risk and the hazard index of trihalomethanes (THMs) through oral ingestion, dermal absorption, and inhalation exposure from supply water of five water treatment plants (WTPs) showed that THMs concentration varied from plant to plant and was found to be in the range of 274–511 μg/l, which is much higher than the prescribed USEPA standards of 80 μg/l and in this study Chloroform was the most dominant THM followed by bromodichloromethane (BDCM), and dibromochloromethane (DBCM) and in this study also indicated that cancer risk analysis through multi-pathways exposure reveals that residents had a higher cancer risk through oral ingestion than other two routes of exposure and this study concluded that the lifetime cancer risks of THMs from supply water are 100 times higher than prescribed USEPA guidelines (Kumari and Gupta, 2018).

Other related study conducted in India showed that the higher cancer risk found for Indian context than those reported for other countries like USA, UK, Japan, Australia, is mainly due to the higher concentration level of THMs, water intake and average body weight and the study also revealed that amongst different THMs, chloroform is the major THMs causing cancer risk through both oral and dermal route of exposure whereas in case of inhalation it was mainly because of BDCM(Villanueva et al., 2017). This study similarly indicated that average lifetime cancer risk analysis showed that females are more prone to cancer risk than males (Paustenbach, 2015).

Another related study of case-control study conducted to test the hypothesis of chronic ingestion of trihalomethanes (THMs), occurring as chlorination byproducts in drinking water validated that it carries a risk of colon cancer and this study showed also lifetime residential and water source histories and information on water-drinking habits, diet, socio-demographics, medical and occupation histories, lifestyle and other factors were the potential predicator variables, however after adjusting for the potential confounding variables does not pose a significant colon cancer risk (Rice, 2017).

Exposure assessment is the most difficult task in a study of this kind. Three factors determine a person's cumulative exposure to an environmental contaminant or risk factor: (1) the environment to which the person was exposed, (2) the level of the proposed agent present in the environment, and (3) the degree to which the person is exposed to that environment (Morris et al., 1992). In the current context, these exposures refer to (1) the source of tap water, (2) concentrations of chlorination byproducts in the tap water, and (3) the amount of tap water consumed. Although exposure at a fixed point in time (e.g., the time of diagnosis or death) often correlates highly with lifetime exposure, a complete assessment of exposure must also include the historical records for each of these three factors. Thus, there are six factors that must be evaluated in each study: three exposure factors plus historical records for each of these factors (Vermeulen et al., 2020). The quality of exposure assessment was scored for each study as the percentage of these factors that were evaluated in the study.

Another related study showed that genetic risk, a product term between alcohol consumption and high fat diet and an interaction term between age and chlorination tend to be positively associated with colon cancer. The association between chlorinated water and colon cancer was found to be highly dependent up on age and duration of exposure. Rate ratio estimates for persons who drank chlorinated water at their residence for 16 or less than 16 years but statistically significant associations between water chlorination and colon cancer, controlling potential confounding variables, were found only for those above age 60. For example, 70 to 79 years old's for who drank chlorinated water for 16 years or more had twice (Relative risk = 2.15) the risk of colon cancer compared with 70 to 79 years old, who drank Unchlorinated water in the same age group the risk of colon cancer was about 50% (RR=1.47) higher in those who drank chlorinated water for less than 16 years as compared with those who drank Unchlorinated water (Craun, 1991).

2.10.3. Dietary Factors and Colorectal cancer

A study conducted in USA using data from the Nurses' Health Study, a prospective study of a cohort of 121,701 female nurses revealed that processed meat consumption and smoking were linked to colorectal cancers (Wei et al., 2017). Another study Shanghai, China showed that Red meat (OR, 1.5; 95 percent CI, 1.0–2.1 for men and OR, 1.5; 95 percent CI, 1.0–2.2 for women), fish (OR, 1.7; 95 percent CI, 1.2–2.4 for men and OR, 1.2; 95 percent CI, 0.8–1.7 for women), and eggs (OR, 1.4; 95 percent CI, 1.0–1.9 for men and OR, 1.3; 95 percent CI, 0.9–1.9 for women) were all linked to consumption of preserved foods, whether from animals or plants, was linked to an increased risk of colon cancer (OR)(Chiu et al., 2003).

A systematic review done on dietary factors and risk of colon cancer by Giovannucci E and his colleague (Huxley et al., 2009) showed that physical inactivity or an excess of energy intake compared to requirements increases the risk of this cancer, according to epidemiological evidence. Consumption of red meat appears to raise risk, but protein-rich foods other than red meat are unlikely to raise risk and may even lower the risk of colon cancer.

Dietary fat at least derived from sources other than red meat does not appear to significantly increase risk. The consumption of fruits and vegetables, as well as the avoidance of highly refined sugar-containing foods, is thought to reduce the risk of colon cancer, though the exact constituents are unknown. Although the evidence is not entirely consistent, alcohol consumption may increase the risk of cancers of the distal colorectal. Other case-control study was conducted on Saudi Arabia revealed that intake of 1–5 servings of dairy products per day, 3–5 servings of legumes per week, 1–5 servings of leafy vegetables per week, 1–5 servings of olive oil per week, three or more cups of black tea per day, and one or more cups of coffee per day were found to reduce the risk of CRC in participants (Azzeh et al., 2017).

2.10.4. Genetic predisposition, family history and colorectal cancers

A genetic predisposition accounts for about 25% of CRC cases, and inherited risk factors contribute to the disease in 5% of CRC patients (Campos, 2017). People were thought to be at higher risk for CRC if they had a family history of the disease or adenomatous polyps. Environmental factors, hereditary risks, or a combination of both were suggested as reasons (Haggar and Boushey, 2009). In a case-control research conducted in Hong Kong, the frequency of advanced colorectal neoplastic was compared between asymptomatic siblings of CRC patients and siblings of those who had no family members with the disease. The prevalence of advanced neoplastic was shown to differ by three times between the case group (7.5%) and control group in the study (2.9 percent) (Ng et al., 2013).

The increase in RR of CRC ascribed to family history was larger in younger subjects, according to a meta-analysis of 9.28 million people (Wong et al., 2018a). Another prospective study that involved 16 nations in the Asia-Pacific region came to the conclusion that it was not required to screen patients with affected first-degree relatives based on prob and identification (Wong et al., 2016).

2.10.5. Shower Water Temperature and colorectal cancer

Trihalomethanes (THMs) can be harmful to humans if they are inhaled or come into contact with the skin while showering or bathing. Warm water (35°C–45°C) is commonly used for showering and bathing. Increased interactions between organics and residual chlorine in chlorinated source water may promote THM production. Exposure evaluation based on THM concentrations in cold water may underestimate the potential health consequences (Chowdhury and Champagne, 2009).

2.11. Conceptual Framework

The conceptual framework of this study emanates from linking the water supply networks of Addis Ababa with Addis Ababa cancer registry. The study encompasses also determination of the association of chlorinated water supply with colorectal cancer. Accordingly, ingestion and non-ingestion pathway of drinking water disinfection byproducts investigated. The key factors contributing for the formation of Trihalomethanes also determined in this study. The dietary factors, genetic and family history of colorectal cancers were identified. The cancer and non-cancer risks of trihalomethanes due to inhalation, ingestion and dermal contacts also identified (Fig. 2.2).

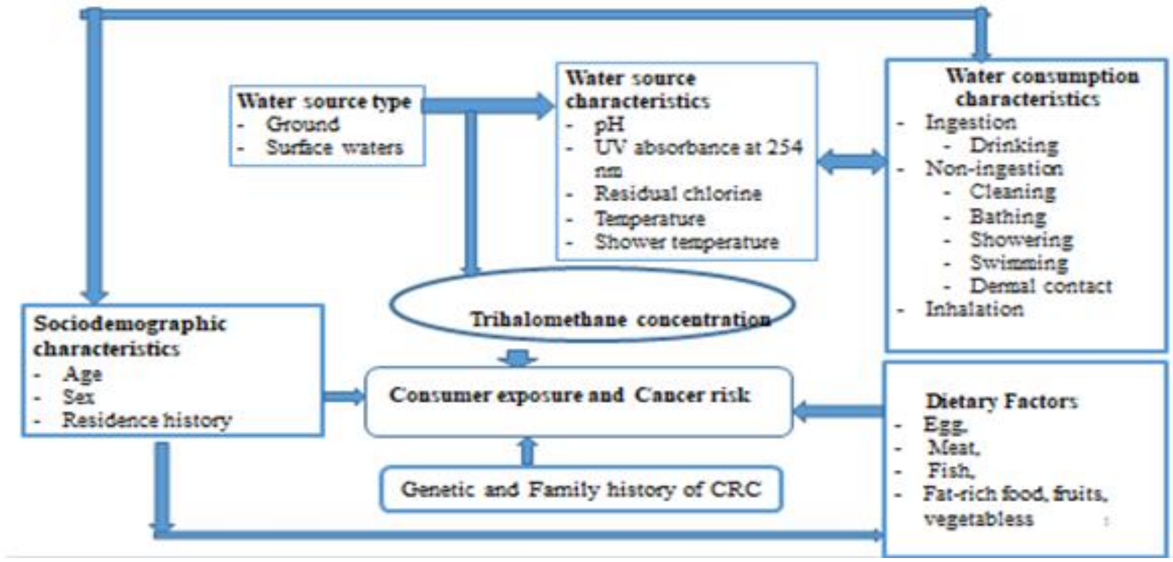


Figure 2.2: *Conceptual Framework of Drinking Water Disinfection byproducts (Trihalomethanes) and Cancer in Addis Ababa, 2022(Cancer, 1991, Crump and Guess, 1982, El-Tawil, 2016, Ghernaout and Elboughdiri, 2020, Koivusalo et al., 1994, Li and Mitch, 2018, Rahman et al., 2014, Nshemereirwe et al., 2022, Simard et al., 2013, Morris et al., 1993)*

Chapter3 : Prevalence and Trends of Drinking Water Disinfection byproducts-related Cancers in Addis Ababa, Ethiopia

3.1. Introduction

The type, occurrence, and levels of these DBPs depend on both the disinfectant used and the characteristics of the source water (Gilchrist et al., 2016, Hong et al., 2017, Zhou et al., 2019, Padhi et al., 2015). The most common organic DBPs include trihalomethanes (THMs), haloacetic acids, haloacetonitriles, halo ketones (HKN), and emerging organic DBPs (Ibrahim et al., 2016). Organic DBPs have attracted the attention of researchers due to their frequent discovery and harmful effects (Righi et al., 2014). The hazardous inorganic DBPs, also known as oxy halide DBPs, include bromates (BrO_3^-), chlorite (ClO_2^-), and chlorate (ClO_3^-) (Michalski, 2005, Saradhi et al., 2015, Padhi et al., 2019a). THMs are routinely treated as illustrative of DBPs in human health risk assessments (Mishaqa et al., 2022). 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, leukemia, stomach, and rectum (Pan et al., 2014, Siddique et al., 2015).

Drinking water disinfection is an essential process for protecting public health and providing safe drinking water because it eliminates pathogenic organisms (Aranda-Rodriguez et al., 2017). Chlorine (gaseous or hypochlorite salt solutions), chloramines, ozone, chlorine dioxide, and UV irradiation have all been used as disinfectants (Righi et al., 2012). Although other technologies and resources have been utilized, chlorine is a frequently used and effective disinfectant (Babaei et al., 2015a, Radwan et al., 2021). However, several undesired inorganics and organic DBPs are produced when a disinfectant reacts with natural organic matter (NOM) and anthropogenic organics, including halides in raw water (Righi et al., 2012, Saradhi et al., 2015, Padhi et al., 2019b).

DBP formation is highly reliant on the composition and concentration of NOM, which can be broadly divided into two fractions of hydrophobic (humic) and hydrophilic (non-humic) substances (Zhong et al., 2019).

The type, occurrence, and levels of these DBPs depend on both the disinfectant used and the characteristics of the source water (Gilchrist et al., 2016, Hong et al., 2017, Zhou et al., 2019, Padhi et al., 2015). The most common organic DBPs include trihalomethanes (THMs), haloacetic acids, haloacetonitriles, halo ketones (HKN), and emerging organic DBPs (Ibrahim et al., 2016). Organic DBPs have attracted the attention of researchers due to their frequent discovery and harmful effects (Righi et al., 2014). The hazardous inorganic DBPs, also known as oxy halide DBPs, include bromates (BrO_3^-), chlorite (ClO_2^-), and chlorate (ClO_3^-) (Michalski, 2005, Saradhi et al., 2015, Padhi et al., 2019a). THMs are routinely treated as illustrative of DBPs in human health risk assessments (Mishaqa et al., 2022). 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, leukemia, stomach, and rectum (Pan et al., 2014, Siddique et al., 2015).

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 (Xie, 2003). The MCL for TTHMs was reduced to 80 µg/L by the Stage 1 D-DBP Rule (Chowdhury et al., 2020b), 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 (Ministry of Water and Energy, 2017). 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) (Villanueva et al., 2015).

Studies have indicated that chlorinated water, particularly chlorinated surface water, has an elevated risk of GIT and UB cancers (Garner et al., 2016, Cragle, 1984). 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.

3.2. Methods

3.2.1. 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 ((CSA), 2013). Data were collected on DBRCs cases using ICD-O (International classification of diseases for oncology) – 31 codes (C15-16, C18-20, C64, C67) (WHO, 2013) for incidence in Addis Ababa between 201 2 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 three public hospitals and twelve private facilities (the only cancer treatment centers) in Addis Ababa, Ethiopia (Assefa M AS GT, 2015). All methods were performed in accordance with relevant guidelines and regulations.

3.1.1. Inclusion criteria

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

3.1.2. Exclusion Criteria

Patients registered but with insufficient information about one of the following vital variables like age sex, diagnosis, stage, region, either in the registration book or in the file are not eligible.

3.1.3. 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 1894 DBRCs from 2012 to 2016 and ArcGIS 14 was used for mapping.

3.1.4. 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 3.1). 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 (Addis Ababa Water & Sewerage Authority, 2019b).

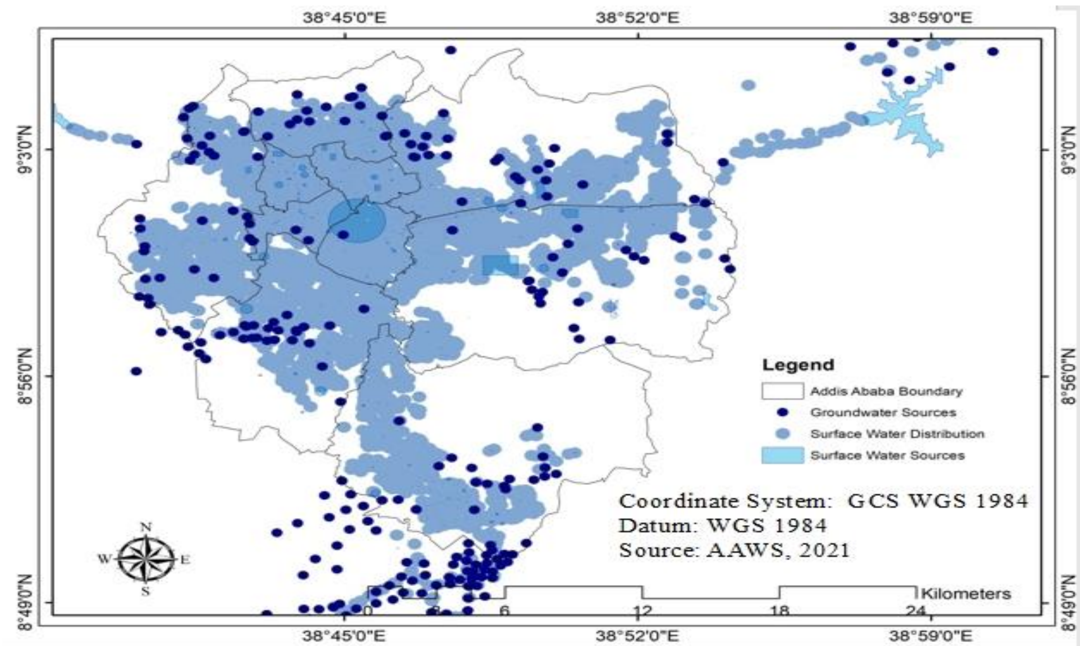


Figure 3.1: Addis Ababa water supply network, Addis Ababa, Ethiopia, 2021

Geocoding was performed on 1894 cancer patients using their address information to identify the type of water source ingested (surface water [chlorinated] or groundwater [non-chlorinated]). Cancer cases with incomplete address information were excluded. Following the distribution network of water sources, each residence was classified as chlorinated or non-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 (Fig. 3.2) & (Fig.3.3) were classified using Addis Ababa's water supply system (Figure 3.1).

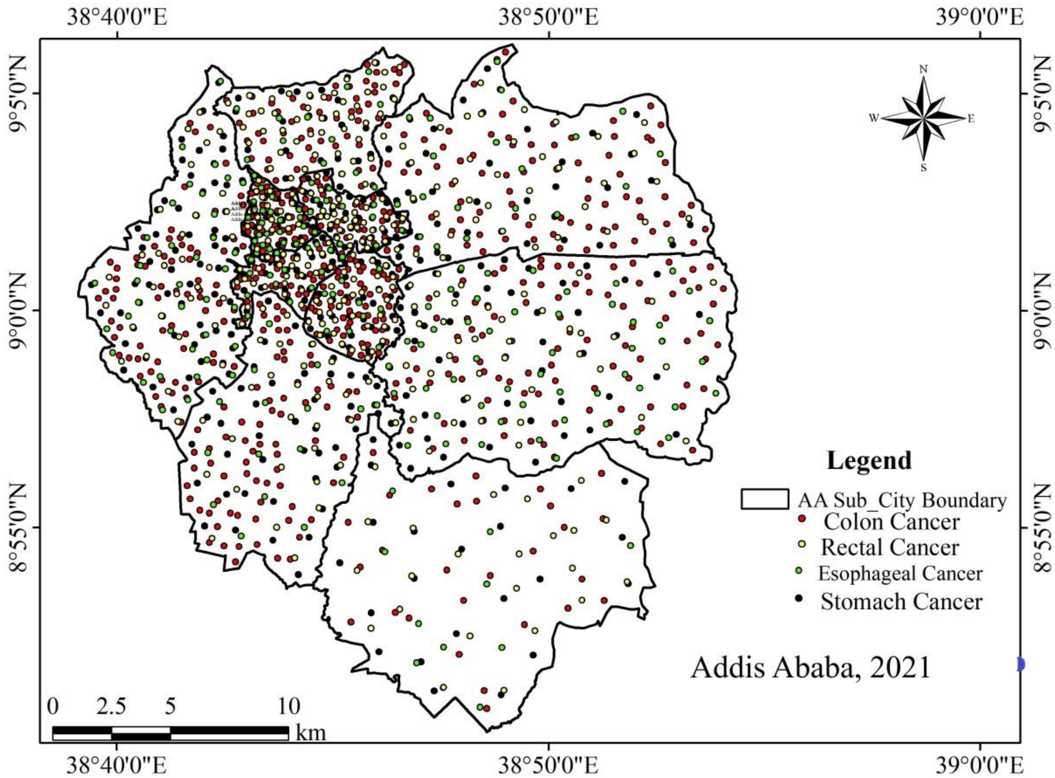


Figure 3.2: GIT-disinfection byproduct-related cancers in Addis Ababa, 2021

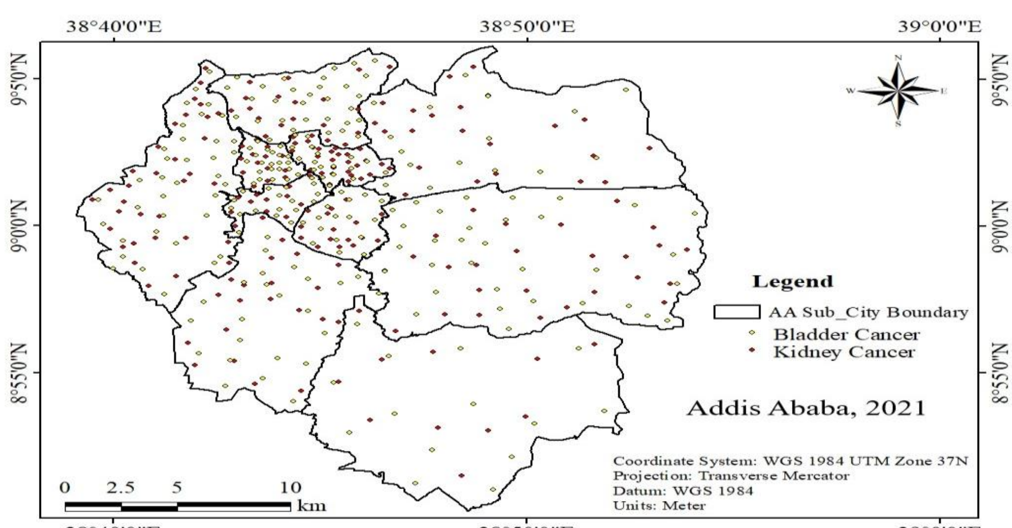


Figure 3.3: UT cancers, Disinfection byproducts-related cancers in Addis Ababa, 2021

3.1.5. Operational Definitions

Chlorinated and unchlorinated water supply

Consumption of surface water (heavily chlorinated) and groundwater (less chlorinated) was used as an acceptable surrogate for comparing exposure vs. non-exposed to DBPs (Morris et al., 1992). 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 (Crump and Guess, 1982).

Disinfection byproduct-related cancers (DBRCs): GIT cancers, namely, colorectal, esophageal, stomach and urological cancers (kidney and bladder cancers), were included in this study.

3.1.6. 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, 3rd edition (ICD-O-32 latest) (WHO, 2013). The data completeness and quality control were checked by the registry. The AACR uses the CanReg5 system for data entry, quality control, and management (Memirie et al., 2018).

3.1.7. 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) (Spss, 2011). To analyze the incidence rate, the total population of Addis Ababa projected for 2017 was used (Central statistical authority 2013b). Negative binomial regression was performed using STATA version 14.0 (Statistical Software: College Station, TX, USA) (StataCorp, 2015) to analyze the incidence rate. Negative Binomial regression analysis was the best fit the model to use when modeling counts data (Zainal Ariffin and Nor Saleha, 2011). The negative binomial regression model fits the data better and accounted for over dispersion better than the Poisson regression model, which assumed the mean and variance were the same (Abdullah et al., 2016). 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.

3.1.8. Ethics approval and informed consent

Ethical approval was obtained from the Institutional Review Board of Natural and Computational Science College of Addis Ababa University. Written permission was obtained from AACR. The Ethical Review Board of Addis Ababa University, Ethiopia, granted the study ethical approval (CNSDO/499/10/2018).

3.2. Results and Discussion

3.2.1. 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 3.1).

Table 3.1: Sociodemographic Characteristics of GIT Cancers from 2012 to 2016, Addis Ababa, Ethiopia, 2021

Variables	Rectal cancer	(%)	Colon Cancer	(%)	Stomach Cancer	(%)	Oesophagus 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

3.2.2. 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 3. 2). The percentages of kidney cancer cases were almost the same in both sexes, a similar finding reported in the US in both sexes (Morris et al., 2017). This could be because both sexes are at equal exposure to potential environmental factors, including drinking water chlorination.

Table 3.2: 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

3.2.3. 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 cancers were 6.1. However, the incidence of CRC in this study was also lower than from Sub-Saharan Africa (SSA) countries (4.04/100,000 population) (Irabor, 2017), middle east and northern Africa in 2016 (8.2/100,000 population) and in Kenya for the period 2013 -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(Benson et al., 2017) (Doci et al., 1991, Jen et al., 1994, Gatta et al., 2000).

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 (Assefa M AS GT, 2015); however, this study incidence was lower than a related report from Kenya, which was 5.2/100,000 (Macharia et al., 2019). With regard to esophageal cancer, its incidence was 1.46, which was higher than a report from 2012-2015 in Addis Ababa (Assefa M AS GT, 2015). Additionally, this study incidence of esophageal cancer was higher than a report from Senegal (0.97%) (Dia et al., 2011); however, this study result of EC was lower than Malawi (27%) (Wolf et al., 2012). This variation could be due to genetic polymorphisms and environmental factors, including drinking water chlorination byproducts (Hendricks and Parker, 2002).

Similarly, urology-based cancer called bladder incidence was observed to be 2.14, which was also slightly higher than the AACR report in 2015 (Assefa M AS GT, 2015). Consistently, this work incidence of BC was comparable with the Eastern Africa report (ASR = 3.3) (Wong et al., 2018b); however, a systematic review by Adeloye D in 2019 showed a higher pooled incidence of bladder cancer (8.8) in Africa, where North Africa is the highest (Adeloye et al., 2019). The GBD (global burden of diseases) also estimated an overall incidence of bladder cancer at 5.3 per 100 000 (Ferlay et al., 2015). 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 (Table 3.3).

Table 3.3: Incidence rate of GIT- and Urology-Based Cancer from 2012 to 2016, 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)

*International classification of Diseases

3.2.4. 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. 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 (Arnold et al., 2017). However, esophageal cancer significantly decreased from the baseline year 2012 to 2016. Even though a contrary study reported that Africa, including Ethiopia, is expected to surpass the incidence of Europe (Malhotra GK, 2017;) (Table 3. 4) (Fig. 3.4).

Table 3.4: Trend test of GIT and urology cancers in Addis Ababa, 2016, 2021

Variable	Regression coefficient	P value	95%CI
Colon	10.3	0.034	1.49-19.10
Rectal	11.9	0.064	1.31-25.10
Stomach	10.5	0.079	2.26-23.26
Esophagus	-6.5	0.018	-10.85- (-2.14)
Kidney cancer	3.8	0.095	1.23-8.83
Bladder cancer	3.1	0.509	10.00-16.21

In the same context, the incidence of kidney cancer showed a rising trend in this study (Figure 3.2.1(2). Another population-based study also highlighted that the temporal trends of kidney cancer are increased(Wong et al., 2017). 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 (Adeloye et al., 2019) (Fig.3.5).

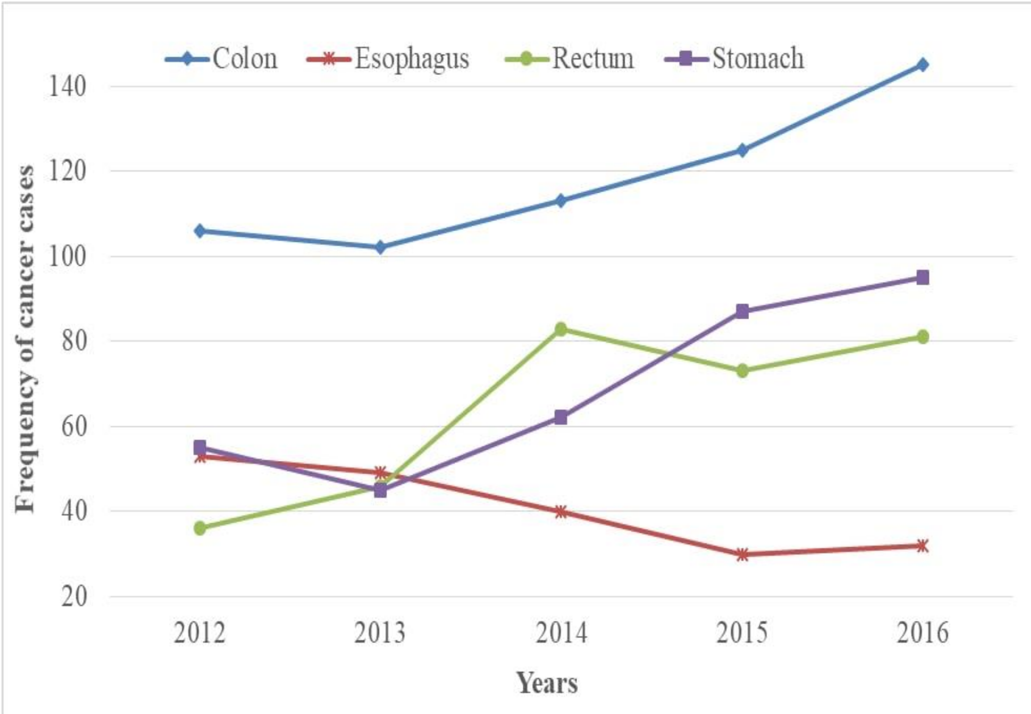


Figure 3.4: Trend of GIT cancers Addis Ababa, 2012-2016, Addis Ababa, Ethiopia

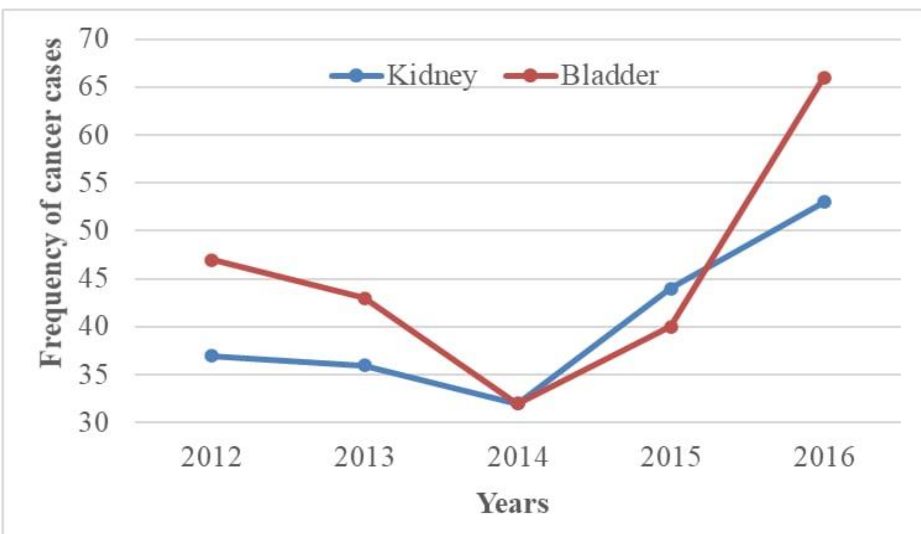


Figure 3.5: Trends of urology-based cancers from 2012 to 2016, Addis Ababa, Ethiopia

3.2.5. 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 3. 5).

Table 3.5: Correlation of DBRCs with sociodemographic characteristics, Addis Ababa, 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 -2016

3.2.6. Proportion of consumption of chlorinated surface and non-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. The proportion of chlorinated surface water utilization by the GIT cancer patients in this study was high. Other related studies reported similar findings (Doyle et al., 1997, Sasada et al., 2015, Rahman et al., 2014) (Table 3.6). However, inconclusive findings were reported from other studies (King et al., 2000, Young et al., 1981, Carlo and Mettlin, 1980, Richardson et al., 2007). This variability could be due to differences in exposure assessment.

In addition, approximately 57.1% and 54% of the kidney and bladder cancer patients, respectively, used chlorinated surface water (Table 3.6). Similar observations were reported in different parts of the world(Jones et al., 2017, Young et al., 1981); however, contradictory findings were reported in other studies(Ackerson et al., 2019, Rahman et al., 2014, Helte et al., 2022, Temraz et al., 2019). In general, the prevalence of DBRCs is higher in communities supplied with chlorinated surface water than in those supplied with unchlorinated groundwater. Another study conducted in Norway showed that chlorination was associated with a 20-40% increase in colorectal cancer rates (FLATEN, 1992), and other related studies are also in line with this study (King et al., 2000, Sasada et al., 2015, Cancer, 1991).

Table 3.6 : Proportion of chlorinated surface water and non-chlorinated groundwater consumed by patients in Addis Ababa, Ethiopia, 2021

Name of cancer	**Consumption of chlorinated water with 95%CI**	**Consumption of non-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

3.3. 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. The prevalence of DBRCs was higher among the 35-54 age category than in the others. Further study is required to validate the association between DBRCs and the chlorination of water

Chapter4 : Drinking Water Source, Chlorination, and Colorectal Cancer: A Matched Case-Control Study in Ethiopia

4.1. Introduction

Colorectal cancer (CRC) represents nearly 10% of all cancer incidences that showed an increasing rate over the last two decades (Villanueva et al., 2017). Studies from African and Asian countries have shown that the annual diagnosis of CRC is increasing (Abdulkareem et al., 2008, Consortium, 2008). Evidence also indicates that the incidence of the disease has increased in most developing countries due to the emergence of potential risk factors such as smoking, obesity, an unhealthy diet, and lifetime exposure to drinking water chlorination by-products (Babaei et al., 2015b, Fitzmaurice et al., 2015, Fitzmaurice et al., 2017, Evlampidou et al., 2020). However, high dietary intake of meat was not identified as risk factor in these countries because of the limited supply to the larger population (Schmitz and Kavallari, 2009, Co-operation and Development, 2016, Abou-Zeid et al., 2002).

Chlorination has been the primary treatment process to improve the quality of drinking water (Babaei et al., 2015b). However, chlorine, as a disinfectant in drinking water, is known to produce trihalomethanes (THMs) (Rook and JJ, 1974). THMs in chlorinated drinking water may cause health threats due to its carcinogenicity (Kumari et al., 2015). In water treatment utilities, DBPs, like chloroform, bromate, trichloroacetic acid, and bromodichloromethane are mostly formed through the reaction of chlorine with natural organic matter (NOM). The DBPs are divided into two categories: hydrophilic and hydrophobic (Villanueva et al., 2017).

THMs were regulated by the USEPA shortly after their discovery in disinfected drinking water, with a maximum contaminant limit (MCL) of 100 µg/l for TTHM (Wang et al., 2015). The Stage 1 D-DBP Rule (Brass, 2000) reduced the MCL for TTHM to 80 g/l and set MCLs of 60 g/L, 10 gL–1, and 1000 gL–1 for HAAs, bromate, and chlorite, respectively. Although the maximum acceptable concentrations (MACs) for TTHM and HAAs are 100 g/L and 80 g/L, respectively, and more DBP species are controlled in Canada (Canada, 2017), the standards are similar to those in the United States. The South African National Standards has set the maximum contaminant levels (MCLs) for total THMs in drinking tap water at 300 µg/L (Mashau et al., 2021). Trihalomethanes (THMs) and haloacetic acids (HAAs), which occur in high amounts in drinking water, are the most commonly investigated and quantified DBPs. THMs are used as a proxy by drinking water utilities in several countries, including Southern Africa, the United States, and Canada, to monitor and control DBPs in drinking water distribution systems (Richardson et al., 2007).

In Ethiopia, water treatment utilities use chlorine for the disinfection of water for public distribution (Ethiopia et al., 2017). However, drinking water utilities in Ethiopia in general and in Addis Ababa in particular not measured drinking water DBPs at all. There is also no monitoring and controlling system of DBPs in drinking water distribution systems in Ethiopia. In addition, the water utilities in Ethiopia not set the maximum allowed concentrations (MAC) of disinfection byproducts for total THMs and other DBPs. Therefore, in the absence of historical data on the level of chlorination byproducts (DBPs), estimates of past exposure have been based on previous information about the water sources (ground and surface water sources) (Villanueva et al., 2015).

Studies showed that people drinking chlorinated water, particularly chlorinated surface water, had increased risk of colon and rectal cancers (Chowdhury et al., 2020a, Lau et al., 2020). Several case-control studies on exposure to chlorination by-products reported positive findings for colon and rectal cancers but the interpretation was limited (Oliver, 2017, Lawrence et al., 1984, Parbery, 2016). Case-control studies of cases related with drinking water chlorination have the potential to overcome the limitations of the early studies, but relatively few have been conducted (Water, 2013, Cragle, 1984, Rahman et al., 2010). Moreover, there is no available study on the association between disinfection byproducts (DBPs) in chlorinated drinking water and colorectal cancer

(CRC) in Ethiopia. Hence, this study aimed to determine the effects of drinking chlorinated water on CRC.

4.2. Methods

4.2.1. Study Area and population

This study was conducted in Tikur Anbessa Specialized Hospital (TASH), College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia. TASH serves as a cancer registry and treatment center for the country. The departments in TASH are gynecology and obstetrics, internal medicine, surgery, pediatrics, radiotherapy, adult oncology, pediatric oncology /hematology, nuclear medicine, psychiatry, laboratory, orthopedics pharmacy and others (Abate et al., 2016). Incident CRC cases were collected from adult oncology and pediatric oncology /hematology respectively. In 2017, the Central Statistical Agency (CSA) projected the population of Addis Ababa to 3,434,000, of which 1,624,999 were males (Central statistical authority 2013a). The target of this study was CRC cases and controls residing in Addis Ababa, Ethiopia (Figure 4.1).

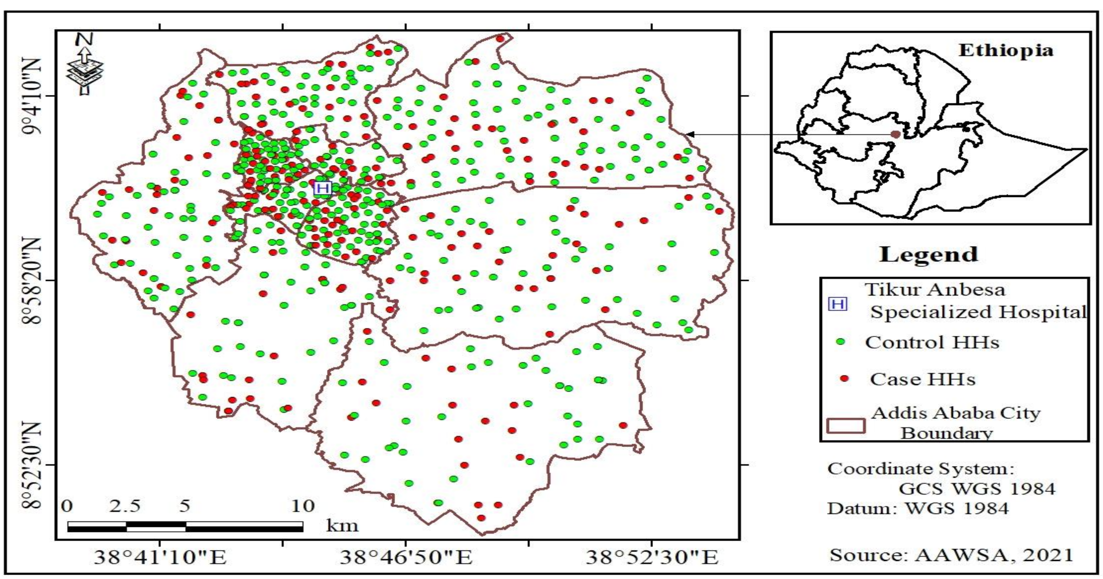


Figure 4.1: Location of Cases households (HHs), Controls households and Study Hospital, 2021

4.2.2. Study design and period

A hospital-based matched case-control study design was employed from June 2020 to May 2021. Histologically confirmed CRC cases were included in the present analysis (ICD-O (C18, C19, C 20)) (Assefa M AS GT, 2015).

4.2.3. Sample Size Determination

The sample size was calculated using a matched case-control study design (Schlesselman, 1982a) by considering the pitman efficiency assumption of the matched pair sample size (Ury, 1975). A matched sample size of 224 pairs using individual matching (1 case to 2 controls: which means 224 cases: 448 controls) was selected by taking into account 1) a type I error of 5%; 2) a probability of type II error 10%; 3) a power of 90%; 4) assumption that 30% of the control households use non-chlorinated water supply in Addis Ababa (Schlesselman, 1982a); 5) expected odds ratio of 2; and 6) a 15 % non-response rate. A 50% of matched pair samples of case and control (112 cases: 224 controls) was taken as the minimum requirement for exposure discordant pairs for testing disease and exposure association (McNemar, 1947). Equations ((7)(8)(9) used to calculate the sample size.

Let $P_\partial\,(P_\partial + \delta)$ and P_∂ be the prevalence of the exposure factor in case and control groups respectively. Thus, $\delta = {(OR-1)P_\partial\,(1-P_\partial)}\big/{[1-P_\partial + P_\partial\,(OR)]}$, where OR is the odds ratio

between cases and controls. For this study with 2 controls per case, conditioned on each matched set with total of m individuals (m ranging from 1 to m exposed), we have than $n_{3,m-1}$, the number of matched sets in which the case and $m-1$controls were exposed is binomially distributed with probability ${m(OR)}\big/{[m(OR)+M-m]}$. Thus, under hypothesis OR=1

$$\left[\left[{\left[\sum_{m=1}^{M}(n_{1,m-3}-T_m m)\right]}\Big/{(M+1)}\right]\right]^2 \Bigg/ \left[{\left[\sum_{m=1}^{M} T_m m(M-m+1)\right]}\Big/{(M+1)^2}\right] \quad (7)$$

Where T_m is the number of matched sets with total individual exposures equal to m, and this statistic given by formula (7) has X^2 distribution with one degree of freedom. Using the input given above Schlesselman and Stolley (Schlesselman, 1982b) suggested the required number of cases, n, given as

$$n = {(M+1)\left[Z_{\alpha/2}(1+OR) + 2Z_{\beta}\sqrt{OR}\right]^2} \Big/ {[2M(OR^2-1)\,s(f,OR)]} \tag{8}$$

Where $s(f,OR) = {(OR-1)f(1-f)} \Big/ {[(1-f)+f(OR)]}$ and f is the prevalence of the exposure factor in the population is approximately equal to P_{∂} .

Assuming a sequence of δ such that $\delta \to 0$ but $\delta\sqrt{n}$ tends to be a constant Taylor (Lachin, 2008) the number of cases to be

$$n = V\left(Z_{\alpha/2} + SZ_{\beta}\right)^2 \Big/ {(M\delta\,)^2} \tag{9}$$

Where $V = M(M-1)\,f(1-f) + \delta M(1-2f)$, and

$$S^2 = {[M(M+1)f(1-f) + \delta M^2(1-2f) - (\delta M^2)]} \big/ {V}$$

4.2.4. Inclusion and exclusion criteria

In both case and control, study participants were in the age range of 20–85 years; residents of Addis Ababa for at least ten years before recruitment and lived at the time of contact and answered study questionnaire. Only CRC cases diagnosed from June 2020 to May 2021 with histological confirmation (C18, C19, C 20), without previous cancer history were included.

4.2.5. Matching of Cases and Controls

Controls were both individual and frequency matched to cases by sex and age (± 5 years) ensuring two controls of the same sex and a 5-year interval for each case (Ury, 1975). In addition, controls were matched based on their residence location.

4.2.6. Case and Control Selection

Cases were interviewed directly after diagnosis and identified through active checkups and periodic visits to hospital departments (adult oncology and pediatric oncology/hematology).

To identify population control subjects, households randomly selected from the ten sub cities Addis Ababa. The matching population controls sample size (428) randomly selected from the ten sub cities in Addis Ababa. Controls were selected from the general population per each sub cities (the largest city under Addis Ababa) and "woredas" (the smallest administrative unit under the sub city) (Fig. 4.2).

The population controls randomly selected from the same residence area for the cases per each sub city. Then the allocated sample size selected from identified household in the "woredas" using matching criteria. Simple random sampling technique was used to select the study participants from selected households (per each woreda). If the household was not had the matching person after interview or refused to participate, the next households were approached. The frequency matching was done based on the age and sex distribution of cases. Person with previous cancer diagnosis was excluded from consideration as controls.

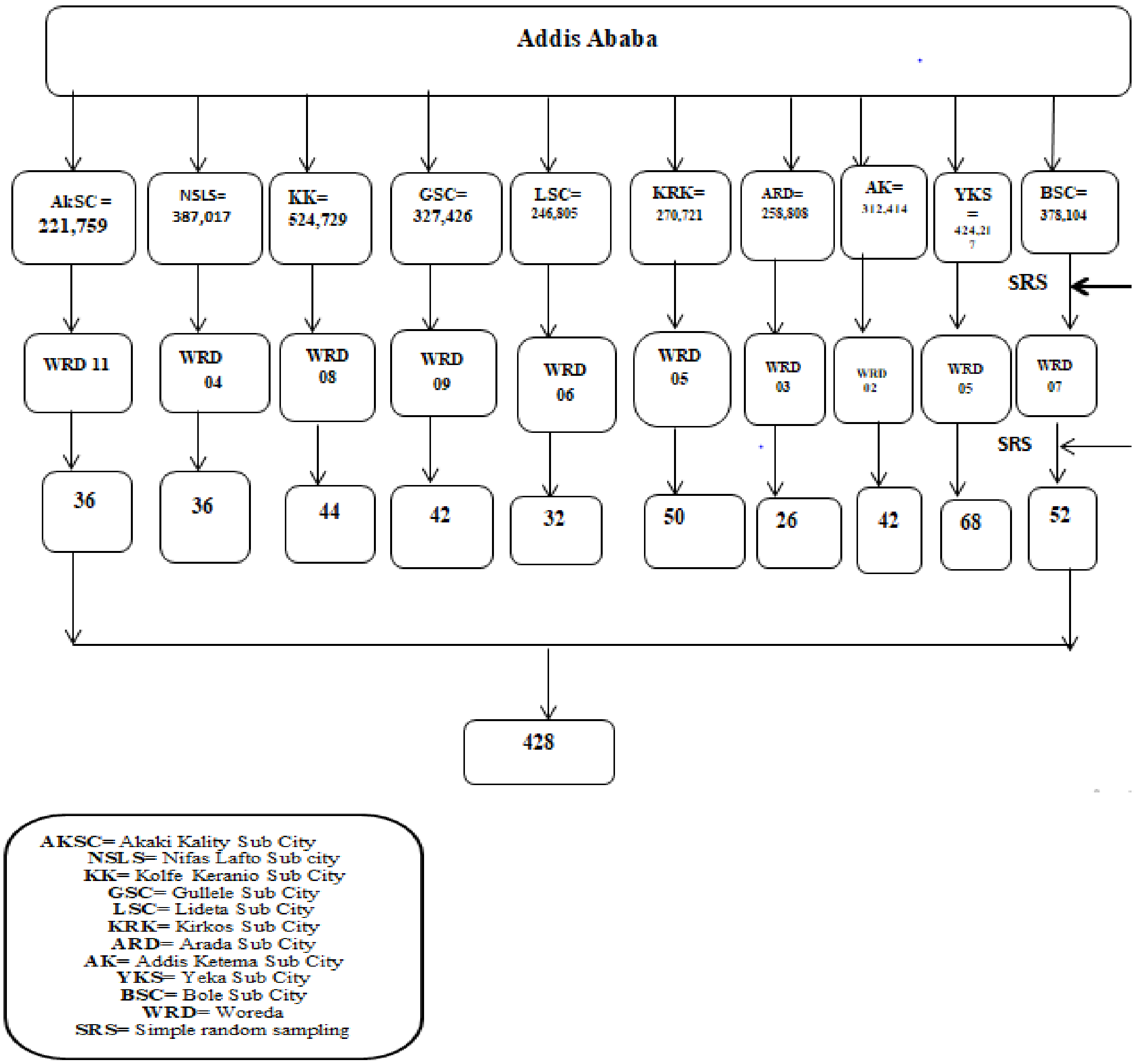


Figure 4.2: Population control selection procedure of colorectal cancer, case control study, Addis Ababa, Ethiopia, 2021

4.2.7. Data Collection

Hospital-based survey data was collected using a standardized and pre-tested questionnaire) and ArcGIS 14 was used for mapping. The questionnaire was adapted from different works of literature and /or developed from other similar studies (Villanueva et al., 2006a, YOUNG et al., 1987, Villanueva et al., 2017, Feyesa et al., 2020, Morris et al., 1992, Crump and Guess, 1982). Some variables signifying these factors were also coded using the operational definitions (Table 4.1).

Table 4.1: Operational definitions for coding variables included in the analysis, Addis Ababa, Ethiopia, 2021

Variables	**Variables Operational definitions**
Chlorinated versus non-chlorinated water supply	Consumption of surface water (heavily chlorinated) and groundwater (less chlorinated) was used as an acceptable surrogate for comparing exposure versus non-exposure to chlorine disinfection by products (DBPs) (Grellier, 2018, Morris et al., 1992).
Regular showering of the body	Categorical response, times per week (≥ 1 or < 1) for the last one year before interview.
Type of water used for showering	Categorical (hot /cold waters) for the last one year before interview.
Piped water supply	Municipally piped water at private and public taps (WHO, 2014). In this study, public water taps included Bono and tanker taps, whereas one household owned a private tap.
Year at place of longest residence	Categorical response, living in years (≥ 40 or < 40)
Swimming History	Categorical (yes /no) for the last one year before interview.
Eggs consumption	Categorical (yes /no) for the last one year before interview.
Daily per capita water consumption (l/c/d)	Volume of tap water consumed was calculated from the reported daily consumption of water and of beverages or foods made with water, 1 year before the interview.
Family history of CRC	Self-reported malignant tumours (yes/no)
Smoking	Categorical (Ever / never) smoke cigarrete) for the last one year before interview.
Herbal drink (times /week)	Categorical (≥ 1 /<1) for the last one year before interview.
Saturated oil consumption (times /week)	Categorical, times per week, (≥ 1 /<1) for the last one year before interview.
Egg's consumption (times /week)	Categorical (≥ 1 /<1) for the last one year before interview.
Meat ingestion (times /week)	Categorical (≥ 1 /<1) for the last one year before interview.
Milk consumption (times /week)	Categorical (≥ 1 /<1) for the last one year before interview.
Body mass index(kg/m2)	Categorical (Low (<24); Medium (24-29) and High (>29) based on the weight 1 year before the interview
Usual physical exercise (times/week)	Categorical (≥ 1 /<1) for the last one year before interview.
Alcohol (drinks/week)	Categorical (0 versus ≥ 8 times) for the last one year before interview.
Coffee (cups/week)	Categorical (0 versus ≥ 21 times) for the last one year before interview.
Tea (cups /week)	Categorical (0 versus ≥ 21 times) for the last one year before interview.

For both cases and controls, twelve trained Oncology professionals (nurses) administered the survey by interviewing study participants using a pre-tested structured questionnaire. Interviewers were health professionals with BSc and above and fluent speaker of Amharic trained on the tools. A three days training was given for the data collectors and supervisors to adhere to the objective of the study. Additionally, COVID-19 prevention protocol training was given. The tools were also pretested (5 % of the sample) in the health care facility (non –selected facility). Based on the pretest findings the tools were validated. The final number of total cases and controls and the water types used are described in Figure 4. 3

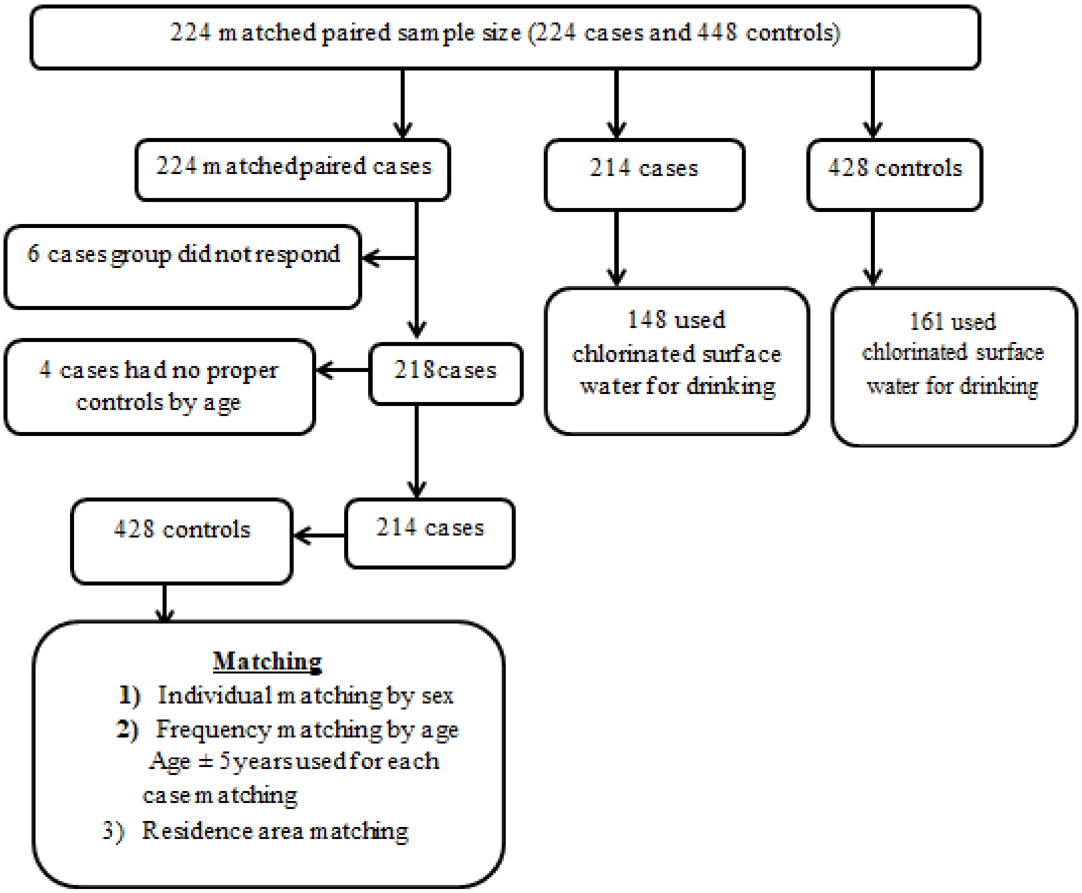


Figure 4.3: Facility-based Matched case-control study flow chart of Addis Ababa, Ethiopia, 2021.

4.2.8. Water Type Verification

To identify the type of water sources used by patients, geocoding was done immediately after data collection of cases using their residential information. Administrative units, roads' lines, and spatial datasets were used for geocoding. The administrative unit data sets included administrative boundaries as areas and allocation centers as points for sub-cities (the largest administrative unit in Addis Ababa City) and woredas (the least administrative unit per sub-city) and geo-referencing of control households were also done. The water supply system of both cases and controls were identified using Geographic Information System (GIS) data from the Addis Ababa Water and Sewerage Authority (AAWSA) water supply network (Addis Ababa Water & Sewerage Authority, 2018). Following the water source distribution network, each household was classified either as chlorinated or non-chlorinated. Then, all cases and controls were classified into chlorinated surface water and non-chlorinated groundwater. AAWSA assisted in the identification of some households where there was a difficulty in distinguishing the source of water supply. The water supply operations in Addis Ababa contain 13 sub-systems. The chlorinated surface water sources are located in the western and eastern parts of the city. The groundwater sources (non-chlorinated) are located in the southeastern and various sites of the Addis Ababa (Addis Ababa Water & Sewerage Authority, 2019a) (Figure 4.4).

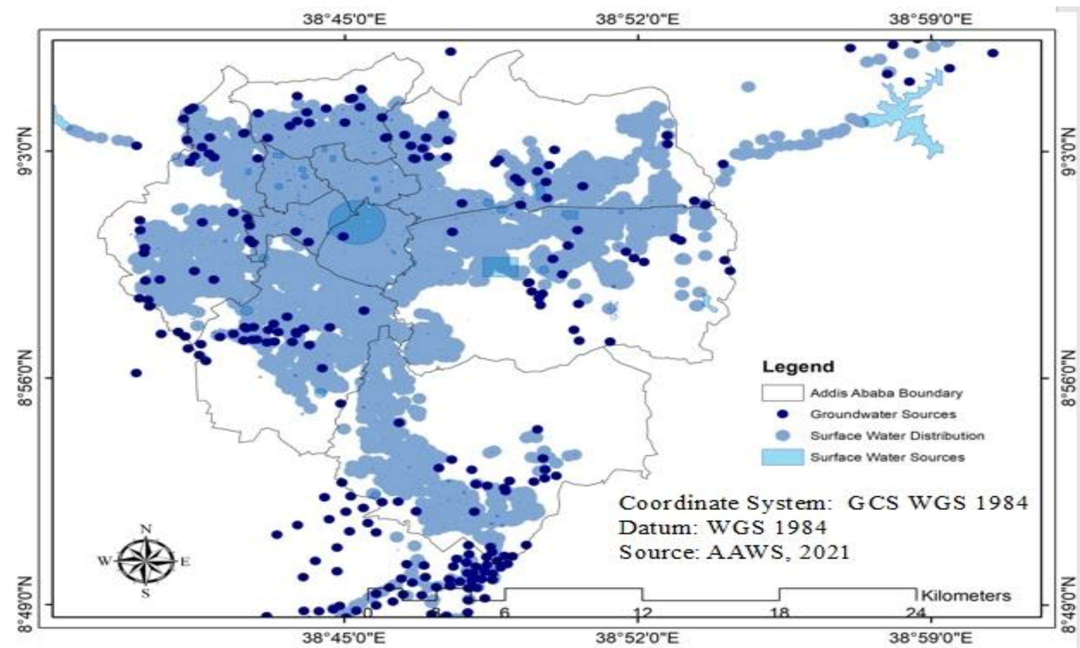


Figure 4.4: Water supply networks of Addis Ababa, Ethiopia, 2021

4.2.9. Dietary History before Diagnosis

Data on major recognized diets related with colorectal cancers were collected by structured interviews using semi-quantitative food frequency questionnaire (FFQ) previously used in a study in Ethiopia and other countries (Abate et al., 2016, YOUNG et al., 1987). Usual dietary intake of the year before the interview was assessed. The FFQ included egg, meat, fish, fat-rich food, fruits, vegetables, sweet food, and beverages. Frequency variables were labeled as “at least once a day”, "4–6 times per week", "2–3 times per week", "once a week", "2–3 times per month", "once a month", and "never or ever in a year (Feyesa et al., 2020)" (Table 4.1).

4.2.10. Survey of Shower Water Temperature

A survey of shower water temperature was conducted in the homes of chosen patients and controls. The study included 45 individuals from the case households and 45 people from the control households. First, the participants' shower water temperature was adjusted as usual in their homes. The water that had been drained from the shower was then collected in a bucket. In addition, household with no facility of shower were requested to bring the type of water used for shower. Finally, the investigator took the temperature of the water with a thermometer. The sample size was proportional to the number of cases and controls (1:1).

4.2.11. Variables and measurements

The outcome variable was CRC. Water supply type (chlorinated surface water or non-chlorinated groundwater) was the primary exposure variable. The remaining variables were covariates (Table 4.1).

4.2.12. Statistical analysis

Data entry and Data analysis was conducted using EpiData Version 3.1 software (EpiData Association, Odense, Denmark) and STATA version 14.0 (Statistical Software: College Station, TX, USA) respectively. For continuous variables, descriptive statistics [n (percent)] were produced, as well as median IQR (interquartile range). For categorical variables, Pearson Chi-square and Fisher's exact tests were employed to assess associations. All reported p-values were two-tailed and considered statistically significant if $p < 0.05$. Conditional Logistic regression model was used to estimate matched odds ratios (unadjusted and adjusted odds ratios. Variables with $p < 0.2$ from bivariate analyses and variables with known biological plausibility were included in the multivariable model. Our analysis did not take account of age and sex, as both were used as matching variables. Cochran Mantel–Haenszel stratified analyses were used to exclude cofactors, and to ascertain and designate effect modifiers. Mantel–Haenszel test of equality of stratum-specific ORs was used to detect effect modifiers. First, the equality of stratum-specific ORs was tested to confirm significant changes, indicating that the exposure and other factors were modifying the effect. The presence of confounding was next investigated if the results were not different. By correcting the effects of the third variable and the crude estimate, the Mantel–Haenszel test provided a single weighed estimate of the predictor. The presence of confounding was then determined by measuring the difference between the crude and adjusted ORs. The evidence of confounding was confirmed using a relative difference in the effect estimate with a limit of 10% (Aschengrau and Seage, 2013). The variables were set a priori to take place, if an interaction term between smoking or meat ingestion and each of the reported variables was significant.

4.2.13. Ethics approval and informed consent

Ethical approval was obtained from the Institutional Review Board of Natural and Computational Science College of Addis Ababa University. Written consent was obtained from both cases and controls prior to the interview.

4.3. Results and Discussion

4.3.1. Socio-demographic characteristics of cases and controls

The response rate for fully matched paired data was 95.5% (214 matched pairs). Ten cases did not match any controls (Fig 4.3). Median ages of the cases were 50 years (Inter Quartile Range (IQR): 40 to 61 years) and of controls 49 years (IQR: 40 to 60 years). The median monthly income was $ 125.0 (IQR: 31.3 to 187.5 USD) and $ 136.6(IQR: 71.9 to 250.0 USD) for the case and control respectively (Table 4.2).

Table 4.2: Characteristics of case and control of study participants in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2021.

Variables	**Case (n = 214)**	**Control (n = 428)**
Age (years) (Median and IQR)	50 (41 - 61)	49(40 - 60)
Monthly income in USD[1](Median and IQR)	125.0(31.3 -187.5)	136.5(71.8,250.0)
Last two years drinking water consumption(l/c/d) (Median and IQR)	1.5 (1.5-2.0)	1.5 (1.5-2.0)
Years at the place of longest residence (Median and IQR)	40 (30-47)	40 (30-50)
BMI (mean $\pm$SD)	22.54±3.70	24.88±3.24

IQR, interquartile range; l/c/d, liter per capita per day; $US, United States Dollars. BMI; Body mass index

[1]The average exchange rate of $ US = 38.0 ETB (Ethiopian birr) from June 2020 to May 2021

4.3.2. Sociodemographic Characteristics of cases and controls

Regarding the age distribution of cases and controls, 133 (20.7%) were between 20–39 years old, 403(62.8%) between 40–64 years old, 83 (12.9%) between 65–74 years old, and 23 (3.5 %) above 75 years old. Out of 214 cases, 43.9 %, and out of 428 controls, 45.3% were males. About 188 (29.3%) of the cases and controls have stable source of income (Table 4.3).

Table 4.3: Sociodemographic Characteristics of cases and controls in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 202

Variables	**Cases (n=214) n, %**	**Controls (n=428) n, %**	**Total n, %**	**Pearson's X^2**
Age category (years)				
20-39	38,17.8	95, 22.2	133,20.7	0.610
40-64	138, 64.5	265, 61.9	403, 62.8,	
65-74	30, 14.0	53,12.4	83, 12.9	
≥ 75	8, 3.7	15, 3.5	23, 3.5	
Sex				
Men	94, 43.9	194, 45.3	288, 44.9	0.736
Women	120,56.1	234, 54.7	354,55.1	
Educational level				
Lower [a]	129,0.58	244, 0.57	373,0.58	0.428
Higher	85,0.40	184, 0.43	269,0.42	
Marital status				
Unmarried	85 , 39.7	173, 40.4	258,40.2	0.864
Married	129, 60.3	255, 59.6	384, 59.8	
Stable source of income				
Yes	59,27.6	129,30.1	188, 29.3	0.500
No	155,72.4	299, 69.9	454, 70.7	
Employment status				
Yes	122, 57.0	251, 58.6	373, 58.1	0.692
No	92, 42.9	177, 41.4	269, 41.9	
Average monthly income				
Greater than 126 ($US)	87, 46.3	177, 51.9	264, 49.9	0.215
Less than 126(($US)	101 ,53.7	164, 48.1	265, 50.1	

[a] includes from not capable to read or write based on self-reporting

4.3.3. Water supply type, chlorination status and residence history

Around 92% of cases and 73.4% of controls consumed water from private taps, whereas 26.6% of controls and 7.9% of cases fetched water from public taps. Similarly, about two–thirds (69.2%) of the cases and one-third of the controls (37.6%) used chlorinated water. About 96.7% of the cases and 93.2% controls used shower. In addition, 54.2% and 41.6 % of the cases and controls had lived more than 40 years at their place of current residence respectively (Table 4.4).

Table 4.4: Water supply type, chlorination status and residence history in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2021

Variable	**Cases (n=224) n, %**	**Controls (n=428) n, %**	**Total n, %**	**Pearson's X^2**
Piped water supply				
Private tap	197, 92.1	314, 73.4	511, 79.6	0.001
Public tap	17, 7.9	114, 26.6	131, 20.4	
Chlorination status				
Chlorinated surface water	148, 69.2	161, 37.6	309, 48.1	0.001
non-chlorinated groundwater	66, 30.8	267, 62.4	333, 51.9	
Drinking of water (litter/day)				
Greater than 1.5	114, 53.7	223, 52.1	337, 52.5	0.780
Less than 1.5	100, (46.7	205, 47.9	305,47.5	
Regular showering				
Yes	207, 96.7	399, 93.2	606, 93.2	0.169
No	7, 3.3	29, 6.8	36, 6.7	
Water used for shower				
Hot water	86, 40.2	59,13.8	145, 22.6	0.001
Cold water	128,59.8	369,86.2	497, 77.4	
Swimming history				
Ever	106, 49.5	134, 31.3	240, 37.4	0.001
Never	108, 50.5	294, 68.7	402, 62.6	
Types of swimming				
Outdoor	58, 37.9	95,62.1	153, 63.7	
Indoor	49, 56.3	38,43.7	87, 36.3	0.567
Years at place of current residence				
≥ 40 years	116, 54.2	178, 41.6	294, 45.8	0.002
< 40 years	98, 45.8	250, 58.4	348, 54.2	

4.3.4. Health related characteristics and dietary information

Around 65.4 % of the cases and 41.1% of the controls had high BMI respectively. Similarly, 13.1%, and 21.3 % the cases and controls ever smoked cigarette respectively. Almost two thirds of the cases and controls drank coffee about 20 times per week. Around 22% of the cases and 27 % of the controls had usual exercise at least once a week. About 82.5% of the women in the cases and 85.6% in the controls were pregnant at least once in the last one year. Around 50% of both cases and controls took sweet food at least once per week for the last one year. Almost 39% of the cases and 14% of the controls consumed meat at least once a week for last one year. About 57% of both cases and controls ate fruit at least once a week for last one year (Table 4.5).

Table 4.5 : Health related characteristics and dietary information in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2021

Variable	**Cases (n=214) n, %**	**Controls (n=428) n, % (95% CI)**	**Total n, % (95% CI)**	**Pearson's X^2/ ****
Regular saturated fat				
Yes	134, 62.6	289, 67.5	423, 65.9	0.216
No	80, 37.3	139, 32.5	219, 34.1	
Meat ingestion (times/week)				
≥ 1	84,39.3	60, 14.0	144, 22.4	0.001
< 1	130, 60.7	368, 85.9	498, 77.6	
Number of pregnancies *				
≥ 1	99, 82.5	199, 85.8	298, 84.6	0.419
< 1	21, 17.5	33, 14.2	54, 15.3	
Drinking tea (times/week)				
≥ 8	152, 71.0	318, 74.3	470, 73.2	0.378
0	62,28.9	110, 25.7	172, 26.7	
Fruit intake (times/week)				
≥ 1	121, 56.5	242,56.5	363, 56.5	0.990
< 1	93, 43.4	186,43.4	279, 43.4	
Vegetable intake (times/week)				
≥ 1	138,64.5	268,62.6	406, 63.2	0.643
< 1	76,35.5	160,37.4	236, 36.7	
Coffee drinking status				
≥ 21 times/week	123, 57.4	280,65.4	403, 62.8	0.050
0	91 ,42.5	148, 34.6	239, 37.2	
Egg's consumption (times/week)				
≥ 1	62, 28.9	147, 34.3	209, 32.6	0.171
< 1	152,71.0	281, 65.7	433,67.4	

*The total not adds to

Table 4.5**(Continued)**

Variable	**Cases (n=214) n, %**	**Controls(n=428) n, %**	**Total n, %**	**Pearson's X^2**
Previous GITD				
Yes	32, 14.9	5, 1.2	38, 5.7	0.231
No	182, 85.1	423, 98.8	605, 94.2	
Family history of CRC				
Yes	45, 21.0	169, 39.5	214,33.3	0.890
No	169,78.9	259, 60.5	509,66.7	
BMI (kg/m^2)				
Low (<25)	165, 77.1	230, 53.70	395, 61.5	0.067
Medium (25-29)	41, 19.6	158, 36.9	199, 30.1	
High (>29)	8, 3.7	40, 9.4	48, 7.5	
Exercise (times/week)				
≥ 1	47, 22.0	117, 27.3	164, 25.5	0.141
< 1	167, 78.0	311, 72.7	498, 74.5	
Smoking Status				
Ever	28, 13.1	91, 21.3	119, 18.5	0.012
Never	186, 86.9	337, 78.7	523, 81.5	
Alcohol (drinks/week)				
≥ 8 times	101, 47.2	228, 53.3	329, 51.2	0.147
0	113, 52.8	200, 46.7	313, 48.8	
Milk (drinks/week)				
≥ 1	129 ,60.3	244,57.0	373,58.0	0.428
< 1	85, 39.7	184,42.9	269, 41.9	

BMI; Body mass index based on the weight 1 year before the interview. GITD: Gastrointestinal tract diseases

4.3.5. Shower temperature

A total of 90 households (45 case households and 45 control households) were used to measure shower temperature. The mean shower temperature among cases and controls were 28.8 and 22.5 °C respectively (Table 4.6). According to one way analysis of variance (ANOVA) depicted that shower temperature does influence colorectal cancers (Table 4.7).

Table 4.6: Measured Shower temperature of cases and control households of colorectal cancers patients, Addis Ababa, Ethiopia, 2021(n= 90).

	Measured Temperature(°C)		
Temperature(°C)	**Freq.**	**per cent**	**Cum.**
17.7	2	2.22	2.22
17.9	1	1.11	3.33
18.4	1	1.11	4.44
18.5	2	2.22	6.67
18.6	1	1.11	7.78
18.7	3	3.33	11.11
18.8	6	6.67	17.78
18.9	6	6.67	24.44
19.3	1	1.11	25.56
19.5	5	5.56	31.11
19.6	2	2.22	33.33
19.7	1	1.11	34.44
19.8	3	3.33	37.78
19.9	3	3.33	41.11
20.1	1	1.11	42.22
20.2	1	1.11	43.33
20.4	1	1.11	44.44
20.5	1	1.11	45.56
20.6	1	1.11	46.67
21.2	1	1.11	47.78
21.5	1	1.11	48.89
22.2	5	5.56	54.44
22.5	3	3.33	57.78
22.9	1	1.11	58.89
23.2	1	1.11	60.00
23.3	2	2.22	62.22
23.5	3	3.33	65.56
23.8	1	1.11	66.67
24.4	1	1.11	67.78
25.5	2	2.22	70.00
27.7	1	1.11	71.11
27.9	1	1.11	72.22
33.5	3	3.33	75.56
33.9	1	1.11	76.67
34.5	1	1.11	77.78
36.7	1	1.11	78.89
37.7	1	1.11	80.00
37.8	1	1.11	81.11
37.9	2	2.22	83.33
38.3	1	1.11	84.44
38.4	1	1.11	85.56
38.6	1	1.11	86.67
38.8	1	1.11	87.78
39.3	1	1.11	88.89
39.9	2	2.22	91.11
40.3	1	1.11	92.22
40.5	1	1.11	93.33
41.4	1	1.11	94.44
41.5	1	1.11	95.56
42.2	3	3.33	98.89
42.5	1	1.11	100.00
Total	**90**	**100.00**	

Table 4.7: One way analysis of variance (ANOVA) to look for mean difference of measured temperature in Addis Ababa, Ethiopia, 2021 (n= 90).

Measured temperature degree Celsius					
	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	904.401	1	904.401	14.773	.000
Within Groups	5387.484	88	61.221		
Total	6291.885	89			

4.3.6. Mantel–Haenszel analysis for proving Co-factors and interactions

The stratified analysis confirmed that there was no significant variation between stratum-specific ORs, showing no interaction between the predictors and smoking or meat consumption. Stratified analysis also depicted no variation between the pooled and adjusted ORs, indicating that both smoking and meat consumption were not co-factors for the effect of predictors on CRC. However, smoking was a co-factor for the effects of alcohol ingestion, educational status, BMI, stable source of income, previous GIT diseases, family history of CRC, physical exercise and meat ingestion (Table 4.8). Additionally, Table 4.9 shows the determinants of CRC by meat ingestion (8)).

Table 4.8 : Stratified analysis by smoking status for predictors of colorectal cancers in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2022.

Variables	**COR**	**Smoking**		**Adjusted (Mantel–Haenszel**			
		Ever	**Never**				
		OR	OR	OR_{MH}	95% CI	X^2_{MH}	P-value
Drinking coffee	0.71	0.84	0.70	0.72	0.51-1.02	0.12	0.7244
Drinking tea	0.84	0.93	0.80	0.83	0.57-1.19	0.09	0.7673
Meat ingestion	3.96	2.82	3.95	3.89	2.54-5.74	0.28	0.5990
Alcohol ingestion	0.78	0.91	0.91	0.81	0.64-1.31	0.00	0.9990
Beer ingestion	0.83	1.00	0.99	0.79	0.69-1.34	0.00	0.9628
White wine	0.73	1.10	0.84	0.83	0.59-1.30	0.23	0.6335
Red wine	0.80	1.00	0.95	0.85	0.65-1.41	0.01	0.9230
Sprite drinks	0.77	0.95	0.94	0.84	0.64-1.40	0.00	0.9730
Traditional alcohol	1.29	1.12	1.09	1.20	0.76-1.57	0.00	0.9790
Saturated fats	0.81	0.75	0.83	0.82	0.58-1.17	0.04	0.8381
Unsaturated fats	0.97	1.59	0.88	0.96	0.68-1.34	1.59	0.2078
Sweet foods	1.27	2.79	1.13	1.28	0.92-1.79	3.24	0.0718
Fruit intake	1.00	1.26	0.96	0.99	0.71-1.39	0.34	0.5558
Vegetable intake	1.08	0.94	1.16	1.12	0.80-1.59	0.15	0.6950
Drinking plant products	0.86	0.50	0.97	0.88	0.63-1.23	1.82	0.1775
Number of pregnancy	0.78	0.37	0.88	0.82	0.45-1.49	0.70	0.4024
Previous GIT diseases	14.87	10.80	15.37	14.79	5.34-40.43	0.07	0.4893
Family history of CRC	1.03	1.03	0.91	1.02	0.67-1.51	1.51	0.2192
Physical exercise	0.74	0.42	0.72	0.69	0.46-1.03	0.44	0.5085
BMI	2.13	1.82	2.24	2.18	1.68-2.84	0.26	0.6072
Educational level	4.20	3.03	4.23	4.08	2.70-6.14	0.30	0.5864
Stable source of income	0.88	0.85	0.85	0.87	0.59-1.24	0.00	0.9980
Average monthly income	0.80	0.77	0.82	0.81	0.56-1.17	0.01	0.9108
Type of water used for showering	0.94	0.61	1.05	0.97	0.70-1.36	1.19	0.2751
Longest residence	1.67	1.42	1.76	1.70	1.21-2.38	0.20	0.6553
Piped water supply	4.20	3.43	4.47	4.32	2.47-7.53	0.10	0.7531
Chlorinated water supply	3.71	5.27	3.51	3.72	2.57-5.38	0.54	0.4644
Showering	2.15	2.92	2.50	2.23	0.96-5.17	0.66	0.4150
Swimming history	2.25	3.65	2.20	2.37	1.66-3.39	0.89	0.3455
Type of swimming	0.87	0.51	1.07	0.82	0.63-1.23	0.58	1.05
Average ingestion of water	1.04	1.11	1.01	1.03	0.73-1.44	0.04	0.8388

Table 4.9: Stratified analysis by meat ingestion for predictors of CRCs in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2021

Variables	**COR**	**Meat ingestion**		**Adjusted (Mantel–Haenszel)**			
		≥ 1	**< 1**				
		OR	OR	OR_{MH}	95% CI	X^2_{MH}	P-value
Drinking coffee	0.71	0.57	0.80	0.73	0.51-1.04	0.63	0.4271
Drinking tea	0.84	0.67	0.92	0.84	0.57-1.25	0.46	0.4975
Smoking	0.57	0.50	0.69	0.56	0.41-1.05	0.28	0.5946
Alcohol ingestion	0.78	0.77	0.89	0.86	0.61-1.21	0.12	0.7271
Beer ingestion	0.84	0.84	0.97	0.94	0.66-1.33	0.11	0.7357
White wine	0.73	0.85	0.88	0.87	0.60-1.27	0.01	0.9382
Red wine	0.81	0.83	0.97	0.94	0.65-1.37	0.12	0.7280
Sprite drinks	0.78	0.70	0.97	0.91	0.63-1.32	0.50	0.4781
Traditional alcohol	1.19	1.14	1.16	1.16	0.81-1.64	0.00	0.9798
Saturated fats	0.81	0.73	0.94	0.87	0.61-1.26	0.37	0.5447
Unsaturated fats	0.97	0.78	1.09	0.99	0.70-1.41	0.69	0.4045
Sweet foods	1.28	1.21	1.32	1.29	0.91-1.82	0.05	0.8256
Fruit intake	1.00	0.80	1.00	1.04	0.73-1.47	0.83	0.3620
Vegetable intake	1.08	0.90	1.12	1.06	0.74-1.51	0.28	0.5969
Drinking plant products	0.86	0.57	0.99	0.86	0.60-1.22	1.77	0.1828
Number of pregnancies	0.98	1.89	0.64	1.00	0.54-1.84	2.78	0.0957
Previous GIT Diseases	14.11	9.83	16.54	14.11	5.09-39.13	0.19	0.6662
Family history of CRC	1.02	0.42	0.64	0.95	0.55-1.33	2.74	0.0978
Physical exercise	0.74	0.67	0.72	0.70	0.47-1.04	0.02	0.8798
BMI	2.13	1.65	2.13	2.02	1.53-2.66	0.56	0.4547
Educational level	4.20	4.09	3.40	3.96	2.58-6.07	1.11	0.2912
Stable source of income	0.88	1.42	0.54	0.74	0.49-1.09	5.14	0.0234
Average monthly income	0.80	0.82	0.95	0.92	0.63-1.33	0.10	0.7475
Type of water used for showering	0.94	0.60	1.31	1.05	0.67-1.30	3.79	0.0517
Longest residence	1.66	1.13	2.01	1.75	1.23-2.48	2.26	0.1325
Piped water supply	4.20	4.07	4.74	4.22	2.52-8.13	0.06	0.8006
Chlorinated water supply	3.71	2.72	3.92	3.67	2.43-5.19	0.73	0.3930
Showering	2.14	5.41	1.58	2.25	0.99-5.12	1.64	0.2001
Swimming	2.15	2.15	1.96	2.38	1.66-3.42	0.37	0.5426
Average ingestion of water	1.05	1.15	1.02	1.05	0.75-1.49	0.09	0.7665

4.3.7. Multivariable conditional logistic regression analysis

In the multivariable analysis, we found that drinking water chlorination status, type of water source, years at place of current residence, and swimming history were significantly associated with CRC. Our main findings show that the odds of developing CRC in households with chlorinated water supply was 2.6 times the odds of non-chlorinated water supply (adjusted mOR= 2.6; (95% CI: [1.7−4.0]). This finding agreed with that of studies from Ontario, Canada (King et al., 2000) and Iowa, USA (Jones et al., 2019) showing that users of surface water had much greater exposure to chlorination byproducts and had a high risk of CRC than consumers of non-chlorinated ground water. A meta-analysis performed by Morris and his colleagues in 1992 supported this finding by indicating chlorinated surface water has substantially larger amounts of chlorination by-products than chlorinated groundwater (medians of 50.7 and 0.8 ppb, respectively) even when the surface water is collected from protected reservoirs (Berg and Burbank, 1972).

Similarly, the odds of CRC of study participants with history of swimming were 2.4 times that of those with no history of swimming (adjusted mOR= 2.4; 95% CI: [1.4−4.1]). A similar related finding was reported from USA Environmental Protection Authority (EPA) indicated that swimming pool has been linked to a threefold increase of cancer risk (all cancers) (EPA, 2005). A similar consistent result was also reported from Thailand (Panyakapo et al., 2008). In the study area tributary rivers (Big and little Akaki rivers) are available but there are no lakes. The rivers in Addis Ababa are simply used as a receptacle of all kinds of wastes released in the city and not used for swimming purpose (Yohannes and Elias, 2017, Mersha, 2012). This implies that the study participants of this study were likely to use swimming pools than streams.

Study participants who lived for more than 40 years in their current residence had 50% higher risk of CRC (adjusted mOR= 1.5; (95% CI: [1.1−2.2]) compared with participants who lived for less than 40 years (Table 4.10). This could be due to dose response relationships of age and risk of colorectal cancers.

Table 4.10: Multivariable analysis of factors associated with CRCs in Addis Ababa, 2021.

Variables	Case (n= 214)	Control (n=428)	UmOR[α](95% CI)[α]	AmOR (95% CI)	P-value
Water used for shower					
Hot water	86	59	4.3(2.8-6.5)	3.8(2.5-5.9) **	**0.001**
Cold water	128	369	1.0	1.0	
Years at longest residence [b]					
≥ 40 years	116	178	1.6(1.2-2.2)	1.5(1.1-2.2) **	**0.027**
< 40 years	98	250	1.0	1.0	
Coffee (drinks/week)					
≥ 21 times	123	280	0.7(0.5-1.0)	0.7(0.50-1.0)	0.058
0	91	148	1.0	1.0	
Chlorination status of drinking water					
Yes	148	161	3.8(2.7-5.5)	2.6 (1.7-4.0) **	**0.001**
No	66	267	1.0	1.0	
Swimming history					
Yes	106	134	2.25(1.57- 3.22)	2.37(1.39-4.07) **	**0.002**
No	108	294	1.0	1.0	
Types of swimming					
Outdoor	58	95	1.51(0.65-3.47)	1.30(0.54-3.13)	0.550
Indoor	49	38	1.0	1.0	
Regular Showering					
Yes	207	399	2.2(1.0 -5.2)	1.5(0.6-3.9)	0.920
No	7	29	1.0	1.0	
Exercise(times/week)					
≥ 1	47	117	0.7(0.5-1.1)	0.7(0.4-1.0)	0.065
< 1	167	311	1.0	1.0	

UmOR: Unadjusted matched odds ratio; AmOR: Adjusted matched odds ratio, CI, Confidence interval.
* Incapable to read or write based on self-reporting
α Denotes unadjusted mOR using 95% confidence interval from bivariate conditional logistic regression analysis in matched case-control pair
. **Statistically significant at $p<0.05$.
[b] years at longest residence

The odds of developing CRCs among those who used hot water for showering were 3.8 times the odds of those who used cold water for showering (adjusted mOR; 3.8= (95% CI: [2.5‒5.9]). This could be due to exposure to THM that is when the water is hot it is higher due to two main reasons: volatility of the THM that may increase the inhalation exposure (and reduce the concentration of the same in water, and the increase diffusivity of the THM inside the body through dermal contact. Similarly, measurement of study participants showers water temperature also indicated significant difference between case and control households. A similar related finding reported from western Massachusetts, USA depicting that the concentrations of trihalomethanes (THMs), trichloroacetic acid (TCAA) and chloropicrin (CP) were substantially higher in the hot water shower than in the cold-water shower (Liu and Reckhow, 2015).

Alcoholic drinks, sweet foods, eggs consumption, coffee and usual physical exercise were not significantly associated with CRCs ($p > 0.05$) (Table 4.10). This might be due to the similarity of the socioeconomic status of case and control households. In contrast to our findings, several studies reported that alcohol intake, even in small amounts (Cai et al., 2014, Fedirko et al., 2011), sweet foods consumption (GAVRILAȘ et al., 2018), usual physical exercise (Haggar and Boushey, 2009) and eggs consumption (Zhang et al., 2003) were significantly associated with CRC.

Table 4.10 (continued)

Variables	Case (n= 214)	Control (n=428)	UmOR (95% CI) [α]	AmOR (95% CI)	P-value
Smoking					
Ever	28	91	0.5(0.3-0.8)	0.4(0.2-0.8)	**0.004**
Never	186	337	1.0	1.0	
Sweet food (times/week)					
≥ 1	120	214	1.3(0.9-1.8)	1.3(0.9-1.9)	0.153
< 1	94	214	1.0	1.0	
Alcohol (drinks/week)					
≥ 8 times	101	228	0.7(0.5-1.1)	0.7(0.3-1.5)	0.344
0	113	200	1.0	1.0	
Meat consumption (times/week)					
≥ 1	84	60	4.6(2.9-7.2)	3.5(2.0-5.9) **	**0.001**
< 1	130	368	1.0	1.0	
Egg's consumption (times /week)					
≥ 1	62	147	0.7(0.5-1.0)	0.8(0.5-1.2)	0.340
< 1	152	281	1.0	1.0	

4.4. Conclusion

Drinking chlorinated water for extended years is a significant risk factor for CRC in Addis Ababa. In addition, hot tap water uses for showering, and swimming history are risk factors for CRC. This information is essential to design integrated interventions that consider chlorination by-products and exposure routes towards the prevention and control of CRC in Ethiopia. Initiating alternative methods to chlorine disinfection of drinking water is also essential.

Chapter5 : Trihalomethanes and physicochemical quality of drinking water in Addis Ababa, Ethiopia

5.1. Introduction

Chlorination is one of the most commonly used methods to disinfect drinking water and to control bio-fouling in water treatment utilities. Among many chemical approaches for disinfection, chlorination is the most familiar method worldwide. This could be due to its (1) demonstrated effectiveness against a wide spectrum of microorganisms, (2) ideal oxidizing potential, (3) accessibility at a relatively cheaper cost, and (4) capacity to provide residual chlorine throughout the water supply network, unlike UV disinfection (Abdullah et al., 2009, Padhi et al., 2019a). However, numerous disinfection byproducts (DBPs) are produced as a result of the interaction between chlorine and natural organic substances (Sadeghi et al., 2019). To date, more than a thousand halogenated DBPs have been reported (Mishaqa et al., 2022).

The most well-known organic DBPs include trihalomethanes (THMs), haloacetonitriles, haloacetic acids, emerging organic DBPs and halo ketones (HKN) (Radwan et al., 2021, Nguyen et al., 2021, Ibrahim et al., 2016). The harmful inorganic DBPs, also recognized as oxy halide DBPs, include bromates (BrO_3^-), chlorite (ClO_2^-), and chlorate (ClO_3^-) (Saradhi et al., 2015, Michalski, 2005, Padhi et al., 2019a). Organic DBPs have attracted the attention of researchers due to their regular discovery and harmful effects (Righi et al., 2014). Due to the presence of chlorination byproducts in the treated water, prolonged exposure to chlorinated water raises the risk of cancer, mutation, kidney and liver damage, retarded fetus growth, congenital disabilities, and possibly miscarriage (Komaki et al., 2014, Du et al., 2020, Avsar et al., 2020, Kim et al., 2020, Liu et al., 2022, Padhi et al., 2019a, Ristoiu et al., 2009, Mashau et al., 2018, Tafesse et al., 2022a).

Disinfection byproducts, such as THMs and HAAs (haloacetic acids), are produced when chlorine undergoes a substitution reaction with organic matter, such as fulvic acids, humic acids, proteins, and amino acids (Andersson et al., 2021, Wu et al., 2020). DBP formation in water is a function of numerous factors, including pH, temperature, residual chlorine, source water characteristics, and organic matter (Padhi et al., 2019a) (Grellier, 2018, Padhi et al., 2019a). THMs are indicated as the most dominant fractions of all the byproducts formed in the chlorination procedure. THMs are a class of DBPs that include chloroform ($CHCl_3$), bromodichloromethane ($CHCl_2Br$), bromoform ($CHBr_3$) and chlorodibromomethane ($CHClBr_2$). THMs were regulated shortly after their discovery in disinfected drinking water, with total trihalomethanes (TTHMs) having a maximum contaminant limit (MCL) of 100 μg/L (Li et al., 2021). The MCL for TTHMs was reduced to 80 μg/L by the Stage 1 D-DBP Rule, (Chowdhury et al., 2020b) while the MCLs for haloacetic acids (HAAs), bromate, and chlorite were set at 60, 10, and 1000 μg/L (Yang et al., 2018), respectively.

In Ethiopia, water treatment centers utilize chlorine to disinfect the water before it is distributed to the general public. However, DBPs in drinking water have not been measured by Ethiopian water utilities, particularly in Addis Ababa. Ethiopia's drinking water supply networks also do not have a system in place to monitor and regulate DBPs. Furthermore, the water treatment plants in Ethiopia did not set the maximum allowed concentrations (MAC) for total THMs and other DBPs. Therefore, this study aimed to explore concentrations of THMs along with various water quality factors in drinking water supply networks of Addis Ababa, Ethiopia.

5.1. Methods

5.1.1. Study Setting and Period

Addis Ababa is the capital city of Ethiopia. Geographically, the city is located 9^o01’29” to the north and 38^o44’48” to the east. Addis Ababa is the largest city in Ethiopia, with a projected population of 3,434,000 in 2017 (Central statistical authority 2013a). The city of Addis Ababa obtains its water supply from both surface water and ground water sources. There are three main dams used to collect run-off water to store in the dams to serve as surface water sources for water supply. The three dams are the Gefersa dam (situated 18 km west of Addis Ababa), Legedadi Dam (situated 25 km east of Addis Ababa), dire dam (situated 10 km north of Legedadi dam) and Akaki groundwater (Akaki well field) (MCE, 2015).

A total of seven surface water reservoirs, two surface water sources and seventy households (36 HHs and 34 HHs from the Gefersa and Legedadi water supplies, respectively) were selected for surface water sampling. For groundwater sampling, five boreholes and thirty-five households were chosen (Figures 5.1, 5.2). Since the water sources are used just once a year and are distributed through a closed system, the samples taken at any time are believed to be consistent throughout the year. Samples were collected from June 1 to July 30, 2022.

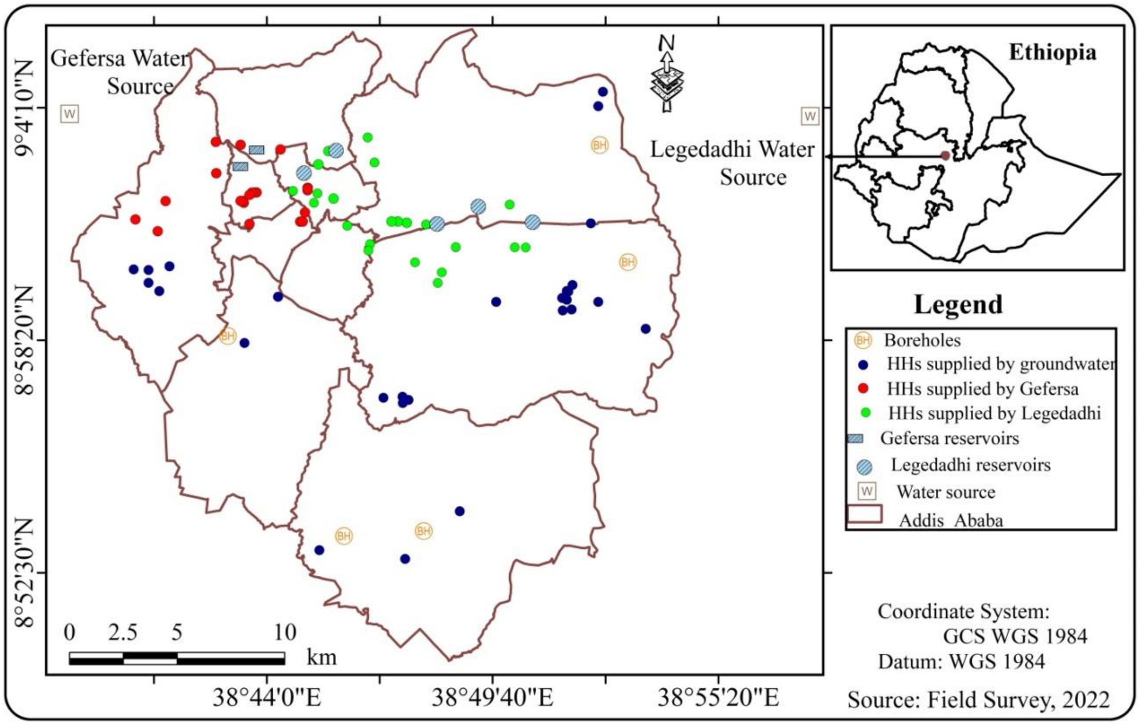


Figure 5.1: Sampling points of the water samples in Addis Ababa, Ethiopia, 2022

5.1.2. Study Design

A cross-sectional study design was used in the water supply networks of the Addis Ababa municipal water system.

5.1.3. Sample size determination

Twenty-one (21) sampling stations were used to gather one hundred twenty (120) drinking water samples. Legedadi, Gefersa, and groundwater sources were the three areas for sampling. Each sampling location produced forty water samples. Samples were collected from several points of use throughout the distribution network, as well as from the raw water source

Location of Sampling Points

The primary requirements for choosing the sampling points were that they be spread out at different distances from the treatment facility, that at least one point represents the distribution system's extreme and that they all be supplied directly by the plant itself, excluding the influence of any re-chlorination facilities. Each locality must be taken into account uniquely when choosing sampling places, although the following standard criteria are frequently used (Fig.5.2) (Kirmeyer and Martel, 2001)

- Sampling stations must be selected so that the samples collected are representative of the various sources from which the general public acquires water.
- A piped distribution system's number of links or branches and the population distribution should be taken into consideration when determining the number of sampling locations.
- Water from reservoirs, etc., must be able to be sampled from sampling sites that are strategically placed. In systems with more than one water source, the placements of the sampling points should take into consideration the number of residents supplied by each source (WHO, 2010).

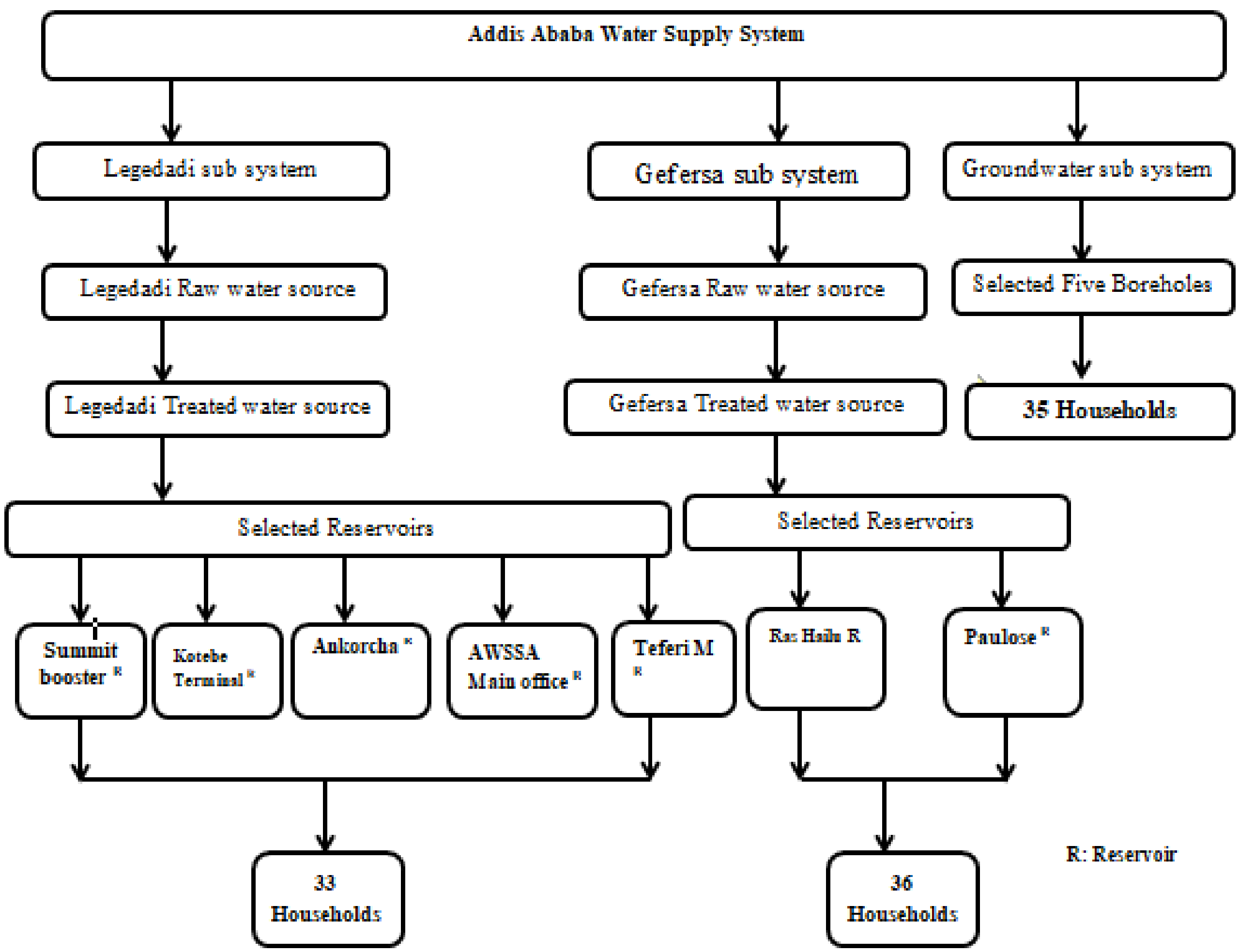


Figure 5.2: Selected sampling points for water collection, Addis Ababa, 2022

5.1.4. Sample Collection and storage for Physico-Chemical Analysis

The water samples were collected from three sampling areas in Addis Ababa, Ethiopia and ArcGIS 14 was used for mapping. A cleaned 350ml plastic polyethylene bottles were used to collect the water samples and carried to the laboratory with an icebox to avoid unusual change in water quality. Prior to the sampling all the bottles are washed and rinsed thoroughly with distilled water. Standard methods (Dirican, 2015) were followed for sample collection and preservation. The Physicochemical analysis of water performed in the Addis Ababa Sewerage and Sanitation Authority (AAWSA) laboratory (Table 5.1).

Table 5.1: Methods Determination of Physicochemical parameters of water samples in Addis Ababa, 2022

Parameter	**Method**	**Summary of the method**
Organic Constituents, UV-Absorbing (UV-254)	DR5000 Spectrophotometer Method 10054 (Clesceri et al., 2005)	The filtered sample is measured at 254 nm to show organic constituents in the sample water. Organic-free reagent water is used for the blank sample cell. Results are given in absorbance per centimetre (cm–1).
Residual chlorine	Insitu measurement (WHO, 2017)	Chlorine can be present in water as free chlorine and as combined chlorine. Both forms can exist in the same water and be determined together as the total chlorine. Free chlorine is present as hypochlorous acid or hypochlorite ion. Combined chlorine exists as monochloramine, chloramine, nitrogen trichloride and other chloro derivatives. The combined chlorine oxidizes iodide in the reagent to iodine. The iodine and free chlorine reacts with DPD (N, N-diethyl-p phenylene diamine) to form a red colour which is proportional to the total chlorine concentration. Test results are measured at 530 nm.
Chloride	Method 8113 (Clesceri et al., 2005)	Chloride in the sample reacts with mercuric thiocyanate to form mercuric chloride and liberate thiocyanate ion. Thiocyanate ions react with the ferric ions to form an orange ferric thiocyanate complex. The amount of this complex is proportional to the chloride concentration. Test results are measured at 455 nm.
EC, TDS	Insitu measurement (WHO, 2017)	The specific conductance of a sample is measured by a self-contained conductivity electrode.
PH and Temperature	Insitu measurement (Skandaraja, 2015)	The pH meter was calibrated using pH 4 and 7 buffers. After calibration, the glass pH electrode was immersed into the water samples and the pH was recorded.
Nitrate (hardness)	Method 8039 (Clesceri et al., 2005)	Cadmium metal reduces nitrates in the sample to nitrite. The nitrite ion reacts in an acidic medium with sulfamic acid to form an intermediate diazonium salt. The salt couples with gentisic acid to form an amber coloured solution. Test results are measured at 500 nm.
Phosphates	Method 10127 (Clesceri, 1998)	Phosphates must be transformed to reactive orthophosphate before examination if they are present in organic or condensed inorganic forms (meta-, pyro-, or other polyphosphates). The sample is pre-treated with heat and acid to create the ideal environment for the condensed inorganic forms to hydrolyse. By heating with acid and per sulphate, organic phosphates become orthophosphates. In an acidic environment, orthophosphate and molybdate combine to form a mixed phosphate/molybdate complex.

5.1.5. Sample collection and storage for Trihalomethane Analysis

The USEPA protocol and practice for sample collection and handling were followed (USEPA, 2016). Duplicate water samples were properly collected from the raw water source, directly after chlorination (DAC), and from the distribution network and tap waters. The sample containers had a total volume of 125 mL and had a screw cap with Teflon-facing silicon septa. Sodium thiosulphate Na_2S2O_3 (0.5% w/v) solution was added to the sample containers (to quench residual chlorine). The sampling point was opened for approximately 3-5 minutes before sampling to ensure that the water came directly from the distribution system.

The sample container filled in such a way to minimize the headspace that no air bubbles pass through the sample as the bottle filled and tightly sealed after collection. The sample containers were filled in such a way to minimize the headspace that no air bubbles pass through the samples as the bottles are filled and tightly sealed. A sampling blank filled with THM-free reagent water was added to the list of samples to be analyzed. Samples were transported to the laboratory using an ice bag and stored at 4 ℃ until analysis.

5.1.6. Chemicals

Certified reference material of EPA 501/601 THM calibration mix (200 µg/ml each of chloroform, chlorodibromomethane, bromodichloromethane, and bromoform component in methanol) was purchased from Sigma–Aldrich, Germany. Solvent (pentane) of GC grade was purchased from Sigma–Aldrich, Germany.

5.1.7. Sample Analysis

The concentrations of THMs in the collected samples were determined following EPA method 551.1(Munch and Hautman, 1995) with some modifications. In brief, 2 mL of pentane was vigorously shaken with 10 mL of the sample to extract the THMs. The extract was transferred in a 2ml vials and 2µl of it was injected in the GC-ECD system, which was placed in Varian auto injector model CP 8400 and then injected into Varian CP-3800 gas chromatography (GC) in the Ethiopian Agriculture Authority (EAA), quality and safety assessment center, physicochemical laboratory, services division. The injector was operated at 220 °C in split mode (split ratio 25:1).

The THMs were separated by an Agilent 122-5032 - GC Column DB-5 (30 m × 0.25 mm x 0.25 μm) capillary column and detected by an electron capture detector (ECD) set at 290°. The carrier gas was nitrogen set at a flow rate of 1.5 mL/min, while the makeup gas was nitrogen set at a flow rate of 40-60 mL/min. The oven temperature was programmed at 40 °C isothermal for 5 min and then ramped to 250 °C at a rate of 15 °C and kept at this temperature for 2 min.

The concentrations of THMs were calculated by the matrix matched calibration method using the aforementioned standard mixture of THMs. With the above setup, the GC was run for more than 12-14 hrs, and the background was checked regularly. The detector current was set to 0.0 nA first and then after the baseline stabilization 0.5-1.0 nA current was applied depending on the signal. After the GC signal stabilized, the blank was run (several times) without any injection, and then after improvement of baseline stability, 1 μL of pentane was injected for THMs quantification.

5.1.8. Quality control and assurance

According to the Eurachem guide, the applied analytical method was verified prior to the analysis of the collected samples in terms of linearity, recovery, minimum detection limit (MDL), and repeatability (Bertil and Örnemark, 2014). The limit of detection (LOD) is the minimum concentration of trihalomethanes that can be detected at a specified level of confidence. To determine the LOD, a concentration of 10 μg/L (one tenth of MAC (maximum allowable concentration)) of matrix-matched samples of the four mixed standards was prepared in seven different replicates. Then, independent measurements of each sample were taken seven times, their standard deviation (SD) was calculated, and the LOD was determined as LOD = 3 X SD. A LOD study is conducted running 10 spiked samples through the entire analytical process from extraction to analysis (Magnusson, 2014) (Table 5.3).
During method verification, as internal quality control, a blank samples and water samples fortified with THM compounds of interest, at six working ranges were prepared as matrix-matched calibrants. Hence, three batches of matrix-matched calibrants were prepared over three different days (Day 1, Day 2 and Day 3). Along with, for determination of recovery and precision, nine (9) spiked samples each in triplicates were prepared by spiking blank samples at 0.5, 1.0- and 1.5-times concentrations of the MACs. Together with each batch of verification samples, matrix-matched reference standards fortified at MACs level post spiked on the water matrix (after sample underwent all preparative steps) and a true blank, reagent blank, which doesn't contain any analytes of interest in order to eliminate false-positive

and ensure that the system is under control. In this study, quality control samples were prepared in triplicates, whereas the test samples were prepared and analyzed in duplicates.

5.1.9. Variables and measurements

The Trihalomethanes concentration was dependent variable and the environmental factors were regarded as predictor variables.

5.1.10.Statistical Analysis

The collected data were entered into Excel spreadsheets, validated, cleaned and exported to Statistical Package for Social Sciences (SPSS) version 23 for analysis. Canonical Correspondence Analysis (CCA) or Redundancy Analysis (RDA) was used for data analysis of trihalomethanes and environmental variables using CANOCO 4.5 (Constante-Pérez et al., 2022) (2). Detrended Correspondence Analysis (DCA) was used to check the gradient lengths. During the interpretation of the results, the statistical significance of a variable was based on a p value < 0.05 and <0.01.

5.1.11.Ethics approval and informed consent

Ethical approval was obtained from the Institutional Review Board of Natural and Computational Science College of Addis Ababa University.

Table 5.2: Trihalomethanes levels found in drinking water samples in previous studies worldwide

* BD (Below Detection); ** ND (Not detected) **

Study drinking water samples, n	Site (country)	$CHCl_3$(µg/l)	CHBrCl2 (µg/l)	$CHCl_2Br$ (µg/l)	$CHBr_3$(µg/l)	TTHMs (µg/l)
Water samples, n=3(Benson et al., 2017)	water treatment plants (WTPs) in Nigeria	950.57	BD*	BD	BD	950.97
Water samples, n=1667(Mishaqa et al., 2022)	Water samples from twenty-three Egyptian governorates over a three-years period	40.5	19.5	10	16.01	86.01
Water samples, n=175(Padhi et al., 2019a)	Sea, open reservoir water samples, and soil in India	-	-	-	-	151.62-198.25
Water samples, n=3(Padhi et al., 2019b)	sea, river, and reservoir	-	-	-	-	18.8 (river), 21.5 (reservoir)
Water samples, n=35 (Uppeegadoo et al., 1999)	Water samples were collected at the Riviere du Poste (RP) and Mont Blanc (MB), southern part of Mauritius					20.3
samples from randomly selected taps in each water zone (Keegan et al., 2001)	United Kingdom water company in the north of England	36.6	8.0	2.8	ND**	46
Water samples, n=72 (Nadali et al., 2019)	Hamadan Province, Iran, two water treatment plants	-	-	-	-	10 to 26
Two sampling sites were selected (Drinking and nondrinking water samples (Kujlu et al., 2020)	Abadan, Khuzestan province (Iran)	-	-	-	-	98.1to 8.88

5.2. Results and Discussion

5.2.1. Characteristics of raw water samples

The results of the characterization of raw water samples collected from the two treatment plants together with the groundwater samples are reported in table 2. The data include determination of pH, temperature, combined chloride, UV absorbing (UV-254), total dissolved solids (TDS), and residual chlorine. The temperature ranged from 19.7±2.5 to 22.7±1.5, and the pH values of the raw water samples taken from the two water treatment plants were between 7.22 and 7.7. The chloride concentrations in the Gefersa and groundwater water samples were above the recommended limits (Alemu et al., 2015). It ranged from 4±3.5 (Legedadi dam) to 10.9±4.9 mg/L (Gefersa dam). The highest TDS level was detected from the groundwater source, which was 105±4.5 mg/L (Table 5.3).

Table 5.3: Summary statistics for raw water samples collected from the two water treatment plants and groundwater sources

Type of water source	PH	Temperature (℃)	TDS (mg/L)	UV-254 (Abs/cm^{-1}).	chloride (mg/L)	NO_3(mg/L)	Res. Cl (mg/L)
Legedadi RW*	7.785±0.28	22.7±1.5	63±3	89±3.2	4±3.5	6.1±2.9	0.00
Gefersa RW	7.22±0.28	19.7±2.5	69±4.2	93.6±2.3	10.9±4.9%WSORL	3.2±4.1	0.00
Groundwater source	7.68±0.05	19.54±0.21	105±4.5	85.24±0.49	10.04±0.22	0.53±0.06	0.05

5.2.2. Method verification

The standard chromatogram depicts a sharp well-separated and resolved peak for each of the THM compounds (Fig. 5.3). The matrix matched calibrations were constructed for six points (S1-4). The minimum detection limit (MDL) was 1.67µg/L. This value is compatible with the USEPA detection limits (ranging from 0.1 to 2.5 µg/L for the THMs), which vary across laboratories and time (Kaufman et al., 2020). The correlation coefficients (r) were higher than 0.989 for all standards, which signifies a good linear response factor for the different THM compounds in the concentration range. The mean recovery ranged from 85.6 to 114.1%, which falls in the acceptable range (80%– 120%) set by EPA method 551.1(Nikolaou et al., 2002b) and showed good accuracy of the method. Similarly, the method repeatability (3.58%–6.79%) ranges were within the EPA method 551.1 guideline (<15%) (Nikolaou et al., 2002b) and indicated good precision of the method (Table 5).

Table 5.4: Method Verification parameters

Parameter	Trihalomethanes (THMs)			
	CHCl3	**CHCl2 Br**	**CHBr2 Cl**	**CHBr3**
Retention time (min.± 5%)	4.21	5.48	7.55	9.95
Linearity correlation coefficients r^2	0.989	0.993	0.989	0.995
Recovery (%)	88.4-109.6	90.8-109.6	85.6-112.4	99.3-114.1
MDL[a] or LOD (µg/L)	1.37	1.73	1.92	1.67
Repeatability [a] (%)	6.18	3.58	6.79	6.41

MDL, Method Detection Limit; [a] for seven replicates.

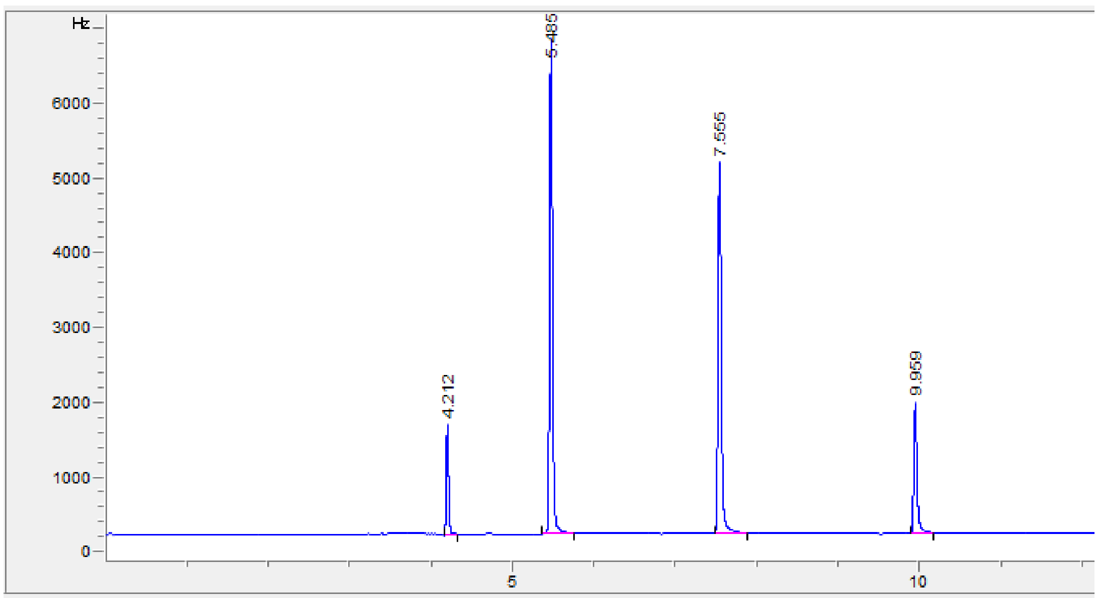


Figure 5.3: Chromatogram of a standard mixture of THMs

Chromatogram for a water sample: CHCl3 (t_R=4.212); CHBrCl2 (t_R=5.485); CHBr2Cl (t_R=7.55) CHBr3 (t_R=9.959)

5.2.3. Number of Measurements below detection limits

The number of measurements recorded below the detection limits for $CHCl_3$, $CHCl_2$ Br, $CHBr_2$ Cl and $CHBr_3$ were 28.3%, 37%, 57.5% and 94.2%, respectively. The presence of certain THMs was below the LOD of the method employed (Table 5.5). Certain THMs were present but at levels below the LOD of the method used. This may be because the water samples were not treated, which prevented them from being subjected to chlorination reactions. These results are comparable with those of a similar study performed in other nations (Zhao et al., 2004, Andreola et al., 2019) (Table 5.5).

Table5.5: Detection Number of Trihalomethanes in Drinking Water

Name of the variable	Number of measurements below detection limit (%)	Number of measurements above detection limit (%)
CHCl3	34 (28.3)	86(71.7)
CHCl2Br	76(63)	44(37)
CHClBr2	51(42.5)	69 (57.5)
CHBr3	113(94.2)	7(5.83)

5.2.4. Trihalomethanes concentration

The mean concentrations of $CHCl_3$, $CHCl_2$ Br, $CHBr_2$ Cl and $CHBr_3$ in the drinking water were 54.3, 10.7, 7.70 and 3.02 µg/L, respectively. The maximum concentration of CHCl3 was 79.40µg/L and the minimum was 4.3µg/L. The total mean concentration of trihalomethanes was 76.3µg/L (Table 5.6 and Fig.5.4). This concentration is below the USEPA MCL of 100 µg/L (Xie, 2003) and the Egyptian water treatment, which was between 29.07 and 86.01 µg/L (Mishaqa et al., 2022). However, the findings of this study were higher than those in Hamadan and Tuyserkan cities, western Iran, in 2016-2017, which were 47.5 µg/L (Nadali et al., 2019). This dissimilarity could be due to differences in methodological and geographical characteristics.

Table 5.6 : Total trihalomethanes and drinking water supplies in Addis Ababa, Ethiopia, 2022

	Mean Concentration µg/L (95% CI)	Min (µg/L)	Max (µg/L)
CHCl3	54.93(50.97-58.53)	4.3	79.40
CHCl2 Br	10.66(9.74-11.53)	2.42	19
CHBr2 Cl	7.70(6.83-8.53)	2.22	13.1
CHBr3	3.02(2.83-3.21)	2.7	3.21
TTHMs	**76.31**		

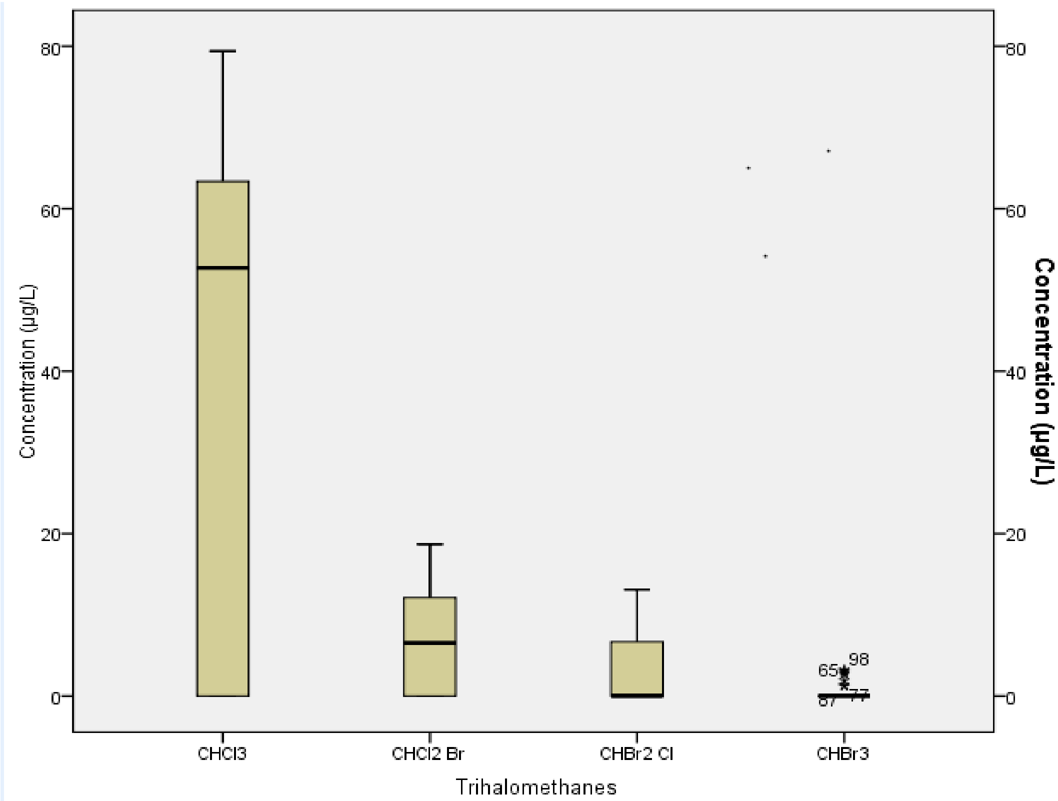


Figure 5.4: Mean trihalomethanes in drinking water in Addis Ababa, Ethiopia, 2022

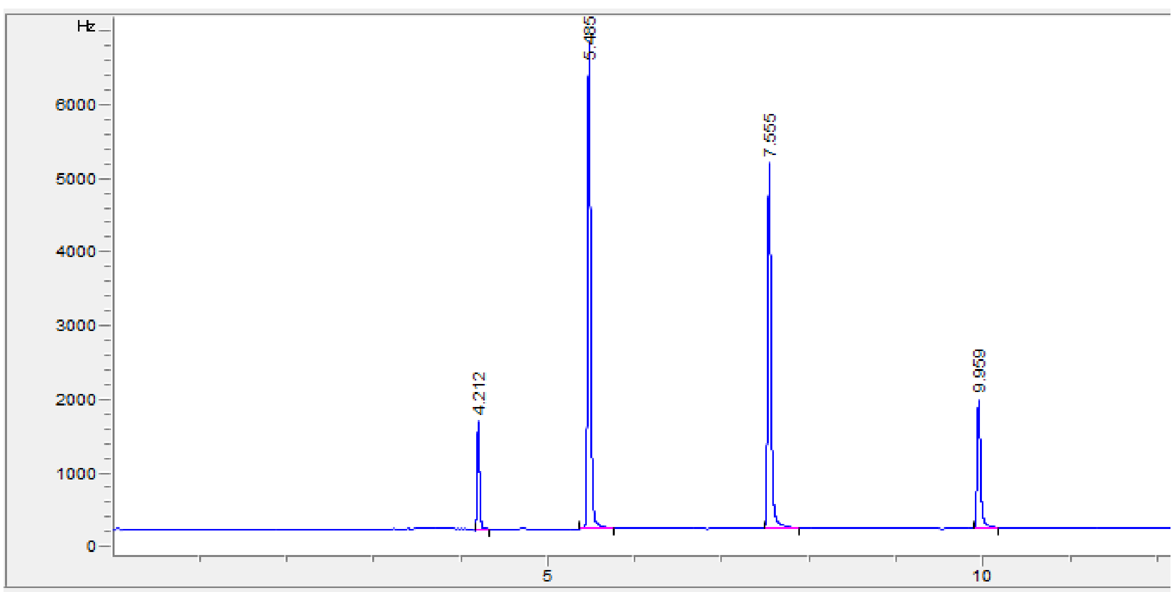


Figure 5.5: Chromatogram of a standard mixture of THMs

Chromatogram for a water sample: $CHCl3$ (t_R=4.212); $CHBrCl2$ (t_R=5.485); $CHBr2Cl$ (t_R=7.55); $CHBr3$ (t_R=9.959)

5.2.5. Distribution of each trihalomethane in the water supply system of Addis Ababa

The mean $CHCl_3$ in the Gefersa reservoirs and Gefersa tap waters were 62.4µg/L and 60.4µg/L, respectively. The mean total THMs in the Gefersa reservoirs and Gefersa tap waters were 76.7µg/L, and 78.07µg/L respectively. Similarly, the mean $CHCl_3$ in the legedadi reservoirs and legedadi tap waters were 49.6µg/L and 59.2µg/L respectively. The mean total THMs in the legedadi reservoirs and legedadi tap waters were 62.2µg/L and 77.1µg/L respectively. The lowest THMs concentration was recorded in the groundwater supply system (15.5µg/L). In addition, the Gefersa water supply system recorded relatively higher mean levels TTHMs compared to others. Very low Bromoform was recorded only from the groundwater supply system (Table 5.7).

Table 5.7 : Comparison of each trihalomethane in the water supply system of Addis Ababa, Ethiopia, 2022

	Gefersa reservoirs (95% CI)	**Gefersa tap waters (95% CI)**	**Legedadi reservoirs (95% CI)**	**Legedadi tap water (95% CI)**	**Groundwater WS (95% CI)**
CHCl3	62.4(53.1-77.0)	60.4(56.1-64.2)	49.64(36.2-63.4)	59.2(55.75-63.07)	8.36(5.98- 10.72)
CHBr Cl2	8.61(7.00-9.65)	11.04(9.81-12.29)	12.6(8.30-15.3)	10.08(8.60-11.60)	3.8(2.7-4.9)
CHClBr 2	5.69(1.13-8.04)	6.63(5.29-7.93)	-	7.80(6.68-8.95)	-
CHBr3	-	-	-	-	3.02(2.77-3.21)
TTHMs	76.7	78.07	62.24	77.08	15.25
Mean TTHMs	**77.4**		**69.66**		**15.25**

*WS: water supply.

These findings could be due to the fact that drinking water is carried over long distances from the treatment plants to the reservoirs, and then to local tap waters. To guarantee that there is residual chlorine in the distribution system, the water is chlorinated after each water booster pump. This chlorine addition increased the reaction time, which in turn increased the concentration of the various THM species and, ultimately, the concentration of TTHMs. The highest concentration of TTHMs (97.4µg/L) was observed in Gefersa tap water. Comparatively, the legedadi water supply system contributed the lower concentration of THMs than Gefersa supply system (Fig. 5.6). This could be because there is high organic matter in the Gefersa dam due to the presence of high forestation coverage (Allochthonous input – such as terrestrial DOM derived from vegetation), fish cultivation and decomposition of fishes and plant remnants. Furthermore, this treatment plant is located in the center of urban and likely to be affected by urbanization activities.

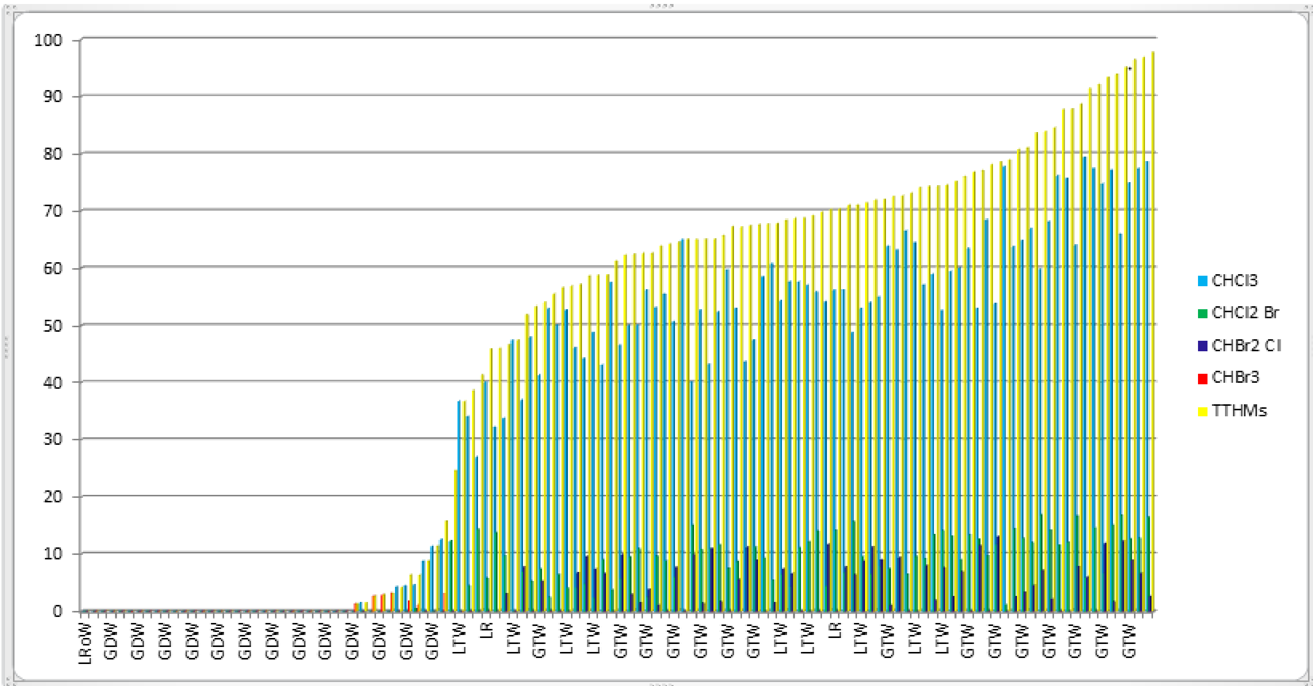


Figure 5.6: Percentage contribution of each THM species to TTHMs. LRow = Legedadi row water, LR= Legedadi reservoir, LTW = Legedadi tap water, GTW= Gefersa tap water, GRW = Gefersa Reservoir Water, and GDW= Groundwater

The measurements of bromodichloromethane (CHBrCl2), chloroform (CHCl3), dibromochloromethane (CHBr2Cl) and bromoform (CHBr3 Cl) in water samples showed that the only species detected was bromoform (CHBr3) in groundwater supplies (3.2µg/L). This could be because the groundwater wells in the city are deepest (> 100meters) containing natural bromide in the water. This bromide might be originated from the soil organic content (SOC) as indicated by the related study that bromoform was the dominant THM produced during Cl2 treatment (Padhi, 2022 #381). Furthermore, this distribution of THM species may be explained by the fact that bromine-carbon bonds are more resistant to dissociation than chlorine-carbon bonds are due to lower dissociation energy (Rasheed, 2023 #38).

5.2.6. Ordination analysis

The data set was first examined in CANOCO for Windows version 4.5 using a detrended correspondence analysis (DCA) to see if a linear or unimodal kind of response was evident along environmental gradients (Van den Brink et al., 2003). Since all environmental gradients were shorter than 2 standard deviation units, redundancy analysis (RDA) was then applied. Trihalomethanes were regarded as response variables in all RDA studies, while environmental factors were regarded as predictor variables (S5). A preliminary analysis was performed to test multicollinearity in environmental variables. Variables with a variance inflation factor of 5 were removed from the analysis (S6). Seven environmental aspects were picked as independent variables using a stepwise forward selection method. Prior to analysis, trihalomethanes and environmental data were log converted [log(x+1)] to reduce variance. Using Monte-Carlo permutations, the statistical significance of the eigenvalues and THMs-environment correlations produced by the RDA were examined.

Trihalomethanes appear to respond linearly to environmental gradients, according to the results of the detrended correspondence analysis (DCA), which indicated a gradient length less than 2 standard deviation units' gradients (Van den Brink et al., 2003). Trihalomethanes and the chosen environmental parameters were shown to be significantly correlated (p 0.05) for both the first axis and all canonical axes combined (Figure 5.7). According to the first two axes of the RDA-biplot of trihalomethanes and environmental variables, 99.6% of the variance in the trihalomethane data and 97.5% of the variation in the correlation and class averages of trihalomethanes with regard to the environmental variables were explained. The first two axes' eigenvalues were 0.527 and 0.012, respectively.

The trihalomethanes-environment correlation in this ordination was 0.784 and 0.327 for the first two axes, respectively. An electron conductivity-related gradient was seen on the first axis of the RDA ordination. Trihalomethanes and this axis had a positive correlation (r = 0.784, p 0.05). The combined chlorine, calcium-based hardness, and UV absorbance were all defined by the second canonical axis.

5.2.7. Multivariate analysis

The first two axes of the RDA biplots explained 99.6% of the variation in environmental data and 53.9% of the total variation in trihalomethanes (Table 5.8). With correlation coefficients of 0.78 and 0.33 for the first and second axes, respectively, the RDA ordination demonstrated a high link between trihalomethanes and environmental variables. Trihalomethanes and residual chlorine, UV absorbance, phosphate and hardness as calcium had a positive correlation with Trihalomethanes species. THMs species except bromoform had negatively correlated with electron conductivity (Fig.5.7).

Table 5.8: Detailed results of the Redundancy Analysis relating the core metrics of trihalomethanes to the environmental variables.

Axes	**1**	**2**	**3**	**4**	**Total variance**
Eigenvalues:	0.527	0.012	0.002	0.000	1.00
Trihalomethanes environmental correlations:	0.784	0.327	0.274	0.192	
Cumulative percentage variance					
of Trihalomethanes data:	52.7	53.9	54.1	54.1	
Trihalomethanes- environmental relation:	97.5	99.6	99.9	100	
Sum of all eigenvalues					1.00
Sum of all canonical eigenvalues					0.541

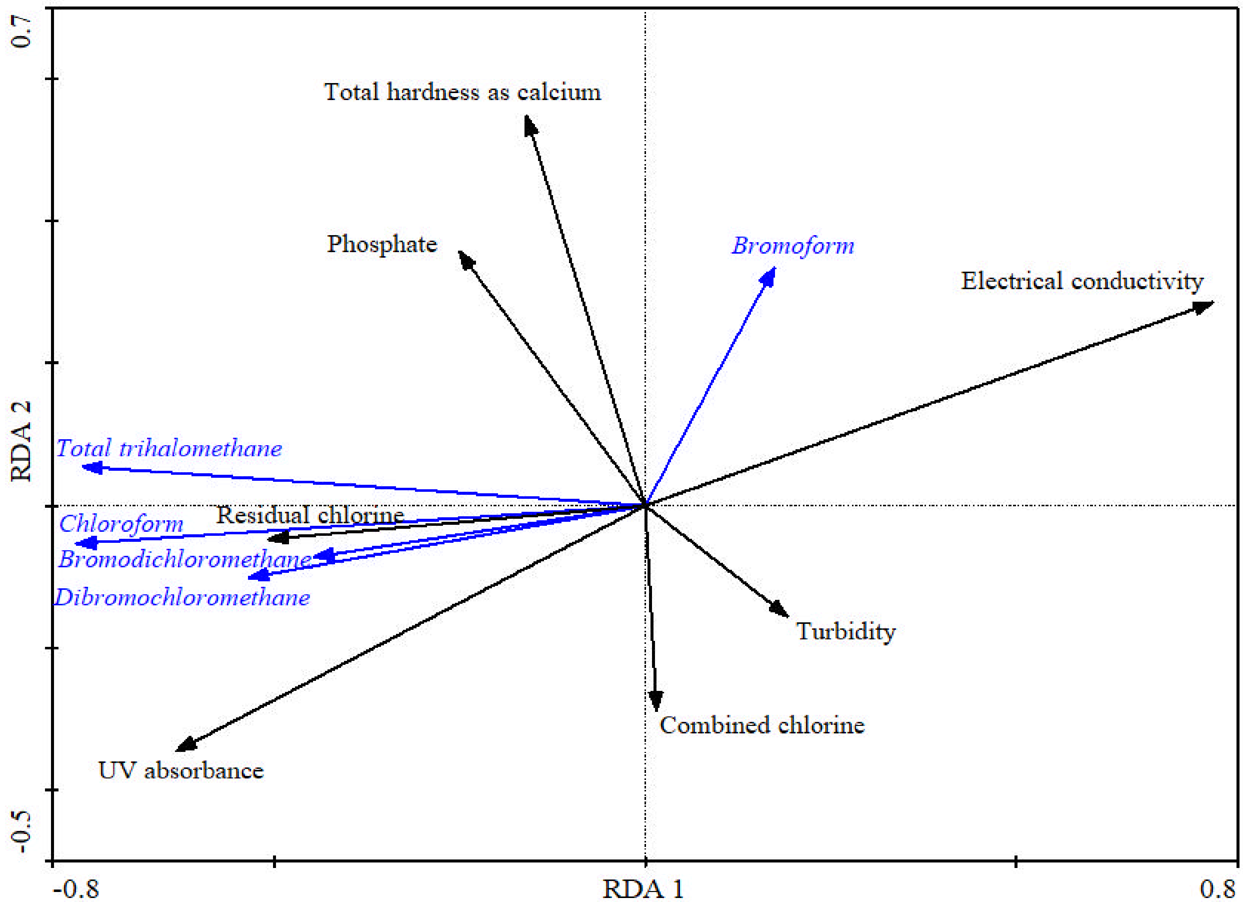


Figure 5.7: Redundancy analysis of Trihalomethanes and environmental variables of drinking water supply in Addis Ababa, Ethiopia

The THM species and residual chlorine had a strong positive correlation in this study. These findings were in line with a related study in Jordan and Iran showing that an increase in the value of residual chlorine has positive effects on the formation of THMs (Babaei et al., 2015c, Saidan et al., 2013). However, another study performed on the drinking water distribution of Ggaba, Kampala, Uganda (Nshemereirwe et al., 2022) indicated that residual chlorine had a negative but significant correlation with trihalomethane formation. This could be due to differences in methodology and water characteristics. Similarly, A similar related study reported a strong positive correlation between UV absorbance at 254 nm (UV254) wavelength and the THM formation potential (THMFP) (Edzwald et al., 1985). Related findings from Scottish and Jordan water treatment utilities (Valdivia-Garcia et al., 2016, Saidan et al., 2013) and several studies (Chowdhury et al., 2009, Nikolaou et al., 2002a, Li et al., 2008, Babaei et al., 2015c) showed a positive correlation between UV absorbance at 254 nm and total THM formation.

The presence of phosphate significantly associated with the formation of trihalomethanes in this work. This could be because of the presence of phosphate in the plumbing systems (certain proportion of it is ductile iron pipe (DCI) in the water supply network in Addis Ababa) promoted a more significant growth of biofilm and this led to increased level of THMs (Jang et al., 2012). The total hardness as calcium had a positive correlation with THMs. This could be likely the result of the protein unfolding at the higher pH and possibly a lack of buffer to mitigate the pH effects of the protein/disinfectant (David, 2014). The THMs formation showed negative correlations with electron conductivity. The causes for the inconsistency of THM and electron conductivity could be due to the co-variation in operational parameters or to the interaction between those parameters.

The combined chlorine negatively associated with THMs formation. These findings are similar to the studies in Gipuzkoa (Basque Country, Spain) (Abilleira, 2023 #379). The probable reason for the negative correlation is as follows: all-natural organic matter does not necessarily result in the formation of disinfectant by-products (Mohammadi, 2016 #380). Similarly, there was significant negative correlation between the amount of turbidity and the THMs formation. This could be because the water turbidity in the investigated treatment plants was not high adequate after the treatment process. In addition, bromoform and combined chlorine not showing correlations. This could be because bromoform only detected in groundwater supply in this study. This variability could be due differences in water characteristics. In addition, bromoform and combined chlorine not showing correlations. This could be because bromoform only detected in groundwater supply in this study and these imply composition of organic constituents is less characterized as its deep holes water.

5.3. Conclusions

The concentrations of THMs in the drinking water of twenty-one sampling points were measured. Surface water supply networks have higher level total THMs than groundwater supply. Chloroform contributed the most to TTHMs in nearly all samples, while bromoform contributed the least. In the present study residual chlorine, UV absorbance, phosphate and hardness as calcium, and electron conductivity were found to be the main predictors determining the abundance and distribution of trihalomethanes. The levels of THMs in Addis Ababa drinking water supply system are generally below the US EPA and WHO drinking water guidelines. However, more attention should be given to TCM, BDCM and DBCM, as they pose high cancer risk even at low levels. Since drinking water containing THMs poses health hazards, precautions must be taken to keep these levels in control. Minimizing the levels of total organic carbon in the water supply sources should be targeted in the future. The monitoring and regulation of the THMs is required on a regular basis to analyze trends and guide the water treatment and distribution system.

Chapter6 : Exposure and carcinogenic risk assessment of trihalomethanes (THMs) from water supply consumers in Addis Ababa, Ethiopia

6.1. Introduction

Chlorination is the most frequently used disinfection method used to destroy pathogenic microorganisms in drinking water (Srivastav et al., 2020, Mazhar et al., 2020). Although disinfection of drinking water lowers the risk of pathogenic infection, when organic and inorganic precursors are present in water, disinfection residues and their byproducts can constitute a chemical threat to human health (Mian et al., 2020).

Disinfection by products (DBPs) creation varies widely depending on the quality of the source water, including natural organic matter (NOM) concentrations and characteristics (as organic precursors) and levels of bromide (as an inorganic precursor), chlorine dose, chlorine contact time with the water, temperature, and pH of the reaction solution (Sadiq and Rodriguez, 2004, Salih and Al-Azzawi, 2016, Pardakhti et al., 2011). Chlorination has been a popular method of water disinfection due to its effectiveness in removing contaminants and affordability. The most often utilized disinfectants at the municipal level are chlorine (Cl_2), chloramines (NH_2Cl, $NHCl_2$), chlorine dioxide (ClO_2), ozone (O_3), and ultraviolet (UV) radiation (Srivastav et al., 2020).

When the naturally occurring natural organic matter present in raw water reacts with chlorine, a variety of DBPs are created, such as trihalomethanes (THMs), haloacetic acids (HAAs), and halogenated acetonitrile (HAN), which may have detrimental effects on human health (Liu et al., 2018, Hamid et al.). Since the discovery of trihalomethanes (THMs), the first DBPs in 1972 during the chlorination of drinking water, major efforts have been made to explore the formation mechanism, toxicity, mitigation measures, and incidence of DBPs (Hamid et al., Wang et al., 2022).

THMs, a class of DBPs that includes bromodichloromethane (BDCM), chlorodibromomethane (CDBM), and bromoform, are among the most common DBPs. Even at very low doses, these DBPs are detrimental to human health. These health hazards could include different malignancies, reproductive issues, birth deformities, and miscarriage (Mishaqa et al., 2022, Hwang and Jaakkola, 2012, McDONALD and Komulainen, 2005, Ewaid et al., 2018). THMs are regularly considered indicative of DBPs in human health risk assessments (Loomis et al., 2018).

THMs were regulated soon after they were found in drinking water that had been treated, and their maximum contaminant limit (MCL) was set at 100 µg/L for total trihalomethanes (TTHMs) (Li et al., 2021). The Stage 1 D-DBP Rule (Chowdhury et al., 2020b) decreased the MCL for TTHMs to 80 µg/L. The maximum allowable concentrations (MAC) for total THMs and other DBPs are not specified by Ethiopia's water quality standards.

The health risk assessments of THMs have been investigated by many researchers worldwide. In Tehran's drinking water, Iran, THMs appear to provide the greatest risk through inhalation, followed by ingestion and dermal contact (Pardakhti et al., 2011). Similarly, in a study of multipath modeling for exposure in lifetime human health risk of THMs in tap water of Karachi, Pakistan, it was discovered that it was mainly caused by the inhalation route (Siddique et al., 2015). In addition, in 10 regions of Fortaleza, Brazil, due to exposure to tap water, cancer risk increased by inhalation compared with oral ingestion and cutaneous absorption (Viana et al., 2009). In Abadan, Iran, inhalation was the main route of exposure, with an approximately 80–90% cancer risk (Kujlu et al., 2020).

Furthermore, a study comparing the cancer risk of THMs in drinking water extracted from two different water supply sources, surface water and well water, was carried out in Tehran. Drinking water extracted from surface water had a higher cancer risk than water extracted from other sources, (Pardakhti et al., 2011). However, a study performed in Dhaka City, Bangladesh, showed that carcinogenic risk via ingestion was higher than the USEPA acceptable limit of 10^{-6}. Carcinogenic risk via inhalation and dermal absorption was lower according to the USPEA acceptable limit (Ahmed et al., 2019).

The aim of this study was to assess the cancer and non-cancer risk from lifetime exposure to THMs via inhalation, drinking water ingestion and dermal contact from twenty-one sampling points in Addis Ababa, Ethiopia. Furthermore, this study also aimed to evaluate the health risks of THMs via a multi-exposure route in both males and females. To accomplish this, the concentrations of THMs in the drinking water of the twenty-one sampling points in the drinking water systems were investigated. Therefore, this study could help water treatment utilities monitor and regulate THMs in drinking water in Ethiopia.

6.1. Methods

6.1.1. Study Setting and Period

Ethiopia's capital is Addis Ababa. The city is situated 9º01’29" to the north and 38º44’48” to the east. 38º44’48”. Both surface water and groundwater are used in the city of Addis Ababa’s water supply. There are three primary dams that are utilized to collect run-off water and store it so that it can be used as surface water sources for water supply. The three dams are the Gefersa dam (18 km west of Addis Ababa), the Legedadi dam (25 km east of Addis Abe), the dire dam (10 km north of Legedadi dam), and the Akaki groundwater (Akaki well field) (MCE, 2015).

For surface water sampling, a total of seven surface water reservoirs, two surface water sources, and 70 households (36 HHs and 34 HHs from the Gefersa and Legedadi water supplies, respectively) were chosen. Five boreholes and 35 homes were selected for groundwater sampling (Fig.6.1). Since the water sources are used just once a year and are dispersed through a closed system, the samples taken at any time are believed to be consistent throughout the year. From June 1 to July 30, 2022, samples were collected.

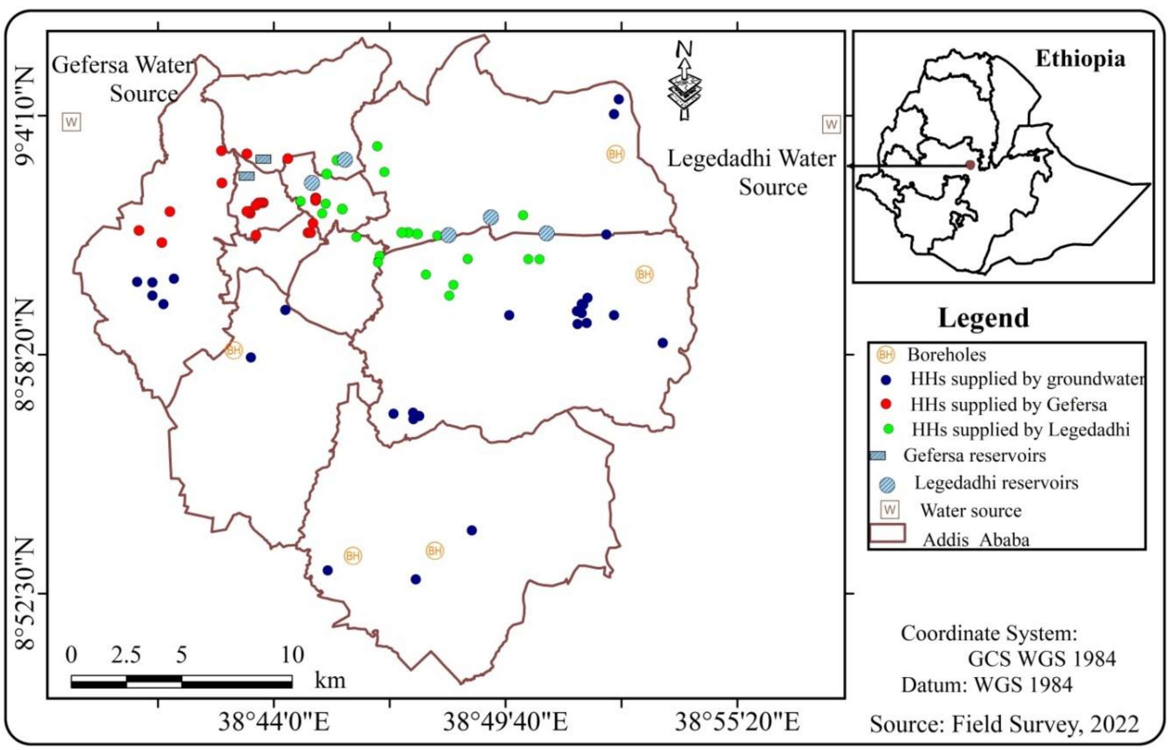


Figure 6.1: Sampling points of the water samples in Addis Ababa, Ethiopia, 202

6.1.2. Study Design

A cross-sectional study design was used in the water supply networks of the Addis Ababa municipal water system.

6.1.3. Sample size determination

Twenty-one (21) sampling stations in Addis Ababa, Ethiopia, were used to gather one hundred twenty (120) drinking water samples, and ArcGIS 14 was used for mapping. Legedadi, Gefersa, and groundwater sources were the three areas for sampling. Each sampling location produced forty water samples. Various areas of usage throughout the distribution network and raw and treated waters produced by drinking water treatment plants were used to collect the samples.

6.1.4. Sample collection and storage

Sample collection and handling procedures were carried out in strict and precise accordance with the US EPA (USEPA, 2016). Duplicate water samples were taken from the raw water sources immediately following chlorination (DAC), the several points of the distribution system, and household taps. Each sample bottle contained 125 mL of material, and the screw caps had silicon septa with Teflon faces. Na2SO3 (0.5% w/v) solution was added to the sample containers to quench residual chlorine. Before sampling, water was allowed to run through the pipe outlets for three to five minutes to ensure that the water came directly from the distribution system. The sample container was filled in a way that minimized headspace after collection to prevent the formation of air bubbles. The bottle was then properly sealed. In addition to the samples that would be examined, a sampling blank was also added. The THM-free reagent water was placed in one of the sampling containers, which was then carried to the sampling site, back to the site where the samples were stored, and then back again. In an ice bag, samples were brought to the lab and kept there until analysis at 4 °C.

6.1.5. Sample Analysis

With a few adjustments, EPA method 551.1(29) was used to determine the THM values in the samples. To extract the THMs, 10 mL of the sample was briskly agitated with 2 mL of pentane. After that, 2 µL of the extract was carefully transferred to a 2 mL glass vial and put in a Varian auto-injector model CP 8400 before being injected into a Varian CP-3800 gas chromatograph (GC). The injector was used in split mode at 220 °C (split ratio 25:1).

Using split mode, the injector was run at 220 °C (split ratio 25:1). The THMs were separated by the capillary Agilent 122-5032 - GC Column DB-5 (30 m 0.25 mm x 0.25 m) column and were discovered using an electron capture detector (ECD) set to 290 °C. The makeup gas was nitrogen, with the carrier gas set to flow at 1.5 mL/min and 40–60 mL/min. The temperature of the oven was set to 40 °C for 5 minutes, and then it was raised to 250 °C at a rate of 15 °C and maintained there for 2 minutes. The aforementioned standard combination of THMs was used to calculate the concentrations of THMs using the matrix matched calibration method. With the aforementioned configuration, the GC ran for more than 12 to 14 hours, and the background was checked often. The detector current was first set to 0.0 nA; then, when the baseline had stabilized, it was adjusted to 0.5–1.0 nA, depending on the signal. Upon the stabilization of the GC signal, the blank was run (several times) without any injection, and following an increase in baseline stability, 1 microL of pentane was injected.

6.1.6. Chemicals

The EPA 501/601 THM calibration mix certified reference material (200 µg/ml of each of the component's chloroform, CDBM, BDCM, and bromoform in methanol) was acquired from Sigma–Aldrich in Germany. Sigma–Aldrich in Germany provided the solvent (pentane), which was of GC quality.

6.1.7. Quality control and assurance

According to the Eurachem guide, the applied analytical method was verified prior to the analysis of the collected samples in terms of linearity, recovery, minimum detection limit (MDL), and repeatability (Bertil and Örnemark, 2014). The limit of detection (LOD) is the minimum concentration of trihalomethanes that can be detected at a specified level of confidence. To determine the LOD, a concentration of 10 µg/L (one tenth of MAC (maximum allowable concentration)) of matrix-matched samples of the four mixed standards was prepared in seven different replicates. Then, independent measurements of each sample were taken seven times, their standard deviation (SD) was calculated, and the LOD was determined as LOD = 3 X SD. A LOD study is conducted running 10 spiked samples through the entire analytical process from extraction to analysis (Magnusson, 2014) (Table 6.1).

During method verification, as internal quality control, a blank samples and water samples fortified with THM compounds of interest, at six working ranges were prepared as matrix-matched calibrants. Hence, three batches of matrix-matched calibrants were prepared over three different days (Day 1, Day 2 and Day 3). Along with, for determination of recovery and precision, nine (9) spiked samples each in triplicates were prepared by spiking blank samples at 0.5, 1.0- and 1.5-times concentrations of the MACs. Together with each batch of verification samples, matrix-matched reference standards fortified at MACs level post spiked on the water matrix (after sample underwent all preparative steps) and a true blank, reagent blank, which doesn't contain any analytes of interest in order to eliminate false-positive and ensure that the system is under control (Table 6.1). In this study, quality control samples were prepared in triplicates, whereas the test samples were prepared and analyzed in duplicates.

Table 6.1: Method Verification parameters

Parameter	**Trihalomethanes (THMs)**			
	CHCl3	**CHCl2 Br**	**CHBr2 Cl**	**CHBr3**
Retention time (min.± 5%)	4.21	5.48	7.55	9.95
Linearity correlation coefficients r^2	0.989	0.993	0.989	0.995
Recovery (%)	88.4-109.6	90.8-109.6	85.6-112.4	99.3-114.1
MDL[a] or LOD (µg/L)	1.37	1.73	1.92	1.67
Repeatability [a] (%)	6.18	3.58	6.79	6.41

MDL, Method Detection Limit; [a] for seven replicates.

6.1.8. Cancer risk assessment

A cancer risk assessment evaluates the likelihood that a person will get cancer as a result of pollutant exposure over the course of their lifetime. There are four steps in this process: assessing exposure and toxicity, gathering and analyzing data, characterizing risks, and managing risks (Wang et al., 2019). THMs were evaluated for their potential to cause human cancer using Equation (10) and three different exposure methods: oral ingestion, skin absorption, and inhalation (Mishaqa et al., 2022) and input values (Table 6.2).

$$Cancer\ risk = CSF \times CDI \qquad (10)$$

where CSF is the cancer slope factor and CDI (mg/kg/day) is the chronic daily intake. The following formulae were used to determine the CDI for each of the exposure routes:

$$CDI_{Oral\ ingestion} = \frac{C_W \times IR \times EF \times ED \times CF}{BW \times AT} \qquad (11)$$

$$CDI_{Absorption} = \frac{C_W \times SA \times F \times PC \times ET \times EF \times ED \times CF}{BW \times AT} \quad (12)$$

$$CDI_{Inhalation} = \frac{C_{Air} \times VR \times AE \times ET \times EF \times CF}{BW \times AT} \quad (13)$$

where AT is the average lifespan (days), BW is the body weight (kg), CF is the mass conversion factor from µg to mg (0.001), SA is the surface area of the skin exposed to water (m^2), F is the fraction of skin in contact with water (%), PC is the permeability coefficient (cm/h), and C_W is the concentration of THM species or TTHMs in the collected drinking water samples. where IR is the rate of water ingestion (L/day), EF is the exposure frequency (days/year), ED is the exposure duration (years), ET is the exposure time (min/day), and VR is the ventilation rate (m^3/h), AE is the absorption efficiency. Based on Eq.$[5-9]$, C_{air} is the concentration of THMs in the air that was calculated using the Little model(Little, 1992). According to Eq. $[10]$ the LCR estimate from multiple exposure routes was calculated by adding the cancer risks from numerous exposure routes for each species of THM. C air is determined by using the following formula:

$$Total\ risk = (CDI_{Oral} \times CSF_{Oral}) + (CDI_{Inhalation} \times CSF_{Inhalation}) + (CDI_{Dermal} \times CSF_{Dermal}) \quad \textbf{(14)}$$

exposure routes for each species of THM. C air is determined by using the following formula:

$$C_{air} = (Y_{s(t)} + Y_{si}) \quad [115]$$

Where

Ysi is the initial THM concentration in the shower room (assumed as 0 mg/l).

Ys(t) is the THM concentration in the shower room at time t (min) assumed to be 30 min in this study.

$$Y_{(s(t))} = [1 - exp(-bt)]\left({}^{a}/_{b}\right) \quad [16]$$

$$b = \left\{\left({}^{Q_1}/_{H}\right)[1 - exp(-N)] + Q_G \middle| V_s\right\} \quad [17]$$

a={Q_1.C_w [1-exp(-N)]}⁄V_s [18]

N=((K_OL A))⁄Q_L

[19]

Where *N is a dimensionless coefficient which is calculated from* K_OL A

$$\textbf{Total risk} = (\mathbf{CDI_{Oral}} \times \mathbf{CSF_{Oral}}) + (\mathbf{CDI_{Inhalation}} \times \mathbf{CSF_{Inhalation}}) + (\mathbf{CDI_{Dermal}} \times \mathbf{CSF_{Dermal}}) \quad [\mathbf{20}]$$

In this work, THMs volatilized from the drinking water into the shower room were calculated using the inhalation exposure model developed on the basis of Little's(Little, 1992) two-resistance theory. C air is determined by using the following formula:

6.1.9. Non-cancer risk assessment

The *hazard* index (HI) of THMs was calculated using Eqs(16) (17) to assess the non-cancer risk

$$HI\ for\ THMs(Oral) = {CDI_{Oral}}/{R_f\ D_{THMs}} \quad (16)$$

$$HI\ for\ THMs\ (\ Dermal) = {CDI_{Dermal}}/{R_f\ D_{THMs}} \quad (17)$$

where RfD is the reference dose (mg/kg/day). The input parameters utilized in the risk assessment studies for cancer and non-cancer are displayed in Table 6.2. Cancer risk is defined into four classes: negligible($CR < 10^{-6}$), acceptable low risk($1 \times 10^{-6} \le CR < 5.1 \times 10^{-5}$), acceptable high risk ($5.1 \times 10^{-5} \le CR < 10^{-4}$) and unacceptable risk$\ge 10^{-4}$.

Table 6.2: Input parameters of cancer and non-cancer risk estimation

Parameter	**Value**	**Reference**
Body weight(BW, kg)	70(male) 60(female)	(Radwan et al., 2020, Radwan et al., 2021, Mishaqa et al., 2022)
Concentration of THMs in water	See table 3	This study
Average lifetime (AT, days)	67.46x365(male) 72.61x365(female) 70x365	(Legay et al., 2011, Health and Group, 1989, UmakantKori and Chandra, 2010)
Exposure frequency (EF, days/year)	365	(Radwan et al., 2020, Radwan et al., 2021)
Exposure duration (ED, year)	30	(Legay et al., 2011, Emergency and Response, 1989, Mishaqa et al., 2022)
Ingestion rate (IR, L/day)	2	(Radwan et al., 2021, Radwan et al., 2020, Health and Group, 1989)
Exposure time$\left({min}/_{day}\right)$	35	(Lee et al., 2004)
Skin surface area (SA, m^2)	1.8	(Health and Group, 1989)
Fraction of skin in contact with water (F, %)	90	(Lee et al., 2004)
Permeability coefficient (PC, cm/h)	Chloroform: 0.00683 BDCM: 0.00402 CDBM: 0.00289 Bromoform: 0.0026	(Pardakhti et al., 2011, Siddique et al., 2015)
Carcinogenic slope factor (CSF, $(mg/kg/day)^{-1}$	Oral/dermal Chloroform: 0.031 BDCM: 0.062 CDBM: 0.084 Bromoform: 0.0079 Inhalation Chloroform: $8.05x10^{-5}$ BDCM: 0.13 CDBM: 0.095 Bromoform: 0.00385	(Pardakhti et al., 2011) (Pardakhti et al., 2011)
THM concentration in air (C air, mg/L)	Little's model	(Little, 1992)
Reference dose (R_fD, mg/kg/day	Chloroform: 0.01 BDCM: 0.02 DBCM: 0.02 Bromoform: 0.02	(Amjad et al., 2013)
Inhalation rate (IR, m^3/h	0.84(male) 0. 66 (Female)	(EPA, 1989)
Bathroom volume (Vs, m^3)	2–18	(Chen et al., 2003)
Water flow rate (QL, L/min)	5	(Little, 1992)
Air flow rate (QG, L/min)	50	(Little, 1992)
Dimensionless Henry's law constants (H)	0.12 (CHCl3) 0.0656 (CHCl2Br) 0.0321 (CHClBr2) 0.0219(CHBr3)	(Basu et al., 2011)
Overall mass transfer coefficient (KOLA, L/min)[a]	7.4 (CHCl3) 5.9 (CHCl2Br) 4.6 (CHClBr2) 3.7 (CHBr3)	(Little, 1992)

KOLA for the other three THMs were calculated according to Wang et al(Wang et al., 2007), [a] The KOLA of chloroform was from Little(Little, 1992)

6.2. Results and Discussion

6.2.1. Method verification

The standard chromatogram depicts a sharp well-separated and resolved peak for each of the THM compounds (S1). The matrix matched calibrations were constructed for six points (S1-4). The minimum detection limit (MDL) was 1.67µg/L. This value is compatible with the USEPA detection limits (ranging from 0.1 to 2.5 µg/L for the THMs), which vary across laboratories and time(Kaufman et al., 2020). The correlation coefficients (r) were higher than 0.989 for all standards, which signifies a good linear response for the different THM compounds in the concentration range. The mean recovery ranged from 85.6 to 114.1%, which falls in the acceptable range (80%– 120%) set by EPA method 551.1(Nikolaou et al., 2002b) and showed good accuracy of the method. Similarly, the method repeatability (3.58%–6.79%) ranges were within the EPA method 551.1 guideline (<15%) (Nikolaou et al., 2002b) and indicated good precision of the method.

6.2.2. Levels of trihalomethanes in Addis Ababa, Ethiopia, drinking water

The average values of the acquired data are displayed in Table 6.3 along with comparisons to the World Health Organization's (WHO) recommended limits (200, 60, 100, and 100 µg/L for $CHCl_3$, $CHCl_2$ Br, $CHClBr_2$, and $CHBr_3$, respectively)(Nottle, 2013). The total THMs in this study was 76.3 µg/L, which was also lower than the prescribed USEPA standards of 80 µg/L(Moya and Phillips, 2002). This finding is lower than those of other studies (Mishaqa et al., 2022, Kujlu et al., 2020, Nadali et al., 2019). However, it is higher than a study report from Southern Mauritius and Iran (Uppeegadoo et al., 1999, Nadali et al., 2019). Chloroform is the most dominant DBP recorded in this study. Other studies reported similar findings (Basu et al., 2011, Siddique et al., 2015).

Table 6.3: Total trihalomethanes and drinking water supplies in Addis Ababa, Ethiopia, 2022

	Mean Concentration µg/L (95% CI)	**Min (µg/L)**	**Max (µg/L)**	**WHO Guideline (µg/L)**
CHCl3	54.93(50.97-58.53)	4.3	79.40	200
CHCl2 Br	10.66(9.74-11.53)	2.42	19	60
CHBr2 Cl	7.70(6.83-8.53)	2.22	13.1	100
CHBr3	3.02(2.83-3.21)	2.7	3.21	100
TTHMs	**76.31**			

6.2.3. Cancer risk analysis of THMs through different routes

6.2.3.1. Ingestion route

The total THM LCR was calculated using Eq. (10) for all possible exposure routes using the input values indicated in Table 6.2 and the average concentration of TTHMs observed in this study. The average LCR for TTHMs via ingestion in drinking water samples in this study was unacceptably high risk(93.4×10^{-2}), which was higher than the unacceptable risk($\geq \ 10^{-4}$). The following was the order in which the risk contribution was noted:$Chloroform\ > BDCM > DBCM > Bromoform$ (Table 6.4). The risk was higher among males than females, and the oral route was the first most common risk factor. Among the four THMs, chloroform showed an acceptable low oral cancer risk of 2.9E-04 for males and 2.5E-04 for females. This is comparable with the results reported by (Hsu et al., 2001), (Lahey and Connor, 1983) and (Mazhar et al., 2022). According to their findings, chloroform's percentage contribution to overall risks was the highest. However, other studies (Lee et al., 2004) and (Mishaqa et al., 2022) reported that BDCM had the highest percentage contributions.

Table 6.4: Chronic Daily Intake of Trihalomethanes through oral ingestion

Parameters	Percentage of $CDI_{Oral\ ingestion}$	$CDI_{Oral\ ingestion\ male}$	$CDI_{Oral\ ingestion\ in\ Female}$
Chloroform	6.73×10^{-4}	2.9×10^{-4}	2.5×10^{-4}
BDCM	1.31×10^{-4}	5.71×10^{-5}	4.86×10^{-5}
DBCM	9.4×10^{-5}	4.11×10^{-5}	3.49×10^{-5}
BF	3.96×10^{-5}	1.72×10^{-5}	1.46×10^{-5}
THMs	93.4×10^{-2}	40.7×10^{-5}	35×10^{-5}

6.2.3.2. Lifetime cancer through dermal absorption

THMs can pass into the body through contact with chlorine treated water while swimming, cleaning dishes, and handling water; therefore, taking a shower and a bath are particularly important (Arman et al., 2016). An average lifetime risk through dermal routes was also of unacceptably high risk (4.3E-02), which was above the unacceptable risk (1.0E-04). The mean skin surface areas for females and males are 1.53 and 1.7 m^2, respectively (Moya and Phillips, 2002). The following was the order in which the risk contribution was recorded:$Chloroform > DBCM > BDCM > Bromoform$ (Table 6.5). The cancer hazards of THMs via dermal contact for females and males were 48.7E-02 and 44.9E-03, respectively, higher than the unacceptable risk (1.0E-04). Although the surface area of skin in males is higher, females have the highest cancer risk through the dermal route, in contrast with other studies (Lee et al., 2004). On the other some other studies are found to have similar results as the present study (Nadali et al., 2019, Kujlu et al., 2020)

Table 6.5: Chronic Daily Intake of Trihalomethanes through Dermal contact

Parameters	$CDI_{Absorption}$	$CDI_{Absorption\ in\ Male}$	$CDI_{Absorption\ in\ Female}$
Chloroform	64.6×10^{-3}	135.4×10^{-4}	146.5×10^{-4}
BDCM	1.5×10^{-3}	5.16×10^{-5}	16.8×10^{-4}
DBCM	26.7×10^{-2}	80.2×10^{-5}	30.1×10^{-2}
BF	11.2×10^{-2}	30.3×10^{-5}	12.6×10^{-2}
TTHMs	4.3×10^{-2}	44.9×10^{-3}	48.69×10^{-2}

6.2.3.3. Cancer risk from inhalation route

Inhalation was the major route of exposure contributing approximately 80–90% of cancer risk mainly due to $CHCl_3$ because this compound is highly volatile having a low boiling point (Kujlu et al., 2020, Babaei et al., 2015a, Siddique et al., 2015). The findings of cancer risk via inhalation are shown in Table 6.6 and Figs.6.2. LCRs due to inhalation exposure were 54.4-E02 for males and 46.3E02 for females. LCR due to total THMs via inhalation route was higher than USEPA unacceptable risk (1.0E-04) in the drinking water. That means approximately 1 in every 10,000 individuals in Addis Ababa, Ethiopia could get cancer from the daily intake of water in their life. The major contributor through inhalation was $CHCl_3$, with a value of 86.5%, followed by $BDCM > BF > DBCM$. A related study reported similar findings (Kujlu et al., 2020).

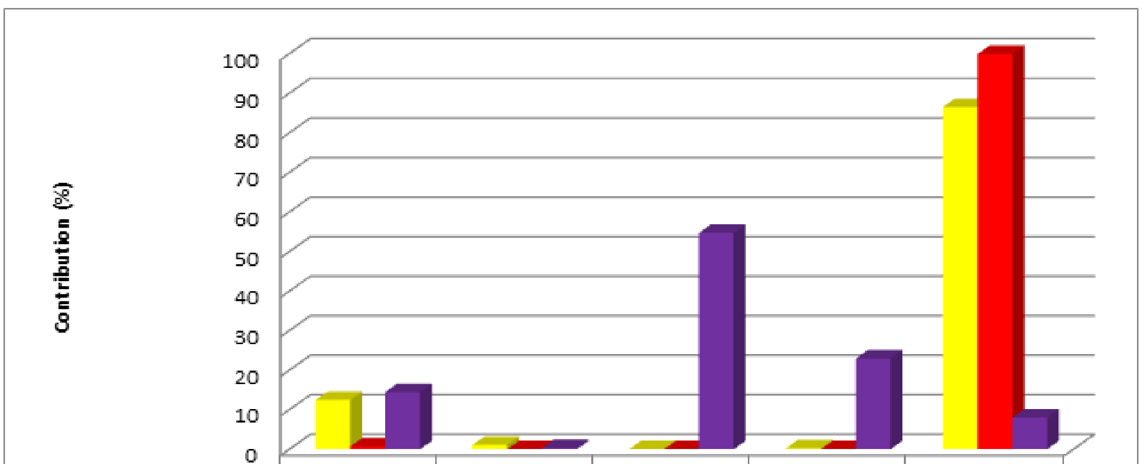
$$Chloroform > BDCM > BF > DBCM$$

Table 6.6: Chronic Daily Intake of Trihalomethanes through Inhalation

Parameters	Percentage of $CDI_{Inhalation}$	$CDI_{Inhalation\ in\ Male}$	$CDI_{Inhalation\ in\ Female}$
Chloroform	18.0×10^{-2}	23.8×10^{-2}	20.3×10^{-2}
BDCM	1.58×10^{-2}	24.3×10^{-3}	5.9×10^{-3}
DBCM	2.69×10^{-5}	1.17×10^{-5}	9.98×10^{-6}
BF	31.5×10^{-4}	13.7×10^{-4}	11.7×10^{-4}
TTHMs	125.3×10^{-2}	54.4×10^{-2}	46.3×10^{-2}

6.2.3.4. Trihalomethanes and cancer risk exposure through different routes

The LCR estimate of trihalomethanes via different routes in this work showed that ingestion is the most common route of exposure (Fig. 6.2). A consistent pattern of exposure route reported from Ivedik Water Treatment Plant, Ankara Turkey (Tokmak et al., 2004) depicting that one of the five million residents of Ankara could develop cancer every year by drinking water on a regular basis . In addition, inhalation was the second most common route of exposure in this work. A similar finding was also reported in other studies that inhalation was the major route of exposure to THMs (Babaei et al., 2015a, Lee et al., 2013, Mosaferi et al., 2021). A recent related study also signified that the utilization of hot water for showering was a risk factor for colorectal cancer that might be due to exposure to THMs; as the volatility of the THMs is higher in hot water (Tafesse et al., 2022b, Pardakhti et al., 2011).



	Chloroform	BDCM	DBCM	BF	TTHM
Inhalation	12.43	1.09	0.02	0.22	86.5
Ingestion	0.719	0.014	0.01	0.004	99.9
Dermal Absorption	14.42	0.31	54.7	22.9	8

Figure 6.2: The percentage contribution of each of the THMs to cancer risk via the different exposure routes

6.2.4. Total cancer risk estimated through different routes

The total cancer risk due to total THMs in this study was 1.66E-3, which was higher than the USEPA acceptable limit of 10E-6 via the three exposure routes. A similar consistent finding was reported from

Abadan, Iran (Kujlu et al., 2020). Ingestion was the dominant contributor to total cancer risk, followed by inhalation and dermal routes (Table 6.7).

Table 6.7: The lifetime total cancer risk estimate of trihalomethanes through different routes, Addis Ababa, Ethiopia, 2022

	Values	Male	Female
CDI *CSF oral	3.72×10^{-5}	7.48×10^{-3}	1.38×10^{-5}
CDI*CSF inhalation	1.06×10^{-3}	9.26×10^{-4}	8.22×10^{-4}
CDI*CSF Dermal	5.60×10^{-4}	1.50×10^{-3}	6.26×10^{-4}
Total cancer risk	1.66×10^{-3}	2.50×10^{-3}	1.46×10^{-3}

6.2.5. Contribution of trihalomethanes to the average TTHM risk

The average percentage of each THM species contribution to the mean LCR of TTHMs (Fig.6.3) depicted that the LCR by chloroform contributes the highest percentage (72%) of the total risk, followed by BDCM (14%), DBCM and finally bromoform. A similar pattern of THM species and LCR(LCR) was reported from India (Mazhar et al., 2022). Although the concentrations of BDCM and CDBM were significantly lower than that of chloroform, they posed a higher LCR. These findings are because BDCM and CDBM have potency factors that are ten times greater than those of chloroform and bromoform (Du et al., 2021, Lee et al., 2004, Semerjian and Dennis, 2007, Bare, 2006, Kumari et al., 2015). The bromoform concentration was very low in Addis Ababa. The concentration was detected only from groundwater sources, which could be due to the presence of natural bromide. Further investigation of brominated THMs in the drinking water supply of Addis Ababa, Ethiopia is needed.

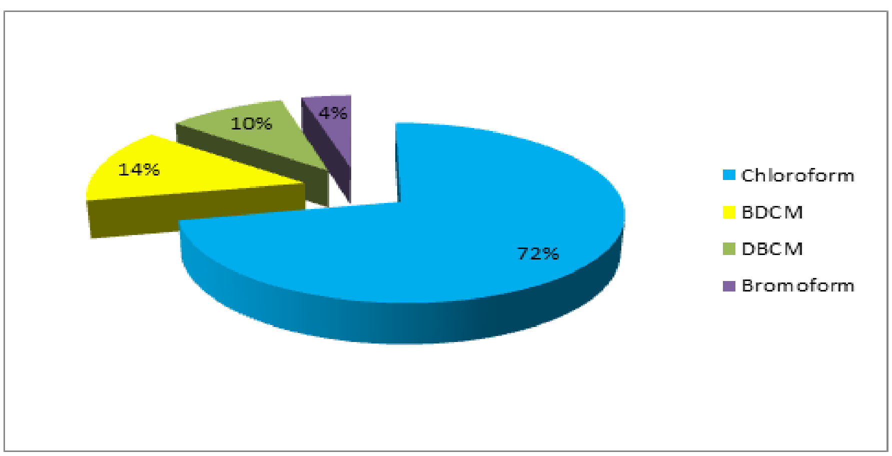


Figure 6.3: Percentage contribution of each THM species to the average TTHM lifetime risk in Addis Ababa, Ethiopia, 2022

6.2.6. Total Cancer Risk and Trihalomethanes by Sex

The risk analysis in this study indicated that the total LCR from the targeted THMs was higher via the three exposure routes than the negligible risk levels (1×10^{-6}). The findings also showed that males were at higher THM cancer risk than females (Fig. 6.4). Other findings reported from other studies showed that males are more susceptible to this cancer(Mishra et al., 2014, Tafesse et al., 2022a) .

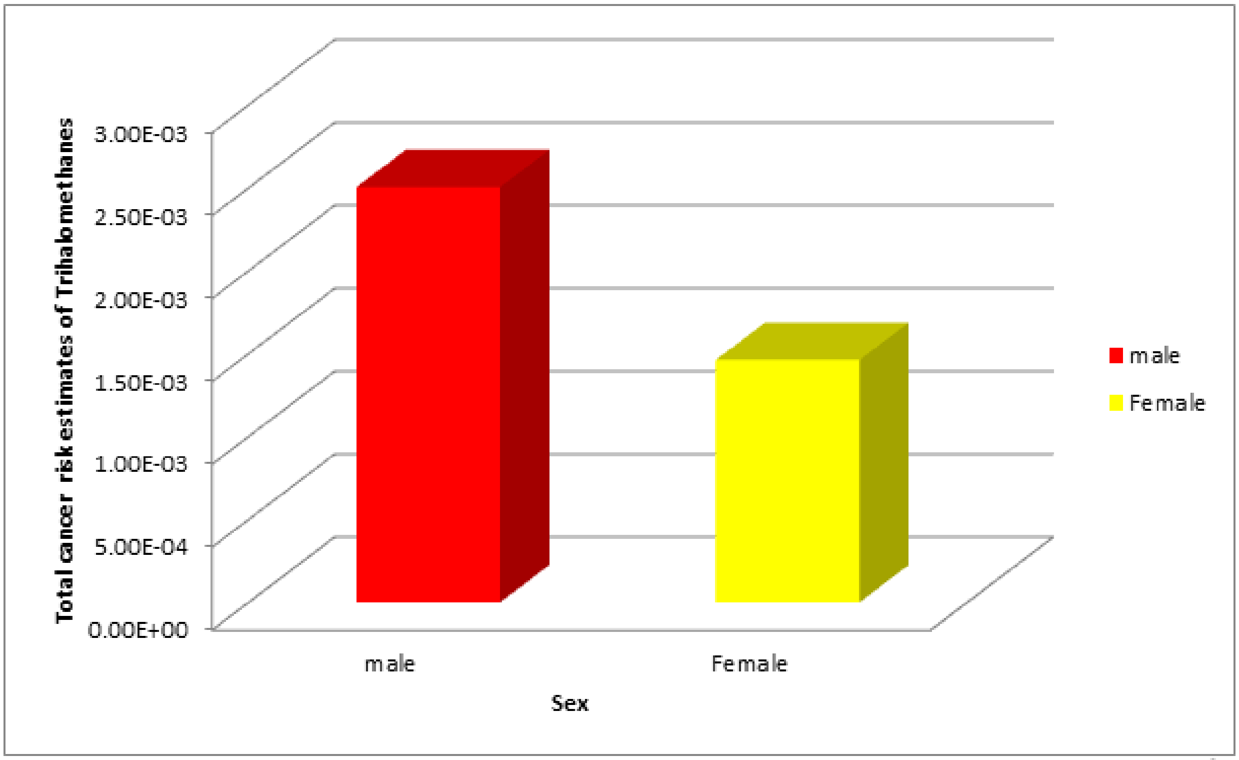


Figure 6.4: Total risk estimates of trihalomethanes by sex in Addis Ababa, Ethiopia, 2022

6.2.7. Trihalomethanes and non-cancer risk

The hazard index (HI) of THMs was calculated using Eqs (16) (17) to assess the non-cancer risk. The hazard index (HI) findings in this study showed that the dermal route caused higher HI values than the ingestion route and that chloroform had the greatest contribution to the HI value. The remaining THM species contributions were below unity, signifying that there would be negligible non-cancer risk (Fig. 6.5).

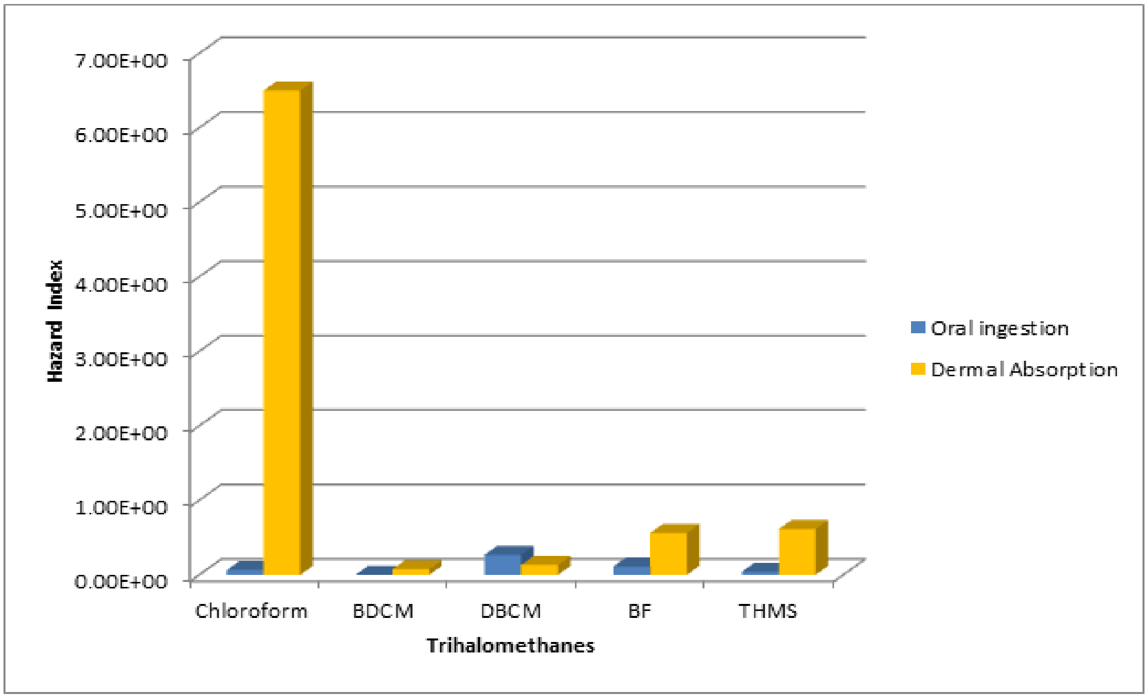


Figure 6.5: Hazard index values of total and individual THM average concentrations for oral and dermal exposure routes, Addis Ababa, Ethiopia, 2022

6.3. Conclusions

This study is the pioneer in its kind to determine the concentration of THMs and their cancer risk investigation through inhalation, dermal absorption and ingestion exposure routes in Addis Ababa, Ethiopia. The findings showed that the THM concentration in the drinking water of Addis Ababa, Ethiopia, was lower than the US EPA limit. $CHCl_3$ had the highest concentration, and $CHBr_3$ had the lowest concentration. The LCRs caused by all pathways were higher than 10^{-6} (negligible risk level defined by the USEPA). The ingestion route carried the greatest lifetime cancer risk for all THMs, which was followed by inhalation and dermal contact. Chloroform was linked to an increased risk of developing cancer through dermal contact. Males had a higher overall cancer risk than females. On the other hand, the hazard index value was below unity, indicating that adverse non-cancer health effects are negligible. In Addis Ababa, Ethiopia, it is crucial to use chlorine dioxide (ClO_2), ozone, and ultraviolet (UV) radiation as alternatives to chlorine. Recently, ClO_2 has been linked to reduced THM formation. The THM concentrations are below the US EPA limit level. However, more attention is required to BDCM and DBCM because they cause high cancer risk even at low levels.

Chapter7 : General Discussion

This study is the first of its kind to investigate the relation between drinking water chlorination byproducts and cancer in Addis Ababa, Ethiopia. The first part of this study tried to show the burden (namely GIT and UBC) cancers related with drinking water chlorination byproducts in Addis Ababa, Ethiopia. The cancer registry in Addis Ababa, Ethiopia was used to conduct the study. It is essential to explore all the possibilities of disinfection byproduct-related cancers due to chlorination of drinking water.

Consumption of surface water (highly chlorinated) and groundwater (less chlorinated) was used as an acceptable surrogate for comparing exposure versus. Non- exposure to DBPs(Morris et al., 1992). The type of water source used per case was classified using the water supply networks of Addis Ababa. The linkage of individual residential addresses with their water supplies permitted improved measures of exposure(Crump and Guess, 1982). Since there is no monitoring and regulation system of DBPs in drinking water distribution systems in Addis Ababa, Ethiopia. In addition, there is no historical data on the level of chlorination byproducts (DBPs) in Addis Ababa, estimates of past exposure have been based on previous information about the water sources (ground and surface water sources) (Villanueva et al., 2015).

The findings of this work concluded in general that the prevalence of DBRCs is higher in communities supplied with chlorinated surface water than in those supplied with non-chlorinated groundwater. A meta-analysis performed by Morris and his colleagues in 1992 supported this finding by indicating chlorinated surface water has substantially larger amounts of chlorination by-products than chlorinated groundwater (medians of 50.7 and 0.8 ppb, respectively) even when the surface water is collected from protected reservoirs(Berg and Burbank, 1972). Therefore, consumption of surface water was found to be an indirect indicator of exposure to chlorination by-products used in different studies (Morris et al., 1993, Doyle et al., 1997). This stage of study also highlighted that the incidence and trends of this two types of cancers was changed significantly from the year 2012 to 2016.

This other objective of this study also attempted to determine the effect of DBPs towards colorectal cancers in Addis Ababa using the type of water sources. In this facility based matched case control study, drinking water chlorination status, years at place of longest residence, types of water used for showering and swimming history were significantly associated with CRC. It was clearly found out that that drinking chlorinated water, particularly chlorinated surface water is linked with colorectal cancers.

The other key findings of this study showed that study participants who used hot water for showering were at more risk of developing CRC. This could be due to the high water temperature that increases the volatility of the THMs that may increase the inhalation exposure (and reduce the concentration of the same in water), and the increase diffusivity of the THMs inside the body through dermal contact. Similarly, measurement of study participants shower water temperature also indicated a significant difference between case and control households. A similar finding were reported from western Massachusetts, USA indicating that the concentrations of trihalomethanes (THMs), trichloroacetic acid (TCAA) and chloropicrin (CP) were substantially higher in the hot water shower than in the cold water shower (57).

This study performed measurements of trihalomethanes in drinking water for the same population in the study area. The concentrations of THMs in the collected water samples were determined following EPA method 551.1(29) with some modifications. The THMs were separated by an Agilent 122-5032 -GC Column DB-5 (30 m × 0.25 mm x 0.25 µm) capillary column and detected by an electron capture detector (ECD). According to the Eurachem guide, the applied analytical method was verified prior to the analysis of the collected samples in terms of linearity, recovery, minimum detection limit (MDL), and repeatability (Bertil and Örnemark, 2014). The verified parameters of THMs determination methods almost all compatible with USEPA limit and can be applied for future application in the study area.

The average concentration value of THMs in the drinking water supply was below the US EPA limit. The results of the average THM concentration followed the order TCM > BDCM > DBCM > TBM. The mean CHCl3 was highest in the Gefersa surface water supply system, which was 62.4 µg/L. TTHMs had strong positive correlations with UV254, temperature of water and residual chlorine. The TDS and pH had strong negative correlations with TTHMs.

The cancer risk study discovered that among the examined routes, ingestion causes the greatest risk. The lifetime cancer risk by chloroform contributes the highest percentage (72%) of the total risk, followed by BDCM (14%), DBCM (10%) and bromoform (4%). The cancer risk for the studied sampling areas in Addis Ababa was higher than the level recommended by the USEPA(1×10^{-6}). The hazard index (HI) findings in this work indicated that the dermal route caused higher HI values than the ingestion route and that chloroform had the greatest contribution to the HI value. In addition, the total cancer risk for males was higher than that for females in this work.

7.1. Strengths

The strengths of this study include the following. The key steps undertaken in this work was integration of the water supply networks to the cancer registry database and this was one of the nobility of this study. The classification of the exposure using this way is original and involves extensive experimentation and research work.

1. The use of a matched case-control study enabled the matching to control for potential confounders. Matched case-control studies have minimal bias relative to unmatched case-control designs due to their internal comparison property.

2. It is a pioneer study to investigate the effect of drinking water chlorination on CRC in Ethiopia, and there was a high response rate (95.5%) for both cases and controls.

3. The use of population controls (in the matched case control study) have the advantage that their exposures are likely to be representative

4. Contrary to the previous studies of chlorination byproducts and CRC (Schwarzenbach et al., 2010b, Wiedenmann et al., 2006, DeMarini, 2020) in which control for confounding was minimal or absent, a number of variables were tested as potential confounders and effect modifiers.

5. The study was able to determine with considerable confidence that THMs in the surface water sources contained higher THMs level compared to groundwater supply.

6. The method validation and verification of THMs in the laboratory set up of Addis Ababa, Ethiopia is one step forward to monitor and regulate the THMs concentration in drinking water.

7.2. Limitations

1. Some households of the cases and controls received a mixed water supply system, which made it difficult to confirm whether the water source is chlorinated or not.
2. Cases and controls study subjects might have changed their residential address in such a way that it may affect the true classification of the exposure.
3. The chlorination status of household water is not based on actual measurement of residual chlorination determination.
4. Cases/controls may use bottled water and water treated with household water treatment

5. The control group is selected from the general population and no confirmatory test whether they are free from colorectal cancer or not.
6. Case selection from health facilities can be prone to bias since patients usually do not represent the general population.
7. Recall bias could have been introduced during historical exposure measurement.

Chapter8 : Conclusion, Recommendation and Future Prospect

8.1. Conclusion

The prevalence of DBRCs was higher in communities supplied with chlorinated surface water. Similarly, the prevalence of DBRCs was higher among males than females. Drinking chlorinated water for extended years is a significant risk factor for CRC in Addis Ababa. In addition, hot tap water use for showering, and swimming history are risk factors for CRC. Surface water supply networks have higher level total THMs than groundwater supply. The average total THM content was lower than the US EPA's MCL. Chloroform contributed the most to TTHMs in nearly all samples, while bromoform contributed the least. Trihalomethane fractions and measured quantities of residual chlorine, UV_{254} and temperature of water showed a strong positive correlation, whereas TDS and pH values showed a negative correlation.

The LCRs caused by all pathways were higher than 10^{-6} (negligible risk level defined by the USEPA). The ingestion route carried the greatest lifetime cancer risk for all THMs. Chloroform was linked to an increased risk of developing cancer after dermal exposure. The primary method of exposure was through ingestion, which was followed by inhalation and dermal contact. Males had a higher overall cancer risk than females.

8.2. Recommendations

Addis Ababa Water and Sewerage Authority (AAWSA) and Ministry of Water and Energy

- The method validation and verification of THMs used in this study can be applied to monitor and regulate the THMs concentration in drinking water.
- It is required to establish maximum allowable concentrations (MAC) of total trihalomethanes for better monitoring and regulation.
- An initiation of alternatives methods to chlorine disinfection of drinking water is also essential.
- It could be highly beneficial implementation of cost effective and efficient removal of natural organic matter thereby reduce DBP formation.
- It is important to design a guideline for monitoring and regulation of drinking water chlorination byproducts, most importantly trihalomethanes.

Ministry of Health

- It is essential to design integrated interventions that consider chlorination by-products and exposure routes towards the prevention and control of CRC in Ethiopia.
- It could be better to create awareness towards the exposure pathways of drinking water disinfection byproducts or trihalomethanes for the public.
- Advocacy work towards utilization of cold shower would be important for lowering the risk of developing colorectal cancer.

8.3. Future Prospect

This study warranted further study on measurements of disinfection by products in urine and / or blood for the same population in the study area. Similarly, molecular characterization and gene typing of biological samples and THMs is central for better featuring of the pollutant. This study directs further epidemiological study towards drinking water chlorination related cancers using cancer registry in Addis Ababa, Ethiopia. It is also essential to perform an additional study on precursors of THMs. It is also required to determine the level of brominated THMs in the drinking water supply system in Addis Ababa, Ethiopia. Though hot shower utilization and swimming history had statistically significant association in this study, it needs further follow up study for confirmation of causation.

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Thesis outputs

1. **Nebiyou Tafesse**, Massimiliano Porcelli, Sirak Robele Gari, and Argaw Ambelu "Prevalence and Trends of Drinking Water Disinfection Byproducts-Related Cancers in Addis Ababa, Ethiopia", Environ Health Insights (2022) 16 (1); DOI. 10.1177/11786302221112.
2. **Nebiyou Tafesse**, Massimiliano Porcelli, Sirak Robele Gari, and Argaw Ambelu "Drinking Water Source, Chlorinated Water, and Colorectal Cancer: A Matched Case-Control Study in Ethiopia", Environ Health Insights (2022) 16 (1); DOI: 10.1177/11786302211064432
3. **Nebiyou Tafesse**, Massimiliano Porcelli , Belachew Bacha, Janvier Gasana, R. K. Padhi, Sirak Robele, Argaw Ambelu "Exposure and carcinogenic risk assessment of trihalomethanes (THMs) from water supply consumers in Addis Ababa, Ethiopia" **published** *Toxicological Reports Journal - ScienceDirect.com by Elsevier*
4. **Nebiyou Tafesse**, Massimiliano Porcelli , Belachew Bacha, Janvier Gasana, R. K. Padhi, Sirak Robele, Argaw Ambelu "Trihalomethanes and physicochemical quality of drinking water in Addis Ababa, Ethiopia" **Under Review in** Heliyon Journal - ScienceDirect.com by Elsevier

List of Conference Presentation

1. Nebiyou Tafesse, Massimiliano Porcelli, Sirak Robele Gari, and Argaw Ambelu "Drinking Water Source, Chlorinated Water, and Colorectal Cancer: A Matched Case-Control Study in Ethiopia", **Oral Presentation** in 5th Ethiopian Environmental Professional Associations (EEHPA) Annual Scientific conference , Dilla , Dilla University, Southern Ethiopia , May 27-28, 2022
2. Nebiyou Tafesse, Massimiliano Porcelli, Sirak Robele Gari, and Argaw Ambelu "Drinking Water Source, Chlorinated Water, and Colorectal Cancer: A Matched Case-Control Study in Ethiopia", **Poster Presentation** in 33rd Ethiopian Public Health Associations (EEHPA) Annual conference from March 13-15, 2022 at Inter Luxury Hotel, Addis Ababa, Ethiopia
3. Nebiyou Tafesse, Massimiliano Porcelli, Sirak Robele Gari, and Argaw Ambelu "Drinking Water Source, Chlorinated Water, and Colorectal Cancer: A Matched Case-Control Study in Ethiopia", **Scholars International Webinar on** Cancer Research and Therapeutics from 14-16 Nov 2022 at Dubai, United Arab Emirates (UAE).

Annex 1: Study Questionnaires

ENGLISH AND AMAHRIC VERSION SURVEY QUESTIONNAIRES

ANNEX 2. SURVEY ENGLISH AND AMHARIC VERSION QUESTIONNAIRES

ENGLISH VERSION OF THE QUESTIONNAIRE

Structured Questionnaire to identify factors to associated with colorectal cancer

Addis Ababa University

Ethiopian Institute of Water Resources

Subject Information Sheet
Good morning/Good afternoon. My name is__________________ and I am a member of a team

Conducting research to assess Drinking Water Source, Chlorinated Water, and Colorectal Cancer: The study is conducted one of the PhD student in collaboration with Addis Ababa University, Ethiopian Institute of Water Resources.

The purpose of my visit today is to take information from you on Drinking Water Source, Chlorinated Water, and Colorectal Cancer: If you are willing to participate, I will ask you few questions. I will visit your home and backyard environment to collect information. In the study if you are found to have a certain health problems, appropriate educational counseling and education will be given to you. However, no financial payment will be made for your participation.

Your name will not be written on this form and will never be used with any information you may tell me. You do not have to answer any questions that you do not want to answer and you may end this interview at any time you want. However, your honest answer to these questions and your continuous interest to participate in study will help as for better understanding of the drinking water source, chlorinated water, and colorectal cancer: eventually help in designing and implementing appropriate intervention Programme to alleviate the problem. We would very much appreciate your participation in this research by genuinely responding to the interviews. Your participation in the study is fully based on your interest and choice. It would take 20-30 minutes to complete the questionnaire. If you have any question during my interview and observation of the home and backyard of the environment, you can ask me at any time so that I can elaborate it. It is also possible to communicate the principal investigator through Tel +251912143906

Questionnaire ID………………………….

Informed Consent Form

With the due understanding of the aforementioned information, would you be willing to participate in the study

Yes ☐

Signature/Finger print of the participant

Signature/Finger print ______________________Date _____________________

No

☐ (Terminate the interview

Signature of the interviewer

Name ______________________Signature ________________ Date __________

Supervisors/Researcher remark and signature

Name ______________________ Signature _______________ Date __________

Addis Ababa University

Ethiopian Institute of Water Resources

Study Two Questionnaire: Drinking Water Source, Chlorinated Water, and Colorectal Cancer: A Matched Case-Control Study in Ethiopia.

Instructions: Put the respondents answer inside the box

Part I: Sociodemographic part

s.no	**Question**	**Response**	**Skip**
001	**Questionnaire number**	_____________	
002	The study participants should be residents of Addis Ababa for minimum of 10 years and above	_____________	
003	Code number	____________	Type of subject 1. Rectal 2. Colon 3. Control
004	Card number	____________	
005	Mobile number		

100.	Gender	A. Male B. female	
101	Sub city	____________	
102	Woreda	____________	
103	Household number	____________	
104	Residential history	1. From birth 2. Not from birth	
105	For how many years lived in the current area?	___________________	
106	Age	____________	
107	Have you attended education?	A. Yes B. No	
108	Educational status	A. Illiterate B. Primary C. Secondary D. College E. University	
109	Marital status	A. Single B. Widowed C. Divorced D. Married **E.** Others	
110	Do you have stable source of income?	A. Yes B. No	If no proceed to Q 112
111	If yes to # 110 how many is your monthly income in ETB?	________________	
112	What is your occupation? Multiple answers possible	A. Farmer B. Government employee C. Merchant D. Private organization employee E. Daily laborer F. House wife G. Other	
113	Occupational type since 18 years old?	A. Farmer B. Government employee C. Merchant D. Private organization employee E. Daily laborer F. House wife G. Other	

114	Occupational type since six months ago?	A. Farmer B. Government employee C. Merchant D. Private organization employee E. Daily laborer F. House wife G. Other	
115	Study participant resident location	A. Longitude __________ B. Latitude __________	

Part II: Water source and drinking water characteristics

s.no	Question	Response	Skip
200	What (is/was) the primary source of drinking water (where you live/when you lived there	A. municipal water supply B. private well C. bottled D. other (specify)/ E. Don't know.	
201	What is the type of water source?	A. Surface water B. Ground water C. Well water D. other (specify)/	
202	Was the water chlorinated?	A. Yes B. No	To be verified by the researcher
203	How did you usually bathe? Did you generally take a bath or did you use a shower?	A. Shower B. bath C. both D. washbowl E. Don't know.	
204	How often did you take a shower/bath?	A. Once per day B. Twice per week C. Three times per week D. Others (Specify)_____	
205	In what form did you use the water when taking shower?	A. Use hot water only B. Use cold water only C. Was warm water only D. Mixing hot water with cold water	

206	During your adult life, did you ever go to a swimming pool for a swim**?**	A. Yes B. No	if no proceed to # 212
207	How many times a year did you go to a swimming pool for a swim	A. Once a year B. Twice per year C. Three times per year D. More than three times per year	
208	What year/age did you start going to a swimming pool	_______________	
209	What year/age did you stop going to a swimming pool	________________	
210	When you went to the swimming pool, for how long did you usually remain in the water	A. 15 minutes B. 30 minutes C. 1 hour D. More than one hour	
211	What was the type of swimming pool?	A. Indoor B. Outdoor	
212	What was the average daily water consumption before 2 years? (liter/day)	________________________________	

Part III: Health profile variables

s.no	**Question**	**Response**	**Skip**
300	Body weight	____________	
301	Height	_____________	
302	BMI	_____________	
303	Have you ever had history of Crohn's disease or colitis before?	A. Yes B. No	
304	If yes to Q# 300please specify	____________	
305	Is there familial history of colorectal cancer?	A. Yes B. No	
306	Did you participate for regular exercise? Multiple response possible	A. Yes, usually (3 times a week for 30 min) B. Yes, occasionally(less than 3 times a week	

		C. No , never	
307	Had you been smoking cigarette?	A. Yes B. No	
308	Did you consume alcohol	A. Yes B. No	
309	If yes to # 308 what type of alcohol you consumed? Multiple response possible	A. Beer B. Red Wine C. White wine D. Beer E. Sprits F. Others specify _________	
310	Have you been pregnant?	A. Yes B. No	
311	If yes to # 310 how many times you were pregnant?	______________	

Part IV-Dietary practice questionnaire

s.no	Question	Response	Skip
400	How many times in a day do you eat?	A. 1 times B. 2 times C. 3times D. greater than 3times	
401	Did you take your meal with appropriate time?	A. Yes B. No	
402	Which one do you use for cooking	A. Saturated fatty acid B. Unsaturated fatty acid	
403	Do you drink sweet and soda drinks Drinks regularly?	A. Yes B. No	
404	If yes to # 4 how many times you use?	A. at least once a day B. 4–6 times per week C. 2–3 times per week”, “once a week”, D. 2–3 times per month”, E. once a month”, and F. never or ever in a year	
405	Do drink herbal drink?	A. Yes B. No	
406	If yes to # 405 how many times you use?	A. at least once a day B. 4–6 times per week	

		C. 2–3 times per week", "once a week", D. 2–3 times per month", E. once a month", and F. never or ever in a year	
407	Do you take meat regularly	A. Yes B. No	
408	If yes to # 407 how many times you use?	A. at least once a day B. 4–6 times per week C. 2–3 times per week", "once a week", D. 2–3 times per month", E. once a month", and F. never or ever in a year	
409	Do you take egg regularly	A. Yes B. No	
409	If yes to # 409 how many times you use?	A. at least once a day B. 4–6 times per week C. 2–3 times per week", "once a week", D. 2–3 times per month", E. once a month", and F. never or ever in a year	
410	Do you take milk regularly	A. Yes B. No	
411	If yes to # 410 how many times you use?	A. at least once a day B. 4–6 times per week C. 2–3 times per week", "once a week", D. 2–3 times per month", E. once a month", and F. never or ever in a year	
412	Do you consume fruits regularly?	A. Yes B. No	
413	If yes to # 14 how many times you use?	A. at least once a day B. 4–6 times per week C. 2–3 times per week", "once a week", D. 2–3 times per month", E. once a month", and F. never or ever in a year	
414	Do you eat vegetables regularly?	A. Yes B. No	
415	If yes to # 415 how many times you use?	A. at least once a day B. 4–6 times per week C. 2–3 times per week", "once a week", D. 2–3 times per month",	

		E. once a month", and F. never or ever in a year	
416	Do you take fruits regularly?	A. Yes B. No	
417	If yes to # 416 how many times you use?	A. at least once a day B. 4–6 times per week C. 2–3 times per week", "once a week", D. 2–3 times per month", E. once a month", and F. never or ever in a year	
418	How do you usually take fruits	A. Juice form B. Whole part	
419	Do drink tea regularly?	A. Yes B. No	
420	If yes to # 419 how many times you use?	A. at least once a day B. 4–6 times per week C. 2–3 times per week", "once a week", D. 2–3 times per month", E. once a month", and F. never or ever in a year	
421	Do you drink coffee regularly?	A. Yes B. No	
422	If yes to # 23 how many times you use?	A. at least once a day B. 4–6 times per week C. 2–3 times per week", "once a week", D. 2–3 times per month", E. once a month", and F. never or ever in a year	
423	Do you wash your hand regularly?	A. Yes B. No	
424	Did you wash dish in the kitchen?	A. Yes B. No	

AMHARIC VERSION OF THE QUESTIONNAIRE

አዲስ አበባ ዩኒቨርሲተ

የኢትዮጵያ ውሀ ሀብት ኢንስቲትዩት

የመጠጥ ውሀ እና ኩሎሪን የተጨመረበት ከ አንጀት ካንሰር ጋር ያለውን መስተጋብር ለማጥናት የታሰበ ነው።

የተጠያቂዎች/መላሾች የመረጃ ቅጽ

እንደምን አደርሽ/ክ/ዋልሽ/ዋልክ/ዋሉ።ስሜ----------------ይባላል የመጠጥ ውሀ እና ኩሎሪን የተጨመረበት ከ አንጀት ካንሰር ጋር ያለውን መስተጋብር በሽታ ወሳኝ ምክንያቶች ለማወቅ የጥናት ምርምር ከሚያደርጉት አባላት ዉስጥ አንዱ ነኝ። ጥናቱን የሚያካሂደዉ አንድ የሦስተኛ ዲግሪ ተመራማሪ ከአዲስ አበባ ዩኒቨርሲቲና ከኢትዮጵያ ውሀ ሀብት ኢንስቲትዩት ጋር በጋራ በመሆን ነዉ። የዛሬዉ የእኔ ጉብኝት/መምጣት አላማ የመጠጥ ውሀ እና ኩሎሪን የተጨመረበት ከ አንጀት ካንሰር ጋር ያለውን መስተጋብርላይ ከእርሰዎ መረጃ ለመሰብሰብ ነዉ።ለመሳተፍ ፈቃደኛ ከሆኑ የተወሰኑ ጥያቄዎችን ለመጠየቅና መረጃዉን ለመሰብሰብ ነዉ የመጣሁት። በጥናቱ ሰአት የጤና ችግር ካጋጠመዎት ተገቢ የሆነ ምክርና ትምህርት ይሰጠዎታል።ለተሳትፎዎ ግን ምንም አይነት ገንዘብ አይከፈልም፡

የሚሰጡኝ መረጃ ከጥናቱ አላማ ዉጭ ለሌላ ለምንም ነገር አልጠቀምበትም ስምዎት በመረጃዉ ቅጽ ላይ አይፃፍም።መመለስ የማይፈልጉት ጥያቄ ካለ አለመመለስና ቃለ መጠይቁን/ምልልሱን በፈለጉት ሰአት ማ ረጥ ይችላሉ።ነገር ግን የእርሰዎ ትክክለኛ መልስና ንቁ ተሳትፎ በጥናቱ የተቅማጥ በሽታ ወሳኝ ምክንያቶችን በደንብ ለመረዳትና ተገቢዉን መፍትሔ በማዘጋጀት ችግሩን ለመፍታት ይረዳናል። በጥናቱ ላይ የእርሰዎ ተሳትፎ ሙሉበሙሉ በእርሰዎ ፍላጐትና ምርጫ ላይ የተመሰረተ ነዉ።ቃለ መጠይቁን/ምልልሱን ለመጨረስ ከ20-30 ደቂቃ ሊወስድ ይችላል። በቃለ መጠይቁ/ምልልሱና ቤትወትን/ግቢዎትን በምጎበኝበት ሰአት ማንኛዉም ጥያቄ ካለዎት በማንኛዉም ሰአት መጠየቅ ይችላሉ ወይም ላብራራልዎት እችላለሁ። የበለጠ መረጃ ከፈለጉ ዋና ተመራማሪዉ በዚህ ስልክ ቁጥር ሊያገኙት ይችላሉ +251912143906

የስምምነት መጠየቂያ ቅጽ

ከላይ በተጠቀሰው መረጃ መሰረት በዚህ ጥናት ለመሳተፍ ፍቃደኛ ነዎት?

አዎ ☐

የተሳታፊ ፊርማ/የጣት አሻራ ______________________ ቀን ______________________

አይደለሁምመጠይቁን/ምልልሱን ያቋርጡ ☐

የጠያቂው ፊረማ

ስም ________________________ፊሪማ________________ ቀን________

…......የተቆጣጣሪ
ዎች/ አስተያየትና ፊርማ--
[redacted]

ሰም_______________________ፊሪማ_____________ _ቀን_________

ክፍል አንድ : **<u>ማህበራዊ እና ኢኮኖሚያዊ መረጃ</u>**

ተ.ቁ	መጠይቅ	አማራጭ መልስ	ዝለል	አስተያየት
001	የመጠይቁ ቁጥር			
002	በአዲስ አበባ ከተማ አስተዳደር ለምን ያህል ጊዜ ኖራዋል ? ለጥናቱ ተሳታፊ የሚሆኑ ቢያንስ 10 ዓመት ና ከዚያ በላይ መሆን አለባቸው	_______________________		
003	መለያ ቁጥር	_______________________	የካንሰሩ ዓይነት 1. ሬክታል 2. ኮለን 3. ኮንትሮል	
004	ካርድ ቁጥር	_______________________		
005	ሰልከ			
100	ፆታ	A. ወንድ B. ሴት		
101	ክ/ከተማ	_______________________		
102	ወረዳ	_______________________		
103	የቤት ቁጥር	_______________________		
104	የመኖርያ አዳርሻ ከውልደት ጀምሮ	A. ከውልደት ጀምሮ አዲስ አበባ የኖርኩ B. አዲስ አበባ ያልተወለድኩ		
105	አሁን በሚኖሩበት ቤት ለምን ያህል ጊዜ ኖሩ	________________		

106	ዕድሜ	_ ______________		
107	የትምህርት ደረጃ	A. ያልተማረ B. የመጀመርያ ደረጃ C. ሁለተኛ ደረጃ D. ኮሌጅ E. ዩንቨርሲቲ		
108	የጋብቻ ሁኔታ	A. ያላገባ/ች B. ባሏ የሞተባት C. የፈታ/ች D. ያገባ E. ሌላ		
109	ቋሚ ገቢ አለዎት ?	A. አዎ B. የለም		መልሱ የለም ከሆነ ወደ ተረ.ቁጥር 111 ሂድ
110	ቋሚ ገቢ ካለዎት (በወር በሙሉ ቤተሰብ ገቢ ምንያህል) ነው) ይጥቀሱ	______________________		
111	የስራ ሁኔታ	A. ሀገበሬ B. የመንግስት ሰራተኛ C. ነጋዴ D. የግል ድርጅት E. የቀን ሰራተኛ F. የቤት እመቤት G. ሌላ ካለ ይጥቀሱ (_________________)		
112	የመኖርያ አካባቢ ታሪክ ከውልደት ጀምሮ	A. ከአንድ ዓመት በፊት ይኖሩበት የነበረው ቦታ ________________ B. መኖር የጀመሩበት ጊዜ ________ C. መኖር ያቆሙበት ጊዜ ___________ D. ሙሉ የመኖርያ ክልል __________ E. ክ/ከተማ ________________ F. ወረዳ ________________		
113	የሰራ ሁኔታ ከ 18 ዓመት ጀምሮ	A. ገበሬ B. የመንግስት ሰራተኛ C. ነጋዴ D. . የግል ድርጅት E. የቀን ሰራተኛ F. የቤት እመቤት		

		G. ሌላ ካለ ይጥቀሱ (________________)		
114	ባለፉት 6 ተከታታይ ወራት ይሰሩት የነበረው ስራ ዘርፍ/ዓይነት	A. ገበሬ B. የመንግስት ሰራተኛ C. ነጋዴ D. የግል ድርጅት E. የቀን ሰራተኛ F. የቤት እመቤት G. ሌላ ካለ ይጥቀሱ (________________)		

ክፍል ሁለት ፡ የመጠጥ ውሀ እና ተያያዥ ጉዳዮች

ተ.ቁ	መጠይቅ	አማራጭ መልስ	ዝለል	አስተያየት
200	በሚኖሩበት አካባቢ የሚጠቀሙት የመጠጥ ውሀ ምንጩ ምንድ ነው ?	A. የመዘጋጃ ውሀ (ቧንቧ) B. የግል ጉድጓድ C. የታሸገ ውሀ D. ሌላ E. አላውቅም		
201	የመጠጥ ውሀው ዓይነቱ ምን አይነት ነው ?	A. የወንዝ ውሀ B. የጉድጓድ ውሀ C. እቤት ውስጥ የተቆፈረ ጉድጓድ D. ሌላ ካለ ይጥቀሱ ________________	በ ተመራማሪው የሚረጋገጥ	
202	ውሀው ክሎሪን የተጨመረበት ነው	A. አዎ B. የለም	በ ተመራማሪው የሚረጋገጥ	
203	ባዝ ወይም ሻወር አጠቃቀምዎት እንዴት ነው ?	A. ሻወር ብቻ B. ባዝ ብቻ C. ሁለቱንም D. ፉል ውሀ E. በፎጣ መታጠብ F. አላውቅም		
204	ሁልጊዜ ባዝ ይጠቀማሉ?	A. አዎ B. የለም		መልስ ሀ ከሆነ ወደ ተራ.ቁ 206
205	ሁልጊዜ ሻወር ይወስዳሉ ?	A. አዎ B. የለም		መልስ ሀ ከሆነ ወደ ተራ.ቁ 207
206	ባዝ የሚጠቀሙት ?	A. አንዳንዴ B. ምንም/የለም		መልስ ሀ ከሆነ ወደ ተራ.ቁ 208

207	ምን ያህል ሻወር ይወስዳሉ ?	A. ምንም በቀን B. በየ ቀኑ C. በሳምንት አንዴ D. በወር አንዴ E. በዓመት አንዴ		
208	ምን ያህል ባዝ ይወስዳሉ ?	A. ምንም በቀን B. በየ ቀኑ C. . በሳምንት አንዴ D. በወር አንዴ E. በዓመት አንዴ		
209	ሻወር ሲወስዱ ምን ዓይነት ውሀ ይጠቀማሉ ?	A. ሙቅ ውሀ ብቻ B. ቀዝቃዛ ውሀ ብቻ C. ለብ ያለ ውሀ ብቻ D. ሙቅ እና ቀዝቃዛ በማወሀድ		
210	በወጣትነትህ/ሽ እድሜ ዋና ዋኝተህ ታውቃለህ ?	A. አዎ B. የለም		መልሱ ለ ከሆነ ወደ ተ.ቁ 216
211	በዓመት ስንት ጊዜ ዋና ይዋኙ ነበር ?	A. በዓመት አንድ ጊዜ B. በዓመት ሁለት ጊዜ C. በዓመት ሶስት ጊዜ D. በዓመት ከ ሶስት በላይ		
212	ቤየትኛው የእድሜ ክልል ነው ዋና መዋነኛት የጀመሩት ?	____________________________ _		
213	በየትኛው እድሜ ነው ዋና መዋኛት ያቆሙት ?	____________________________ _		
214	ዋና ሲዋኙ ለምን የህል ጊዜ በውሀ ውስጥ ይቆያሉ ?	A. አስራ አምስት ደቂቃ B. ሰላሳ ደቂቃ C. አንድ ሰዓት D. ሌላ (ይጠቀስ)		
215	የዋናው ዓይነት ምን ዓየንት ነው ?	A. ከቤት ውስጥ B. ከቤት ውጪ		
216	በባለፈው ሁለት ዓመት በቀን በአማካይ ምን ያህል ውሀ ይጠጣሉ ? በቀን በሊትር ቢሰላ	____________________________ _		

ክፍል ሶስት ፡ አጠቃላይ የጤና ሁኔታ በተመለከተ

ተ.ቁ	መጠይቅ	አማራጭ መልስ	ዝለል	አስተያየት
300	የሰውነት ክብደት በኪ.ግ	_______________		
301	ቁመት	_______________		
302	ቦዶ ማስ ኢንዴክስ (BMI)	_______________		

303	ከ አሁን በፊት የአንጀት ህመም ነብርዎት ?	A. አዎ B. የለም		
304	መልሶ አዎን ከሆነ ምን ዓይነት ህመም ነው ቢጠቅሱልን ?	______________		
305	በቤተሰብዎ ውስጥ የአንጀት ካንሰር የያዘው ሰው አለ ?	A. አዎ B. የለም		
306	የ አካል ብቃት እንቅስቃሴ ይሰራሉ ?	A. አዎ በቀን ሶሰት ጊዜ B. አዎ በቀን ከ ሶስት ጊዜ በታች C. የለም ሰርቼ አላውቅም		
307	ሲጋራ ያጨሱ ነበር ?	A. አዎ B. የለም		
308	አልኮል ይጠጡ ነበር ?	A. አዎ B. የለም		
309	መልስዎ አዎ ከሆነ ምን ዓይነት አልኮሎችን ይጠጡ ነበር ?	A. ቢራ B. ነጭ ወይን C. ቀይ ወይን D. ስፐሪትስ E. ባህላዊ መጠጥ(ጠላ ፤አረቄ) F. ሌላ______________		
310	ተጠያቂው ፆታ ሴት ከሆኑ ይህንን ይጠይቁ ነፍሰ ጡር ነበሩ ?	A. አዎ B. የለም		ተጠያቂው ሴት ካልሆኑ ወደ ክፍል አራት ይሂዱ
311	ልጅ አለዎት	A. አዎ B. የለም		መልሱ የለም ከሆነ ወደ ክፍል አራት ይሂዱ
312	መልስዎ አዎ ከሆነ ስነት ልጆች አለዎት ?	______________		

ክፍል አራት ፡ የአመጋገብ መረጃን በተመለከተ

ተ.ቁ	መጠይቅ	አማራጭ መልስ	ዝለል	አስተያየት
400	በቀን ምን ይህል ጊዜ ይመገባሉ ?	A. አንድ ጊዜ B. ሁለት ጊዜ C. ሶስት ጊዜ D. ከ ሶሰት ጊዜ በላይ		
401	የመመገቢያ ሰዓቶትን ጠብቀው ይመገባሉ?	A. አዎ B. የለም		
402	የሚጠቀሙት የዘይት ዓይነት የትኛው ነው ? ከአንድ በላይ መምረጥ ይቻላል ?	A. የሚረጋ B. የማይረጋ		
403	ለስላሰና ጣፋጭ በመደበኛነት (በሳምንት ከሁለት) በላይ ይወስዳሉ ?	A. አዎ B. የለም		
404	ለ ተራ ቁጥር 4 መልሶ አዎ ከሆነ ምን ያህል ጊዜ ይጠቀማሉ ?	A. ቢያንስ በቀን አንዴ B. ከ 4 እስከ 6 ጊዜ በሳምንት C. ከ 2 እስከ 3 ጊዜ በሳምንት D. በሳምነት አንድ ጊዜ E. ከ 2 እስከ 3 ጊዜ በወር F. በወር አንድ ጊዜ G. ምንም		
405	ስጋን አዘወትረው ይመገባሉ ?	A. አዎ B. አይደለም		
406	በተራ ቁጥር 5 መልስዎ አዎ ከሆነ ምን ያህል ጊዜ ይጠቀማሉ ?	A. ቢያንስ በቀን አንዴ B. ከ 4 እስከ 6 ጊዜ በሳምንት C. ከ 2 እስከ 3 ጊዜ D. በሳምንት በሳምነት አንድ ጊዜ E. ከ 2 እስከ 3 ጊዜ በወር H. በወር አንድ ጊዜ I. ምንም		
407	እንቁላል አዝወትረው ይመገባሉ ?	A. አዎ B. የለም		
408	በተራ ቁጥር 7 መልስዎ አዎ ከሆነ ምን ያህል ጊዜ ይጠቀማሉ ?	A. ቢያንስ በቀን አንዴ B. ከ 4 እስከ 6 ጊዜ በሳምንት C. ከ 2 እስከ 3 ጊዜ D. በሳምንት በሳምነት አንድ ጊዜ E. ከ 2 እስከ 3 ጊዜ በወር F. በወር አንድ ጊዜ G. ምንም		
408	ወተት አዝወትረው ይጠጣሉ ?	A. አዎ B. የለም		

409	በተራ ቁጥር 9 መልስዎ አዎ ከሆነ ምን ያህል ጊዜ ይጠቀማሉ ?	A. ቢያንስ በቀን አንዴ B. ከ 4 እስከ 6 ጊዜ በሳምንት C. ከ 2 እስከ 3 ጊዜ D. በሳምንት በሳምነት አንድ ጊዜ E. ከ 2 እስከ 3 ጊዜ በወር F. በወር አንድ ጊዜ G. ምንም		
410	የዕፅዋት መጠጥ ይጠጣሉ ?	A. አዎ B. የለም		
411	በተራ ቁጥር 410 መልስዎ አዎ ከሆነ ምን ያህል ጊዜ ይጠቀማሉ ?	A. ቢያንስ በቀን አንዴ B. ከ 4 እስከ 6 ጊዜ በሳምንት C. ከ 2 እስከ 3 ጊዜ D. በሳምንት በሳምነት አንድ ጊዜ E. ከ 2 እስከ 3 ጊዜ በወር F. በወር አንድ ጊዜ G. ምንም		
412	አትክልት ይመገባሉ ?	A. አዎ B. የለም		
413	በተራ ቁጥር 412 መልስዎ አዎ ከሆነ ምን ያህል ጊዜ ይጠቀማሉ ?	A. ቢያንስ በቀን አንዴ B. ከ 4 እስከ 6 ጊዜ በሳምንት C. ከ 2 እስከ 3 ጊዜ D. በሳምንት በሳምነት አንድ ጊዜ E. ከ 2 እስከ 3 ጊዜ በወር F. በወር አንድ ጊዜ H. ምንም		
414	ፍራፍሬ ይመገባሉ ?	A. አዎ B. የለም		
415	በተራ ቁጥር 414 መልስዎ አዎ ከሆነ ምን ያህል ጊዜ ይጠቀማሉ ?	A. ቢያንስ በቀን አንዴ B. ከ 4 እስከ 6 ጊዜ በሳምንት C. ከ 2 እስከ 3 ጊዜ D. በሳምንት በሳምነት አንድ ጊዜ E. ከ 2 እስከ 3 ጊዜ በወር F. በወር አንድ ጊዜ G. ምንም		
416	ፍራፍሬን በምን መልኩ ነው የምትጠቀመው?	A. በጭማቂ መልኩ B. እንዳለ በሙሉ		
417	ሻይ በመደበኝነት ይጠጣሉ ?	A. አዎ B. የለም		
418	በተራ ቁጥር 417 መልስዎ አዎ ከሆነ ምን ያህል ጊዜ ይጠቀማሉ ?	A. ቢያንስ በቀን አንዴ B. ከ 4 እስከ 6 ጊዜ በሳምንት C. ከ 2 እስከ 3 ጊዜ		

		D. በሳምንት በሳምነት አንድ ጊዜ E. ከ 2 እስከ 3 ጊዜ በወር F. በወር አንድ ጊዜ H. ምንም		
419	ቡና በመደበኝነት ይጠጣሉ ?	A. አዎ B. የለም		
420	በተራ ቁጥር 419 መልስዎ አዎ ከሆነ ምን ያህል ጊዜ ይጠቀማሉ ?	A. ቢያንስ በቀን አንዴ B. ከ 4 እስከ 6 ጊዜ በሳምንት C. ከ 2 እስከ 3 ጊዜ D. በሳምንት በሳምነት አንድ ጊዜ E. ከ 2 እስከ 3 ጊዜ በወር F. በወር አንድ ጊዜ G. ምንም		
421	እጅዎትን ሁልጊዜ በውሐ እና በሳሙና ይታጠባሉ ?	A. አዎ B. የለም		
422	የማዕድ ቤት ዕቃዎችን በውሀ ሁልጊዜ ያጥባሉ ?	A. አዎ B. የለም		

አመሰግናለው !!!

Annex 2: Chromatographic Analysis , Calibration Curves and Redundant Analysis

CHROMATOGRAPHIC ANALYSIS AND CALIBRATION CURVE

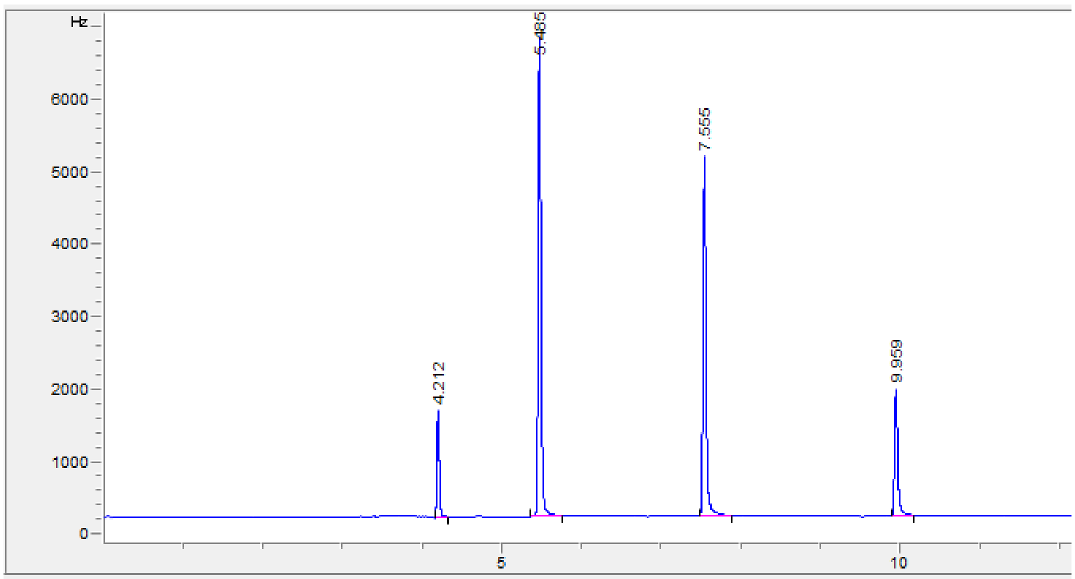


Figure S1: Chromatogram of standard mixture of THMs

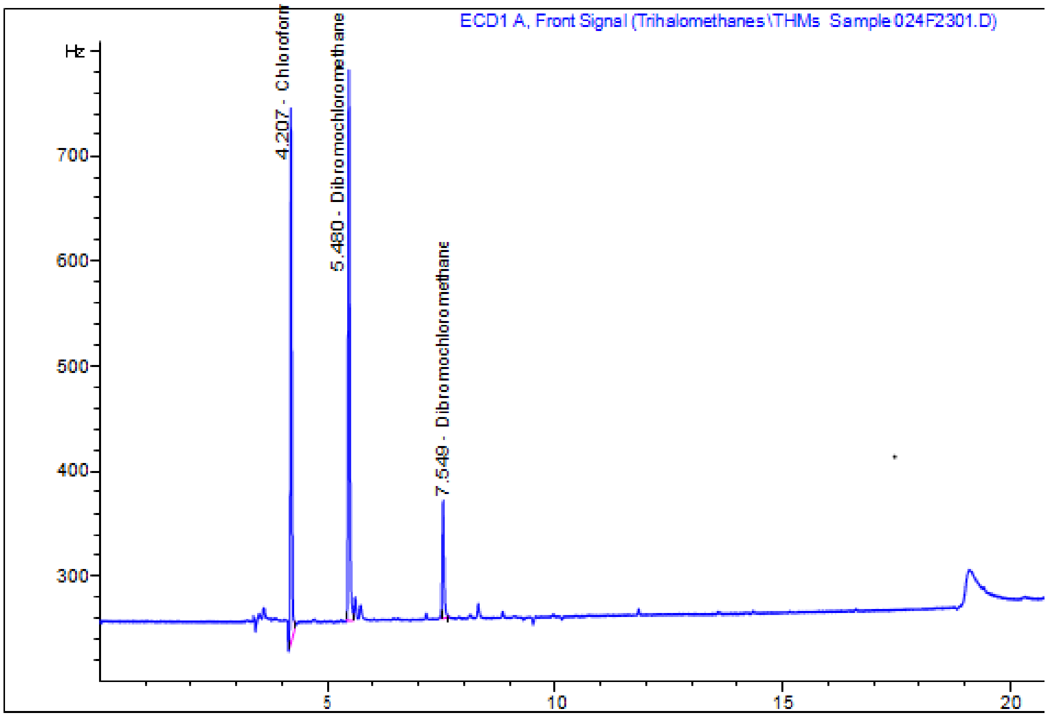


Figure S0.1: Chromatogram of THMs in a real drinking water sample

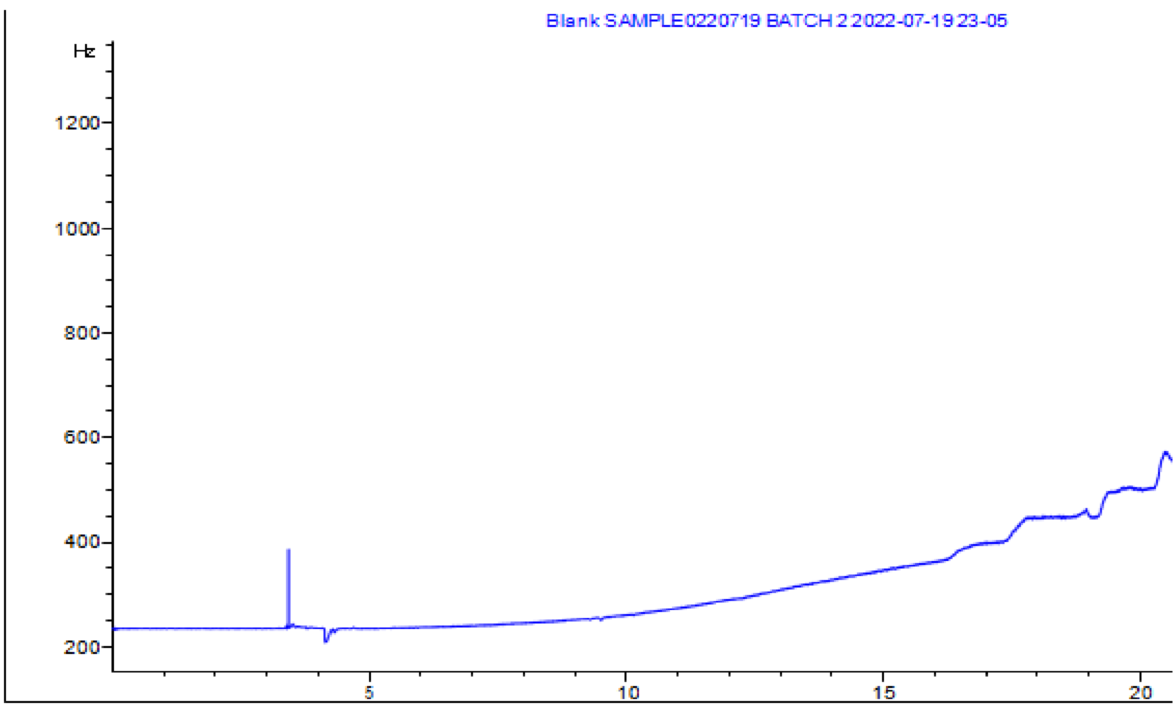


Figure S3: Chromatogram of Blank sample

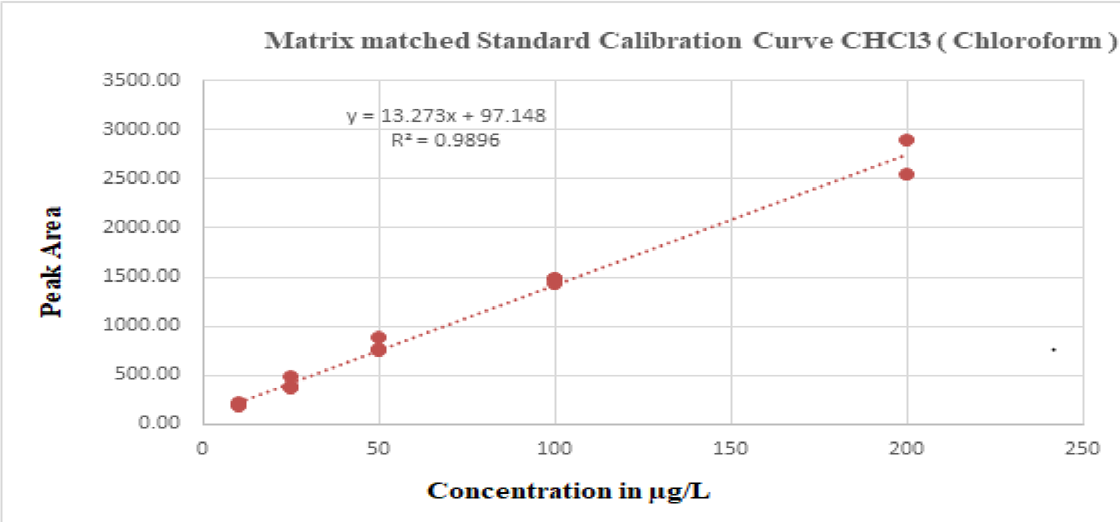


Figure S4: Matrix-matched calibration curves of Chloroform at 50, 100, 150

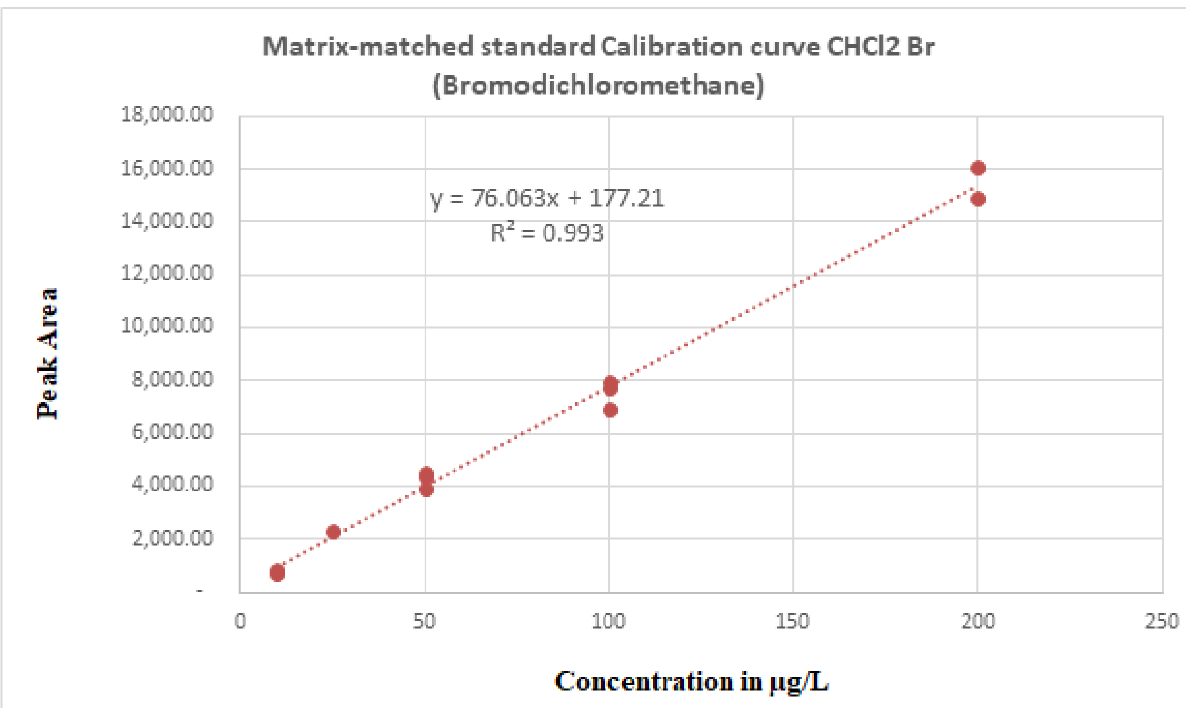


Figure S5: Matrix-matched calibration curves of Bromodichloromethane at 50, 100, 150

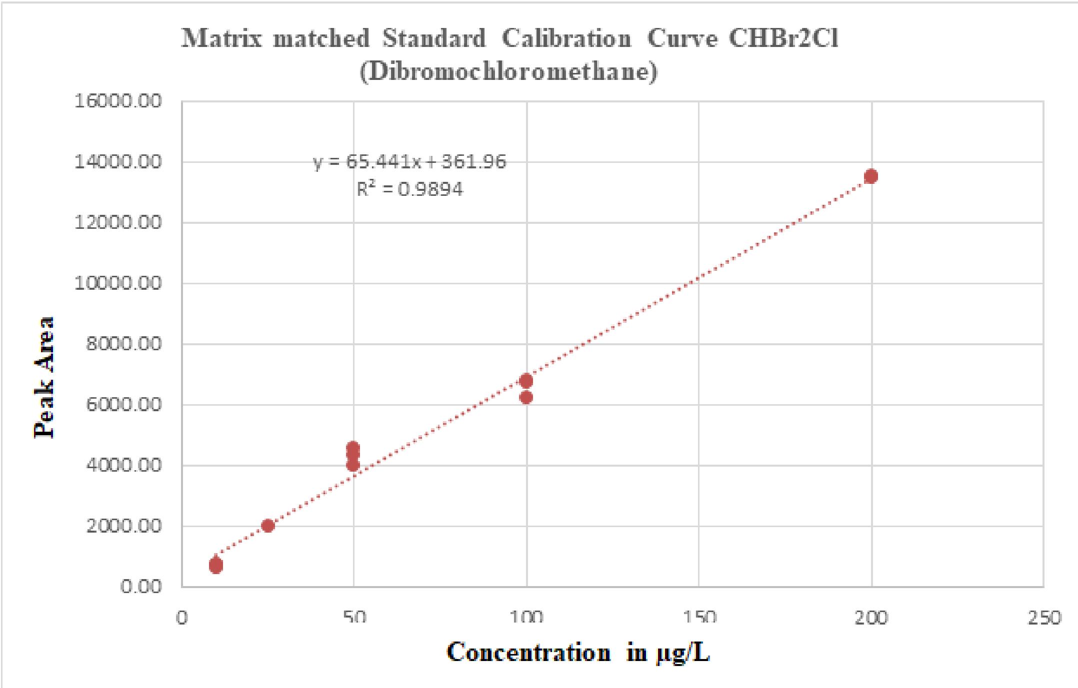


Figure S6: Matrix-matched calibration curves of Dibromochloromethane at 50, 100, 150

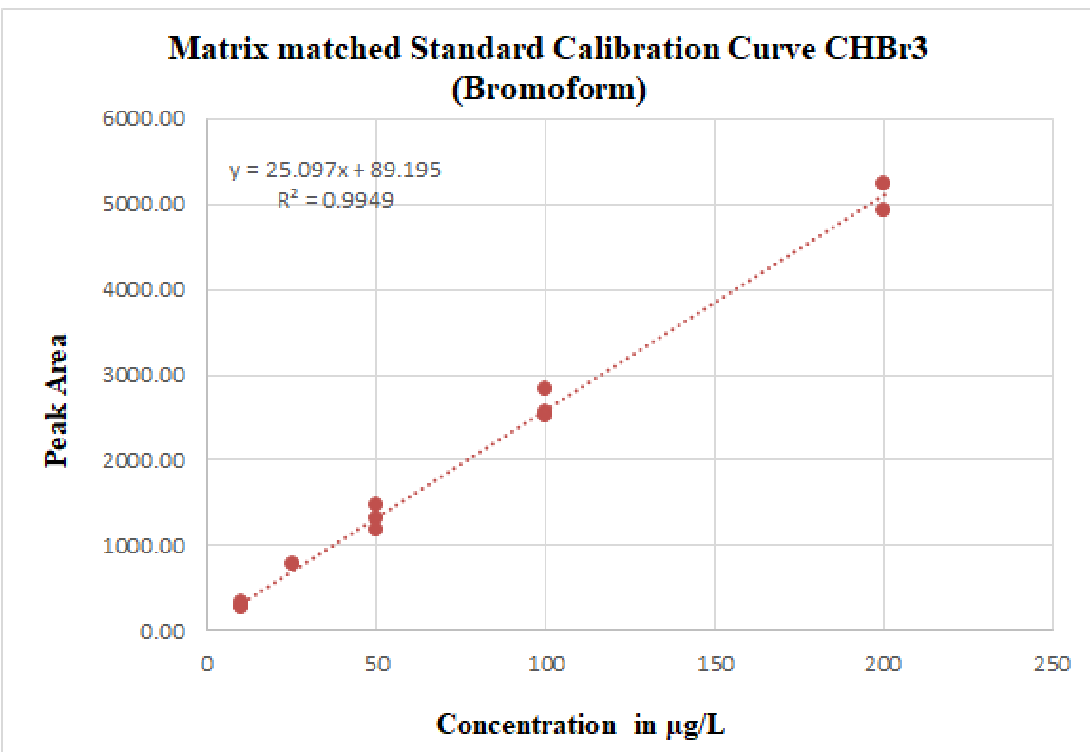


Figure S7: Matrix-matched calibration curves of Bromoform at 50, 100, and 150

Table S5: Stepwise Analysis of Trihalomethanes and environmental variables

N	Name	Weighted mean	Stand.dev.	Inflation factor
1	SPEC AX1	0.0000	1.2749	
2	SPEC AX2	0.0000	3.0575	
3	SPEC AX3	0.0000	3.6542	
4	SPEC AX4	0.0000	5.2104	
5	ENVI AX1	0.0000	1.0000	
6	ENVI AX2	0.0000	1.0000	
7	ENVI AX3	0.0000	1.0000	
8	ENVI AX4	0.0000	1.0000	
1	Residual chlorine	0.5063	0.3898	1.2569
2	Turbidity	1.8609	13.9506	1.2227
6	Electron conductivity	237.1533	110.8028	1.2701
8	UV absorbance at 254	85.2392	5.4289	1.4035
9	Hardness (calcium)	69.2100	6.8422	1.1068
15	Combined chlorine	10.0422	2.4498	1.2308
16	Phosphate	0.2824	0.2333	1.3580

Table S6: Selection of Environmental variables for redundancy analysis of Trihalomethanes

Environmental variable	Number of permutations	F-ratio	Variance explained by the variables selected	Variance explained by all the variables	p-value
Electron conductivity	499	53.04	0.31	0.58	0.0020
Residual chlorine	499	21.31	0.42	0.58	0.0020
UV absorbance	499	7.05	0.45	0.58	0.0040
Turbidity	499	7.19	0.48	0.58	0.0060
Combined chlorine	499	3.95	0.53	0.58	0.0260
Hardness as calcium	499	2.92	0.54	0.58	0.1020
Phosphate	499	7.11	0.51	0.58	0.0040

Annex 3: Selected Pictures of Field Work and Laboratory Analysis

Geferesa Treatment Plant 1

Legedadi Treatment Plants 1

Reservoir water 1

Gefersa Dam 1

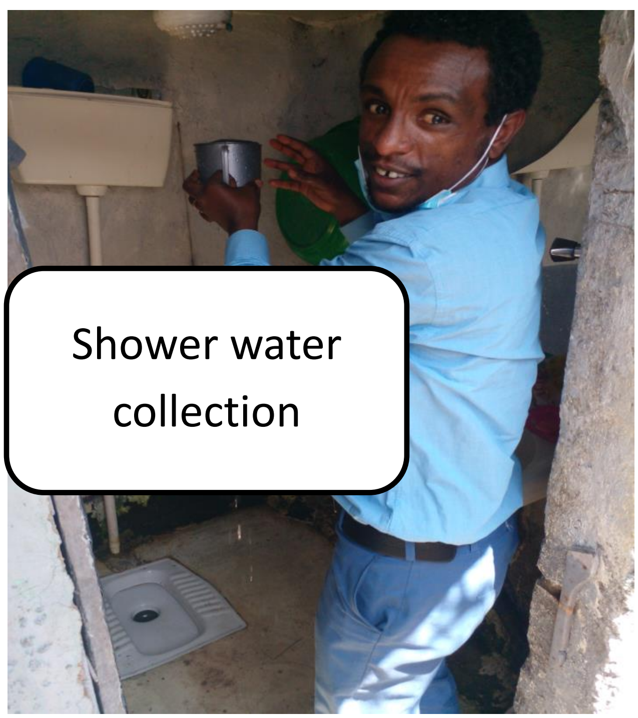
Tap water collection 1

Sample containers 1

Sample Extraction and Preparation 1

Running GC-ECD for THMs determination 1


TASH
Oncology
Department


Shower water
collection


Population
control
survey

Annex 4: Interventional action plan

Interventional action plan

Background

The study findings showed that the prevalence and trends of drinking water disinfection byproducts related cancers are increasing in Addis Ababa, Ethiopia. The study also highlighted that the prevalence of DBRCs was higher in communities supplied with chlorinated surface water. The matched case control study depicted the linkage between drinking water sources, chlorination and colorectal cancers in Addis Ababa, Ethiopia. In the case control study it was confirmed that hot tap water use for showering, and swimming history are risk factors for CRC. The cross-sectional study conducted in the water supply networks in Addis Ababa also indicated surface water supply networks have higher level total THMs than groundwater supply network. The levels of THMs determined in this study in Addis Ababa drinking water supply system were generally below the US EPA and WHO drinking water guidelines. However, more attention should be given to TCM, BDCM and DBCM, as they pose high cancer risk even at low levels. The LCRs of THMs caused by all pathways were higher than 10^{-6} (negligible risk level defined by the USEPA). The ingestion route carried the greatest lifetime cancer risk for all THMs, which was followed by inhalation and dermal contact. Chloroform was linked to an increased risk of developing cancer through dermal contact. The study also indicated that males had a higher overall cancer risk than females. Based on the study findings the following interventional action plan prepared to be conducted by the Ethiopian Institute of Water Resources (EIWR) and other key stakeholders working in the area .

Implementation Plan of Drinking Water Chlorination Byproducts and Cancer Risks in Addis Ababa, Ethiopia

	Activity	Target date	Person responsible	Outcome/ Deliverables	Progress
1.	**Monitoring and regulation of Trihalomethanes in the water supply networks in Addis Ababa, Ethiopia :** a) Identification of key stakeholders working in the water and related area b) Invitations of those stakeholders for validation workshops c) Ensure project lead has clear mandate and resources required to start the planning process d) Assign and plan to implement the responsible individual		Advisor of the study, Investigator, and EIWR Director	• Set up of the procedures for monitoring and regulation • Number of workshops conducted • Established monitoring tool by the key stakeholders	
2.	**Designing a guidelines for monitoring and regulation of the trends of Trihalomethanes** a) Identify stakeholders who will participate in the validation workshops b) Preparing the TOR to organize and conduct the validation workshops c) Ensure the findings of the study clearly communicated to the key stakeholders in Addis Ababa, Ethiopia d) Install the proper equipment's required to analyze the THMs level in water in Addis Ababa e) Organize training for the water technicians towards how to run the GC-ECD or other related advanced equipment's f) Establish proper recording and documentation of THMs in the water supply networks in Addis Ababa, Ethiopia		Advisor of the study, Investigator, and EIWR Director	• Set up of the procedures for designing guidelines • Number of workshops conducted • Established monitoring tool by the key stakeholders	
3.	**Awareness creation towards drinking water chlorination byproducts and cancers in Addis Ababa**		Advisor of the study, Investigator,	• Set up of the procedures for awareness creation	

	a) Identify stakeholders-- use team approach to identify. b) Using team, collect data about the stakeholders c) Organize the data and analyze--again use a team approach d) Determine strategies that will be used to influence, support and engage stakeholders in different capacities. e) Update the action plan based on strategies identified.		and EIWR Director	• Number of workshops conducted • Established monitoring tool by the key stakeholders	
4.	**Preparation of brochures about the importance of cold shower** a) Design of brochures regarding the importance of cold showering b) Distribution of the brochures to the community c) Update the action plan based on strategies identified.			• Set up of the procedures for designing brochures • Number of brochures distributed to the users • Established monitoring tool by the key stakeholders	
5.	**Establishment of the maximum allowable concentration of trihalomethanes in Ethiopia** a) Initiate the importance of establishing the MAC of trihalomethanes b) Involve the relevant stakeholders, choose intervention strategies. Choose interventions based on available information, effectiveness, and fit with the organization and its members			• Set up of the procedures for designing MAC of trihalomethane s • Number of workshops conducted • Established monitoring tool by the key stakeholders	

Annex 5: CV

Nebiyou Tafesse has earned his BSc from University of Gondar. Nebiyou obtained his MSc in Tropical and Infectious Diseases from Addis Ababa University. He has taught in Menelik II Medical and Health Sciences College, Kotebe University of Education. At the moment he is a PhD candidate of Water and Public Health under supervision of Prof. Dr Argaw Ambelu and Dr .Sirak Robele at Ethiopian Institute of Water Resources, Addis Ababa University, Ethiopia. His research interest includes drinking water chlorination byproducts and cancer risks in Addis Ababa, Ethiopia.