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REVIEW ARTICLE

A Review on Arsenic Toxicity Induced Keratosis and its Prevalence

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ABSTRACT

Background: Rapidly increasing discharge of arsenic (As) is a major health concern due to its cancer-causing effects. Excessive exposure of As causes the cancer of many organs including skin, liver, kidney, lungs. Precancerous skin condition due to the exposure of As is called As-keratosis, which is marked by hyperpigmentation and plaques and lump formation. The article focal point is the skin cancer which is the most concerning one.
Objective: The purpose of this review article is to synthesize an up-to-date knowledge of As induced keratosis including its prevalence, diagnosis, treatment.
Methodology: This review was conducted by using major database including Google Scholar and PubMed.
Review findings: Toxicity due to As is a global health related issue which affect people globally. As-keratosis is inveterate clinical or subclinical deadly harmful because of the presence of As metalloid in the body at higher level. A cross-sectional analysis was held to investigate the exposure of As is due to the number of reasons which includes contaminated water and sanitary landfills, etc. Diagnosis is based on the laboratory examination and histopathological examination. It is also diagnosed by the measuring the amount of As in blood, urine and hairs sample. Pathophysiology of the keratosis describe that the trivalent arsenide and methylation of As cause hyperpigmentation.
Conclusion: For the prevention of As keratosis make sure the usage of As treatment plant for the availability of As free water for drinking purposes. Options for the treatment purpose include the use of the oral and topical medications and surgical excision. For the management of As keratosis nanotechnology use to remove As from ground water.

INTRODUCTION

Contamination and the filthy pollutants caused due to Arsenic (As), which is a heavy metal is a universal considerable challenge, it becomes a major issue, a health hazard to humans who are being exposed to this heavy metal. As is known for its cancer-causing properties, called as King of poisons, which shows the acuteness of its toxicity (Li *et al*. 2025). As-keratosis is a precancerous causing skin cancer, pigmentation changes, and neurological changes by long-term chronic exposure to heavy metal. As is carcinogenic metalloid which is present in groundwater, soil, rock and air (Tao and Wang 2024). Due to high illiteracy rate and lack of knowledge among people living in such areas and being exposed through As poisoning and peak level of extremities of detrimental health related issues due to As by drinking such polluted water is ambiguous and inadequately evidenced, which carries a high risk of proceeding into cutaneous squamous cell carcinoma and can be represented with clinical and subclinical lesions (Ibrahim *et al*. 2006). Humans have had a very long, hysterical and chaotic relationship with heavy metals. Their prevalent nature and human's dependency on heavy metals for production, have outgrowth consequences that causes systemic toxicity. In spite of clinical knowledge and related experience more than a decade ago, toxicity and poisoning effects caused due to heavy metals have now become representative and most problematic point of interest and

perverted outcome in clinical toxicology is potentially fatal and it is a notion that is mainly and primarily aided by studies and performing experiments on animals and collecting data. Due to restricted research and experiments performed on animals may escalate the rate of heavy metal excretion, their curative effectiveness regards to morbidity and mortality is large (Kosnett 2010).

This article scrutinizes the clinical exemplar and pathophysiology of As poisoning, a heavy metal. The term "arsenic" is a derivative word from the Latin, "*Arsenicum*" that usurp from a Syriac word "(al)zarniqa", which means "yellow orpiment". Antecedently, As is thought as a metalloid due to its dual properties such as they consider to possess metallic and non-metallic characteristics, for time bein in accordance to the reference book of toxicology, As accounts as a toxic metal, which is translucent, odorless, and tasteless (Hall, 2002; Rajiv *et al.* 2023). As metal possess two compounds having chemical-valences of three and five. The chemical compound of As (As_2O_3), which possess tri-valent property, has high level of toxicity than the compound which is penta-valent. As is metabolized by the liver and excreted mainly through the kidneys about 90–95% (Sy, Salud-Gnilo *et al.* 2017). The purpose of this review article was to synthesize an up-to-date knowledge of As induced keratosis including its prevalence, diagnosis, treatment and prevention.

HEAVY METAL EXPOSURE

Exposure due to heavy metal and their core root are natural sources and industrial as well as medicinal. It can invade in humans through absorption, nasal route, and ingestion. As contamination due to natural source involves soil, water, rocks, of which the most common is by drinking tap water comes from underground sources (Lee 2017; Demissie *et al.* 2023). Peak level of As metal stratum was noticed and then reported in deep aquifers. As can endow in industry for manufacturing pesticides, dyes, HED, and semiconductors. It is suggested that the surplus As amount in cosmetic product's preparation should be within the specified limit and must be less than 5 ppm (Tao and Wang 2024). Research have proclaimed that As is present in color pigments used as a cosmetic product in eye-shadows, leads to dermatitis of eyelid and even promote cancers of skin on its long-term use. As metal is broadly classified as and used in striated medicinal preparations as an ingredient of many natural preparations, by use of herbs and allopathic formulations, in various diseases treatment such as asthma, psoriasis, eczema, and Hodgkin's disease, leprosy, squamous cell carcinoma, followed by long-term administration of conventional medicinal therapy which contains As metal for chronic psoriasis (Rajiv *et al.* 2023).

KERATOSIS CAUSED BY ARSENIC

Keratosis due to heavy metal As is a pre-malignant and venomous plague in human beings that shows chronic exposure due to As has become an outgrowth effect. Toxicity of As is the most acute and primitive biomarker (Ganie *et al.* 2024). Lesions erupt as firm, punctate, symmetric papules corn-like in appearance fuse to form scaly, hyper pigmented, warts on skin (Huang *et al.* 2019; Table 1). They are on areas of body which prone to produce friction like soles of feet and palm of hands, moreover they can be enact on the dorsum of extremities, genitalia, eyelids. There is no specific grading level and severity classification for toxicity induced by As metal (Pratt *et al.* 2016). It can be acute, sub-acute and chronic. Severity of As poisoning depends upon the various elements, whichincludes the type and grade of As compound, state of valence chemical compounds, toxic dose, rate of exposure of heavy metal, duration of exposure and underlying disease illness (Çöl *et al.* 1999).

PATHOPHYSIOLOGY

After exposure to As, it absorbs in the body and goes to different organs. During transit from blood to tissues, it metabolizes into reactive trivalent arsenite. Trivalent arsenite have ability to bind to sulphahydral group present in keratin filament, skin, hair, nails (Sarma, 2015). After binding to sulphahydral group of proteins, it activates transcription factors, alters the level of growth factors and cytokeratin's. Due to alteration of cytokeratin's and p53, As affect differentiation and proliferation of keratinocytes, which are the cells of epidermis (Rossman *et al.* 2004). In the cells demand of energy, DNA damage and mutation of mitochondria due to As exposure cause differentiation of epidermal keratinocytes. As up-regulates interleukin 1 & 2, beta factors and keratin. Abnormal proliferation of keratinocytes starts to form, and lesions develop in skin, which may coalesce to form hyper pigmented plaques (Palma-Lara *et al.* 2020). Keratosis mostly occur in areas prone to friction and trauma such as palm of hands and soles of feet. Lesions may develop squamous cell carcinoma (Fig. 1). Abnormal differentiation of keratinocytes, apoptosis and aberrant inflammation cause carcinogenesis. In liver As is methylated into mono-methyl arsenic acid and it is further reduced to mono-methylarsonous acid (Paul *et al.* 2015). Methylation increases the oxidative stress, this stress cause DNA repair, altered chromosomal abnormalities i.e. sister chromatid changes and gene expression. As acts on P53 compromised cells to cause chromosomal abnormality this cause carcinogenesis of skin (Tao and Wang 2024).

PREVALENCE

The prevalence rates of As keratosis across the world and countries of South-Asia such as Pakistan, India, Bangladesh, narrative for the highly polluted domain of the world due to As prevalence. Inorganic As has demonstrated gene amplification, a major potential finding, since gene

Table 1: Level of grading of As-keratosis according to papule size

Severity	Papule sizes	Characteristics
Grade-1; Mild level	<2 millimeter	Thickened and gritty papules, apparent
Grade-II; Moderate level	2–5 millimeter	Papules corn-like in appearance, apparent
Grade-III; Severe level	>5 millimeter	Warts or papules with fissures

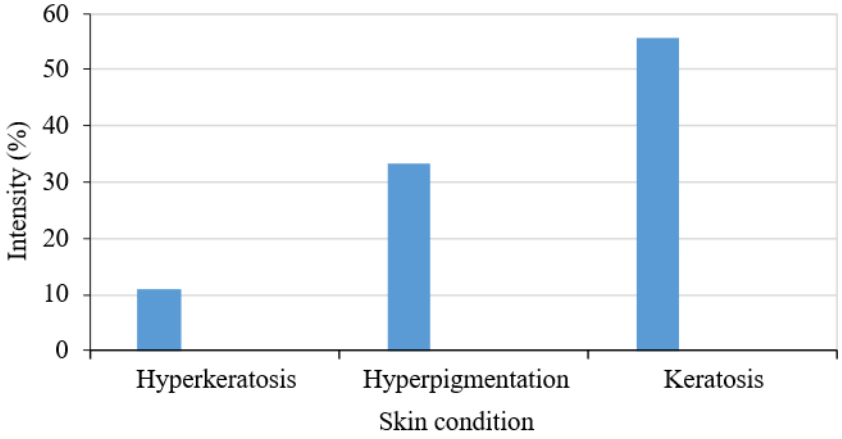

Fig. 1: Prevalence of keratosis in comparison to hyperkeratosis and hyperpigmentation

amplification of oncogenes has been seen in number of human tumors with epidemiologic work (Rajiv *et al.* 2023). Heavy metal poisoning is interlinked with a number of occupations. It is directly linked by drinking contaminated tap water, washing in ground water without any use of filters and potential soil exposure. A major concern is that the safe disposal of waste of heavy metals include As, lead, copper, etc. The concentration of these heavy metals is higher than the prescribed limit as set by the United States Food and Drug Administration and World Health Organization (Somé *et al.* 2012).

To guarantee compliance with regulatory limits, quality control measures should be implemented to monitor metal concentrations. Of the 116 residents surveyed, 81 had clinically diagnosed As keratosis and pigmentation changes. Among them were 52 males and 29 females in the age ranging between 4–82 years (Lonergan *et al.* 2010). Two cases of squamous cell carcinoma were detected through skin biopsy in situ. High grades of As in the groundwater and topsoil aided the prevalence of chronic As poisoning. A revelatory quota of groundwater in Pakistan is contaminated with As noticed. As contaminated wells were found around Indus River, suggest that poisoning is due to heavy metal. The very first noticed and reported epidemiological case of experimental data based on clinical evidence of As metal causing lesions on skin's surface and into deep tissues carried out alongside Indus River (Chakrabarty 2015). A case in point with cluster of multi stage survey was conducted and documented among people (3874) ≥ age of 15 years, is to conclude the prevalence of arsenicosis, based on its relation with increasing level of drinking contaminated groundwater in urban as well as in rural areas (population ratio: 1.8 million of people) in Pakistan due to lack of awareness programs. Pakistan has low levels of As metal exposure in tap water compared with India, Philippines, Bangladesh and China. A large population in West of Bengal, India and Uttar Pradesh, susceptible to inorganic As through their drinking contaminated water (Singh *et al.* 2007). A survey was conducted involving 7683 study population of all ages in an affected As territory, noticed skin keratosis, pulmonary effects and pigmentation alterations between April 1995 and March 1996. Recently, disease prevalence odd-ratio estimates evidently raised the sample population who take part in clinical experimental studies and have had high grades of As in their sources of drinking contaminated water (≥500 mcg/L) as compared with such individuals who had normal skin appearance and exposed to low levels of As (<50 mcg/L) (Table 1). Such territories are exaggerated due to the As-rich sediments grounds in the Gangetic River of Brahmaputra (Ganga-Jumna) sink, which flows orderly millions of years ago (Rahman and Hasegawa 2011; Järup 2003).

DIAGNOSIS

Skin signs are specific for diagnosis. Reports show that chronic As toxicity affects various bodily systems. Clinical evidence of chronic As poisoning depends on the dose, exposure duration, and host vulnerability (Das and Sengupta 2009). It is difficult to diagnose since its symptoms resemble those of common ailments. As the blood exits quickly, thus diagnosing long-term exposure necessitates hair or nail testing, which are not always available. Because trace levels present in food and water, even a positive test

can be difficult to interpret. Many people are unaware they have been exposed until major health conditions, such as nerve damage or cancer, arise years later, making diagnosis even more difficult. Concentration of As in the urine used as an indicator for the exposure of As (Fatmi *et al.* 2013). Route for the elimination of As from the body is urine. As concentration in urine has been shown to compare with presence of As in tap water (groundwater) concentration. As concentration present in seafood also affect As measurement in urine.

Organic As have no toxicity on mammals. If the seafood has been taken from last 2 days then it affects the laboratory As measures that's why laboratories only measure inorganic As or its metabolites. Urine sample should be collected over 24 h time period. More presence indicates the maximum exposure of As. Typically, human hair and nails contain higher levels of As than other body parts due to keratin content. Levels of As metal in hair give important point of interest which gives meaningful information about chronic poisoning induced by As exposure to skin (Singh *et al.* 2007). There is only a very rough correlation among As concentration in hairs and As toxicity, which presents a number of challenges for the toxicologist utilizing this test. Thus, hair concentrations in patients with chronic As poisoning can range from 10 parts per million deaths linked to As have been documented to have levels of about 45 ppm. Chances of variation of hairs from inside and outer-side due to As content could be significant, which makes results of a single hair less accurate than from larger hair samples. Therefore, samples should be taken from multiple locations on the head, containing only one gram of hair clipped near the area of scalp, the entire sample should be examined (Son *et al.* 2008; de Luzuriaga *et al.* 2011). To evaluate toxicity using hair As concentrations, contamination outside of the hair should be eliminated.

The majority of inorganic and organic As in human blood is removed quite quickly. As in blood will only reflect exposure for a brief period, making it highly time dependent. Continuous and consistent exposure, such as drinking water, can lead to steady state As levels in the blood, allowing for a correlation between As exposure and As blood levels (Vahter 2008; Ali *et al.* 2013). However, there is no quantitative evidence linking As exposure to blood As concentrations in humans. The half-life of As in the body in comparison to its half-life in the blood makes it challenging to determine the link between body As concentrations and total concentration of As in blood and organs. The pigmentary and keratotic alterations observed in arsenicosis can be mimicked by a variety of disorders (Khan *et al.* 2015). The study of pathology Hyperkeratosis, parakeratosis, acanthosis, and papillomatosis are epidermal alterations associated with As keratosis (Fig. 1). Basal pigmentation and dysplastic alterations are also infrequently observed. Both benign and malignant forms of arsenical hyperkeratosis are distinguished by the presence or lack of cellular atypia. There are no distinct histological characteristics that distinguish As-induced cutaneous cancers from their non-As-induced counterparts. Diagnostics in laboratories, the primary method of determining the environmental burden is to test the amounts (Ahamed *et al.* 2006; Ghosh 2013).

TREATMENT APPROACH

In China, As poisoning was commonly treated using As removal agents i.e. sodium thiosulphate and Dimercaptopropyl sulfonate. Concentration of As in blood and urine were reduced after these drugs were given to 18 (43.90%) patients who were cancer free and 6 (14.6%) patients who were cancerous (Camaclang *et al.* 2019). Two patients received sodium thiosulphate noticed a drop in blood As levels, whereas 4 patients received dimercaptopropyl sulfonate saw their levels return to normal. Following treatment with dimercaptopropyl sulfonate, two cancer patients had higher urine As levels (Balali-Mood *et al.* 2025; Islam *et al.* 2025).

Leaves of Drumstick tree (*Moringa oleifera*) and leaves of spinach (*Ipomea aquatica*) and the raised parts of them, had increased effects in the toxicity due to As. *Silybum marianum*, Garlic (*Allium sativum*), Turmeric (*Curcuma longa*), and some algae along with fibers was the most beneficial herbs for the intoxication treatment due to As. Chelating agents work by attaching themselves to the metal ion, making it more soluble in water and facilitate quicker kidney elimination. As a result, it lowers the body's total As load and lowers the risk of cancer (Verma *et al.* 2025; Zahra *et al.* 2025). The clearance of skin lesions is accelerated by keratolytic treatment like 20% of urea and 6–10% of salicylic acid in combination with agents which forms chelates and complex compound formulation. Retinoid have anti-keratinizing properties, their therapy has been utilized to treat As keratosis. By influencing the gene expression, which may impact cell distinction, proliferation, multiplication and induction of apoptosis, they also aid in the chemo-prevention of malignancies linked to As (Ullah *et al.* 2024). Drinking contaminated groundwater tanned with As, people who take a high calorie, antioxidants rich meals had lessened effects of As toxicity (Das and Sengupta 2009). Numerous studies have demonstrated that polyphenols, black tea and leaves of green tea, Vitamin A (Retinol), Vitamin C (Ascorbic acid), Vitamin E (Tocopherol) all reduced the effects of As toxicity. After six weeks of topical treatment with 5%imiquimod cream once daily, the neoplasms completely resolved clinically and didn't reappear throughout more than three years of clinical observation. In order to identify and eradicate cancer cell, it activates immune cells like T-cells and dendritic cells (Tang *et al.* 2023).

PREVENTION STRATEGIES

Prevention is the core step in lowering chronic As toxicity. The best way is the prevention rather to cure. The health impacts and prevention of As have been the attention of many nations. Acknowledge the severity of the arsenicosis epidemic, which affects a sizable portion of the global population and for which there is currently no cure (Rajiv *et al.* 2023). Increased prevention measures are of importance to us because to the substantial impact on the population at risk as well as the additional conditions linked to ongoing drinking water exposure to As. Filtration is the most used clean up method (Hye 2018). SONO filters, iron filters, membrane filters and nanoparticle filters are the common techniques used to remove the As from water. Different filters work better at different water pH level. It is important to understand that As cannot be removed by boiling the water (Tao and Wang 2024). It offers a promising solution for removing As from water and soil. It is the natural and cheap way to remove As. Plants can remove As regardless of water pH, it clears the contaminated area of As. In reality, these plants are hyper accumulating (Hassan 2018). It doesn't eliminate contaminations from polluted areas instead, it reduces the contaminated mobility, As which prevents plants from absorbing it. As can be absorbed by certain hyper accumulating plants, which then move it to their aerial parts and release it into the atmosphere as arsine (Saha 2003). This should not be attempted form an environmental perspective. Using plant metabolism, this is a combination of phytodegradation and phytostabilization. As is absorbed by hyper accumulating plants in watery environments (Shajil *et al.* 2024).

CONCLUSION

As keratosis can cause variable incorporations. Its prevalent nature and their huge presence globally, makes it a difficult chore to prevent these aspects of poisoning. The outcome of this experimental study and limited research on keratosis revealed that the contemporary prevalence of skin lesions caused by As in the community was 2.21%. Moreover, beside the cases of arsenicosis, the primarily clinical manifestation was keratosis, which is then followed by hyperpigmentation and then comes the hyperkeratosis, were observed. There must be checkpoints to evaluate the As exposure and related poisoning in between the population in the area under-study by using body biomarkers. A global epidemic, global agencies i.e. World Health Organizations and the UNEP (United Nations Environment Program) can help the communities by encouraging hyperawareness, and the surroundings global etiquette for acceptable limits of As exposure in periodic history. People who are affected by these heavy metals and have had previously developed history of keratosis should must pay attention to decrease improbability of malignant modification and they must hold identical preventive steps. Lesions are cancerous in nature and these cancerous cells may invade into other body tissues and can also cause damage to them, so they should be closely monitored, and surgical treatment strategies should be followed and implemented to affected individuals.

AUTHOR CONTRIBUTIONS

NUA: Topic decision in publication, Journal approach, publication process, data defining, writing and data collection; HK: Introduction to Arsenic, Heavy metal poisoning, Prevalence; ZB Intervention traditional and modern strategies; AZ: Abstract and diagnosis; KA: Introduction to arsenic keratosis and conclusion; RK Pathophysiology; HS: Diagnosis; ZS: Pathophysiology; RI: Intervention traditional and modern strategies; MY: Introduction to arsenic keratosis and conclusion, data collection and in writing.

CONFLICTS OF INTEREST

No conflict of interest among the authors to declare

DATA AVAILABILITY

Not applicable to this paper

ETHICS APPROVAL

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REFERENCES

Ahamed S, Sengupta MK, Mukherjee A, Hossain MA, Das B, Nayak B, Pal A, Mukherjee SC, Pati S, Dutta RN, Chatterjee G, Mukherjee A, Srivastava R, Chakraborti D (2006) Arsenic groundwater contamination and its health effects in the state of Uttar Pradesh (UP) in upper and middle Ganga plain, India: A severe danger. *Science of The Total Environment* 370: 310–322. https://doi.org/10.1016/j.scitotenv.2006.06.015.

Ali SS, Karim N, Munshi AB, Siddqui I, Khan FA (2013) Health hazards among coastal villagers of Pakistan due to arsenic contaminated drinking water. *Journal of Water Resource and Protection* 5: 41104. https://doi.org/10.4236/jwarp.2013.512132.

Balali-Mood M, Eizadi-Mood N, Moghaddam HH, Etemad L, Moshiri M, Vahabzadeh M, Sadeghi M (2025) Recent advances in the clinical management of intoxication by five heavy metals: Mercury, lead, chromium, cadmium and arsenic. *Heliyon* 11: e42696. https://doi.org/10.1016/j.heliyon.2025.e42696.

Camaclang MLA, Cubillan ELA, Yap-Silva C (2019) Arsenicosis presenting with cutaneous squamous cell carcinoma: A case report. *Acta Medica Philippina* 53: 171–176.

Chakrabarty N (2015) *Arsenic Toxicity: Prevention and Treatment*. Boca Raton, FL: CRC Press.

Çöl M, Çöl C, Soran A, Sayli BS, Oztürk S (1999) Arsenic-related Bowen's disease, palmar keratosis, and skin cancer. *Environmental Health Perspectives,* 107: 687–689. https://doi.org/10.1289/ehp.107-1566498.

Das NK, Sengupta SR (2009) Arsenicosis: Diagnosis and treatment. *Indian Journal of Dermatology, Venereology and Leprology* 2008;74:571–581. https://doi.org/10.4103/0378-6323.45098.

de Luzuriaga AMR, Ahsan H, Shea CR (2011) Arsenical keratoses in Bangladesh—update and prevention strategies. *Dermatologic Clinics* 29: 45–51. https://doi.org/10.1016/j.det.2010.09.003.

Demissie S, Mekonen S, Awoke T, Teshome B, Mengistie B (2023). Prevalence of arsenic-induced skin lesions and associated factors in Ethiopia: Community-based study. *Toxicology Reports* 11: 153–161.. https://doi.org/10.1016/j.toxrep.2023.07.007

Fatmi Z, Abbasi IN, Ahmed M, Kazi A, Kayama F (2013) Burden of skin lesions of arsenicosis at higher exposure through groundwater of taluka Gambat district Khairpur, Pakistan: A cross-sectional survey. *Environmental Geochemistry and Health* 35: 341–346. https://doi.org/10.1007/s10653-012-9498-3.

Ganie SY, Javaid D, Hajam YA, Reshi MS (2024) Arsenic toxicity: Sources, pathophysiology and mechanism. *Toxicology Research* 13: tfad111. https://doi.org/10.1093/toxres/tfad111.

Ghosh A (2013) Evaluation of chronic arsenic poisoning due to consumption of contaminated ground water in West Bengal, India. *International Journal of Preventive Medicine* 4: 976–979.

Hall AH (2002) Chronic arsenic poisoning. *Toxicology Letters* 128: 69–72. https://doi.org/10.1016/S0378-4274(01)00534-3.

Hassan MM (2018) *Arsenic in Groundwater: Poisoning and Risk Assessment*. Boca Raton, FL: CRC Press.

Huang H-W, Lee C-H, Yu H-S (2019) Arsenic-induced carcinogenesis and immune dysregulation. *International Journal of Environmental Research and Public Health* 16: 2746. https://doi.org/10.3390/ijerph16152746.

Hye MA (2018) Arsenicos is: A review of its diagnosis and treatment. *Medicine Today* 30: 81–88. https://doi.org/10.3329/medtoday.v30i2.37816.

Ibrahim D, Froberg B, Wolf A, Rusyniak DE (2006) Heavy metal poisoning: Clinical presentations and pathophysiology. *Clinics in Laboratory Medicine* 26: 67–97. https://doi.org/10.1016/j.cll.2006.02.003.

Islam M, Roy D, Singha D (2025) Metal ion toxicity in human body: Sources, effects, mechanisms and detoxification methods. *Chemistry Africa* 8: 779–797. https://doi.org/10.1007/s42250-025-01233-z.

Järup L (2003) Hazards of heavy metal contamination. *British Medical Bulletin* 68: 167–182. https://doi.org/10.1093/bmb/ldg032.

Khan S, Shah IA, Muhammad S, Malik RN, Shah MT (2015) Arsenic and heavy metal concentrations in drinking water in Pakistan and risk assessment: A case study. *Human and Ecological Risk Assessment* 21: 1020–1031. https://doi.org/10.1080/10807039.2014.950925.

Kosnett M (2010) Chelation for heavy metals (arsenic, lead, and mercury): Protective or perilous? *Clinical Pharmacology & Therapeutics* 88: 412–415. https://doi.org/10.1038/clpt.2010.132.

Lee C-H (2017) Pathophysiology of arsenic-induced adverse health effects. *Hong Kong Journal of Dermatol* 25: 171–177.

Li Z, Lu F, Zhou F, Song D, Chang L, Liu W, Yan G, Zhang G (2025) From actinic keratosis to cutaneous squamous cell carcinoma: The key pathogenesis and treatments. *Frontiers in Immunology* 16: 1518633. https://doi.org/10.3389/fimmu.2025.1518633.

Lonergan CL, McNamara EK, Cordoro KM, Greer KE (2010) Imiquimod cream 5% for the treatment of arsenic-induced cutaneous neoplasms. *Cutis* 85: 199–202.

Palma-Lara I, Martínez-Castillo M, Quintana-Pérez JC, Arellano-Mendoza MG, Tamay-Cach F, Valenzuela-Limón OL, García-Montalvo EA, Hernández-Zavala A (2020) Arsenic exposure: A public health problem leading to several cancers. *Regulatory Toxicology and Pharmacology* 110: 104539. https://doi.org/10.1016/j.yrtph.2019.104539.

Paul S, Majumdar S, Giri AK (2015) Genetic susceptibility to arsenic-induced skin lesions and health effects: A review. *Genes and Environment* 37: 23. https://doi.org/10.1186/s41021-015-0023-7.

Pratt M, Wadden P, Gulliver W (2016) Arsenic keratosis in a patient from Newfoundland and Labrador, Canada: Case report and review. *Journal of Cutaneous Medicine and Surgery* 20: 67–71. https://doi.org/10.1177/1203475415599342.

Rahman MA, Hasegawa H (2011) Aquatic arsenic: Phytoremediation using floating macrophytes. *Chemosphere* 83: 633–646. https://doi.org/10.1016/j.chemosphere.2011.02.045.

Rajiv SV, George M, Nandakumar G (2023) Dermatological manifestations of arsenic exposure. *Journal of Skin and Sexually Transmitted Diseases* 5: 14–21. https://doi.org/10.25259/JSSTD_3_2022.

Rossman TG, Uddin AN, Burns FJ (2004) Evidence that arsenite acts as a cocarcinogen in skin cancer. *Toxicology and Applied Pharmacology* 198: 394–404. https://doi.org/10.1016/j.taap.2003.10.016.

Saha KC (2003) Diagnosis of arsenicosis. *Journal of Environmental Science and Health Part A* 38: 255–272. https://doi.org/10.1081/ESE-120016893.

Sarma N (2015) Skin manifestations of chronic arsenicosis. In: *Arsenic: Exposure, Sources, Health Risks, and Mechanisms of Toxicity*, pp: 127–136. States C (Ed.). Hoboken, NJ: Wiley. https://doi.org/10.1002/9781118876992.ch6.

Shajil C, Chen P, Mahabal GD (2024) *Arsenical Keratosis*. Treasure Island, FL: StatPearls Publishing.

Singh N, Kumar D, Sahu AP (2007) Arsenic in the environment: Effects on human health and possible prevention. *Journal of Environmental Biology* 28: 359–365.

Somé IT, Sakira AK, Ouédraogo M, Ouédraogo TZ, Traoré A, Sondo B, Guissou PI (2012) Arsenic levels in tube-wells water, food, residents' urine and the prevalence of skin lesions in Yatenga province, Burkina Faso. *Interdisciplinary Toxicology* 5: 38–41. https://doi.org/10.2478/v10102-012-0007-4.

Son S, Song H, Son S (2008) Successful treatment of palmoplantar arsenical keratosis with a combination of keratolytics and low-dose acitretin. *Clinical and Experimental Dermatology* 33: 202–204. https://doi.org/10.1111/j.1365-2230.2007.02596.x.

Sy SMT, Salud-Gnilo CM, Yap-Silva C, Tababa EJL (2017) A retrospective review of the dermatologic manifestations of chronic arsenic poisoning in the Philippines. *International Journal of Dermatology* 56: 721–725. https://doi.org/10.1111/ijd.13615.

Tang GT, Elakis J, Scardamaglia L (2023) Cutaneous manifestations and treatment of arsenic toxicity: A systematic review. *Skin Health and Disease* 3: ski2.231. https://doi.org/10.1002/ski2.231.

Tao R, Wang R (2024) Arsenical keratosis in China: A case report and review of the literature. *Skin Research and Technology* 30: e13903. https://doi.org/10.1111/srt.13903.

Ullah H, Aslam S, Mustafa G, Waseem A, de Freitas Marques MB, Gul Z, Alvi MU, Anwar S, Sabir M, Hamid A, Ibrahim M (2024) Potential toxicity of heavy metals in cosmetics: Fake or fact: A review. *International Journal of Environmental Analytical Chemistry* 104: 8878–8909. https://doi.org/10.1080/03067319.2023.2217406.

Vahter M (2008) Health effects of early life exposure to arsenic. *Basic & Clinical Pharmacology & Toxicology* 102: 204–211. https://doi.org/10.1111/j.1742-7843.2007.00168.x.

Verma M, Chivate MS, Singh V, Mishra V (2025) Arsenic and antimony. In: *Visceral Leishmaniasis and Post-kala-azar Dermal Leishmaniasis: Pathogenesis, Treatment and Disease Control*, pp: 194–202. Singh V, Kumar A (Eds.). Boca Raton, FL: CRC Press.

Zahra A, Ali M, Ali N, Khan A, Zairov R, Sinyashin O, Wang Y, Zafar S, Khan F-A (2025) A comprehensive analysis of the impact of arsenic, fluoride, and nitrate–nitrite dynamics on groundwater quality and its health implications. *Journal of Hazardous Materials* 487: 137093. https://doi.org/10.1016/j.jhazmat.2025.137093.