The Open Public Health Journal
DOI: 10.2174/0118749445379342250304042227, 2025, 18, e18749445379342

ISSN: 1874-9445
1

SYSTEMATIC REVIEW ARTICLE
OPEN ACCESS

Effect of Drinking Water Quality on Birth Outcomes: A Systematic Review

Tria Rosemiarti[1,*], Diana Sunardi[2] and Netta M. Putri[3]

[1]*Department Nutrition and Science of The Tirta Investama, Jakarta-12940, Indonesia*
[2]*Department of Nutrition, Faculty of Medicine, Universitas Indonesia - Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia*
[3]*Department of Nutrition, Universitas Tidar, Magelang, Indonesia*

Abstract:

Objective: This review aimed to analyze the effects of drinking water contaminants during pregnancy on birth outcomes, focusing on chemical contaminants, including heavy metals, nitrates, and disinfection byproducts.

Methods: A literature search was conducted using SCOPUS, EBSCO, PubMed, Cochrane, and Google Scholar databases. The review included English-language prospective cohort studies and clinical trials published between 2007-2022 that focused on healthy pregnant women and measured birth outcomes. From 269 articles identified, 30 met the inclusion criteria.

Results: Analysis of 30 studies encompassing over 4 million births demonstrated significant associations between water contaminants and adverse birth outcomes. Arsenic exposure below 10 µg/L was associated with an increased risk of very low birth weight (AOR 1.14) and preterm birth (AOR 1.10). Nitrate concentrations of 5-10 mg/L were linked to higher rates of spontaneous preterm birth. Combined exposure to multiple contaminants demonstrated stronger effects than individual exposures, particularly during the second trimester.

Conclusion: Evidence demonstrates that exposure to water pollutants during pregnancy, even at levels below current regulatory guidelines, has a significant impact on birth outcomes. Recommendations include increased monitoring during pregnancy, particularly for private well users, reviewing regulatory standards, and implementing tailored treatments for vulnerable populations.

Keywords: Birth outcome, Contamination, Drinking water, Pregnancy, Water quality, Water quality regulation, Contaminants during pregnancy, Chemical contaminants.

* Address correspondence to this author at the Department Nutrition and Science of the Tirta Investama, Jakarta 12940, Indonesia; E-mail: dr_tria_rosemiarti@yahoo.co.id

Cite as: Rosemiarti T, Sunardi D, Putri N. Effect of Drinking Water Quality on Birth Outcomes: A Systematic Review. Open Public Health J, 2025; 18: e18749445379342. http://dx.doi.org/10.2174/0118749445379342250304042227

Received: December 30, 2024
Revised: January 27, 2025
Accepted: February 06, 2025
Published: March 20, 2025

1. INTRODUCTION

The health and well-being of expectant mothers and their developing fetuses during pregnancy represent a critical public health concern, with numerous environmental factors influencing outcomes. Among these factors, drinking water quality has emerged as a significant focus in maternal-fetal health research. Drinking water quality, defined as the chemical, physical, and biological characteristics of water in relation to established standards for safety and public health [1], plays a fundamental role in determining health outcomes worldwide. Birth outcomes, encompassing measures such as birth weight, gestational age at delivery, congenital anomalies, and fetal growth parameters, are sensitive indicators of environmental influences during pregnancy.

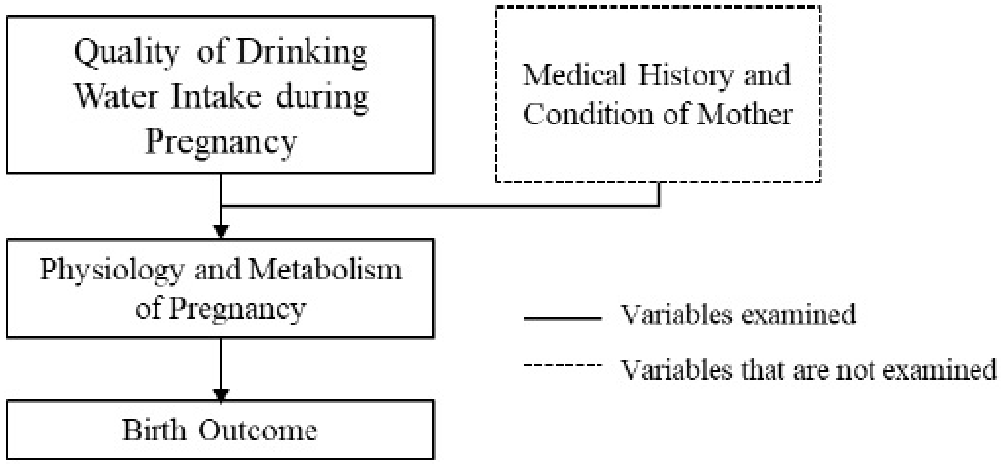

Fig. (1). Conceptual framework.

Recent epidemiological studies have demonstrated an alarming increase in adverse birth outcomes potentially linked to environmental exposures. The World Health Organization estimates that approximately 2 billion people globally consume drinking water contaminated with chemical or biological agents that exceed safety thresholds [2]. This exposure risk is particularly concerning for pregnant women, as demonstrated by comprehensive biomonitoring studies. A landmark collaborative investigation between the Harvard School of Public Health and the Centers for Disease Control examined 87 distinct chemicals in mother-fetus pairs, revealing that nearly all these substances could traverse the placental barrier [3]. This finding fundamentally challenged previous assumptions about fetal protection and highlighted the urgent need to address water quality issues, especially for pregnant women.

The scope of water contamination concerns has expanded significantly in recent years. While traditional focus centered on microbial contamination, emerging research has identified various chemical contaminants as potential threats to fetal development. These include heavy metals (*e.g.*, arsenic, lead), agricultural chemicals (*e.g.*, nitrates, pesticides), and disinfection byproducts [4, 5]. A meta-analysis by Smith *et al.* [6] found that exposure to these contaminants during pregnancy was associated with a 20-40% increased risk of adverse birth outcomes.

Despite growing evidence linking water quality to birth outcomes, several critical research gaps persist such as limited understanding of the combined effects of multiple contaminants, as most studies focus on single agents [7], insufficient data on exposure timing and critical windows of vulnerability during pregnancy [8], inadequate assessment of how different water sources (municipal, private wells, bottled water) may influence exposure risks [9], and limited research on the effectiveness of current water quality standards in protecting fetal health [10].

Furthermore, existing reviews have typically focused on specific contaminants or particular birth outcomes, leaving a need for a comprehensive analysis of the broader relationship between water quality and birth outcomes. Maternal exposure to contaminated drinking water has been linked to various adverse outcomes, including low birth weight, preterm birth, and congenital anomalies [11, 12]. However, the strength and consistency of these associations vary across studies, highlighting the need for an evaluation of the evidence.

The primary objective of this review was to consolidate and analyze existing research on the relationship between various parameters of drinking water quality and adverse birth outcomes. Through meticulous examination and synthesis of findings from diverse studies, this review aims to provide a comprehensive understanding of these relationships. These insights are vital for informing public health policies, guiding targeted interventions, and identifying areas requiring further research. The knowledge gained will be instrumental in promoting access to safe drinking water for pregnant individuals, with the ultimate goal of reducing the incidence of adverse birth outcomes.

2. METHODS

This review examined the relationship between drinking water quality during pregnancy and birth outcomes, focusing on summarizing and synthesizing current evidence from the literature. The review methodology employed a narrative approach to analyze and interpret findings from diverse studies (Fig. **1**).

2.1. Literature Search Strategy

A comprehensive literature search was conducted using five electronic databases: SCOPUS, EBSCO, PubMed, Cochrane, and Google Scholar. The search strategy combined MeSH terms and free-text words using Boolean operators. The primary search string was: (“water quality”[MeSH Terms]) OR ((“pregnant”[All Fields] AND “birth outcome”[All Fields])). Additional search terms included: “drinking water quality” OR “water quality” OR “contamination” AND “pregnancy” OR “birth” OR “fetal”

Table 1. Search strategies results.

Databases	Search Strategies	Found	Used
SCOPUS	*"water quality" [MeSH Terms] OR ("pregnant"[All Fields] AND "birth outcome" [All Fields])*	185	29
EBSCO	*"water quality" [MeSH Terms] OR ("pregnant"[All Fields] AND "birth outcome" [All Fields])*	8	0
PUBMED	*"water quality" [MeSH Terms] OR ("pregnant"[All Fields] AND "birth outcome" [All Fields])*	18	0
COCHRANE	*"water quality" [MeSH Terms] OR ("pregnant"[All Fields] AND "birth outcome" [All Fields])*	5	0
Google search	*"water quality" [MeSH Terms] OR ("pregnant"[All Fields] AND "birth outcome" [All Fields])*	53	1

AND "outcome" OR "birth outcome" OR "birth weight." The search was restricted to English-language publications from January 2007 to December 2022. The complete search results by database are presented in Table **1**.

2.2. Study Selection

2.2.1. Inclusion Criteria

Studies were selected based on the following criteria *i.e.*, original research published in English, published between 2007-2022, peer-reviewed journal articles, and full text available. The population criteria were pregnant women without pre-existing medical conditions (defined as the absence of chronic diseases such as diabetes, hypertension, or autoimmune disorders documented at the first prenatal visit), singleton pregnancies, and women aged 18-45 years. The study design criteria were clinical trials or prospective cohort studies, clear documentation of exposure assessment methods, birth weight as a primary or secondary outcome measure, and sample size ≥50 participants.

Studies were excluded if they focused on animals or in vitro studies, included only women with pre-existing conditions, were case reports or series, or lacked quantitative exposure assessment.

2.2.2. Types of Contaminants Considered

The review examined studies investigating both inorganic and organic contaminants in drinking water. Inorganic contaminants included heavy metals (arsenic, lead, mercury) and nitrates, while organic contaminants encompassed pesticides and disinfection byproducts. Only studies with clearly defined exposure assessments and contaminants with established regulatory standards were included. Studies focusing solely on radioactive or microbiological contaminants were excluded due to their different exposure mechanisms and health outcomes.

2.3. Quality Assessment Protocol

The quality of the included studies was evaluated by examining several key aspects of research design and reporting. Studies were assessed based on their methodological approach, including the clarity of population descriptions, appropriateness of sampling methods, and reliability of exposure and outcome measurements. Particular attention was paid to how studies handled potential confounding factors and whether they adequately discussed study limitations. The review also considered whether studies employed appropriate statistical analyses and clearly presented their results. This evaluation helped inform the interpretation and synthesis of findings across studies while acknowledging the varying strengths and limitations of different research approaches.

2.4. Data Extraction

Data extraction was performed using a standardized approach that captured key study characteristics, including authors and publication year, study design and location, sample size, and population characteristics. Information about exposure assessment included contaminant types and levels, measurement methods, exposure duration and timing, and quality control procedures. Outcome measures, including both primary and secondary outcomes, measurement methods, timing of assessment, and statistical analyses, were also recorded.

2.5. Evidence Synthesis

The synthesis of evidence followed a structured approach that integrated findings across multiple dimensions. Studies were first organized by contaminant type, followed by identification of patterns across different research contexts. The synthesis examined temporal and geographic variations in findings while carefully considering the effects of exposure timing. Evidence from different water sources was evaluated, and the consistency of findings across studies was assessed. This comprehensive approach allowed for a thorough understanding of how various aspects of water quality affect birth outcomes while acknowledging the complexity and interrelated nature of the factors involved (Fig. **2**).

3. RESULTS AND DISCUSSION

From an initial pool of 269 articles identified using the specified keywords, 30 met all the inclusion criteria (Table **1**). This review synthesized evidence from 30 methodologically rigorous studies encompassing over 4 million births across diverse geographical and socioeconomic contexts (Table **2**). The results showed a number of clear trends in the relationship between birth outcomes and drinking water quality. The crucial finding by Needham *et al*. that environmental pollutants can easily pass through the placental barrier is at the heart of our knowledge of how water contaminants impact pregnancy outcomes [3]. This landmark finding demonstrated that of 87 distinct chemicals examined, nearly all could traverse the placental membrane, fundamentally challenging previous assumptions about fetal protection. The placenta, while serving as a selective barrier, cannot fully shield the developing fetus from environmental contaminants present in maternal drinking water.

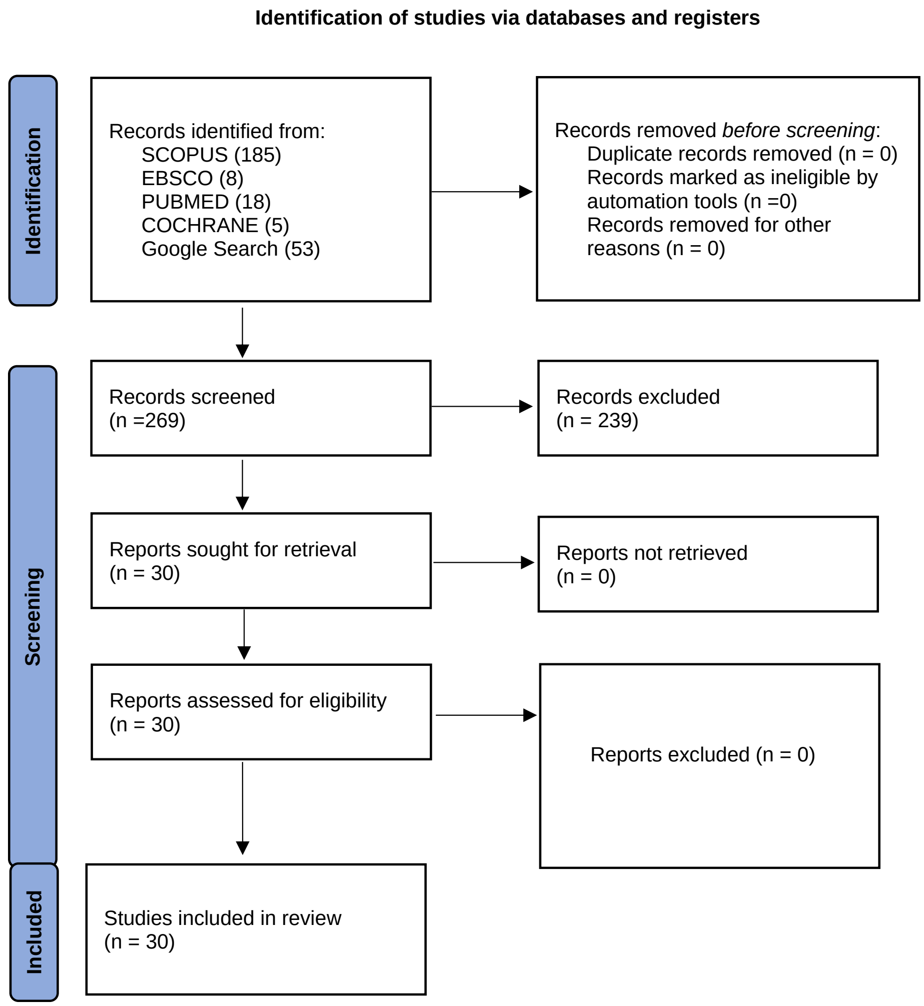

Fig. (2). Literature search flow diagram (PRISMA).

Table 2. Descriptive analysis of trials included in the review.

No.	Researcher and Journal Year/Refs	Design and Methods (sample size and inclusion criteria)	Details of the Study Conducted (measurements)	Research Result	Conclusion and Suggestions of the Research (strengths and weaknesses of the study)
1.	Yang *et al* 2002 [13]	Case-control and ecological approach; 1,781 women in 252 cities	Calcium levels from Taiwan Water Supply Corporation.	Significant trend towards decreased risk of VLBW with increasing calcium levels	Protective effect of calcium intake from drinking water on VLBW risk. Future studies should use more precise estimates of individual calcium intake.
2.	Yang *et al*, 2003 [14]	Semi-individual design; 18,259 first parity singleton live births	Arsenic measurements from 3901 well water samples	Babies in arsenic-endemic areas were on average 30g lighter; higher preterm birth rate	Arsenic exposure through drinking water was associated with increased risk of low birth weight. Limitations: Ecological design, lack of individual-level exposure data.
3.	Yang, 2004 [15]	Retrospective cohort study; 182,796 women in 128 cities	Chlorination proportion (CP) data from Taiwan Water Supply Corporation	No evidence of increased risk of LBW associated with chlorinated water; some support for preterm birth risk	Methodological limitations: more accurate exposure assessment methods needed.

(Table 2) contd.....

No.	Researcher and Journal Year/Refs	Design and Methods (sample size and inclusion criteria)	Details of the Study Conducted (measurements)	Research Result	Conclusion and Suggestions of the Research (strengths and weaknesses of the study)
4.	Agazzotti, 2004 [16]	Case-control study; 1,194 subjects	Exposure assessed by questionnaire and direct water sampling	No significant association between Trihalomethanes (THMs) and term-small for gestational age (SGA) or preterm birth; weak associations with high chlorite levels	THM concentrations were negligible. High chlorite levels associated with term-SGA. Strength: Individual-level exposure assessment.
5.	Villanueva *et al*, 2005 [17]	Ecological study; 3,510 births	Atrazine measurements in drinking water at treatment plants	No significant associations with SGA or very preterm birth (VPTB); suggestive association with LBW	Low atrazine levels and narrow exposure ranges explain lack of association. Strength: Consideration of seasonal patterns.
6.	Manassaram *et al*. 2005 [18]	Comprehensive review of epidemiologic studies	Review focusing on maternal exposure and reproductive effects	Unclear evidence for direct exposure-response relationship between drinking water nitrate levels and adverse reproductive effects	Current literature insufficient for causal relationship. Future studies should incorporate individual exposure assessments, especially for private well users.
7.	Yang *et al*, 2007 [19]	Retrospective cohort study; 90,848 women in 65 cities	Total trihalomethane (TTHM) concentrations from Taiwan Environmental Protection Administration (EPA) method	No association between THM exposure and LBW, SGA, or preterm delivery at relatively low THM concentrations	More accurate exposure assessment methods needed. Strength: Large sample size. Weakness: Lack of individual-level exposure data.
8.	Huyck *et al*, 2007 [20]	Prospective study; 52 pregnant women	Hair, toenail, and drinking water samples collected	Maternal hair arsenic in early pregnancy associated with reduced birth weight	Limitations: small sample size, low-precision birth weight measurement. Strength: Use of biomarkers.
9.	Aschengrau *et al*, 2008 [21]	Retrospective cohort study; 1,353 exposed and 772 unexposed children	PCE (tetrachloroethylene) exposure estimated using EPANET modeling	No significant association between PCE exposure and birth weight or gestational duration	Results suggest prenatal PCE exposure doesn't adversely affect birth outcomes at observed levels. Strength: Use of modeling for exposure estimation.
10.	Ochoa-Acuña *et al*, 2009 [22]	Retrospective cohort study; 24,154 births	Atrazine concentrations from US EPA's monitoring program	Atrazine exposure associated with increased rates of SGA when averaged over 4-6 months before birth	Suggests association between atrazine and increased prevalence of SGA. Strength: Consideration of exposure timing.
11.	Migeot *et al*, 2013 [23]	Cohort study; 11,446 women-neonates	Nitrate and pesticide measurements from water distribution systems	Increased risk of SGA status with exposure to nitrate/atrazine metabolite mixture, especially in second trimester	Effects of exposure to mixture of atrazine and nitrate metabolites should be further studied. Strength: Consideration of mixture effects.
12.	Weyer *et al*, 2014 [24]	Multi-site population-based case-control study; 1,410 cases, 1100 controls	Bottled water samples analyzed using EPA Method 300.0	No significant association between nitrate intake from bottled water and birth defects	Bottled water nitrate levels were very low and didn't significantly impact risk of birth defects. Strength: Consideration of bottled water.
13.	Rodenback *et al*, 2000 [25]	Ecological epidemiological study; births in specific US census tracts	Trichlorethylene (TCE) exposure from contaminated wells	Association between TCE exposure and VLBW babies	Further evidence that maternal consumption of TCE-contaminated drinking water is associated with VLBW infants. Weakness: Lack of individual-level exposure data.
14.	Bloom *et al*, 2014 [26]	Comprehensive review of 18 English-language papers	Review assessing birth weight, gestational age, and birth size	Limited evidence for decreased birth weight associated with arsenic exposure; insufficient evidence for effects on preterm birth or birth size	Published results suggest lower birth weight may be associated with maternal arsenic exposure. Strength: Comprehensive review.
15.	Ruckart *et al*, 2014 [27]	Cross-sectional study; 11,896 births	Birth certificates identify mothers living at Camp Lejeune	Association between in utero exposure to TCE and reduced SGA, term low birth weight (TLBW) and mean birth weight (MBW)	Suggests association between TCE exposure and adverse birth outcomes. Strength: Large sample size. Weakness: Lack of data on other maternal characteristics.
16.	Iszatt *et al*, 2014 [28]	Intervention study; 429,599 live births and 2279 stillbirths	Information on chloroform, Bromodichloromethane (BDCM), Dibromochloromethane (DBCM), bromoform and water zone limits	Enhanced coagulation intervention not associated with significant reduction in birth outcome rates; large decreases in chloroform associated with decreases in very low birth weight rates	Disinfection by product (DBP) is a public health concern; future research should focus on narrow outcome definitions. Strength: Intervention design. Weakness: Ecological nature of exposure assessment.
17.	Ileka-Priouzeau *et al*, 2015 [29]	Population-based case-control study; 330 SGA cases, 1100 controls	Haloacetaldehydes (HA) and haloacetonitriles (HAN) concentrations estimated using spatial-temporal strategy	No statistically significant association between HAs and HANs exposure and SGA in newborns	The approach may provide a way to incorporate multiroute exposure in situations with limited data. Strength: Consideration of multiple exposure routes.

(Table 2) contd.....

No.	Researcher and Journal Year/Refs	Design and Methods (sample size and inclusion criteria)	Details of the Study Conducted (measurements)	Research Result	Conclusion and Suggestions of the Research (strengths and weaknesses of the study)
18.	Kogevinas *et al*, 2016 [30]	Cohort study; 14,005 mothers (2002-2010) and their children from France, Greece, Lithuania, Spain and the UK	This study determined the levels of trihalomethane in residential areas using regulatory records and ad hoc sampling campaigns. It also estimated the amount of trihalomethane absorbed by trimester and the entire pregnancy.	There was no association between birth weight, LBW, SGA, preterm birth and total trihalomethane exposure during pregnancy	The study found no connection between trihalomethane exposure and birth outcomes in pregnant women. The evaluation of exposure levels has been a significant limitation in many studies.
19.	Smith *et al* 2016 [6]	Prospective cohort study; 7,438 women with term babies	Residential drinking water DBP levels measured	Increasing daily internal dose of total THMs during third trimester significantly increased risk of term LBW in Pakistani infants	THM exposure associated with reduced birth weight, but differed by ethnicity. Strength: Individual water use data. Weakness: Unable to account for mobility during pregnancy.
20.	Stayner *et al*, 2017 [31]	Ecological study; 134,258 singleton births	Monthly data on sex, race, and ethnicity from state data	Atrazine exposure associated with increased rates of preterm delivery (PTD) when averaged over 4-6 months before birth	Findings raise concerns about potential adverse effects of atrazine on human development. Strength: Large sample size. Weakness: Ecological design limits causal inference.
21.	Almberg *et al*, 2017 [32]	Ecological study; 428,804 live singleton births in Ohio	This study used birth certificate data (from the 2003 revision of the US Certificate of Live Birth) for births occurring in the state of Ohio between 2006 and 2008. There were 428,804 live singleton births in Ohio between 2006 and 2008.	Arsenic in drinking water was linked to a higher likelihood of having VLBW (AOR 1.14) and PTB (AOR 1.10) in singleton births from areas where <10% of the people used private wells.	The presence of arsenic in drinking water was linked to VLBW and PTB in areas where people was drinking water with arsenic levels below the current limit of 10 µg/L. This suggests that the current regulations standards might not be enough to prevent the reproductive risks of prenatal arsenic exposure.
22.	Almberg *et al*, 2018 [33]	Cross-sectional study; 14,445 live singleton births	Atrazine drinking water measurements in finished water from 2005 to 2008 were obtained from the USEPA AMP public data portal for all 22 AMP water systems in Ohio	Significantly increased odds of LBW birth at term were associated with atrazine exposure during the entire gestational period (OR 1.27, 95% CI 1.10, 1.45), as well as the first (OR 1.20, 95% CI 1.08, 1.34) and second (OR 1.13, 95% CI 1.07, 1.20) trimesters of pregnancy	Atrazine exposure may lead to lower birth weight in term infants, with the highest risk observed when exposure occurs during the early and middle stages of pregnancy.
23.	Mashau *et al*, 2018 [34]	Systematic review of 32 studies	Comprehensive search and screening	Twleve studies (38%) reported association between maternal DBP exposure and adverse pregnancy outcomes	Maternal consumption of water exposed to DBP (THM, Haloacetic acid (HAA)) is associated with adverse pregnancy outcomes. Strength: Comprehensive review. Weakness: Heterogeneity in exposure assessment methods across studies.
24.	Mashau *et al*, 2019 [35]	Cross-sectional study; 205 pregnant women	Samples were analyzed for urinary creatinine and trichloroacetic acid (TCAA).	Increased creatinine adjusted for TCAA concentrations showed increased risk of preterm birth, SGA and low birth weight	The urinary TCAA concentrations identified in this study indicate potential health risks to women and fetuses. Limitation: Cannot establish temporal relationship.
25.	Mashau *et al*, 2021 [36]	Prospective cohort epidemiological study; 1,167 pregnant women	For each district, this study measured residential drinking water DBP levels (measured in THM) through regulatory data and routine water sampling	Increasing daily internal dose of total THMs during the third trimester of pregnancy significantly increased the risk of preterm birth (AOR 3.13, 95% CI 1.36-7.17)	This study suggests that THM exposure is associated with certain negative pregnancy outcomes. Limitation: Did not adjust for some potential confounders.
26.	Coffman *et al*, 2021 [37]	Population-Based Study; 898,206 births in Denmark during 1991--2011	Maternal nitrate exposure estimated using spatial model	Evidence of decreasing trend in models for term birth weight using either categorical or continuous exposure measures	Findings suggest maternal nitrate intake from drinking water may reduce term birth weight and length. Strength: Large sample size. Weakness: Lack of data on dietary nitrate sources.
27.	Sherris *et al*, 2021 [38]	Retrospective study; 1,443,318 consecutive sibling births	The concentration of nitrate in the drinking water at each woman's home during pregnancy.	Positive association between tap water nitrate concentrations of 5 to <10 mg/L and spontaneous preterm birth.	Findings suggest nitrate in drinking water may lead to spontaneous preterm birth. Strength: Within-mother design. Weakness: Lack of individual-level water consumption data.

(Table 2) contd.....

No.	Researcher and Journal Year/Refs	Design and Methods (sample size and inclusion criteria)	Details of the Study Conducted (measurements)	Research Result	Conclusion and Suggestions of the Research (strengths and weaknesses of the study)
28.	Stayner *et al*, 2022 [39]	Cohort study; 1,018,914 births	Nitrate exposure estimated using spatial model linked to individual addresses	Exposure-response relationship between nitrate during pregnancy and eye Birth Defects (BD); increased risk in highest exposure group	Evidence of increased risk of ocular BD. Interaction with maternal age observed. Strength: Large sample size. Weakness: Potential for exposure misclassification.
29.	Arun *et al*, 2022 [40]	Cross-sectional study; 7,147 and 6,858 women	Samples analyzed for urinary creatinine and fluoride	Women with LBW infants were exposed to significantly higher levels of water fluoride	Findings may inform public health strategies regarding water fluoride as a potential risk factor during pregnancy. Strength: Use of NHANES data. Weakness: Cross-sectional design limits causal inference.
30.	Pintaningrum *et al*, 2023 [41]	Meta analysis	Search for published scientific articles using the PRISMA method	Statistically significant positive relationship between arsenic contamination and congenital heart disease incidence, but in the low category	Arsenic contamination in drinking water during pregnancy has a low effect on the incidence of congenital heart disease. Strength: Meta-analytic approach. Weakness: Limited number of included studies.

3.1. Major Contaminants and Their Effects

3.1.1. Arsenic Exposure

Arsenic exposure consistently showed adverse effects on birth outcomes. Yang *et al*.'s study of 18,259 births in arsenic-endemic areas demonstrated significant associations with reduced birth weight [14]. The underlying mechanism, as demonstrated by subsequent research, involves arsenic's ability to interfere with cellular metabolism and DNA methylation patterns. Notably, Almberg *et al*.'s research revealed that even arsenic levels below the current regulatory limit of 10 μg/L were associated with increased risks of very low birth weight (VLBW) and preterm birth [15-34]. This suggests current standards may not adequately protect fetal development. The mechanism involves oxidative stress induction in placental tissue, disruption of cellular energy metabolism, interference with DNA repair mechanisms, and alteration of gene expression patterns crucial for fetal development. These effects manifest most prominently in reduced birth weight, increased risk of preterm birth, alterations in fetal growth patterns, and potential developmental disruptions.

3.1.2. Nitrate Contamination

Recent large-scale studies have illuminated the mechanisms by which nitrates affect fetal development. Coffman *et al*.'s analysis of 898,206 Danish births revealed a dose-dependent relationship between nitrate exposure and reduced birth weight [35-37]. The mechanism operates primarily through the conversion of maternal nitrate intake to nitrites, which can cross the placental barrier and form methemoglobin in fetal blood. Additionally, the mechanism also disrupts oxygen transportation by interfering with hemoglobin's oxygen-carrying capacity. This reduced oxygen delivery to developing fetal tissues, particularly during critical developmental windows. Sherris *et al*.'s innovative within-mother analysis of 1,443,318 consecutive sibling births provided compelling evidence of these mechanisms, showing an increased risk of spontaneous preterm birth at nitrate concentrations of just 5-10 mg/L [38]. This suggests that even relatively low nitrate levels can significantly impact fetal development through oxygen transport disruption.

3.1.3. Disinfection Byproducts (DBPs)

The evidence for DBPs showed notable geographic and demographic variations. Smith *et al*.'s prospective study of 7,438 women found significant associations between trihalomethane exposure and reduced birth weight in specific ethnic groups, with Pakistani infants showing particular vulnerability to term low birth weight when exposed to higher THM levels during the third trimester [6]. However, Kogevinas *et al*.'s European study of 14,005 mother-child pairs found no consistent associations between THM exposure and birth outcomes [30], suggesting potential genetic or environmental modifiers of DBP effects. This geographic variation was further explored in Mashau *et al*.'s systematic review of 32 studies, which found that 38% of studies reported associations between maternal DBP exposure and adverse pregnancy outcomes [34]. The varying results were particularly evident in studies examining different types of DBPs, with Mashau *et al*.'s subsequent research showing that increased urinary trichloroacetic acid (TCAA) concentrations were specifically associated with higher risks of preterm birth, small for gestational age (SGA), and low birth weight [35]. Ileka-Priouzeau *et al*.'s population-based case-control study of 330 SGA cases and 1,100 controls found no statistically significant association between halo acetaldehyde (HA) and halo acetonitrile (HAN) exposure and SGA in newborns [29].

The disparate findings across studies point to several critical considerations in understanding DBP effects. First, the variation in results between Smith *et al.* [6] and Kogevinas *et al.* [30] suggests that population-specific factors, including genetic polymorphisms and environmental co-exposures, may modify DBP effects on fetal development. This interpretation is strengthened by

Aggazzotti *et al.*'s earlier work [16], which found that while THM concentrations were generally negligible, high chlorite levels showed associations with term-SGA, indicating that different DBP species may have distinct biological effects. Second, the methodological advances in exposure assessment, particularly the use of urinary TCAA as a biomarker [30], have provided more precise measurements of individual exposure compared to earlier studies that relied solely on water sampling. This improvement in exposure assessment methodology may partly explain the more consistent associations found in recent studies.

3.2. Critical Windows of Exposure

3.2.1. Timing Effects

The timing of exposure to water contaminants during pregnancy has emerged as a crucial factor in determining the severity and nature of adverse birth outcomes. This temporal sensitivity reflects the precisely orchestrated nature of fetal development, where different organ systems and developmental processes show heightened vulnerability during specific gestational periods. The review identified crucial periods of vulnerability during pregnancy. Almberg *et al.*'s research on atrazine exposure demonstrated the strongest associations with low birth weight during early and middle pregnancy [33]. This timing effect was consistent across multiple contaminants, suggesting particular sensitivity during specific developmental stages.

3.2.2. Cumulative Exposure Impacts

The temporal vulnerability pattern is further illuminated by Migeot *et al.*'s groundbreaking research on the combined effects of nitrates and atrazine metabolites [23]. Their study revealed that exposure during the second trimester was particularly critical, with evidence suggesting that this period represents a unique window of vulnerability where the developing fetus is especially susceptible to environmental insults. This increased sensitivity appears to be linked to the rapid cellular proliferation and organ development occurring during this phase, coupled with the increased efficiency of placental transfer. The researchers observed that exposure during this critical window was associated with a significantly increased risk of small-for-gestational-age births, with the effect being notably more pronounced than similar exposure levels during other periods of pregnancy. Importantly, their work also highlighted how the combination of multiple contaminants during these sensitive periods could produce synergistic effects, suggesting that the temporal aspect of exposure must be considered alongside the complex interactions between different water contaminants.

3.3. Synergistic Interactions

A novel finding emerged regarding contaminant interactions. Multiple studies demonstrated that combined exposure to different contaminants produced effects greater than individual exposures would suggest. This was particularly evident in Migeot *et al.*'s work showing synergistic effects between nitrates and pesticide metabolites [23]. These findings challenge current regulatory approaches that typically assess contaminants in isolation.

The complexity of these synergistic interactions is further illuminated by their relationship with timing and exposure patterns. When nitrate exposure occurred alongside other agricultural contaminants, the risk of spontaneous preterm birth increased significantly beyond what would be expected from simple additive effects. Although nitrates mainly impact oxygen transport and cellular metabolism, their presence appears to increase the capacity of other pollutants to pass past the placental barrier and impair fetal development. This synergistic link appears to function through a number of complementary processes. This finding is particularly significant in agricultural regions, where seasonal patterns of pesticide application coincide with naturally occurring nitrate fluctuations in groundwater. The researchers observed that women exposed to combined contaminants showed significantly higher risks of adverse birth outcomes compared to those exposed to individual contaminants at similar concentrations, demonstrating that the combined effect was greater than what would be expected from adding the individual effects alone [23] These observations highlight the urgent need for a paradigm shift in water quality regulation, moving from single-contaminant standards to more comprehensive approaches that consider the real-world complexity of multiple interacting exposures.

3.4. Methodological Advances

Recent studies introduced improved exposure assessment techniques. Mashau *et al.* demonstrated the utility of urinary trichloroacetic acid as a biomarker for DBP exposure [35], representing a significant advancement in exposure assessment accuracy. Additionally, the use of sophisticated spatial modeling and within-mother designs has strengthened the evidence base considerably.

3.5. Regional and Socioeconomic Disparities

3.5.1. Geographic Variations

Significant regional differences emerged in both contaminant profiles and associated outcomes. Rural areas showed particularly high risk due to reliance on unregulated private wells, while urban areas faced different challenges related to aging infrastructure and disinfection byproducts.

3.5.2. Socioeconomic Factors

Lower-income regions with limited water treatment infrastructure demonstrated stronger associations between contamination and adverse outcomes. This disparity highlights the intersection of environmental justice and public health concerns.

3.6. Water Source Considerations

This review revealed important variations in birth outcomes based on drinking water sources, with distinct risk patterns emerging across different supply systems:

3.6.1. Municipal Water Systems & Private Wells

Large-scale studies through municipal water systems provided the most robust data on contaminant levels. Coffman *et al.*'s analysis of Danish public water supplies (n=898,206) demonstrated that even regulated municipal systems showed concerning associations between contaminant levels and birth outcomes [37]. However, these systems generally maintained better monitoring and treatment protocols compared to other sources.

Several studies highlighted elevated risks associated with private well usage. Almberg *et al.*'s research in Ohio found significantly higher risks of very low birth weight and preterm birth in areas where private wells were common [32]. Private wells often lack regular monitoring and treatment systems, potentially exposing users to higher contamination levels. This is particularly concerning as Brender *et al.*'s research suggested that well-water users might be exposed to elevated nitrate levels without adequate warning [10].

The implications of Coffman *et al.*'s findings are particularly significant because they demonstrate that even well-regulated municipal systems face challenges in maintaining optimal water quality for fetal development [37]. Their large-scale population-based study in Denmark revealed a decreasing trend in term birth weight associated with increasing nitrate exposure, even within systems that meet current regulatory standards. This suggests that current acceptable thresholds for contaminants may need reevaluation specifically in the context of prenatal development, as impacts may occur at levels previously considered safe [37].

The findings from Almberg *et al.* and Brender *et al.* collectively highlight a critical public health challenge regarding private well water [10, 32]. Almberg *et al.*'s research in Ohio demonstrated that areas with higher reliance on private wells showed increased risks of adverse birth outcomes, particularly in regions where arsenic levels were below current regulatory limits [32]. This finding is especially noteworthy when considered alongside Brender *et al.*'s work on nitrate exposure [10], as it suggests that private well users may face multiple concurrent exposure risks without the benefit of regular monitoring systems. Together, these studies emphasize the need for enhanced monitoring and support systems for private well users, particularly for pregnant women in areas where private wells serve as the primary water source.

3.6.2. Bottled Water

An interesting finding emerged from Weyer *et al.*'s analysis of bottled water consumption during pregnancy [24]. Their case-control study found that bottled water generally contained very low nitrate levels and showed no significant association with congenital disabilities. However, the authors noted that the source and quality of bottled water varied considerably, emphasizing the need for consistent regulation and monitoring.

Weyer *et al.*'s multi-site population-based case-control study included 1,410 cases and 1,100 controls, analyzing bottled water samples using EPA Method 300.0 [24]. This methodologically rigorous approach provided valuable insights into nitrate concentrations in bottled water sources. Their research was particularly significant as it was one of the first large-scale studies to specifically examine bottled water as a distinct exposure source during pregnancy, with the findings suggesting that bottled water consumption might represent a way to reduce nitrate exposure during pregnancy. Bottled water might offer certain advantages in terms of contaminant reduction, but comprehensive monitoring and regulation of bottled water sources remains crucial for ensuring consistent quality and safety for pregnant women.

3.6.3. Surface Water vs Groundwater

The review identified distinct contamination patterns between surface and groundwater sources. Yang *et al.*'s study of arsenic exposure in arsenic-endemic areas demonstrated significant impacts on birth outcomes, with their research showing babies were, on average, 30g lighter and had higher preterm birth rates [14]. These findings were particularly notable as they examined groundwater contamination in areas with naturally occurring arsenic.

Regarding surface water sources, Ochoa-Acuña *et al.*'s research in Indiana provided evidence of herbicide exposure effects through drinking water, showing associations between atrazine exposure and increased rates of small-for-gestational-age births when exposure was averaged over 4-6 months before birth [22].

The differences between these two studies help illustrate how contaminant profiles can vary between water sources, with each presenting unique challenges for monitoring and regulation. This understanding is crucial for developing appropriate water quality management strategies that address the specific risks associated with different water sources.

3.7. Understanding Variability in Findings

The observed variations in study findings can be attributed to several key factors that warrant careful consideration. First, methodological differences significantly influenced results across studies. Research using biomarkers, such as Mashau *et al.*'s [35] use of urinary trichloroacetic acid measurements, demonstrated stronger and more consistent associations compared to studies relying solely on environmental monitoring. This methodological distinction was particularly evident in the assessment of disinfection byproducts, where Kogevinas *et al.* [30] found no consistent associations using environmental data alone, while Smith *et al.* [6] identified significant effects when incorporating individual exposure assessments.

Geographic and demographic factors also contributed to result variability. Yang *et al.* [14] demonstrated significant impacts in arsenic-endemic areas of Taiwan, with babies averaging 30g lighter at birth, while studies in regions with lower baseline contamination levels showed more modest effects. This geographic variation was further complicated by population-specific vulnerabilities, as evidenced by Smith *et al.*'s [6] finding of increased susceptibility among Pakistani infants to trihalomethane exposure.

Exposure timing emerged as another crucial source of variation. Migeot *et al.* [23] found that second-trimester exposure to nitrate-atrazine mixtures had particularly strong effects on fetal growth, while Almberg *et al.* [33] identified early pregnancy as the critical window for atrazine exposure. These temporal variations in susceptibility help explain apparently contradictory findings across studies with different exposure assessment periods.

3.8. Integration with Existing Literature

Our findings both confirm and extend previous research in several important ways. The association between arsenic exposure and adverse birth outcomes aligns with earlier work by Milton *et al.* [39-43] and Von Ehrenstein *et al.* [44]. However, our review adds crucial evidence about the effects at lower exposure levels. Particularly significant is Almberg *et al.*'s [32] demonstration of risks below current regulatory limits, which builds on Bloom *et al.*'s [26] earlier review of arsenic exposure effects.

Regarding nitrate exposure, our findings extend Manassaram *et al.*'s [18] seminal review by incorporating newer evidence from large-scale studies. Coffman *et al.*'s [37] analysis of 898,206 Danish births provides robust evidence for dose-dependent effects, while Sherris *et al.*'s [38] within-mother analysis of 1,443,318 siblings offers methodologically robust support for causality.

The evidence for disinfection byproducts shows interesting evolution from earlier work. While Aggazzotti *et al.* [16] found minimal effects from trihalomethanes, more recent studies like Mashau *et al.* [34] have identified specific susceptible subgroups and particular byproduct species of concern, suggesting more complex relationships than previously recognized.

3.9. Implications for Practice and Policy

These findings have several concrete implications for water quality management and maternal health care. First, current regulatory standards for arsenic (10 μg/L) may need reconsideration, given evidence of adverse effects at lower levels [32]. We recommend implementing more stringent standards, particularly in areas serving pregnant women.

Second, the timing of exposure monitoring should be adjusted to align with critical windows of vulnerability. Based on Migeot *et al.*'s [23] and Almberg *et al.*'s [33] findings, we recommend enhanced monitoring during early pregnancy and the second trimester, particularly for nitrates and agricultural contaminants.

Third, private well users require special attention. Brender *et al.*'s [10] work suggest that well-water users face elevated exposure risks without adequate warning systems. We recommend implementing mandatory testing programs for private wells used by pregnant women, with particular attention to nitrate and arsenic levels.

3.10. Future Research Directions

Several critical areas require further investigation. First, the interaction between multiple contaminants needs a more detailed study. While Migeot *et al.* [23] demonstrated synergistic effects between nitrates and pesticides, similar investigations are needed for other common contaminant combinations, particularly in agricultural areas.

Long-term health consequences of early-life exposure represent another crucial research gap. While our review focused on birth outcomes, the potential for developmental effects extending into childhood and beyond requires investigation, following the methodological approach of longitudinal studies like Sherris *et al.* [38].

Research is also needed on cost-effective intervention strategies, particularly for resource-limited settings. While Weyer *et al.* suggested bottled water as a potential intervention, more sustainable solutions require investigation, especially for communities relying on private wells or unregulated water sources[24].

Finally, the role of genetic susceptibility in modifying contaminant effects, as suggested by Smith *et al.*'s [6] findings regarding ethnic differences in trihalomethane susceptibility, warrants further investigation. This could help identify particularly vulnerable subpopulations requiring enhanced protection.

This review substantially advances our understanding of how water quality affects birth outcomes. By synthesizing evidence from diverse study designs and populations, it reveals patterns and associations that were not apparent in individual studies, particularly regarding timing effects and contaminant interactions. These insights provide a strong foundation for future research and policy development aimed at protecting maternal and fetal health through improved water quality standards.

CONCLUSION

This review of 30 studies conclusively demonstrates that drinking water quality during pregnancy significantly influences birth outcomes, with effects varying by contaminant type, exposure timing, and water source. Key findings revealed that even exposure to contaminant levels below current regulatory standards can adversely affect birth outcomes, particularly for arsenic and nitrates. The timing of exposure proved crucial, with particular vulnerability during early pregnancy. At the same time, the synergistic effects of multiple contaminants indicate that current regulatory approaches focusing on individual contaminants may underestimate real-world risks.

These findings call for several crucial actions: integration of water quality monitoring into standard prenatal care, particularly for women relying on private wells; reevaluation of regulatory standards for drinking water contaminants specifically considering fetal health outcomes; and prioritization of interventions for vulnerable populations, especially in areas with limited water treatment infrastructure. Healthcare providers, water quality regulators, and public health officials must work together to implement these changes while researchers continue investigating long-term health consequences and developing cost-effective intervention strategies. Through these coordinated efforts, we can better protect maternal and fetal health through improved water quality standards and comprehensive public health interventions.

AUTHORS' CONTRIBUTION

All three authors have contributed to all processes in this review. TR, DS, and NMP contributed to the conception and design of this study, prepared, gathered data and conducted analysis. TR, DS, and NMP drafted the manuscript. All authors have read and approved for publication of this final manuscript.

LIST OF ABBREVIATIONS

AMP	=	Atrazine monitoring program
BD	=	Birth defect
BDCM	=	Bromodichloromethane
CI	=	Confidence interval
CP	=	Chlorination proportion
DBCM	=	Dibromochloromethane
DBP	=	Disinfection by-product
DDT	=	Dichlorodiphenyltrichloroethane
EPA	=	Environmental protection administration
HA	=	Haloacetaldehydes
HAN	=	Haloacetonitriles
IUGR	=	Intrauterine growth restriction
LBW	=	Low birth weight
MBW	=	Mean birth weight
OR	=	Odds ratio
PAH	=	Polycyclic aromatic hydrocarbon
PCE	=	Perchloroethylene tetrachloroethylene
PRISMA	=	Preferred reporting items for systematic reviews and meta-analyses
PTB	=	Preterm birth
PTD	=	Preterm delivery
SGA	=	Small for gestational age
TCAA	=	Trichloroacetic acid
TCE	=	Trichloroethylene
THM	=	Trihalomethane
TLBW	=	Term low birth weight
TTHM	=	Total trihalomethane
USEPA	=	United States Environmental Protection Agency
VLBW	=	Very low birth weight
VPTB	=	Very preterm birth

CONSENT FOR PUBLICATION

Not applicable.

STANDARDS OF REPORTING

PRISMA guidelines and methodology were followed.

AVAILABILITY OF DATA AND MATERIALS

All data included in this review are from previously published papers.

FUNDING

This study was funded by PT Tirta Investama, Indonesia.

CONFLICT OF INTEREST

The authors authors declare no potential conflicts of interest.

ACKNOWLEDGEMENTS

The authors express their sincere thanks and appreciation to Dr. Irene Indriani Gumuljo for her assistance and support.

SUPPLEMENTARY MATERIAL

PRISMA checklist is available as supplementary material on the publisher's website along with the published article.

REFERENCES

[1] Guidelines for Drinking-water Quality: Fourth Edition Incorporating the First and Second Addenda. (4th Ed..). Geneva: World Health Organization 2022; pp. 1-6.

[2] Progress on Drinking Water, Sanitation and Hygiene: 2021 Update and SDG Baselines. (1st Ed..). Geneva: World Health Organization/UNICEF 2021; pp. 1-8.

[3] Needham LL, Grandjean P, Heinzow B, *et al.* Partition of environmental chemicals between maternal and fetal blood and tissues. Environ Sci Technol 2011; 45(3): 1121-6. http://dx.doi.org/10.1021/es1019614 PMID: 21166449

[4] National Primary Drinking Water Regulations EPA 816-F-09-004. (9th Ed..). Washington, DC: Environmental Protection Agency 2021; pp. 1-12.

[5] European Food Safety Authority. Risks to human health related to the presence of chemical contaminants in water intended for human consumption. EFSA J 2020; 18(4): 6064.

[6] Smith RB, Edwards SC, Best N, Wright J, Nieuwenhuijsen MJ, Toledano MB. Birth weight, ethnicity, and exposure to trihalomethanes and haloacetic acids in drinking water during pregnancy in the born in bradford cohort. Environ Health Perspect 2016; 124(5): 681-9. http://dx.doi.org/10.1289/ehp.1409480 PMID: 26340797

[7] Ferguson KK, O'Neill MS, Meeker JD. Environmental contaminant exposures and preterm birth: A comprehensive review. J Toxicol Environ Health B Crit Rev 2013; 16(2): 69-113. http://dx.doi.org/10.1080/10937404.2013.775048 PMID: 23682677

[8] Polanska K, Hanke W, Sobala W. Predictors of environmental exposure to pollutants during pregnancy: The Polish mother and child cohort study. Int J Occup Med Environ Heal 2019; 32(4): 527-42.
PMID: 31241624

[9] Villanueva CM, Kogevinas M, Cordier S, *et al.* Assessing exposure and health consequences of chemicals in drinking water: Current state of knowledge and research needs. Environ Health Perspect 2014; 122(3): 213-21.
http://dx.doi.org/10.1289/ehp.1206229 PMID: 24380896

[10] Brender JD, Weyer PJ, Romitti PA, *et al.* Prenatal nitrate intake from drinking water and selected birth defects in offspring of participants in the national birth defects prevention study. Environ Health Perspect 2013; 121(9): 1083-9.
http://dx.doi.org/10.1289/ehp.1206249 PMID: 23771435

[11] Grellier J, Bennett J, Patelarou E, *et al.* Exposure to disinfection by-products, fetal growth, and prematurity: A systematic review and meta-analysis. Epidemiology 2010; 21(3): 300-13.
http://dx.doi.org/10.1097/EDE.0b013e3181d61ffd PMID: 20375841

[12] Rahman A, Kumarathasan P, Gomes J. Infant and mother related outcomes from exposure to metals with endocrine disrupting properties during pregnancy. Sci Total Environ 2016; 569-570: 1022-31.
http://dx.doi.org/10.1016/j.scitotenv.2016.06.134 PMID: 27378155

[13] Yang CY, Chiu HF, Chang CC, Wu TN, Sung FC. Association of very low birth weight with calcium levels in drinking water. Environ Res 2002; 89(3): 189-94.
http://dx.doi.org/10.1006/enrs.2002.4369 PMID: 12176002

[14] Yang CY, Chang CC, Tsai SS, Chuang HY, Ho CK, Wu TN. Arsenic in drinking water and adverse pregnancy outcome in an arseniasis-endemic area in northeastern Taiwan. Environ Res 2003; 91(1): 29-34.
http://dx.doi.org/10.1016/S0013-9351(02)00015-4 PMID: 12550085

[15] Yang CY. Drinking water chlorination and adverse birth outcomes in Taiwan. Toxicology 2004; 198(1-3): 249-54.
http://dx.doi.org/10.1016/j.tox.2004.01.032 PMID: 15138048

[16] Aggazzotti G, Righi E, Fantuzzi G, *et al.* Chlorination by-products (CBPs) in drinking water and adverse pregnancy outcomes in Italy. J Water Heal 2004; 2(4): 233-47.
http://dx.doi.org/10.2166/wh.2004.0021 PMID: 15666965

[17] Villanueva CM, Durand G, Coutté M-B, Chevrier C, Cordier S. Atrazine in municipal drinking water and risk of low birth weight, preterm delivery, and small-for-gestational-age status. Occup Environ Med 2005; 62(6): 400-5.
http://dx.doi.org/10.1136/oem.2004.016469 PMID: 15901888

[18] Manassaram DM, Backer LC, Moll DM. A review of nitrates in drinking water: Maternal exposure and adverse reproductive and developmental outcomes. Environ Health Perspect 2006; 114(3): 320-7.
http://dx.doi.org/10.1289/ehp.8407 PMID: 16507452

[19] Yang CY, Xiao ZP, Ho SC, Wu TN, Tsai SS. Association between trihalomethane concentrations in drinking water and adverse pregnancy outcome in Taiwan. Environ Res 2007; 104(3): 390-5.
http://dx.doi.org/10.1016/j.envres.2007.01.006 PMID: 17324396

[20] Huyck KL, Kile ML, Mahiuddin G, *et al*. Maternal arsenic exposure associated with low birth weight in Bangladesh. J Occup Environ Med 2007; 49(10): 1097-104.
http://dx.doi.org/10.1097/JOM.0b013e3181566ba0 PMID: 18000415

[21] Aschengrau A, Weinberg J, Rogers S, *et al.* Prenatal exposure to tetrachloroethylene-contaminated drinking water and the risk of adverse birth outcomes. Environ Health Perspect 2008; 116(6): 814-20.
http://dx.doi.org/10.1289/ehp.10414 PMID: 18560539

[22] Ochoa-Acuña H, Frankenberger J, Hahn L, Carbajo C. Drinking-water herbicide exposure in Indiana and prevalence of small-for-gestational-age and preterm delivery. Environ Health Perspect 2009; 117(10): 1619-24.
http://dx.doi.org/10.1289/ehp.0900784 PMID: 20019915

[23] Migeot V, Albouy-Llaty M, Carles C, *et al.* Drinking-water exposure to a mixture of nitrate and low-dose atrazine metabolites and small-for-gestational age (SGA) babies: A historic cohort study. Environ Res 2013; 122: 58-64.
http://dx.doi.org/10.1016/j.envres.2012.12.007 PMID: 23340115

[24] Weyer PJ, Brender JD, Romitti PA, *et al.* Assessing bottled water nitrate concentrations to evaluate total drinking water nitrate exposure and risk of birth defects. J Water Heal 2014; 12(4): 755-62.
http://dx.doi.org/10.2166/wh.2014.237 PMID: 25473985

[25] Rodenbeck SE, Sanderson LM, Rene A. Maternal exposure to trichloroethylene in drinking water and birth-weight outcomes. Arch Environ Heal 2000; 55(3): 188-94.
http://dx.doi.org/10.1080/00039890009603405 PMID: 10908102

[26] Bloom MS, Surdu S, Neamtiu IA, Gurzau ES. Maternal arsenic exposure and birth outcomes: A comprehensive review of the epidemiologic literature focused on drinking water. Int J Hyg Environ Heal 2014; 217(7): 709-19.
http://dx.doi.org/10.1016/j.ijheh.2014.03.004 PMID: 24713268

[27] Ruckart PZ, Bove FJ, Maslia M. Evaluation of contaminated drinking water and preterm birth, small for gestational age, and birth weight at Marine Corps Base Camp Lejeune, North Carolina: A cross-sectional study. Environ Heal 2014; 13(1): 99.
http://dx.doi.org/10.1186/1476-069X-13-99 PMID: 25413571

[28] Iszatt N, Nieuwenhuijsen MJ, Bennett JE, Toledano MB. Trihalomethanes in public drinking water and stillbirth and low birth weight rates: An intervention study. Environ Int 2014; 73: 434-9.
http://dx.doi.org/10.1016/j.envint.2014.08.006 PMID: 25244706

[29] Ileka-Priouzeau S, Campagna C, Legay C, Deonandan R, Rodriguez MJ, Levallois P. Women exposure during pregnancy to haloacetaldehydes and haloacetonitriles in drinking water and risk of small-for-gestational-age neonate. Environ Res 2015; 137: 338-48.
http://dx.doi.org/10.1016/j.envres.2015.01.005 PMID: 25601737

[30] Kogevinas M, Bustamante M, Gracia-Lavedán E, *et al.* Drinking water disinfection by-products, genetic polymorphisms, and birth outcomes in a european mother-child cohort study. Epidemiology 2016; 27(6): 903-11.
http://dx.doi.org/10.1097/EDE.0000000000000544 PMID: 27468006

[31] Stayner LT, Almberg K, Jones R, Graber J, Pedersen M, Turyk M. Atrazine and nitrate in drinking water and the risk of preterm delivery and low birth weight in four Midwestern states. Environ Res 2017; 152: 294-303.
http://dx.doi.org/10.1016/j.envres.2016.10.022 PMID: 27816866

[32] Almberg KS, Turyk ME, Jones RM, *et al.* Arsenic in drinking water and adverse birth outcomes in Ohio. Environ Res 2017; 157: 52-9.
http://dx.doi.org/10.1016/j.envres.2017.05.010 PMID: 28521257

[33] Almberg K, Turyk M, Jones R, Rankin K, Freels S, Stayner L. Atrazine contamination of drinking water and adverse birth outcomes in community water systems with elevated atrazine in Ohio, 2006−2008. Int J Environ Res Publ Heal 2018; 15(9): 1889.
http://dx.doi.org/10.3390/ijerph15091889 PMID: 30200320

[34] Mashau F, Ncube EJ, Voyi K. Drinking water disinfection by-products exposure and health effects on pregnancy outcomes: A systematic review. J Water Heal 2018; 16(2): 181-96.
http://dx.doi.org/10.2166/wh.2018.167 PMID: 29676755

[35] Mashau F, Ncube EJ, Voyi K. Maternal urinary levels of trichloroacetic acid and association with adverse pregnancy outcomes. J Water Heal 2019; 17(6): 884-95.
http://dx.doi.org/10.2166/wh.2019.109 PMID: 31850896

[36] Mashau F, Ncube EJ, Voyi K. Association between exposure to drinking water disinfection byproducts and adverse pregnancy outcomes in South Africa. J Water Heal 2021; 19(1): 174-89.
http://dx.doi.org/10.2166/wh.2020.214

[37] Coffman VR, Jensen AS, Trabjerg BB, *et al.* Prenatal exposure to nitrate from drinking water and markers of fetal growth restriction: A population-based study of nearly one million Danish-

born children. Environ Health Perspect 2021; 129(2): 027002. http://dx.doi.org/10.1289/EHP7331 PMID: 33539179

[38] Sherris AR, Baiocchi M, Fendorf S, Luby SP, Yang W, Shaw GM. Nitrate in drinking water during pregnancy and spontaneous preterm birth: A retrospective within-mother analysis in California. Environ Health Perspect 2021; 129(5): 057001. http://dx.doi.org/10.1289/EHP8205 PMID: 33949893

[39] Stayner LT, Jensen AS, Schullehner J, *et al.* Nitrate in drinking water and risk of birth defects: Findings from a cohort study of over one million births in Denmark. Lancet Reg Health Eur 2022; 14(100286): 100286. http://dx.doi.org/10.1016/j.lanepe.2021.100286 PMID: 35141697

[40] Arun AK, Rustveld L, Sunny A. Association between water fluoride levels and low birth weight: National health and nutrition examination survey (NHANES) 2013–2016. Int J Environ Res Publ Heal 2022; 19(15): 8956. http://dx.doi.org/10.3390/ijerph19158956 PMID: 35897326

[41] Pintaningrum Y, Juliardi NRAD, Ermawan R. Effect of arsenic contamination in drinking water during pregnancy with the incidence of congenital heart disease: A meta-analysis. J Kedokte Unram 2023; 12(1): 1359-63.

[42] Milton AH, Smith W, Rahman B, *et al.* Chronic arsenic exposure and adverse pregnancy outcomes in bangladesh. Epidemiology 2005; 16(1): 82-6. http://dx.doi.org/10.1097/01.ede.0000147105.94041.e6 PMID: 15613949

[43] Milton AH, Rahman H, Smith W, Shrestha R, Dear K. Water consumption patterns in rural Bangladesh: Are we underestimating total arsenic load? J Water Heal 2006; 4(4): 431-6. http://dx.doi.org/10.2166/wh.2006.0027 PMID: 17176814

[44] von Ehrenstein OS, Guha Mazumder DN, Hira-Smith M, *et al.* Pregnancy outcomes, infant mortality, and arsenic in drinking water in West Bengal, India. Am J Epidemiol 2006; 163(7): 662-9. http://dx.doi.org/10.1093/aje/kwj089 PMID: 16524957