JPRM
Journal of Preventive and Rehabilitative Medicine

2023; 5(2): 54-65
PublishedOnline:08/11/2023
(https://journals.unza.zm/index.php/medicine/about)
DOI: https://doi.org/10.21617/jprm20232.529

ISSN: 2415-038X (Print)

ORIGINAL ARTICLE Open Access

Uranium exposure-associated health complications and their environmental-exposure pathways: A baseline survey among residents near uranium mining sites in Siavonga, Zambia

Titus Haakonde [1,2,3] *, Kennedy Choongo [2], Gershom Chongwe [5,6], Gilbert Nchima [7], Md. Saiful Islam [8,9], Kutemba Kaina Kapanji-Kakoma [10] and John Yabe [2,4]

[1] Environmental Health Section, School of Applied and Health Sciences, Evelyn Hone College of Applied Arts and Commerce, Lusaka, Zambia. [2] Department of Para-clinical Studies, School of Veterinary Medicine, The University of Zambia, Lusaka, Zambia. [3] Department of Clinical Sciences, School of Medicine and Health Sciences, University of Lusaka, Lusaka, Zambia. [4] School of Veterinary Medicine, University of Namibia, Windhoek, Namibia. [5] Department of Biostatistics and Epidemiology, School of Public Health, The University of Zambia, Lusaka, Zambia. [6] Tropical Diseases Research Centre, Ndola, Zambia [7] Toxicology and Biochemistry Unit, Central Veterinary Research Institute, Ministry of Livestock and Fisheries, Balmoral, Chilanga, Zambia. [8] Department of Soil Science, Patuakhali Science and Technology University, Dumki, Patuakhali,8602, Bangladesh; [9] Centre for River and Coastal Engineering (CRCE), Universiti Teknologi Malaysia (UTM), 81310, Johor Bahru Malaysia [10] National Institute for Scientific and Industrial Research, Lusaka, Zambia.

*Corresponding author: thaakonde@evelynhone.edu.zm

Abstract

To cite: Haakonde T, Choongo K, Chongwe G, Nchima G, Silam Md, Kapanji-K K, Yabe J., Uranium exposure-associated health complications and their environmental-exposure pathways: A baseline survey among residents near uranium mining sites in Siavonga, Zambia. JPRM 2023, 5(2): 54-65. doi: https://doi.org/10.21617/jprm20232.529

Background: Uranium (U), a naturally occurring actinide may exhibit radio-toxic or chemo-toxic health effects in exposed populations. Increased cases of environmental uranium pollution have recently gained attention owing to its potential threats to human health and adverse effects on animals and aquatic life. Among the toxicological effects known to arise from environmental exposure to U in humans include neurotoxicity, hepatotoxicity, pulmonary toxicity, reproductive toxicity and bone toxicity. Anecdotal evidence indicating that residents of communities in the vicinity of U-mining sites in Siavonga, Zambia, were experiencing some health complications associated with U exposure have been recorded. Therefore, the current study was conducted with the aim of assessing the associations between specific U exposure-associated health complications, and the potential environmental exposure pathways among residents in the vicinity of the U mining sites in Siavonga, Zambia.
Methods: A comparative cross-sectional study design was used. A total of 698 study participants who met the study's inclusion criteria were randomly included in the study. Pre-tested interviewer-administered semi-structured questionnaires were used for data collection, The collected data was thereafter statistically analysed using a binary logistic regression through SPSS (v 20).
Results: The current study results are suggesting that one's place of residence and the location of drinking water sources had an effect ($p < 0.05$) on one's chances of experiencing U exposure-associated health complications. The odds of experiencing U exposure-associated health complications among the U-mining area community residents were at minimum >1.2 among the general populations, >1.6 among pregnant women and >2.014 among children compared to the residents of the non-mining area communities.
Conclusions: The findings of the study revealed that the residents of the U-mining area were exposed to high U levels. Therefore, awareness programs targeting local communities should be initiated to sensitise them on the means and ways of limiting and avoiding exposure to U.

Keywords: *Uranium exposure; Children; Maternal-related; Health complications; Zambia*

Received: *18 December 2022* ***Accepted:*** *9 May 2023* ***Published:*** *8 November 2023*

INTRODUCTION

Uranium (U) is an actinide that naturally occurs in small concentrations in the environment. Geogenic processes and anthropogenic activities have been implicated in raising the concentration of U in the environment [1]. Variations in the geological deposits of U in different compartments of the environment are usually responsible for elevated levels of U levels [2]. Geological and geochemical processes such as leaching of U contaminated surface water into underground aquifers can contaminate groundwater [3]. Weathering can also exacerbate environmental U contamination as weathering agents such as wind or water may carry U contaminated soil particles to non-contaminated environments [4]. Some geochemical processes such as low environmental pH levels and oxidation processes may enhance the oxidation of uraniferous rocks or the decomposition of U-carbonate complexes thereby contributing to the elevation of U levels in the environment [5]. In addition to geological and geochemical processes, anthropogenic activities can alter the geologic distribution of U and result in its release into the environment [6]. Mining and mineral exploration, agricultural, nuclear facilities and military activities are among the most reported anthropogenic activities cited as sources of U environmental contamination [6-11]. Therefore, geological processes, geochemical reactions and anthropogenic activities can render U more bio and chemo-available in the environment.

Reports on environmental U pollution have recently gained much attention, probably owing to uranium's potential threats to human health and its adverse effects on animals and aquatic life [11-16]. Evidence from some toxicological and epidemiological studies suggesting possible associations between environmental U exposure and potential human health effects has been documented. For instance, studies by Keith et al. [17] suggest that most of the U exposure-associated health complications arise from uranium's chemotoxicity and not radiotoxicity. Other studies have also indicated that consumption of food contaminated with U, particularly water containing U concentrations exceeding 30 µg/L, may pose chemo-toxic effects to the cardiovascular and the renal systems [18-21]. Even exposures to U levels lower than 30 µg/L should not be ignored if the exposure happens to be chronic. An association between chronic exposure to U concentrations lower than 30 µg/L and some health complications such as some cancers, impairments to the nervous, endocrine and reproductive systems have been reported [22-23]. Acute and subacute exposures to U levels above 30 µg/L have also shown associations with prenatal-related and kidney-associated health complications in humans [15-16,24]. Uranium from contaminated environments has several routes of entry into the body systems, as shown in Fig 1.

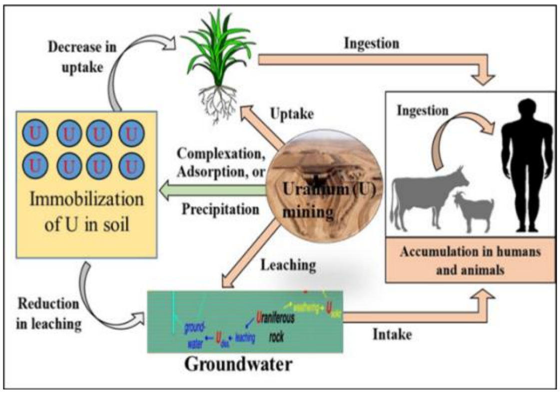

Fig. 1: Schematic illustration of exposure pathways of U to humans [25].

The routes of exposure to U include inhalation, dermal contact and the oral route. Among the three, the oral route account for the majority of the exposure through consumption of water contaminated with U, intake of agricultural products such as cereals, meat and meat products such as cow milk [26]. Preliminary studies by Haakonde et al. [25,27] showed elevated U levels above the World Health Organisation's recommended guideline limit of 30.00 µg/L for drinking water, and high urinary U levels up to 110.00 µg/L in Siavonga district, Zambia. This indicated increased health risk from U exposure to residents in the vicinity of U mining sites in the area. Reports alleging that residents in the vicinity of the U mine were experiencing U health complications that could be linked to U exposure in Siavonga [28-31] have persisted. According to the literature search using the following key words; uranium exposure, children, maternal-related, health complications and Zambia on google scholar did not reveal any publication on this topic. Therefore, to the best of our knowledge, nothing is currently known about the association between environmental U exposure risk factors and health complications alleged to be prevailing among the residents near U mining sites in Siavonga district, Zambia. Hence, the current study was conducted to determine the prevailing U exposure-associated health complications among residents in the vicinity of the U mining sites in Siavonga. Further, associations between each of the identified health complications and the environmental exposure risk factors were assessed.

MATERIALS AND METHODS

Study design

A comparative cross-sectional study design was used in the current study. A semi-structured questionnaire, mostly with closed-ended questions was used for collecting data on the prevailing U exposure-associated health complications and the associated environmental exposure risk factors. The same type of questionnaire administered in U-mining area communities was also administered in the non-mining area communities. The total number of households from the communities in the U-mining area was used to determine the sample size of the respondents. Only one person participated in the study from each selected household.

Using the modified Cochran formula [63] and the outlined parameters, the sample size of the respondent households was determined. From each of the study areas, i.e., U-mining area and the non-mining area, 349 study participants were targeted for sampling. The sampling activities were conducted between November 2019 and October 2020. The sampling sites are shown in Fig. 2. The Stratified sampling technique was used when sampling the households from communities in the U-mining area. For each community, a list of serial numbers of households was developed from each of the current village registers. A raffle draw was performed to randomly select households from which the study participants were selected. Only one volunteering person meeting the inclusion criteria from the selected household was required to respond to a questionnaire. The same procedure was done when selecting respondents from the non-mining area communities. Residents who had resided in the U-mining area communities for a continuous period of not less than one year were included in the current study. The one-year period of residence for the study participants' inclusion into the study was based on the biological half-life of U in the bones, which is estimated to be between 70 and 200 days for chronic exposure to U and much lesser (about 15 days) in the blood for acute exposure to U [3,34]. The residents targeted for inclusion in the study had to be at least 18 years at the time of data collection with no history of smoking or working in the U-mining or processing facilities. The age of 18 years and above for to be included in the study was based on ethical reasons as it is the age of informed consent. A history of smoking or working in U-mining or processing facilities could have confounded the signs and symptoms of U chemical toxicity.
Regarding study participants from the non-mining area communities, only those who resided in the area for a continuous period of not less than a year were included in the current study as long as they were at least 18 years, and with no history of smoking or working in U-mining or processing facilities. Additionally, they were expected to have never resided in the U-mining area communities or any mining area elsewhere for a continuous period of more than a year from the time of data collection.

Any resident of either the U-mining area or the non-mining area communities who did not meet the outlined criteria for a respective study area was excluded from the current study.

Study Area

The current study focused on the communities around U mining sites in Siavonga district, Zambia (Fig. 2). Siavonga district is located between latitude -16o 32'17" South and longitude 28° 42'31.54" East and 511 meters elevation above the sea level. The district covers about 2514 km2 with a population density of 25.21persons per km2 [32]. The U-mining areas are surrounded by Nanyanga, Simamba, Sinadambwe and Manchahvwa communities. These study sites were selected because of U-mining activities which have been ongoing since the early 1960s in the area [33]. For purposes of comparing our results, Siavonga town, about 67 km away from the U-mining area and with no U mining history, was also included in the study. Details of population distributions about the study area are shown in Fig. 2

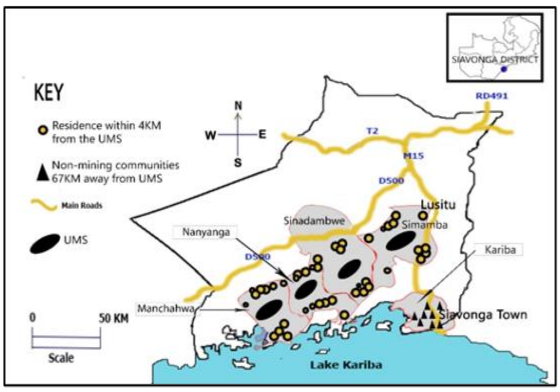

Fig. 2: Location of Mining and Non-Mining Communities near Uranium Mining Sites in Siavonga, Zambia.

Data collection and analysis

Data collection was conducted between November 2019 and October 2020. A pre-tested questionnaire by Yabe et al. [35] was slightly modified and thereafter used for data collection. A total of eight enumerators, particularly Community Health Assistants, were oriented and trained for two days to interviewer-administer questionnaires. Five were assigned to collect data from the U-mining area communities and three to the non-mining area communities. Prior to data collection, the questionnaire was translated from English into Tonga, a dominant language in the study area, by a Secondary School trained teacher for Tonga language.

Prior to interviewing the study participants informed consent was obtained from them. The relevance of the study, its nature, and expected level of participation were well explained to them. They were also assured of confidentiality about the information they were to disclose, was treated with the utmost confidentiality, as only the principal investigator (PI) had access to the entered data through encryption of data files. There was equally restricted access to the filled-up questionnaires by any individual without permission from the (PI). Participation in the current study was on a voluntary basis and any study participant was free to opt out of the survey without giving notice to the principal investigator.

Associations between specific U exposure-associated health complications and the environmental U-exposure pathways were examined using a binary logistic regression analysis with the aid of the statistical software, SPSS version 20 (IBM Analytics, Year of version release). Gender, age and the number of pregnancies a respondent had before, were all adjusted for when assessing for associations between specific U exposure-associated health complications and the environmental U-exposure pathways. A p-value of less than 0.05 indicated a statistical significance in all the statistical tests.

RESULTS

Participant's demographic characteristics

The study participants from the U-mining area communities were of ages ranging from 19 to 66 years, and their median age was 31. From the non-mining communities, the age range of the of the study participants was 18 to 73 years with a median age of 33. The majority of the study participants were in the informal sector of employment, mainly as subsistence farmers (95%) in the U mining area communities and in the non-mining area communities (65%), mainly as subsistence farmers, fishermen and marketeers. Other socio-demographic characteristics of the study participants are shown in Table 1.

Table 1: Participants' demographic characteristics

Variable		Study site	
		Mining area	Non-mining area
Gender	Male (%)	42.5	28.3
	Female (%)	57.5	71.7
Age (in years)	Minimum	19	18
	Maximum	66	73
	Median	31	33
Marital status	Married	80.2	79.1
	Unmarried	19.8	20.9
Household size	Mean	6	5
Education	None (%)	8.0	6.0
	Primary (%)	42	40
	Secondary (%)	33	30
	Tertiary (%)	17	24

Self-reported U exposure-associated health complications and exposure risk factors

As shown in Table 2, the logistic regression analysis suggested that one's place of residence, and the location of their drinking water sources had an effect ($p< 0.05$) on the U exposure-associated self-reported cases (SRCs) of chronic lower abdominal pain, and abnormal menstruations among the female respondents ($p<0.05$) among the residents of the U-mining area when the respondent's age was kept fixed. Additionally, one's place of residence and location of drinking water source, i.e., in U-mining area or non-mining area, showed statistical evidence of having an effect ($\beta= 1.531$, $p< 0.05$) on the self-reported cases of experiencing pain when urinating among respondents of the U-mining area communities where age and gender were adjusted for. The history of consuming water sourced from water sources located in the vicinity of U-mining areas showed a significant regression relationship (β= 1.600, p< 0.05) with the self-reported respiratory-related complications when age and gender of the study participants was kept fixed during regression analysis. Further, the study results showed that the odds of experiencing chronic lower abdominal pain [OR= 11.554; 95% CI (3.251, 41.054)], abnormal menstruations [OR= 3.490; 95% CI (2.621, 19.629)] and experiencing pain when urinating [OR= 6.943; 95% CI (1.180, 40.842)] among respondents living in the U-mining area communities were all above 1.180 times higher than those living in the non-mining area. On the other hand, the odds of experiencing respiratory-related complications among the study participants whose water sources were located in the U-mining area were 1.700 times higher than those who consumed from water sources located in the non-mining area in Siavonga, Zambia.

Table 2: Regression analysis of the SRCs and U exposure-associated factors in Siavonga district

Variable	Pseudo r^2	Percentage correct	β	Exp(β)	95% CI for Exp(β)	
Chronic lower abdominal pain *versus*	0.892	77.5 (21.2) [90.0]			Lower	Upper
Residence			2.247*	11.554	3.251	41.054
Duration of Residence			-1.376	0.252	0.106	0.601
Consumption of water			2.111*	1.365	1.590	3.159
Consumption of cow milk			-0.137	0.872	0.192	3.957
Abnormal menstruations (Among female respondents) *versus*	0.799	88.6 (10.1) (98.7)				
Residence			2.490*	3.490	2.621	19.629
Duration of Residence			1.250	1.262	0.494	3.229
Consumption of water			1.095*	2.990	1.482	18.551
Consumption of cow milk			1.088	2.968	0.649	13.578
Pain when urinating *versus*	0.65 9	71.6 (17.9) [91.6]				
Residence			1.538*	6.943	1.180	40.842
Duration of Residence			-0.238	0.788	0.242	2.572
Consumption of water			1.531*	4.621	1.121	19.059
Consumption of cow milk			-0.325	0.722	0.244	2.140
Respiratory-related complications *versus*	0.874	84 (19.2) [98.2]				
Residence			0.903	2.468	0.626	9.722
Duration of Residence			0.689	1.992	0.483	8.212
Consumption of water			1.600*	5.471	1.837	16.294
Consumption of cow milk			0.493	0.960	0.366	2.522

**Implies that the associations were statistically significant at p< 0.05. The percentages in () are for the logistic regression model's specificity, while [ ] are for the logistic regression model's sensitivity.*

Maternal-related Self-Reported Health Complications (SRHCs) and U exposure-associated environmental risk factors

The logistic regression analysis between the respondents' area of residence and the location of the drinking water sources with the U exposure-associated health complications area shown in Table 5. After adjusting for age and the number of previous pregnancies which the female respondents had, the analysis showed that ones' residence and the location of the sources of drinking water, i.e., U-mining area or non-mining area, had a regression relationship ($p < 0.05$) with the U exposure-associated self-reported cases of miscarriages and stillbirths. Similarly, U exposure-associated self-reported cases of low birth weights and births with congenital defects, suggested that ones' residence had an effect ($p < 0.05$) on the self-reported low birth weights and births with congenital defects when the ages and previous pregnancy records were kept fixed.

The current study further showed that the odds of having a miscarriage [OR= 1.672; 95% CI (1.272, 10.275)], stillbirth [OR= 9.546; 95% CI (6.616, 12.023)], child a with low birthweight [OR= 2.868; 95% CI (1.825 9.972)] or births with congenital defects [OR= 4.815; 95% CI (1.263,13.726)] were all above 1.672 times higher among U-mining area community respondents than their counterparts from the non-mining area (Table 5). Further, the odds of experiencing miscarriages and stillbirths were 1.071 and 2.129 times higher among the study participants from the U-mining area communities than those from the non-mining area with 95.0 per cent Confidence Intervals (CIs) of 1.068 to 4.513 and 1.011 to 3.939, respectively (Table 3).

Table 3: Regression analysis of U exposure-associated maternal-related complications and U exposure-associated *factors*

Variable	Pseudo r^2	Percentage correct	β	Exp(β)	95% CI for Exp(β)	
Miscarriages *versus*	0.724	88.1 (16.8) [93.4]			Lower	Upper
Residence			0.514	1.672	1.272	10.275
Duration of Residence			0.709	1.686	0.420	6.768
Consumption of water			1.071	0.554	1.068	4.513
Consumption of cow milk			-1.020	0.761	0.028	4.629
Stillbirths *versus*	0.742	86.1 (8.8) [97.8]				
Residence			3.495*	9.546	6.616	12.023
Duration of Residence			-0.944	0.389	0.122	1.241
Consumption of water			2.002*	1.103	1.011	3.939
Consumption of cow milk			1.276	0.067	0.005	0.813
Low birth weights *versus*	0.545	65 (26.9) [80.2]				
Residence			1.173*	2.868	1.825	9.972
Duration of Residence			2.326	0.805	0.162	3.996
Consumption of water			1.054	1.087	0.334	3.539
Consumption of cow milk			0.709	2.868	0.825	9.972
Births with congenital defects *versus*	0.851	95.9 (11) [98.8]				
Residence			2.511*	4.815	1.263	13.726
Duration of Residence			1.333	3.791	0.755	19.034
Consumption of water			-3.389	0.966	0.174	5.373
Consumption of cow milk			0.425	1.530	0.162	14.477

**Implies that the associations were statistically significant at p< 0.05. The percentages in ( ) are for the logistic regression model's specificity, while [ ] are for the logistic regression model's sensitivity.*

Children's U exposure-associated health complications and environmental risk factors for prenatal exposure to U

The logistic regression analysis showed that when the ages of the mothers adjusted for, the mothers' area of residence and history of experiencing a U exposure associated health complication during pregnancy had a significant ($p < 0.05$) effect on the child's health status; low birth weights, hearing impairments and physical disabilities water (Table 4). Concerning the parents' area of residence, the odds of having a child with low birth weight [OR= 2.014; 95% CI (1.535, 7.577)], hearing impairment [OR= 2.016; 95% CI (1.994, 49.510)] or a physical disability [OR= 1.048; 95% CI (1.879, 2.268)] were all above 1.048 times higher among parents living in communities in the U-mining area than those from non-mining area communities. Further, the odds of having a child with low birth weight [OR= 1.138; 95% CI (1.057, 3.332)], hearing impairment [OR= 1.231; 95% CI (1.064, 1.838)] or physical disabilities [OR= 1.959; 95% CI (1.062, 3.615)] were all above 1.138 times higher among mothers with a self-reported history of experiencing a U exposure-associated health complication than the mothers who did not self-report to have ever experienced the same health complications.

Table 4: Regression analysis of children's U exposure-associated health complications and prenatal U exposure-associated environmental factors

Variable	Pseudo r^2	Percentage correct	β	Exp(β)	95% CI for Exp(β)	
Low birth weights versus	0.834	89.8 (10.8) [93.7]			Lower	Upper
Residence			1.071*	2.014	1.535	7.577
Duration of Residence			-0.295	0.745	0.154	3.593
Consumption of water			3.944	1.208	1.093	5.670
Consumption of cow milk			0.189	0.389	0.048	3.160
Mother's history of experiencing a UEAHC			1.980*	1.138	1.057	3.332
Hearing impairments versus	0.743	94.6 (20.0) [99.1]				
Residence			1.948*	2.016	1.994	49.510
Duration of Residence			-0.832	0.435	0.056	3.409
Consumption of water			-2.943	0.653	0.132	4.547
Consumption of cow milk			-0.865	0.421	0.087	2.030
Mother's history of experiencing a UEAHC			1.467*	1.231	1.064	1.838
Physical disabilities versus	0.579	74.6 (28.4) [96.7]				
Residence			3.034*	1.048	1.879	2.268
Duration of Residence			2.595	13.401	4.823	37.232
Consumption of water			-0.103	0.902	0.273	2.982
Consumption of cow milk			0.519	1.680	0.804	3.510
Mother's history of experiencing a UEAHC			0.672*	1.959	1.062	3.615

DISCUSSION

The current study findings showed that the most prevailing U exposure-associated self-reported health complications among the residents of the U-mining area communities included chronic lower abdominal pain, pain when urinating, abnormal menstruations among women and respiratory-related health complications. Further, a significant association between the prevailing U exposure-associated health complications and U exposure-associated environmental risk factors i.e., area of residence, duration of residence in communities in the vicinity of U mining sites, consumption of cow milk and water sourced from the U mining area communities suggested correlations with the prevailing U exposure-associated health complications. Earlier studies done in the same area also showed significant correlations between U contamination levels in drinking water and in cow milk sampled from the same area in Siavonga [25,27]. Elsewhere, researchers have also reported a high prevalence of cases of nephrotoxicity [14,36], altered menstrual cycles [16,37] and respiratory-related health complications [38] in populations residing in well-known U-contaminated environments. Therefore, these findings from the current study strongly suggest that the reported health complications among the residents in the vicinity of the U-mining sites could be due to them being exposed to U by virtue of their area of residence, sources of the water they drink and the food they consume.

Jenny-Burri *et al.* [39] reported that only place of residence and duration of residence in the place influenced the prevalence of U exposure-associated health complications among the Swedish population exposed to natural U. Similarly, our study findings showed that, one's place of residence and one's duration of residence in the same area had strong associations with the prevailing U exposure-associated health complications i.e., chronic lower abdominal pain, experiencing of chronic pain when urinating, abnormal menstruations and respiratory-related health complications. As reported in the findings from this study, other studies have equally indicated that prolonged duration of residence in a place and frequency of visits to U-mining sites have an impact on ones' blood uranium levels [40-41].

The current study results suggest that consumption of U-contaminated water may be associated with adverse health complications, contrary to the findings by Kurttio *et al.* [36]. Kurttio *et al.* [36] concluded that U contamination of drinking water had no direct relationship with the adverse health effects manifesting among the consumers of U-contaminated water as there were no apparent clinical symptoms among consumers of water with high U-levels (3410 µg/L). Further, Prat *et al.* [42] suggested that calcium-dependent U-species [CaUO2(CO3)3(aq) and CaUO2(CO3)32-] in drinking water inhibit the chemo-toxicity of U upon ingestion. Prat's conclusion on the role of calcium-dependent U-species in drinking water could be the likely explanation for the non-existence of statistical relationships between U exposure through drinking water and the adverse health effects in the exposed populations that were not observed by Kurttio *et al.* [36]. Although not investigated, the current study results could suggest that calcium-dependent U-species were negligible in the drinking water sources in Siavonga. Hence, the suggested statistical association between U contamination of the drinking water sources and the overall SRHCs among the U-mining area residents in Siavonga, Zambia. Otherwise, an increasing volume of literature has continued to suggest potential associations between U exposure-associated health complications and U exposure environmental risk factors globally [38,43-45].

In the current study, self-reported adverse birth outcomes were more prevalent among women from communities in the vicinity of the U-mining sites than the women from the non-mining area. The self-reported miscarriages, stillbirths and births with congenital disabilities demonstrated significant associations with some of the environmental exposure risk factors, i.e., the women's residence and duration of residence, their sources of drinking water and foods. Previous studies in Wuhan in China, Central Michigan and the Texas Gulf Coast in the USA have so far indicated a possible association between stillbirths and pre-term labour with maternal U-exposure in women who resided in U-contaminated environments for up to 20 years [16,46-47]. Unlike the studies that only demonstrated the association between stillbirths and place of residence as an environmental U exposure risk factor, the current research suggests that synergistic environmental exposure risk factors could be responsible for the observed association between the self-reported cases of stillbirths and environmental exposures to U.

According to the current study results, environmental exposure factors, i.e., the women's place of residence and the location of drinking water had an association with the self-reported birth outcome such as congenital disabilities. Similarly, Guo *et al.* [48] and Wei *et al*. [49] reported that births with congenital disabilities, particularly orofacial clefts were more prevalent among women whose residences were located in environments contaminated with U. However, scientific explanations for the association between orofacial clefts in children and maternal exposure to U is still scanty, making it difficult to exclude the latent effects from other environmental pollutants and determine the possible reproductive toxicity of U in humans [50-52].

A meta-analysis by Ma *et al.* [2] on U studies conducted between 2000 and 2020 showed that none of the studies found evidence to associate U-exposure with miscarriages. On the contrary, our study suggests that a combination of environmental risk factors could induce miscarriages, as alleged through self-reports among women that were interviewed. Our study findings further concur with few documented reports which suggest possible associations between U exposure-associated maternal complications (stillbirths and births with congenital disabilities) and environmental exposure to U [16,53].

In the current study, the self-reported cases of children's low birth weights, hearing impairments and physical disabilities demonstrated an association with the parental place of residence and their mothers' history of experiencing a U exposure-associated health complication during the period of pregnancy. Studies by Bloom *et al.* [47], Yang *et al.* [53], Chen *et al.* [54] and Wang *et al.* [15] observed that low birth weights were prominent among pregnant women concurrently exposed to U and other toxic heavy metals. These researchers only considered the association between maternal exposures to natural U through drinking water and the prevalence of lower birth weights. Apart from drinking water as the possible route of maternal and prenatal exposure to natural U, the current study also considered the synergistic effects that could arise from a parental place of residence, duration of residence, consumption of drinking water and cow milk from known U contaminated area. Although evidence of mechanisms of prenatal exposure to U is scanty, it is concerning to note that U environmental-exposure risk factors could amplify uranium's dose-time dependent toxicological effects during the gestation and lactation periods and subsequently manifest multifarious health complications during foetal and neonatal stages [44,55].

The most self-reported physical disability among children from communities in the vicinity of U mining sites was bone-related deformations. Since U is implicated in replacing Ca^{2+} ions on the bone surface and accumulating in the skeleton [56-60]. Therefore, the present study suggests that U exposure could be responsible for self-reported bone-related physical disabilities.

Scientific evidence associating U exposure with hearing impairments in humans, both children and adults, is still scarce. However, Wright *et al.* [60] observed an association between hearing impairments in infants and exposure to Lead (Pb). Wright *et al.* [60] further suggested that hearing impairments in children could also be attributed to brain damage resulting from prenatal exposure to Pb, a neurotoxicant. A series of uranium's alpha and beta decay processes result in progenies, including Pb [1]. The connection of U and Pb could be responsible for the reported relationship between maternal exposure to U due to the parents' area of residence and the self-reported cases of hearing impairments among children whose parents reside in communities in the vicinity of U mining sites. Similarly, such a connection of Pb with U could also suggest possible relationships between the cases of brain damage among children whose parents were environmentally exposed to U in China, the USA and Japan [17,62].

LIMITATIONS

The current study only considered U exposure as a possible cause of the self-reported health complications among residents of the study area. However, uranium's decay process produces even more toxic metals such as Radon, Polonium, and Pb, which could cause various health complications. Additionally, the current study only assessed associations between U exposure pathways and the self-reported health complications among the study participants. Further, the unavailability of diagnostic equipment, particularly, for screening environmental exposure-associated health complications in most of the local health facilities in Siavonga may have the potential to mislead clinicians and researchers to attribute the causation of the self-reported health complications U exposure alone while ignoring other risk factors. Therefore, the current study results should be cautiously interpreted as they do not signify causation but rather associations between the environmental exposure pathways and the prevailing self-reported U exposure-associated health complication prevailing among residents in the vicinity of the U mining area in Siavonga, Zambia.

CONCLUSION

By assessing more synergistically interacting environmental risk factors, the present study is the first study which identified the associations which U exposure have with the prevailing U exposure-associated SRHCs among communities in the vicinity of the U-mining sites in Siavonga, Zambia. Further, the present study findings, could suggest a possible confirmation of findings from the earlier studies conducted in the same area [25,64] which revealed increased likelihood of health risks from environmental exposure to U among the U-mining area community residents. Thus, the alleged health complications being experienced by the U-mining area residents could be emanating from exposure to high U levels. Therefore, the local authority and the ministry of health should initiate awareness programmes targeting the local communities to sensitise them on the means and ways of limiting and avoiding exposure to U. Finally, epidemiological studies should be conducted in future to verify and explore possible cause-effect models such as U excretion and creatinine tests for nephrotoxicity, and the antibody-antigen studies for inflammatory effects associated with U exposure.

DECLARATION

Acknowledgement The authors thankfully acknowledge the Ministry of Technology and Science formerly the Ministry of Higher Education's Department of Science and Technology for the support. The authors also express their gratitude to Prof. Md. Saiful Islam and Dr. Kutemba Kaina Kapanji-Kakoma for reviewing earlier versions of the manuscript and providing scientific advice.

Author contribution TH, JY, KC and GC conceived and designed the study. TH collected data. TH, GC and GN analysed and interpreted the results. TH drafted the manuscript. All the authors had input in the manuscript. All authors have read and approved the final manuscript.

Ethics The current study's ethical clearance was obtained from the Excellence in Research Ethics in Science Converge Institutional Review Board under approval reference number "2019-Oct-015", and permission to conduct research was obtained from the Zambia Health Research Authority. Siavonga District Health Office granted permission for conducting interviews in the district.

Competing interests There were no competing interests from all authors in this study.

Funding The research was jointly funded by the Ministry of Technology and Science of the Government of the Republic of Zambia through the Post-graduate Scholarships grant. However, TH supplemented the funding from personal sources.

REFERENCES

1. Sahoo S.K, Jha V.N, Patra A.C, Jha S.K, Kulkarni M.S. Scientific background and methodology adopted on derivation of regulatory limit for uranium in drinking water-A global perspective. Environmental Advances. 2020; 2:100020; doi: 10.1016/j.envadv.2020.100020.
2. Ma W, Gao B, Guo Y, Sun Z, Zhang Y, Chen G, et al. Occurrence and Distribution of Uranium in a Hydrological Cycle around a Uranium Mill Tailings Pond, Southern China. Int J Environ Res Public Health. 2020; 17:773; doi:10.3390/ijerph17030773.
3. Banning. A, and M. Benfer. Drinking Water Uranium and Potential Health Effects in the German Federal State of Bavaria. Int. J. Environ. Res. Public. Health.2017;14(12), 927-931.
4. Masindi, V, and K.L. Muedi. Environmental contamination by heavy metals. Heavy metals. 2018; 10(5), 115-132
5. Stetten, L., A. Mangeret, J. Brest, M. Seder-Colomina, P. Le Pape, M. Ikogou, N. Zeyen, A. Thouvenot, A. Julien, and G. Alcalde. Geochemical control on the reduction of U (VI) to mononuclear U (IV) species in lacustrine sediments. Geochemistry and Cosmochemistry. 2018; 222(19), 171-186.
6. Vengosh, A., R.M. Coyte, J. Podgorski, and T.M. Johnson. A critical review on the occurrence and distribution of the uranium-and thorium-decay nuclides and their effect on the quality of groundwater. Sci. Total Environment. 2022; 808, 151914.
7. Chavoshi, E., M. Afyuni, M.A. Hajabbasi, A.H. Khoshgoftarmanesh, K.C. Abbaspour, H. Shariatmadari, and N. Mirghafari. Health Risk Assessment of Fluoride Exposure in Soil, Plants, and Water at Isfahan, Iran. Human and Ecological Risk Assessment: 2011; 17, 414-430. doi.org/10.1080/10807039.2011.552397.
8. Stajnko, A., R. Tuhvatshin, G. Suranova, D. Mazej, Z. Šlejkovec, I. Falnoga, Z. Krušič, E.Lespukh, and P. Stegnar. Trace elements and ALAD gene polymorphisms in general population from three uranium legacy sites-A case study in Kyrgyzstan. Science of the Total Environment. 2020; 719, 134427.
9. Teh, T., N.A.R. Nik Norulaini, M. Shahadat, Y. Wong, and A.K. Mohd Omar. Risk assessment of metal contamination in soil and groundwater in Asia: a review of recent trends as well as existing environmental laws and regulations. Pedosphere. 2016; 26 (4), 431-450.
10. Neiva, A.M.R., M.T.D. Albuquerque, I.M.H.R. Antunes, P.C.S. Carvalho, A.C.T. Santos, C. Boente, P.P. Cunha, S.B.A. Henriques, and R.L. Pato. Assessment of metal and metalloid contamination in soils trough compositional data: the old Mortórios uranium mine area, central Portugal. Environmental and Geochemistry in Health. 2019; 41, 2875-2892.

11. Castrillejo, M., R. Witbaard, N. Casacuberta, C.A. Richardson, R. Dekker, H.A. Synal, and M. Christl. Unravelling 5 decades of anthropogenic 236U discharge from nuclear reprocessing plants. Sci. Total Environment. 2020; 717, 137094.
12. Canu IG, Laurent O, Pires N, Laurier D, Dublineau I. Health Effects of Naturally Radioactive Water Ingestion: The Need for Enhanced Studies. Environmental Health Perspectives. 2011; 119:1676–1680; doi:10.1289/ehp.1003224.
13. Williams LJ, Chen L, Zosky GR. The respiratory health effects of geogenic (earth derived) PM10. Inhalation toxicology. 2017; 29: 342–355.
14. Deyssenroth MA, Gennings C, Liu SH, Peng S, Hao K, Lambertini L, et al. Intrauterine multi-metal exposure is associated with reduced fetal growth through modulation of the placental gene network. Environment international. 2018;120: 373–381.
15. Wang, S., Y. Ran, B. Lu, J. Li, H. Kuang, L. Gong, Y. Hao. 2020. A review of uranium-induced reproductive toxicity. Biological and Trace Elements Research. 2019; 196, 204-213.
16. Zhang, W., W. Liu, S. Bao, H. Liu, Y. Zhang, B. Zhang, A. Zhou, J. Chen, K. Hao, and W. Xia. Association of adverse birth outcomes with prenatal uranium exposure: A population-based cohort study. Environmental Research International 2020; 135, 105391.
17. Keith, S., O. Faroon, N. Roney, F. Scinicariello, S. Wilbur, L. Ingerman, F. Llados, D. Plewak, D. Wohlers, and G. Diamond. Toxicological Profile for Uranium, Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles. 2013a; [Online] Available from https://www.ncbi.nlm.nih.gov/books/NBK158802/ [Accessed 2 July 2019].
18. Katz S. The Chemistry and Toxicology of Depleted Uranium. Toxins 2014; 2:50–78; doi:10.3390/toxics2010050.
19. Ali, W., M.W. Aslam, C. Feng, M. Junaid, K. Ali, S. Li, Z. Chen, Z. Yu, A. Rasool, and H. Zhang. Unravelling prevalence and public health risks of arsenic, uranium and co-occurring trace metals in groundwater along riverine ecosystem in Sindh and Punjab, Pakistan. Environmental Geochemistry Health. 2019; 7(41), 2223-2238.
20. Hon, Z., J. Österreicher, and L. Navrátil. Depleted Uranium and Its Effects on Humans and Sustainability. 2015; 7(63), 4063-4077.
21. Redvers, N., A, M, Chischilly, D. Warne, M. Pino, and A. Lyon-Colbert. Uranium Exposure in American Indian Communities: Health, Policy, and the Way Forward. Environmental Health Perspectives., 2021; 129, 035002.
22. Hossein-Asghari, M., S. Saeidnia, M. Amin Rezvanfar, and M. Abdollahi. A Systematic Review of the Molecular Mechanisms of Uranium-Induced Reproductive Toxicity. Inflamation & Allergy-Drug Targets. 2015; 14(9), 67-76.
23. Sanchez, B., X. Zhou, A.S. Gardiner, G. Herbert, S. Lucas, M. Morishita, J.G. Wagner, R. Lewandowski, J.R. Harkema, and C. Shuey. Serum-borne factors alter cerebrovascular endothelial microRNA expression following particulate matter exposure near an abandoned uranium mine on the Navajo Nation. Particulate and Fibre Toxicology, 2020; 17, 1-14.
24. van Gerwen, M., N. Alpert, W. Lieberman-Cribbin, P. Cooke, K. Ziadkhanpour, B. Liu, and E. Genden. Association between uranium exposure and thyroid health: a National Health and Nutrition Examination Survey analysis and ecological study. International Journal of Environmental Research and Public Health. 2020; 17, 712.
25. Haakonde T, Yabe J, Choongo K, Chongwe G, Islam MS. Preliminary Assessment of Uranium Contamination in Drinking Water Sources Near a Uranium Mine in the Siavonga District, Zambia, and Associated Health Risks. Mine Water and the Environment 2020; 39: 735–745.
26. Goussen, B., F. Parisot, R. Beaudouin, M. Dutilleul, A. Buisset-Goussen, A.R.R. Péry, and J.M. Bonzom. Consequences of a multi-generation exposure to uranium on Caenorhabditis elegans life parameters and sensitivity. Ecotoxicology. 2013; 22(6), 869-878.
27. Haakonde T, Yabe J, Choongo K, Chongwe G, Islam M.S., Nchima G. Uranium contamination of Cow milk near uranium mining sites in Siavonga, Zambia. Bulletin of the National Research Centre. 2021; 2021(18).
28. National Assembly of Zambia. Parliamentary debate: Ministerial statement by Honourable Minister of Mines, Mr. Maxwell Mwale on Uranium mining in Siavonga. (27.07.2010).
29. Times of Zambia Newspaper. Uranium mining in Siavonga causing serious health complications. (20.07.2018).
30. Zambia Environmental Management Agency (ZEMA). 2018. Zambia Environmental Outlook Report 3, Zambia Environmental Management Agency, Lusaka.
31. Daily Nations Newspaper. Siavonga villagers to petition minister over uranium contamination. (30.10.2021).
32. Zambia Statistics Agency (ZSA). (2019). Zambia Demographic and Health Survey, Lusaka, Zambia.
33. Van Aardt J, Bowell R, BéruBé K, Jones T, Lusambo V. (2018). Geochemical and Bioreactivity Assessment of Future Mining Operations at Mutanga Uranium Project, Southern Province, Zambia.
34. Arzuaga, X., M. Gehlhaus, and J. Strong. Modes of action associated with uranium induced adverse effects in bone function and development. Toxicology Letters. 2015; 236, 123-130.
35. Yabe, J., S.M. Nakayama, Y. Ikenaka, Y.B. Yohannes, N. Bortey-Sam, A.N. Kabalo, J. Ntapisha, H. Mizukawa, T. Umemura, and M. Ishizuka. Lead and cadmium excretion in faeces and urine of children from polluted townships near a lead-zinc mine in Kabwe, Zambia. Chemosphere. 2018; 202, 48-55.
36. Kurttio P, Auvinen A, Salonen L, Saha H, Pekkanen J, Mäkeläinen I, et al. Renal effects of uranium in drinking water. Environmental Health Perspectives. 2002; 110:337-342; doi:10.1289/ehp.02110337.
37. Bao, S., W. Xia, S. Xu, Y. Li, B. Lu, C. Wu, J. Liao, H. Liu, X. Sun, and A. Zhou. Multiple metal exposure and platelet counts during pregnancy: A repeated measure study. Environmental International. 2020; 136(2), 105-119.
38. Williams LJ, Chen L, Zosky GR. The respiratory health effects of geogenic (earth derived) PM10. Inhalation toxicology. 2017; 29: 342–355.
39. Jenny-Burri, J., A. Blanc, R. Aubert, M. Haldimann, U. Zürcher, M. Burnier, F. Paccaud, M. Bochud, and V. Dudler. Uranium exposure of the Swiss population based on 24-hour urinary excretion. Swiss Medical Weekly. 2020; 150, 15-16.
40. Benson, R., O.D. Conerly, W. Sander, A.L. Batt, J.S. Boone, E.T. Furlong, S.T. Glassmeyer, D.W. Kolpin, H.E. Mash, and K.M. Schenck. Human health screening and public health significance of contaminants of emerging

concern detected in public water supplies. Science of the Total Environment. 2017; 579(2), 16423-1648.

41. Buononato, E.V., D. De Luca, I.C. Galeandro, M.L. Congedo, D. Cavone, G. Intranuovo, C.M. Guastadisegno, V. Corrado, and J. Ferri. Assessment of environmental and occupational exposure to heavy metals in Taranto and other provinces of Southern Italy through scalp hair analysis. Environmental Monitoring and Assessment., 2016; 188(5), 337-350.
42. Prat, O., T. Vercouter, E. Ansoborlo, P. Fichet, P. Perret, P. Kurttio, and L. Salonen. Uranium speciation in drinking water from drilled wells in southern Finland and its potential links to health effects. Environmental Science and Technology. 2009; 43, 3941-3946.
43. Ministry-of-Health-Canada. Guidelines for Canadian Drinking Water Quality Guideline Technical Document Uranium. [online]. 2020; (May);31. Available from https://www.canada.ca/en/health-canada/services/publications/healthy-living/guidelines-canadian-drinking-water-quality-guideline-technical-document-uranium.html.
44. Duggal V, Sharma S, Singh A. Toxicological risk and age-dependent radiation dose assessment of uranium in drinking water in southwest-central districts of Haryana State, India. Groundwater for Sustainable Development. 2021; 100577.
45. Lu, B., Y. Ran, S. Wang, J. Li, Y. Zhao, X. Ran, R. Li, and Y Hao. Chronic oral depleted uranium leads to reproductive damage in male rats through the ROS-hnRNP A2/B1-COX-2 signaling pathway. Toxicology. 2021; 449, 152666.
46. Ashrap, P., D.J. Watkins, B. Mukherjee, J. Boss, M.J. Richards, Z. Rosario, C.M. Vélez-Vega, A. Alshawabkeh, J.F Cordero, and J.D. Meeker. Maternal blood metal and metalloid concentrations in association with birth outcomes in Northern Puerto Rico. Environment International. 2020; 138, 105606.
47. Bloom, M.S., G.M.B. Louis, R. Sundaram, J.M. Maisog, A.J. Steuerwald, and P.J. Parsons. Birth outcomes and background exposures to selected elements; the Longitudinal Investigation of Fertility and the Environment (LIFE). Environmental Research. 2015; 138(4), 118-129.
48. Guo, Y., L. Liu, W. Ni, Y. Pan, Y. Chen, Q. Xie, Y. Liu, L. Jin, Z. Li, and A. Ren. Uranium concentration in umbilical cord may increase the risk for orofacial clefts. Environmental Research. 2020; 182, 109103.
49. Wei, Y., L. Jin, Z. Li, J. Liu, L. Wang, X. Pi, S. Yin, C. Wang, and A. Ren. Levels of uranium and thorium in maternal scalp hair and risk of orofacial clefts in offspring. Journal of Environmental Radioactivity. 2019; 204, 125-131.
50. Al-Shammari, A.M. Environmental pollutions associated to conflicts in Iraq and related health problems. Reviews in Environmental Health. 2016; 31(24), 245-250.
51. Goodrich, J.M., M.E. Ingle, S.E. Domino, M.C. Treadwell, D.C. Dolinoy, C. Burant, J.D. Meeker, and V. Padmanabhan. First trimester maternal exposures to endocrine disrupting chemicals and metals and fetal size in the Michigan Mother Infant Pairs Study. Journal of Development and Original Health Distributions. 2019; 10(4), 447-458.
52. Sharma, N. and J. Singh. Radiological and chemical risk assessment due to high uranium contents observed in the groundwaters of Mansa District (Malwa region) of Punjab state, India: an area of high cancer incidence. Exposure and Health. 2016; 8(2), 513-525.
53. Yang, X., Y. Li, J. Li, S. Bao, A. Zhou, S. Xu, and W. Xia. Associations between exposure to metal mixtures and birth weight. Environmental Pollution. 2020; 263, 114537.
54. Chen, M. H., S. Ng, M.S. Tsai, C.C Lin, and P.C. Chen. Birth Cohort Consortium of Asia (BiCCA): Current Children's Environmental Health Issues in Asia and Future Perspectives, in Pre-Emptive Medicine: Public Health Aspects of Developmental Origins of Health and Disease. 2019. doi.org/10.1007/978-981-13-2194-8_12.
55. Foster, W.G., J.A. Evans, J. Little, L. Arbour, A. Moore, R. Sauve, J. Andrés León, and W. Luo. Human exposure to environmental contaminants and congenital anomalies: a critical review. Crit. Reviews in Toxicology. 2017; 47(7), 59–84.
56. Gritsaenko, T., V. Pierrefite-Carle, G. Creff, B. Simoneau, A. Hagège, D. Farlay, S. Pagnotta, F. Orange, X. Jaurand, and C. Den-Auwer. Low doses of uranium and osteoclastic bone resorption: key reciprocal effects evidenced using new in vitro biomimetic models of bone matrix. Archives of Toxicology. 2021; 95(8), 1023–1037.
57. Younes, A., J.S Ali, A. Duda, C. Alliot, S. Huclier-Markai, J. Wang, F. Kabalan, D. Nemirovsky, R. Deng, and M.T. Nur. Uptake and Removal of Uranium by and from Human Teeth. Chemical Research and Toxicology. 2021; 34 (3), 880-891.
58. Grimstead, D.N., A.E. Clark, and A. Rezac. Uranium and vanadium concentrations as a trace element method for identifying diagenetically altered bone in the inorganic phase. J. Archaeol. Method Theory, 2018; 25(4), 689-704.
59. Kurttio P, Komulainen H, Leino A, Salonen L, Auvinen A, Saha H. Bone as a possible target of chemical toxicity of natural uranium in drinking water. Environmental Health Perspectives. 2005; 113: 68-72.
60. Wang, S., Y. Ran, B. Lu, J. Li, H. Kuang, L. Gong, and Y. Hao. A review of uranium-induced reproductive toxicity. Biological and Trace Elements Research. 2019; 196, 204-213.
61. Wright, R.O., S. Teitelbaum, C.Thompson, D. Balshaw, and C. Network. The Child Health Exposure Analysis Resource (CHEAR) is a vehicle to measure the environment in the Environmental influences on Child Health Outcomes (ECHO) Program. Current Opinions in Paediatrics. 2018; 30, 285.
62. Vicente-Vicente, L., Y. Quiros, F. Pérez-Barriocanal, J.M. López-Novoa, F.J. López-Hernández, and A.I. Morales. Nephrotoxicity of uranium: pathophysiological, diagnostic and therapeutic perspectives. Toxicology. Sci., 2010; 118, 324-347.
63. Ott, R.L, and M.T. Longnecker. (2015). An Introduction to Statistical Methods and Data Analysis. Cengage Learning. New York, U.S.A.
64. Haakonde T, Yabe J, Choongo K, Chongwe G, Nchima G. Uranium exposure and associated health risk implications among the residents living around uranium mining sites: a preliminary study in the Southern Province of Zambia. Environmental Advances. 2021; 5(100098).