Interaction Between Zinc, Cadmium, and Lead in Scalp Hair Samples of Pakistani and Irish Smokers Rheumatoid Arthritis Subjects in Relation to Controls

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Abstract

The incidence of rheumatoid arthritis (RA) has been associated with cigarette smoking. The aim of our study was to assess the trace essential and toxic metals, cadmium (Cd), lead (Pb), and zinc (Zn), in scalp hair samples of 32 Irish and 46 Pakistani smokers and non-smokers RA male patients with age range 42-56 years. For comparison purpose, the scalp hair samples of 27 Irish and 55 Pakistani non-RA male subjects of the same age group were collected. The concentrations of trace and toxic elements were measured by inductive coupled plasma atomic emission spectrophotometer and atomic absorption spectrophotometer prior to microwave-assisted acid digestion. The validity and accuracy of the methodology was checked using certified reference materials and using conventional wet acid digestion method on the same certified reference materials (CRMs). The recovery of all studied elements was found to be in the range of 97.5-99.7% of certified reference values of CRMs. The results of this study showed that the mean values of Cd and Pb were significantly higher in scalp hair samples of both smoker and non-smoker RA patients than in referents ($P<0.001$), whereas the concentration of Zn was lower in the scalp hair samples of smokers and non-smokers rheumatoid arthritis patients. The deficiency of Zn and the high exposure of Cd and Pb as a result of cigarette smoking may be synergistic risk factors associated with rheumatoid arthritis.

Keywords: Scalp hair • Zinc • Toxic elements • Pakistani rheumatoid arthritis patients • fish rheumatoid arthritis patients • Atomic absorption spectrophotometer • Inductively coupled plasma atomic emission spectrophotometer.

Introduction

Rheumatoid arthritis (RA), a systemic skeletal disease characterized by a low bone mass, is a major public health problem in elderly persons resulting in high incidence of fragility fractures, especially hip and vertebral fracture. In these people, the high incidence of osteoporotic fractures leads to considerable mortality, morbidity, reduced mobility, and decreased quality of life [1].

A variety of trace elements are found in bones including iron, copper (Cu), zinc (Zn), manganese (Mn), fluoride, strontium, and boron [2]. Although they are present in only minute amounts, trace elements influence normal metabolic processes through interaction

with, or incorporation into, proteins, particularly enzymes [3]. The role of Zn in healthy aging is particularly important as it prevents neoplastic cell growth and is involved in mitotic cell division, and DNA and RNA repair. Chronic diseases associated with alterations in Zn status are bronchial asthma and rheumatoid arthritis [4]. Zinc plays an important role in nucleic acid synthesis, transcription, and translation as a cofactor for some of the enzymes involved and may therefore participate in a broad range of metabolic activities in bone. Alkaline phosphate is required for bone calcification, and collagenase is required for bone resorption and remodeling [5]. It has been demonstrated that Zn deficiency reduces the synthesis and activity of alkaline phosphate in rats [6], and the activity of collagenase in chicks [7]. Zinc deficiency has also been reported to interfere with glycosami-noglycan metabolism of membranous bone and osteoblastic activity in experimental animals [8]. In addition, Zn has been shown to stimulate bone formation and to inhibit osteoclastic activity in vitro [9].

Cigarette design has evolved considerably over the last few decades with the incorporation of new tobacco process-es, papers, filters, and several ingredients (flavor, humectants, and casing materials), which either alone or in combination have the potential to modify the quantity and/ or the quality of the smoke yielded [10]. The tobacco plant absorbs heavy metals most probably from the soil, fertilizers, or pesticides [11]. Other environmental factors that may influence the uptake of toxic elements by tobacco plants include the pH of soil, and contaminated irrigated water and sewage sludge used as fertilizers. Tobacco smok-ing delivers 87 organic carcinogens to the lungs, in addition to toxic elements [12], which may partition into the smoke phase on combustion [12]. Some of these [cadmium (Cd), nickel (Ni), and lead (Pb)] readily pass into the bloodstream and may accumulate in specific organs, such as the kidney and liver [13]. There are a few studies that have reported on the large variations of toxic elements in the compositions of commercial tobacco products, which have tried to link smoking-related diseases with toxic elements derived from tobacco combustion [14]. The intake of trace and toxic elements may promote rheumatoid arthritis disorders by increasing oxidative stress (for example, by catalyzing the production of reactive oxygen species or inhibiting their degradation) due to the deficiency of antioxidant elements (Zn, Cu, and Mn). The deficiency of essential nutrients, lack of homeostatic control, or an excess intake of some toxic elements causes chronic physiological disorders, such as hypertension, cardiovascular disease, and rheumatoid arthritis [15] .

Determinations of trace elements in human tissues and fluids were used to obtain information on nutritional status for diagnosis of diseases, indication of systemic intoxication, and to obtain information on environmental exposure. In the majority of cases, whole blood, serum, plasma, and urine were analyzed [16]. Hair can provide a more permanent record of trace and toxic elements associated with normal and abnormal metabolism as well as toxic elements assimilated from the environment. In addition, hair is easily collected, conveniently stored, and easily treated. Therefore, the analysis of human hair has become an important way to understand any quantitative change in certain elements in-side the body [17].

One of the most widely used analytical techniques for the determination of different elements in biological and environ-mental materials are atomic absorption spectrometry and inductively coupled plasma atomic emission spectrometry due to its advantages over other

analytical techniques [18]. The mineralization method is most frequently applied for the analysis of biological samples or wet digestion with concentrated acids using either conventional heating or microwave energy for oxidizing the organic matter [16].

The main advantage of microwave-assisted samples pretreatment is its requirement of small amount of mineral acids and a reduction in the production of nitrous vapors. Microwave systems keep blank levels low because only small volumes of reagents are required and allow more samples to be processed per hour than conventional digestion systems [19].

The aim and objective of our present study was to assess the concentrations of Cd, Pb, and Zn in the scalp hair samples of Pakistani and Irish male smoker rheumatoid arthritis patients. For a comparative study, 27 Irish and 55 Pakistani non-rheumatoid arthritis individuals (smoker and non-smokers) of the same age group (range 42-56 years), socioeconomic status, localities, and dietary habits were selected as referents. The metal levels were also examined for a possible mutual correlation and were compared with reported metal levels for donors from other regions of the world. It was anticipated that the comparative metal levels in hair of Pakistani and Irish referent segments would bring out distinct sources responsible for the distribution of selected metals to help assess the nutritional status and environmental exposure of the two categories of subjects compared with those from other nations where different environmental and living conditions prevail.

Materials and Methods

Apparatus

The analysis of elements in Ireland was carried out by means of a Varian Liberty 220 (Mulgrave, Victoria, Australia) Inductively Coupled Plasma Atomic Emission Spectrometer using the axially viewed plasma. The Liberty Series II ICP features a 40-MHz free running RF generator and a 0.75-m Czerny—Turner monochromator with 1,800 grooves/mm holographic grating used in up to four orders. The resolution of the spectrometer is typically 0.018 nm in first order, 0.009 nm in second order, 0.007 nm in third order, and 0.006 nm in fourth order. The instrument was controlled with a Digital Equipment Corporation (DEC) Venturis computer with an Intel Pentium processor and Varian Plasma 96 software running under Microsoft Windows 95 operating system. The instru-mental conditions are shown in Tables 1 and 2. A Hinari Life style (Elstree, Hertfordshire, UK) domestic microwave oven (maximum heating power of 800 W) was used for digestion of the scalp hair samples.

The analysis of elements in Pakistan was carried out by means of a double beam Perkin-Elmer atomic absorption spectrometer model 700 (Norwalk, CT, USA) equipped with a flame burner and graphite furnace HGA-400, a pyrocoated graphite tube with an integrated platform, and an autosampler AS-800 (Perkin Elmer).

Table 1 Measurement conditions for inductive coupled plasma atomic emission spectroscopy Liberty 220 ICP-AES

Parameters	Cd	Pb	Zn
Wavelength (nm)	226.502	220.553	213.8
Height (mm)	3	3	5
Windows (nm) (above the coil)	0.027	0.027	0.027
Scan (nm)	0.040	0.040	0.040
Integration (s)	3	3	3
Replicates	3	3	3
Sample uptake (s)	30	30	30
PMT (V)	650	650	650
Power (kW)	1.10	1.10	1.10
Plasma flow (l/min)	15.0	15.0	15.0
Auxiliary flow (l/min)	1.50	1.50	1.50
Pump speed (rpm)	15	15	15
Background mode	Dynamic	Dynamic	Dynamic
Max curve order	1	1	1
C.C. limit	0.995	0.995	0.995

Table 2 Liberty 220 common parameters

Nebulizer type	V-groove
Nebulizer pressure	150 kPa
Stabilization time	10 s
Sample delay time	30 s
Rinse time	10 s
Pump–tube	Orange–orange (inlet)
	Blue–blue (outlet)
Snout purge	Off
Fast pump	On

The instrumental parameters are shown in Table 3. Zn was measured under optimized operating conditions using FAAS with an air—acetylene flame, whereas Cd and Pb were determined using ETAAS. Signals were measured as absorbance peaks in the flame absorption mode, whereas integrated absorbance values (peak area) were determined in the graphite furnace. A Pel (PMO23, Osaka, Japan) domestic microwave oven (maxi-mum heating power of 900 W) was used for digestion of the scalp hair samples. Acid-washed PTFE (polytetrafluoro-ethylene) vessels (Kartell, Milan, Italy) and flasks were used for preparing and storing solutions.

Table 3 Measurement conditions for elements using flame and electrothermal atomic absorption spectrometry

Parameters	Cd	Pb	Zn
Lamp current (MA)	6.0	8.0	7.5
Wavelength (nm)	228.8	283.3	213.8
Slit width (nm)	0.7	0.7	0.7
Dry temperature (°C)/ramp/hold (s)	140/15/5	140/15/5	Burner height=7.5 mm
Ashing temperature (°C)/ramp/hold (s)	850/10/20	700/10/20	Oxidant (air)=17.0 $l min^{-1}$
Atomization temperature (°C)/ramp/hold (s)	1,650/0/5.0	1,800/0/5.0	Fuel (acetylene)=2.0 $l min^{-1}$
Cleaning temperature (°C)/ramp/hold (s)	2,600/1/3	2,600/1/3	
Chemical modifier	$Mg(NO_3)_2$+Pd $(NO_3)_2$	$Mg(NO_3)_2$	

Sample volume=10 µl, cuvette=cup, carrier gas=200 ml/min. Background correction (D_2 lamp) used for all elements

Reagents and Glasswares

Ultrapure water obtained from ELGA Lab Water system (Bucks, UK) was used throughout the work. Concentrated nitric acid (65%) and hydrogen peroxide (30%) were obtained from Merck (Darmstadt, Germany) and checked for possible trace metal contamination. Working standard solutions of Cd, Pb, and Zn were prepared immediately prior to their use, by stepwise dilution of certified standard solutions (1,000 ppm) Fluka Kamica (Buchs, Switzerland), with 0.5 M HNO_3. All solutions were stored in polyethylene bottles at 4°C.

For the accuracy of methodology, the certified reference materials (CRMs), human hair NCSZN 81002b (Beijing, China), and certified reference materials (CRMs) of human hair BCR 397 (Brussels, Belgium) were used (Table 4). All glassware and plastic materials used were previously soaked for 24 h in 5 M nitric acid, washed with distilled water and finally rinsed with ultrapure water, dried, and stored in class 100 laminar flow hoods.

Table 4 Determination of trace elements in certified sample of human hair (CRM) by conventional (CDM) and microwave digestion method (MWD) (n=10)

Elements	Conventional digestion method CDM	Microwave digestion method MWD	T value[a]	% recovery[b]	Certified values
Certified human hair reference material (NCS ZC 81002b) (µg/g)					
Cd	0.0716±0.003 (4.19)	0.0714±0.006 (8.40)	0.305	99.7	0.072±0.010
Pb	3.80±0.37 (9.74)	3.72±0.35 (9.41)	0.081	98.05	3.83±0.18
Zn	191±7.28 (3.81)	187±9.53 (5.09)	0.648	97.9	191±16
Certified human hair material CRM 397 (µg/g)					
Cd	0.53±0.025 (4.72)	0.524±0.024 (4.58)	0.2256	98.87	0.52±0.024
Pb	33.29±1.21 (3.63)	32.56±1.18 (3.62)	0.096	97.8	33±1.2
Zn	197±12.8 (6.2)	194±11.3 (5.7)	0.0345	98.6	199±5

[a] Paired t test between CDM and MWD, df=9, T (critical) at 95% CI=2.262, P=0.05. Means in percentage. Values in parentheses are RSD

[b] % recovery was calculated according to the following: $\frac{[MDM]}{[CDM]} \times 100$

Sample Collection and Pretreatment

This study was completed in two phases. Phase 1 was completed during January 2005 to June 2006 and phase 2 during July 2010 to October 2010. The sampling locations were Hyderabad, Pakistan and Dublin, Ireland. The donor ages of both countries ranged between 42 and 56 years from each location. Before the start of this study, all referents and rheumatoid arthritis patients of both countries were in-formed through a consent form by the administration about the aim of study, and all agreed to participate and signed the form. A questionnaire was also administered to them to collect details regarding physical data, ethnic origin, health, duration and frequency of smoking, dietary habits, age, and consent. The RA patients were grouped according to their habits—non-smokers (NSRA) and smokers (SRA). While control groups were also divided into two groups, referent non-smokers (RNS) and smokers (RS) are shown in Table 5.

Table 5 The number of subjects as control and rheumatoid arthritis patients of age group 42–56 years

Countries	Referents		Rheumatoid arthritis	
	Smokers	Non-smokers	Smokers	Non-smokers
Pakistan	47	52	39	34
Ireland	22	19	23	20

All the patients had active disease defined by the following criteria: erythrocyte sedimentation rate (ESR) of at least 30 mm/h, six or more tender joints, three or more swollen joints, and morning stiffness of at least 30-min duration. Thirty Irish and 37 Pakistani patients had IgM-positive rheumatoid factor. None of the patients had been treated with steroids, immunosuppressives, or penicillamine within the 3 months before the study. They all were receiving non-steroidal anti-inflammatory drugs (NSAIDs) (diclofenac so-dium, 100 mg/day).

Physical examinations were carried out in a basic health unit of Hyderabad, Pakistan and Dublin, Ireland to measure participant's weight, height, blood pressure, and biochemical data.

For all patients and referents, anthropometric parameters including weight, height, and waist circumference were measured using the standard protocols. There were no statistically significant differences between both groups of patients and referents with regard to height and weight. The study protocol was approved by the local ethics committee of higher education commission, Islamabad, Pakistan. The criteria of healthy subjects included no history of symptoms of any related disease to arthritis documented in their medical notes. All control subjects underwent a routine medical examination. The dietary habits of Pakistani

people (elder age group) depend upon animals (chicken, mutton, beef) and plants (vegetables, beans and grain) while the Irish people used chicken, vegetables, and beans.

Collection of Scalp Hair Samples

The hair samples (-1.0 g each) were taken from the nape of the neck. Hair samples were put into separate plastic envelopes for each participant on which the identification (ID) number of the participant was indicated. The plastic envelope of each subject was tightly sealed and attached to a questionnaire.

Before analysis, each individual hair sample was cut into approximately 0.5-cm-long pieces and mixed to allow a representative subsampling of the hair specimen. After cutting, each sample was washed with diluted Triton X-100; samples were then rinsed with distilled water and then with deionized water. The samples were rinsed three times with acetone [19]. All samples were then dried in an oven at 75±5°C for 2 h. Dried samples were stored separately in polyethylene bags.

Microwave-Assisted Acid Digestion (MWD)

Duplicate samples of scalp hair (200 mg) of each RA patients and control individuals were directly placed into Teflon PFA flasks. Two milliliters of a freshly prepared mixture of concentrated HNO3—H202 (2:1, v/v) was added to each flask and kept for 10 min at room temperature then placed in a covered PTFE container. This was then heated following a one-stage digestion program at 80% of total power (800 W). Complete digestion of scalp hair samples required 5-8 min. After the digestion, the flasks were left to cool and the resulting solution was evaporated to semidried mass to remove excess acid. About 5 ml of 0.1 M nitric acid was added to the residue and filtered through a Whatman no. 42 filter paper and diluted with deionized water up to 10.0 ml in volumetric flasks.

Blank extractions were carried through the complete procedure. Blanks and standard solutions were prepared in a similar acid matrix. The validity and efficiency of the MWD method was checked with certified values of human hair NCSZC 81002b and certified human hair CRM 397 and with those obtained from conventional wet acid digestion method [17].

Analytical Figures of Merit

Statistical analyses were performed using computer program Excel XL State (Microsoft Corp., Redmond, WA, USA) and Minitab 13.2 (Minitab Inc., State College, PA, USA). Calibration was performed with a series of Cd, Pb, and Zn standards. Sensitivity (m) was the slope value obtained by least-square regression analysis of calibration curves based on peak area measurements. The linear range of the calibration curve ranged from the quantification limit up to 100 μg/1 was used for all trace and toxic elements.

Results

The concentrations of Zn in the scalp hair samples of Irish male referent non-smokers (RNS) and referent smokers (RS) were significantly higher at 95% confidence interval (CI) (196-207) and (175-182) µg/g, respectively, than those values observed for rheumatoid arthritis non-smokers (RANS) and rheumatoid arthritis smokers patients (RAS) (CI=131-140 and CI=120-124 µg/g, respectively, with P<0.001). In Pakistani subjects, Zn levels in the scalp hair samples of RANS and RAS (CI=130-146 and CI=106— 118 µg/g, respectively) were found to be lower than those in RNS and RS (CI=239-258 and CI=216-233 [µg /g, respectively, P<0.001) (Table 6). An elevated level of Cd content was observed in the scalp hair of Irish RANS and RAS. The ranges of Cd in the scalp hair samples of RNS and RS were CI 0.64-0.73 and CI 0.87-1.00 µg/g, respectively, whereas those in RANS and RAS were CI 1.98-2.32 µg /g and CI 3.06-3.68 µg/g, respectively (P <0.001). The same trend was observed in Pakistani subjects (Table 6). The Pb concentration in the scalp hair samples of Irish RAS was found in the range of CI 3.15-3.56 µg /g, whereas in the RANS, the Pb level was in the range of CI 4.38-4.71 µg (Table 6). Similarly, a higher level of Pb was observed in RAS (CI 5.22-6.08 µg/g) than in RS (P<0.001). The same trend was observed in Pakistani subjects (Table 6).

Table 6 Concentrations of trace and toxic metals in scalp hair samples of Irish and Pakistani male smokers and non-smokers referent and rheumatoid arthritis (RA) subjects (µg/g)

Elements	Non-smokers			Smokers		
	Referents	Rheumatoid arthritis	*P* value	Referents	Rheumatoid arthritis	*P* value
Irish subjects						
Cadmium	0.68±0.07	2.13±0.37	0.001	0.94±0.12	3.35±0.61	0.001
Lead	3.36±0.41	4.55±0.34	0.009	3.75±0.28	5.62±0.87	0.003
Zinc	203±7.53	135±9.42	0.001	178±5.28	122±4.63	0.001
Pakistani subjects						
Cadmium	1.55±0.42	4.59±0.51	0.001	2.38±0.29	5.86±0.63	0.001
Lead	5.79±0.74	9.34±0.72	0.003	6.82±0.65	11.6±1.05	0.002
Zinc	250±19.3	138±16.5	0.001	225±17.1	112±9.67	0.001

It was observed that the levels of all three elements were significantly higher in scalp hair samples of Pakistani population as compared to Irish subjects of same age group (P=0.01-0.001).

Discussion

The present study brings out data related to the metal distribution in hair with related to arthritis disease and smoking habits in two different countries. Table 6 presents the concentration of essential trace and toxic elements (Zn, Cd, and Pb) in scalp hair samples of Irish and Pakistani RA and referent donors. Rheumatoid arthritis is an autoimmune disease, a disorder in which the body attacks its own healthy cells and tissues. The result shows that the level of Zn in scalp hair samples of smokers and non-smokers RA patients was low-er than

referents (Table 6). Zn deficiency is associated with delayed bone growth, but few studies have been done to elucidate its potential role in bone turnover regulation.

The skeleton is a major bone store of Zn, and in humans approximately 30% of total body Zn is found in bone, probably bound to hydroxyapatite [20]. It has been proposed that since urinary Zn excretion is almost uninfluenced by variation in diet, urinary Zn excretion may be used as a marker of changes in bone metabolism [21]. Zinc supplementation was reported to decrease periarticular osteoporosis in RA patients [22]. Defects in skeletal development have been reported in man due to Zn deficiency and also due to the acrodermatitis enteropathica, an inherited congenital disorder of Zn absorption [23]. It has been reported that forearm bone mineral content is correlated with Zn intake in pre-menopausal women, suggesting a possible role of Zn in the maintenance of bone mass [24].

It was reported in literature that amino acid complex of Zn ((3-alanyl-L-histidinato zinc) has more potent effect than Zn sulfate on bone metabolism in experimental animals, and this Zn chelate has been pro-posed as a possible treatment for osteoporosis [25, 26]. The mean levels of Pb and Cd in the scalp hair samples of non-smoker referents of both countries were found to be lower than those recorded in smokers and non-smokers RA patients (Table 6). Pb has an exceptionally long half-life in bone (more than 20 years) compared to other elements (Cu, Fe, Zn) [27]; it is not the only metal which can deposit in bone from respiratory exposure. Other metals which can accumulate in bone as a result of respiratory exposure include arsenic, Cd, cobalt, and antimony [27]. Pb can in-crease osteoporosis and it may disrupt the normal formation of Ca hydroxyapatite, thus critically weakening the bone [28].

Tandon et al. [4] in his study noted that the effects of Pb on humans include anemia, abdominal colic, and gum wastage, while Cd alters calcium (Ca) and phosphorus metabolism, thus contributing to arthritis, osteoporosis, and neuromuscular diseases. Toxic elements (Cd, Pb, and Ni) may deplete glutathione and protein-bound sulfhydryl groups, resulting in the production of reactive oxygen species, such as superoxide anion, hydrogen peroxide, and hydroxyl radical [29]. Tobacco leaves naturally accumulate and concentrate relatively high levels of Cu (7.1-68.8), Cd (5.73-7.96), Pb (0.04-14.4), and Ni (2.21-3.45) as compared to medicinal and edible plants Cu (0.686-0.953), Cd (0.072-0.12), Pb (0.374-0.615), and Ni (0.31-0.523) [30, 31]; therefore, smoking of tobacco is an important source of these metals exposure for smokers [32]. The total amount of carcinogens in cigarette smoke ranges from 1 to 3 µg per cigarette [13]. The country of origin and type of the product play major roles in determining the chemical composition of cigarette tobacco [32]. It was investigated that one pack of cigarettes deposits 2-4 µg Cd, 1-2 µg Pb, and 0.96-1.34 µg Ni into the lungs of a smoker, whereas some of the smoke passes into the air to be inhaled by smokers and non-smokers alike [33, 34]. It was also consistent with another study that smokers generally exhibit significantly higher Cd, Ni, and Pb body burdens than non-smokers [32].

The results suggested that although these toxic elements (Cd, Ni, Pb) pose a hazard to essential trace metal homeostasis of various organs, co-exposure can pose a major threat, while consumption of ethanol may absorb much more Cd and Pb than their unexposed counterparts [35]. In the past few years, increasing consideration has been given to

interactions occurring in the organism between toxic metals and bioelements essential for life. These inter-actions are complex and involve biometals such as Zn, Cu, Fe, Se, Ca, and toxic elements, including Cd [36]. The basis of Cd toxicity is its negative influence on enzymatic systems of cells, resulting from substitution of other essential metal ions (mainly Zn, Cu, and Ca) in metalloenzymes and its very strong affinity to biological structures containing —SH groups, such as proteins, enzymes, and nucleic acids [37].

The relevance of Cd and Pb—Zn interactions should be considered in the light of the general population exposure to toxic metals [38] and common deficiency of Zn in the world, mainly due to nutritional factors [39]. This is the first study with comprehensive data on toxic and essential elements in the scalp hair samples of male rheumatoid arthritis and referent smokers and non-smokers subjects of two countries (Pakistan and Ireland). The con-centrations of essential trace and toxic elements in scalp hair samples of the Irish referent subjects were close to those reported from other European [36-42], American [43-45], and Australian [46] countries (Table 7). The elemental con-centrations of Cd and Pb in Pakistani referents were almost higher than in European countries, which are in agreement with the studies carried out in Asian [2, 47-59] and African countries [60-64] (Table 7).

Humans are also affected by Cd through smoking and consumption of foods and beverages. Rice is the main source of Cd in rice-eating countries. Human Pb exposure is mainly through air and food. In most developed countries, the fuel content of Pb has been controlled but still remains an issue of immediate consideration in developing countries, including Pakistan. Other sources of Pb exposure include Pb-based paints, Pb pipelines in water supply systems, and ceramics. The Pb-based products, including paints and food containers, are not completely banned in Pakistan [65].

Conclusion

It can be concluded that impaired trace element metabolism of the essential trace and toxic elements may have a role in the pathogenesis and progression of arthritis. The really overlooked issue here is the dramatic impact of the toxic metals on human health.

Commonly, when the body burden of these metals is in excess, the symptoms manifest in the form of muscle and joint complaints. This is because heavy metals interfere with the normal biochemical processes involving Zn and other nutrients in the cells of human body. When these essential minerals in the body are disrupted by heavy metals, musculoskeletal symptoms such as muscle and joint pain commonly occur. These toxic metals impair the immune system, cause abnormal cell responses, and may aggravate our sign and symptom of arthritis disorders. It is necessary to add these minerals via food supplements.

The results of this study provided guidance to clinicians and other professional investigating deficiency of essential trace metals and excessive level of toxic metals in biological samples of healthy and arthritis patients.

Table 7 Comparison of different elemental contents (μg/g) in scalp hair of people from various parts of the world

Authors	Elements	Age (years)	*N*	*x*±*s* (μg/g)
Europe				
Sweden				
Rodushkin and Axelsson [40]	Pb	1–75	114	0.22–7.26
	Cd	1–75	114	0.010–0.356
	Zn	1–75	114	68–198
Poland				
Nowak and Chmielnicka [41]	Pb	25–39	624	4.8–5.7
	Cd	25–39	624	0.56±2.3
	Zn	25–39	624	132.7±135.7
Trojanowski et al. [42]	Pb	26–50	109	3.71±0.29
	Cd		109	0.401±0.035
	Pb	51–75	121	3.88±0.35
	Cd		121	0.260±0.022
Italy				
Sturaro et al. [43]	Zn	21–60	50	171–314
	Pb	21–60	50	6.5–8.7
France				
Goulle et al. [44]	Zn	40–60	45	129–209
	Pb	40–60	45	0.13–4.57
Netherlands				
Iyengar and Wolttlez [45]	Zn	21–60	50	176±38
South America				
Nagra et al. [46]	Cd	22–59	50	31.6±38
North America				
Saiki et al. [47]	Zn	50–70	50	45–162
	Zn	71–87	50	30–202
Australia				
McKenzie [48]	Zn	16–56	118	189±24
Asia				
Pakistan				
Pasha et al. [49]	Pb	15–94	86	14.62±8.01 (0.577–31.8)
	Cd	15–94	86	2.13±1.74 (0.196–9.17)
	Zn	15–94	86	154.2±117.1 (12.4–729.2)
Pasha et al. [50]	Pb	37–65	37	15.50±8.11
	Cd	37–65	37	1.675±1.13
	Zn	37–65	37	140.7±79.5
Shah et al. [51]				
(Pak)	Pb	3–54	62	15.97±5.56
(Lib)		3–54	62	24.95±8.69
(Pak)	Cd	3–54	62	0.38±0.186
(Lib)		3–54	62	0.53±0.26
(Pak)	Zn	3–54	62	226±53.7
(Lib)		3–54	62	190±34.0
Khalique et al. [52]	Cd	41–50	18	0.300±0.140
	Zn	41–50	18	270±46.5
India				
Vishwanathan et al. [53]	Pb	36±1.23	25	24.8±5.92
	Cd	36±1.23	25	5.12±3.41
	Zn	36±1.23	25	265.2±17.3
Sukumar and Subramanian [54]	Pb	31–45	17	8.9±1.9
		46–60	11	4.5±2.8
	Cd	31–45	17	1.5±0.3
		46–60	11	1.9±0.5
	Zn	31–45	17	87.0±1.9
		46–60	11	112.8±25.3
Mehra and Juneja [55]	Pb	1–30	50	7.60±6.44
	Cd	1–30	50	0.32±0.21
	Zn	1–30	50	182.4±45.2
Rao et al. [56]	Cd	17–60	20	0.12–0.61
	Zn	17–60	20	45.44–123.5
	Pb	17–60	20	0.75–4.1
Turkey				
Sasmaz et al. [57]	Pb	–	26	3.06±1.42
	Cd	–	26	0.67±0.33
Ulvi et al. [58]	Zn	47.76±13.11	29	176.96
Hong Kong				
Man and Zheng [59]	Pb	20–50	30	12.04±7.0
	Zn	20–50	30	184.85±60.89
Man et al. [60]	Zn	30–69	95	355–503
Africa				
Nigeria				
Nnorom et al. [61]	Pb	1–30	46	63.6
	Cd	1–30	46	1.0
	Zn	1–30	46	128.6
Syria				
Khuder et al. [62]	Pb	21–59	281	10.7±8.9
	Zn	21–59	281	260±113
Sudan				
Eltayeb and Van-Grieken [63]	Zn	30–50	35	89–170
	Pb	30–50	35	3–17
Egypt				
Mortada et al. [64]	Pb	28–40	93	1.8–9.7
	Cd	28–40	93	0.08–0.82

This study also provides some support for the hypothesis that dietary intake or inhalation of toxic elements (Cd and Pb), most probably through smoking cigarette, may increase the risk of rheumatoid arthritis and related disorders, which indicates that the causal link may be stronger among cigarette smokers. We propose that essential and toxic elemental

measurements may be performed on patients reaching in the emergency department to test whether its concentration may serve not only as markers of rheumatoid arthritis and its remedies but also as predictors of adverse outcomes.

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