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Human health risk assessment of Cd, Cu, Pb and Zn through consumption of raw goat's milk in Jijel province (Algeria)

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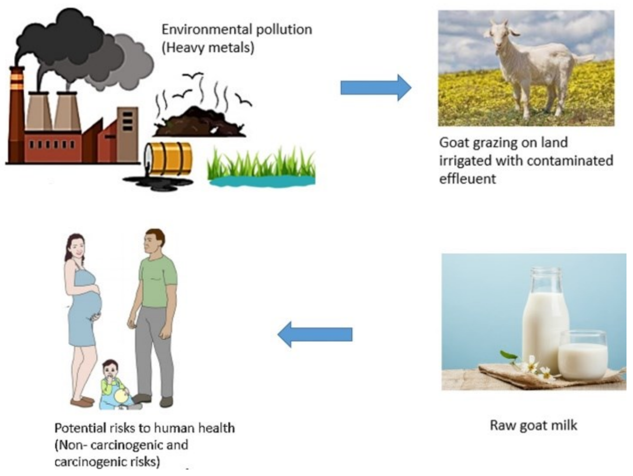
Graphical abstract



Abstract

Contamination of the food chain by toxic metals is one of the main concerns for human health. Milk is part of a balanced diet; essential for proper growth, but can also contains hazardous chemicals and contaminants including heavy metals which can be a risk for health. The aim of this study is to estimate the concentration of heavy metals in goat's milk and to assess infants and children health risks related to milk consumption in Jijel province. Metals, namely Cd, Cu, Pb and Zn were determined by FAAS. In parallel, an online survey was carried out to estimate the daily consumption of milk. Then, non-carcinogenic and carcinogenic health risk values were calculated. The results indicated common to low levels of essential elements (Cu: 0.05 ± 0.001 mg/kg, Zn: 1.87 ± 0.069 mg/kg) in comparison with toxic elements (Cd: 0.018 ± 0.001 mg/kg, Pb: 0.38 ± 0.004 mg/kg). Cadmium content bordered its limit (0.01mg/kg), whereas, lead was higher twenty time the permissible limit. While, daily estimated intake of lead exceeds the limit value (282.35%), target hazard quotient and hazard index of the mixture were below one the safe limit, representing the absence of non-carcinogenic risk. Contrariwise, the carcinogenic risk of Pb and Cd, and their cumulative risk were observed higher than the acceptable limit (Pvalue < 0.001). Based on these results, the consumption of goat's milk in Jije lprovince seems to be not safe for infants.

Keywords: Cancer risk, goat's milk, health risk assessment, heavy metals, Jijel

1. Introduction

Milk and dairy products are important components of the human diet, milk has been described as nearly complete food since it contains vital nutrients including proteins, essential fatty acids, lactose, vitamins and major minerals in balanced proportions, all these nutrients contribute to the development and maintenance of human life and health (Hussain *et al*. 1996; Meshref *et al*. 2014). Of note, milk and dairy products continue to be an essential part of nutrition throughout life, being recommended as an essential food group for daily consumption (Verduci *et al*. 2019). Nowadays, due to health consciousness, people tend to consume medicinal value added food items, such as goat milk. Naturally, reduced form of fat globule in the goat milk suits well for young population (Dhanalakshmi and Gawdaman 2013). Dairy goats produce about 15.2 million metric tons (MT) of milk accounting for 2.3% of global production (Verduci *et al*. 2019). According to the Food and Agriculture Organization (FAO), developing countries are home to more than 90% of the world's goat population; Asia has the largest proportion of the world's goat population, followed by Africa which contributes 24% of the global world production (Bilandžić *et al*. 2016; Nayik*et al*. 2021). Thus, there is a great interest for the production of goat milk due to the composition and high

Lebsir D., Balli N., SafiaHabila, Boussouf L., Boutenoun H., Belkouicem I.S., Bouchekhou N. and Leghouchi E. (2023), Human health risk assessment of Cd, Cu, Pb and Zn through consumption of raw goat's milk in Jijel province (Algeria), *Global NEST Journal*, **25**(8), 122-130.

quality of the product, particularly for population groups with particular needs, such as infants, and children suffering from hypersensitivity to cows’ milk (Bilandžić *et al*. 2016; Nayik *et al*. 2021). Goat's milk is defined as a substance composed of 77 to 80% water, and 20 to 23% of total solids (Salvador *et al*., 2006). In 100 ml of goat’s milk we have 3.3 g proteins, 2.5 g casein, 0.4 g lactoalbumin, 4.1g fat, and 3.8 g lactose (caprahispana 2011). The main minerals found in goat’s milk are K, Cl, Ca, P, Na, S and Mg at the amount of 181,150, 134, 121, 41, 28 and 16 mg in 100 g of goat’s milk (Park 2006). Also, we find all fat-soluble vitamins represented: A, D, E and K and a large majority of water-soluble vitamins: thiamine, niacin, pantothenic acid, biotin, pyridoxine, folic acid and cobalamin. Their quantity varies considerably depending on the time of the year and the animal's diet. The amount of riboflavin is very high and, to a lesser extent, that of vitamins A, B1 and B12. However, the figures for vitamins C and D are relatively low (Pece *et al*. 2005). It is well established that the most frequent consumers of milk and dairy products are infants and children, two age demographics described as particularly vulnerable to heavy metal exposure risks (Ismail *et al*. 2017). One of the main concerns with metals is their ability to bioaccumulate (Pilarczyk *et al*. 2013). In general, milk can contain a variety of xenobiotic compounds as an excretion of the mammary gland, including toxic heavy metals (Pilarczyk *et al*. 2013; Ismail *et al*. 2017), which are released from fixed and mobile sources such as petrochemicals, gas extraction, refinery processes, dumping sites of industrial wastes, and agricultural fertilizers and can be transferred to water, air, and soil, and even to plants the first part of the food chain. The feed of livestock from forage and water containing heavy metals leads to intake and accumulation of these elements in the edible tissues and other products like milk (Homayonibezi *et al*. 2021). Some mineral elements like Zn and Cu can also be categorized as heavy metals when they are found in food commodities beyond certain limits. Whereas, the four most toxic heavy metals typically found in food items are Hg, As, Cd, and Pb. When entering the human body through inhalation, skin contact, and ingestion (food or water), the toxic impacts of the heavy metals on human health include lung and blood cancer, kidney failure, osteoporosis, skeletal damage, gastrointestinal and hormonal disorders, some metabolic disorders, as well as neurodevelopmental and cognitive impairment (Ismail *et al*. 2017; Santa Maria, Hill, and Kline 2019). Therefore, to ensure consumers health, it is necessary to determine the residual concentrations of metals in milk and evaluate their associated health risks. In Jijel province, a northeastern town of Algeria, the intensive traffic jam and the industrial activities such as thermal power plant, Bellara steel complex, and the tannery may result in a high risk of heavy metals contamination (Querol *et al*. 2007; Leghouchi, Laib, and Guerbet 2009; Amodio *et al*. 2013). Although, there have been a reduced number of studies about metal contamination in food in Algeria (Amrane and Bouhidel 2019; Mehouel *et al*. 2019; Bounar, Boukaka, and Leghouchi 2020), but information regarding the heavy metal contents in milk and its products and the evaluation of their health risks still limited. It is now of interest to determine the risks of cancer and non-carcinogenic diseases derived from the consumption of milk in regions exposed or suspected of being exposed to this kind of pollution. Therefore, this work aimed to determine the concentration of heavy metals in goat’s milk and to evaluate the associated health risk in sensitive population with respect to daily consumption of milk for infants and children, in three different locations of Jijel province namely El-Milia, Texenna and Djimla.

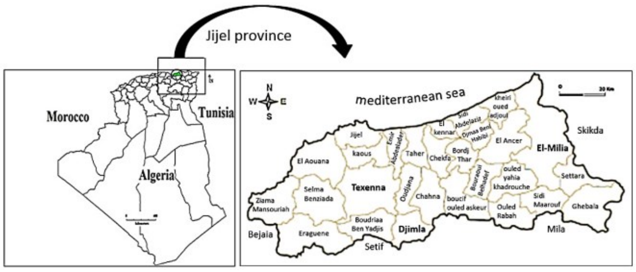


Figure 1. Geographical location of Jijel province (northeastern Algeria), and the targeted areas of the study (DPAT 2021; Lotfi and Karima2021)

2. Materials and methods

2.1. Study site

This study was conducted in the province of Jijel in the north-east of Algeria (Figure 1). Jijel is located between 36°48’N and 5°46’E, covering 2,577 km^2 (DPAT2021; Lotfi and Karima 2021). Three different locations of Jijel province were targeted in this study. The first, El-Milia the largest city area of the region, located in north-east of Jijel province, it occupies 332 km^2 (DPAT2021), and encompasses 99,515 inhabitants, Algerian Qatari Steel operates in the industrial zone of Bellara, in the commune of El-Milia (60 km east of Jijel) where it operates a steel complex with a total area of 523 hectares (Medjita and Boukerzaza2018). This steel complex occupies a privileged position midway the cities of Jijel, Mila, Constantine and Skikda. The second location, Texenna is located at 20Km southeast of the city of Jijel, it occupies 125.79 km^2 and includes 19,985 inhabitants. And the third one Djimla, located 45 km south-east of Jijel, it covers a total area of 65.28 km² and has a population of 22,140 according to DPAT censuses (2021) (DPAT 2021). Between the municipalities of Texenna and Djimla, we have The Tabellout dam a gravity type dam about 70 km south of the Jijel district. It is built between 2010 and 2018, with a height of 115 m, it is the fifth largest dam in Algeria with a capacity of 294 million m^3. According to the Directorate of Agricultural Statistics and Information Systems (DSASI) of Jijel district, and according to the agricultural campaign of (2019/2020) the consumption of goat's milk in El-Milia, Texenna, and Djimla was estimated at 29.40 × 10^3, 15.00 × 10^3 and 12.50 × 10^3 L/year respectively (DSASI 2020). The survey was focused on infants and children populations (0 to 10 years old).

Table1. FAAS measurement conditions

Parameters metals	Wavelength (nm)	Light intensity (mA)	Slitwidth (nm)	Burner height (mm)	Fuel gas (C2H2) flow (l/min)
Lead (Pb)	283.3	10	0.5	7	0.8
Cadmium(Cd)	228.8	8	0.5	7	0.8
Copper (Cu)	324.7	6	0.5	7	0.8
Zinc (Zn)	213.9	8	0.5	7	0.8

2.2. Reagents

Standard solutions of Cd, Cu, Pb and Zn at 1gL-1 in 2% nitric acid (SIGMA-ALDRICH, Germany) were used to calculate calibration curves. All the standards were prepared with high purity metals, HNO_3 and water. For the steps of sampling and extraction the reagent used HNO3 65% w/w, H2SO4 95% w/w (SIGMA-ALDRICH, Germany), and H2O2 30% v/v (Fisher scientific, Sweden) were of analytical reagent grade. Finally, the standard solutions were diluted in ultrapure water to obtain concentrations that were used to construct the calibration curves: 0.5, 1, 2, 4, and 6 mgL^{-1} of Cu; 0.1, 0.2, 0.4, 1, 2 and 4 mgL^{-1} of Cd; 0.5, 1, 2, 5, 10 and 20 mgL^{-1} of Pb; and 0.75, 1, 1.5, 2, and 3 $mg\ L^{-1}$ of Zn.

2.3. Sampling

A total of twentyseven goat's milk samples (250 mL) were collected at small dairy farms from rural areas of three different targeted locations (Texenna, Djmila, el-Milia) in Jijel province (Figure 2), from each location we selected three dairy farms and from each farm we collected three samples (250ml). To avoid any contamination, security measures have been applied such as washing of the hands and the udders of the animal before milking, the elimination of the first jet of each milking, and the decontamination of polyethylene bottles with nitric acid (Quemerais and Cossa1997). Then, the collected milk was stored immediately in the decontaminated polyethylene bottles, and transported in a cool box to the laboratory refrigerator before use. A pooled sample was prepared from three samples from each farm to obtain a three representative pool from each region.

2.4. Milk samples analysis

The milk samples were then analyzed for heavy metal elements using flame atomic absorption spectrometry (FAAS), model Shimadzu AA 6800 (Shimadzu®, Tokyo, Japan), under the conditions described in Table 1. The limit of detection (concentration of an element that gives a signal equal to three standard deviations of the background noise) varied from 0.001 to 0.02 µl with an accuracy of 1 to 2 % on relative error. Before FAAS was done, goat's milk extracts were prepared according to the method of Shahbazi *et al*. (2016). 15 ml of goat's milk was mixed with 20 ml of HNO_3, and heated to dryness using a hotplate. Then, 5 ml of H2SO4 wad added and heated to dryness. After that, 5 ml of H2O2 was added and heated until the sample becomes colorless and dry. Finally, residues were dissolved and completed to 5.0 ml using distilled water (Shahbazi, Ahmadi, and Fakhari 2016). Each extraction was performed in triplicate for each targeted location. The extract obtained was then filtered, and the filtrates were stored in sealed bottles in the refrigerator until the day of FAAS assay.

2.5. Online survey

An online survey was conducted on April 2022, all citizens of Jijel were eligible to participate, 198 parents participate to the survey among them 47 % have infants aged 0 to 4 years old, and 36.9 % have children aged 4 to 10 years old. So the number of infants and children was estimated to 93 and 73 respectively.

Parents were asked to answer online two kinds of questions regarding:

- The weight of the kids and,
- The daily (24h) amount of goat's milk consumed by infants and children.

The questions were set in Arabic and French languages, and the online survey link is as follows: https://docs.google.com/forms/d/1mZMy99bEL-5gcMFvL6mID4PCs3pu6cdfnXb1EnMSxtA/edit?ts=63e35f52&fbclid=IwAR2JbNb2_x2oY_SRf84HnwVxbWZZUf7iC2ICQexHxOQnE67mc9w1Kpv0koI#responses

2.6. Health risk assessment

According to the accredited methodology of the risk assessment by the Environmental Protection Agency of the United States, Human health risk assessment is a process used to estimate the health effects that might result from exposure to carcinogenic and non-carcinogenic chemicals (US EPA 1989). The risk assessment process is made up of four basic steps: hazard identification, exposure assessment, toxicity (dose-response) assessment, and risk characterization. The non-carcinogenic health risks of a single metal *via* consumption of goat's milk were assessed based on the target hazard quotient (THQ), a ratio of determined doses for one pollutant to its reference dose (RfD), and can be calculated as the following equations (1) and (2) (US EPA 1999; Giri *et al*. 2021):

$$THQ = \frac{\mathrm{EDI}}{\mathrm{RFD}} \tag{1}$$

$$EDI = \frac{\mathrm{Cmetal} \times \mathrm{Wmilk}}{\mathrm{BW}} \tag{2}$$

Where EDI is the estimated daily intake of heavy metals (mg/kg/d), and RFD is the oral reference dose; the RFD values of Pb, Cd, Cu, and Zn are set to be 0.0036 (JECFA

2003), 0.001, 0.04, and 0.3, mg/kg/d (US EPA 2014). C_{metal} is the mean concentration of heavy metals in milk samples (mg/kg), W_{milk}/BW is the intake of milk per kg body weight per day (kg/day.bw (kg)). The mean intake of milk as well as the average infants and children body weight have been set according to the online survey. The severity of health risks caused by toxic compounds is enhanced with the increasing THQ value, if the THQ is less than one; the exposed population is unlikely to experience obvious adverse effects (Zhuang *et al*. 2009). Since the exposure to more than a single metal may result in additive and/or interactive effects, the health index (HI) was used to evaluate the total non-carcinogenic health risk caused by a mixture of heavy metals (US EPA 1986). HI was estimated by the equation:

$$\mathrm{HI} = \sum_{i=0}^{n} \mathrm{THQ} \tag{3}$$

On the other hand, for carcinogens, the risks are estimated as the incremental probability of an individual developing cancer over a lifetime as a result of exposure to the potential carcinogen. The cancer risk (CR) for toxic metals Cd and Pb was calculated based on the equation:

$$CR = \mathrm{EDI} \times \mathrm{CSF0} \tag{4}$$

Where CSF (Cancer Slope Factor) is the carcinogenic slope factor that converts the estimated daily intake of the heavy metal averaged over a lifetime of exposure directly to incremental risk of an individual developing cancer (US EPA 1989), for the oral route of the metals, CSF Pb and Cd is estimated at 0.0085 and 15mg/kg/day respectively (USEPA 2002). The US Environmental Protection Agency (US EPA) considers acceptable for regulatory purposes a cancer risk limit to be 1×10^{-6} to 1×10^{-4}(US EPA 2004). In our study, to evaluate the plausible additive carcinogenic risk due to the exposure to the mixture Pb and Cd, the cumulative risk of cancer (CRc) was calculated as the sum of the individual risks of these two metals, according to the equation:

$$\mathrm{CRc} = CR(Cd) + CR(Pb) \tag{5}$$

2.7. *Statistical analysis*

The concentrations of heavy metals (Pb, Cd, Cu and Zn) were expressed in milligram per kilogram of raw milk, and presented as the mean ± SEM for each metal. A one-way analysis of variance (ANOVA) was performed to assess the differences in the metallic profile of milk between the three regions targeted by the study. The p-value < 0.05 was considered to indicate a statistically significant difference. Significantly different groups are processed by post hot analysis with the Tukey test.

Descriptive statistics were performed by Microsoft Excel 2016 spreadsheet, while hypothesis testing and factor analysis were performed by GraphPad Prism5.

3. Results and discussion

3.1. *Concentrations of metals in goat’s milk*

The contents of heavy metals (Pb and Cd), and trace elements (Cu and Zn) in all samples and their relevant limit values of international standardsare summarized in Table 2, One-way analysis of variance shows that the concentration of lead significantly exceeds the threshold value in all regions, especially El-Milia 0.425±0.0065 *vs* 0.02 mg/kg (P=0.012). In the same way, cadmium concentration highly exceeds the safe limit value especially in Djimla 0,0359 ± 0,0025 *vs* 0.01 mg/kg (p < 0.0001). Contrariwise, copper and zinc concentrations were within the acceptable limit and did not exceed the threshold value.

Table 2. Concentrations of metals and the threshold values are expressed as mean ± SEM in mg/kg. (*) p<0.05 a significant difference heavy metals concentration *vs* threshold limit, (a) p=0.012 a significant difference El-Milia*vs*Djimla, (b) p<0.0001 a significant difference Djimla*vs* El-Milia and Texenna, (c) p=0.03 a significant difference Texenna*vs*Djimla, (d) p = 0.0003 a significant difference Texenna*vs* El-Milia and Djimla

Metals	**Regions**				
	El-Milia	**Texenna**	**Djimla**	**Threshold values**	**References**
Lead (Pb)	0.425±0.0065^{*a}	0,382 ± 0,0026*	0,338 ± 0,0223*	0.02	(FAO/WHO 2012)
Cadmium(Cd)	0,0155 ±0,0021*	0,00397 ± 0,0007*	0,0359 ± 0,0025^{*b}	0.01	(Codex Alimentarius Commission 1999)
Copper (Cu)	0,0500± 0,0024*	0,0633± 0,0044^{*c}	0,0369± 0,0019*	0.40	(Shahbazi, Ahmadi, and Fakhari2016)
Zinc (Zn)	1,425 ±0,1042*	2,712± 0,1148^{*d}	1,467± 0,1298*	3.28	(IDF 1979)

This could underscore the release of toxic metals into the ambient air of Jijel province. Lead is one of the most harmful heavy metals for children; it causes fallback in their intellectual development (Tepanosyan *et al*. 2017). The average lead concentration of goat’s milk samples in our study (0.338 – 0.425) mg/kg was significantly higher than the limit 0.02 mg/kg set by the world health organization, the 24th Codex Committee on Food Additive and Contaminants (CCFAC), and the Regulation No. 1881/2006 of EU (Codex 2001; EU 2006; FAO/WHO 2012), these results are in accordance with those of El Sayed *et al*. (2011), with Pb values close to our results (0.327 mg/kg) (El Sayed *et al*. 2011).However, in Nigeria lower values were obtained (0.168 – 1.394) mg/kg(Garba, Abdullahi, and Abdullahi 2018), on the other hand, in Egypt,and Iran higher values of lead were reported (0.044 mg/kg) and (0.141 mg/kg) respectively (Meshref *et al*. 2014; Homayonibezi *et al*. 2021). The increase of lead concentration in goat’s milk observed in the present study could be explained by the pollution of the environment, due to agricultural and industrial activities (particularly in El-Milia), and road transport. Many countries banned the fuel by the 1980s, but it was only in July 2021 that Algeria became the last country to ban it; according to a study day conducted by Sonatrach on the media coverage of unleaded petrol, the global consumption of fuels containing lead in Algeria reached 2.71 million tons in 2017(Sellami *et al*. 2020). As result, lead alkyl additives in gasoline were burned and emitted into the atmosphere and may be responsible for the high concentration of lead in certain vegetation, roadsides, soil, air, water and plants (Tunegova, Toman, and Tancin 2016).Likewise, cadmium (Cd) is one of the most toxic industrial and environmental pollutants due to its long half-life (15-30 years), bioaccumulation (WHO 2005), and multifaceted deleterious effects on human health such as: teratogenic, carcinogenic, hepatotoxic, nephrotoxic, skeletal and reproductive (WHO 2005; Matović *et al*. 2011; Garba, Abdullahi, and Abdullahi 2018). The maximum permissible level of Cd in dairy products has been 0.01 µg/g of wet weight in FAO/WHO limits (Shahbazi, Ahmadi, and Fakhari 2016). By comparing our data results with the FAO limit, it seems that El-Milia and Texenna are safe; however, the content of Cd in Djimla is three times the allowed value. However, other studies reported lower values of Cd 0.0004, 0.003, 0.004 and 0.002 mg/kg, respectively (SolaLarranaga and Navarro-Blasco 2009; Bilandžić *et al*. 2011; Pilarezyk *et al*. 2013; Khan *et al*. 2014). The sources of this high concentration of Cd in our study can be due to both natural sources (altered bedrock) and anthropogenic (road traffic, activities related to the Tabellout dam and local farming), also the use of fertilizers in Jijel could be a potential source of Cd contamination (Bounar, Boukaka, and Leghouchi 2020).On the other hand, our results are in accordance with other studies where the level in milk exceeded the permissible limit (Raghu 2015; Iqbal *et al*. 2016; Imam, Muhammad, and Zakari 2017).

3.2. Online survey results

The weight of infants and children was estimated to 15.54±0.079 and 27.27±0.162 Kg respectively. As demonstrated in the Figure 3 the daily consumption of goat's milk for infants was around 600 ml; whereas, the daily consumption for children was around 400 ml.

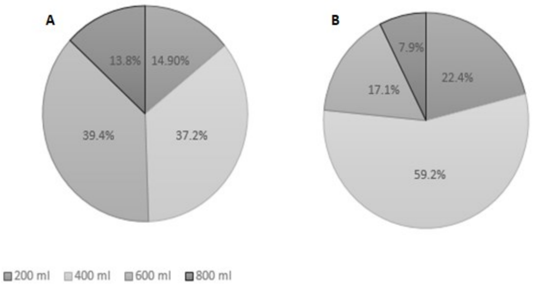


Figure 2. The daily consumption amount of goat's milk of children (A), and infants (B)

3.3. Estimated daily intake of metals and their respective human health risks

3.3.1. Estimated daily intake (EDI)

Although the estimation of metals concentration is a crucial step, but it is insufficient to assume toxicity or non-toxicity of milk, because the exposure of milk consumers to heavy metals and associated health risk is determined not only by pollutant concentrations in milk, but also by milk consumption rates. Therefore, it is necessary to carry out health risk assessments according to the daily intake of metals (EDI), which is used to assess the non-carcinogenic health risk. The mean EDI values of metals for each group *via* the consumption of milk were calculated and represented in Figure 3, (Cu and Zn) EDI values did not exceed threshold values (0.04 and 0.3) mg/kg Bw/d, respectively (US EPA 2014). However, Cd EDI values exceed the allowed limit in the region of Djimla among infants (US EPA 2014), likewise, Pb EDI values exceed threshold value both in infants, and children for all region groups (JECFA 2003). We noticed that EDI values of infant groups were significantly higher than those of children groups.

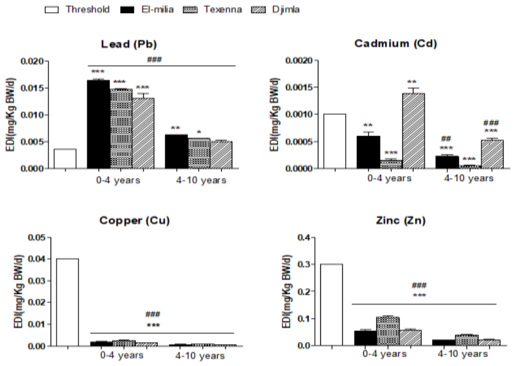


Figure 3. Estimated daily intake (EDI) of Cd, Pb, Cu and Zn in infants (0-4 years old) and children (4-10 years old), through goat's milkconsumption, in El-Milia, Texenna and Djimla. Expressed as Mean ± SEM, (***): $p<0.001$ vs threshold, (**) : $p<0.01$ vs threshold, (*) : $p<0.05$ vs threshold, (###) : $p<0.001$ vs (0-4 years old) and (##) : $p<0.01$ vs (0-4 years old)

3.3.2. Target hazard quotient (THQ)

As shown in Table 3, no THQ value over 1 was observed for both age groups in all regions ($p<0.001$). It is found that the highest non-carcinogenic risk for Pb and Cd is observed in El-Milia and Djimla respectively. However, Texenna presented the higher risk for Cu and Cd.

3.3.3. Hazard index (HI)

The Hazard index calculated as the sum of all the THQ of the individual heavy metals, and determines the non-carcinogenic risk induced by simultaneous exposure to a mixture of several metals. As shown in Figure 4,the region of Texenna presents the highest estimated value of this risk compared to other regions, but there is no obvious risk to the population as all HI values do not exceed one ($p<0.001$).

Table 3. The target hazard quotient values of heavy metals on infants and children in the three sites of study. Results are expressed as Mean ±SEM. (***) p<0.001, (**) p<0.01 Infants *vs* Children

Regions	Groups	Pb	Cd	Cu	Zn
El-Milia	**Infants**	5.74E^{-05} ± 3.41E^{-07***}	5.98E^{-07} ± 3.26E^{-08**}	7.73E^{-05} ±1.67E^{-06***}	1.65E^{-02} ±4.65E^{-04***}
	Children	2.18E^{-05} ±1.30E^{-07}	2.27E^{-07} ±1.24E^{-08}	2.94E^{-05} ±6.35E^{-07}	6.27E^{-03} ±1.77E^{-04}
Texenna	**Infants**	5.16E^{-05} ± 1.37E^{-07***}	1.53E^{-07} ± 1.26E^{-08}	9.78E^{-05} ±3.05E^{-06***}	3.14E^{-02} ±5.88E^{-04***}
	Children	1.96E-05 ±5.21E-08	5.82E-08 ±4.78E-09	3.71E-05 ±1.16E-06	1.19E-02 ±2.23E-04
Djimla	**Infants**	4.57E^{-05} ±1.16E^{-06***}	1.39E^{-06} ±4.06E^{-08***}	5.70E^{-05} ±1.20E^{-06***}	1.70E^{-02} ± 5.35E^{-04***}
	Children	1.74E^{-05} ± 4.41E^{-07}	5.27E-07 ±1.54E-08	2.17E-05 ±4.56E-07	6.46E-03 ±2.03E-04

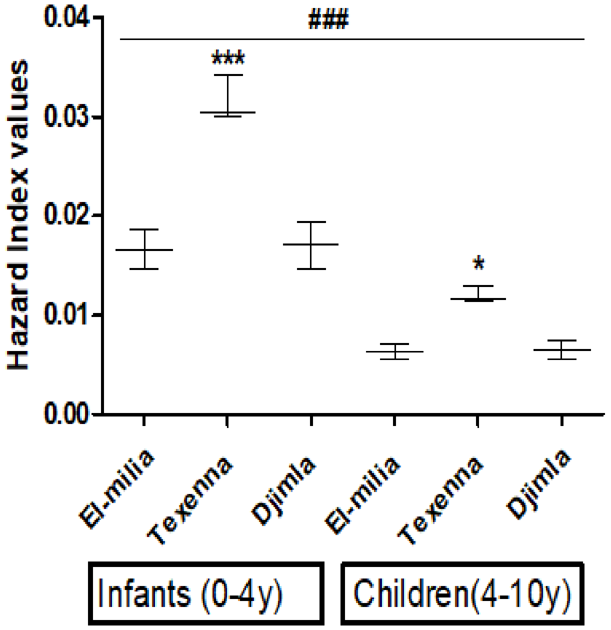


Figure 4. Hazard index (HI) values for metals in infants (0-4 years old) and children (4-10 years old); through goat's milk consumption, in El-Milia, Texenna and Djimla. Expressed as Mean ± SEM, (***): p<0.001 vs Texenna, (*) p<0.05 vs Texenna, (###): p<0.001 vs (0-4 years)

Despite the high values of EDI for heavy metals, Table 3 and Figure 5 showed that all THQ and HI (sum of individual metal THQs) values did not exceed the threshold value set at one, and have an acceptable level of non-carcinogenic adverse health risk, which indicate that the consumption of goat's milk in these regions do not represent a significant health risk (Zhuang *et al*. 2009; US EPA 1986).

3.3.4. *Cancer risk (CR)*

The carcinogenic risk was calculated based on Pb and Cd. As shown in Figure 5, we notice an accurate risk in infant group compared to children, especially in the region of El-Mila for lead and the region of Djimla for cadmium. The carcinogenic risk of Pb was achieved to be 1.25E-04 for infants and 4.76E-05 for children, based on this, their chance of cancer is 1 per 10.000 and 4 per 100.000, respectively. As can be observed, the estimated carcinogenic risk is in the accepted range of E−04 to E−06. According to the grades based on the Delphi method, carcinogenic risk of Pb belongs to Grade III (Low-medium risk) for children and Grade V (Medium-high risk) for infants (Dashtizadeh *et al*. 2019). On the other hand, the carcinogenic risk of Cd was estimated to 1E-02 for infants and 4E-03 for children. Which implies that 1 infant per 100, and 4 children per 1000 are at risk for cancerous diseases. Those values exceed highly the threshold; based on the Delphi method the carcinogenic risk of Pb is associated to Grad VI (high risk) for children and Grad VII (extremely high risk) for infants (Dashtizadeh *et al*. 2019).

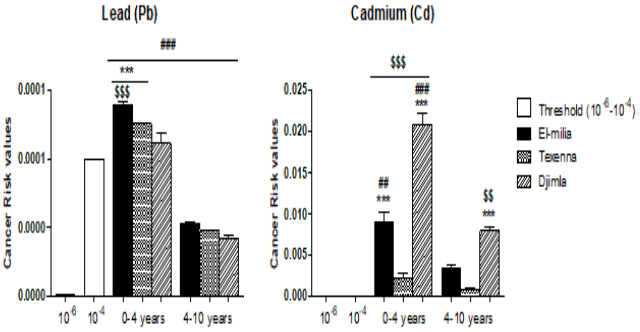


Figure 5. Cancer risk values of heavy metals for infants (0-4 years old), and children (4-10 years old) from goat's milk consumption. Results are expressed as Mean ± SEM. (*) vs threshold values (10-6 – 10-4), ($) vs other regions, (#) vs (4-10 years). (***), ($$$) and (###) p<0.001, ($$) and (##) p< 0.01

3.3.5. *Cumulative cancer risk (CRC)*

To assess the reasonable additive carcinogenic risk of a mixture of tow heavy metals Pb and Cd, cumulative cancer risk was calculated as shown in Figure 6. The values of cumulative cancer risk are significantly above the threshold limit in both El-Milia and Djimla (p<0.001), and the values of infants group greatly exceed those of children group.

In our study, we notice that Lead and cadmium cancer risk values were significantly higher than the threshold values set at 1× 10^{-6} to 1× 10^{-4}(US EPA 2004). In addition, the values of the cumulative cancer risk of both metals exceed the allowed limit value (Mohammadi *et al*. 2019) especially in the infants group.

4. Conclusion

This is the first study to assess the health risk related to goat's milk in Algeria targeting infants and children, two sensitive age groups of the population. The results showed that the average concentrations of heavy metals in goat's milk varied significantly and decreased in the order Zn > Pb > Cu > Cd. Compared with the recommended maximum allowable limits of WHO, USEPA, CODEX and IDF the concentration of trace elements Zn and Cu was lower than the threshold; contrariwise, the concentration of heavy metal Pb was twenty time the allowed limit. In addition, the carcinogenic risk of Cd and Pb varied from low medium to extremely high risk. The results obtained in this study are alarming and reflect a significant level of pollution in Jijel province. Preventive and remedial measures and awareness rising are needed. To ensure the safety of children and infants, implementation of targeted investigations and monitoring of heavy metal contents are required, data showed the cancer risk associated with goat's milk consumption. Therefore, this study will be quite helpful for both government officials in reducing heavy metals contamination, and inhabitants in taking protective measures especially regarding the quantity and frequency of consumption.

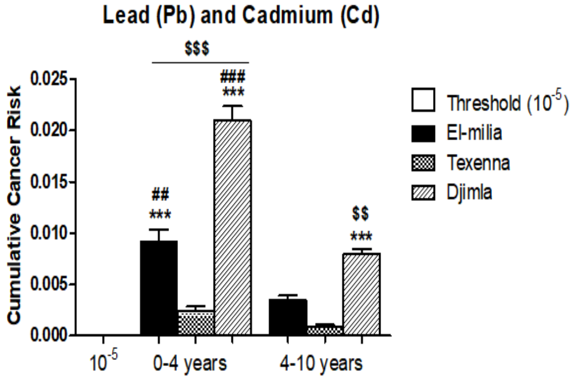


Figure 6. Cumulative Cancer risk values of heavy metals for infants (0-4 years old), and children (4-10 years old) from goat's milk consumption. Results are expressed as Mean ± SEM. (*) vs threshold values (10-5), ($) vs other regions, (#) vs (4-10 years). (***), ($$$) and (###) p<0.001, ($$) and (##) p< 0.01

Declaration of interests

The authors do not report conflict of interests regarding the publication of this paper.

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