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Review

Review on Lead Contamination in Drinking Water of Pakistan, Consequences on Animal Health and Environmental Integrity: Modulation Through Possible Bioremediation

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Abstract. Lead, a non-biodegradable element, pervades the environment through both natural processes and anthropogenic activities. Its presence in air, food, soil and water poses significant health risks, with workers and young children being particularly vulnerable. Lead exposure can remain undetected due to the absence of obvious symptoms, yet it contributes to approximately 0.6% of the global disease burden. World Health Organization recognizes lead as a toxicant, with detrimental effects on various bodily systems including neurological, hematological, gastrointestinal, cardiovascular and renal systems. Chronic lead exposure is especially concerning, leading to neurological disorders in children, including antisocial behavior and cognitive impairments. Additionally, it impacts male reproductive function and increases the risk of spontaneous abortion in pregnant individuals. Furthermore, inorganic lead compounds are classified as carcinogenic to humans by the International Agency for Research on Cancer (IARC). Lead toxicity manifests in various ways, including anemia due to decreased red blood cell production and hemoglobin synthesis. Its strong affinity for sulfhydryl groups on proteins leads to enzyme dysfunction and structural protein alterations, primarily affecting the central nervous system. The accumulation of lead in living organisms through the food chain presents a significant environmental and health concern, with even low concentrations posing risks to human and aquatic life. Higher concentrations are extremely toxic to livestock, humans and plants. However, studies in Pakistan reveal that lead contamination in groundwater often exceeds these standards, with alarming concentrations observed in various regions. In summary, lead pollution poses significant health risks to both humans and the environment, with widespread implications for public health and ecosystem. Efforts to mitigate lead exposure and contamination are crucial to safeguarding human health and environmental integrity.

Keywords: non-biodegradable, lead poisoning, toxicant, carcinogenic, toxic metal, low concentration

Introduction

Water, essential for all living organisms, primarily originates from two main sources: surface water, including rivers, canals, lakes and streams and groundwater extracted from wells (Mishra, 2023). Due to its polarity and hydrogen bonding properties, water can suspend, dissolve, absorb and adsorb various compounds. Consequently, it rarely remains in a pure state and is vulnerable to contamination from environmental factors, human activities, and biological processes (Chitmanat and Traichaiyaporn, 2010). In Pakistan, groundwater is a critical source for drinking, agricultural and industrial purposes. However, factors such as overpopulation, rapid urbanization, unsustainable policies and improper waste disposal practices have led to a decline in groundwater quality (WWF, 2007). Similar to many other developing nations, Pakistan grapples with significant water scarcity and contamination challenges. The nation has already depleted much of its available water

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resources (PCRWR, 2005) and resulting in a water-stressed status and the likelihood of future water shortages (Perveen, 2023).

In Pakistan, the rate of water precipitation is lower than the rate of evapouration, resulting in a continual decrease in water levels in rivers, lakes and groundwater sources. This situation is exacerbated by factors such as prolonged droughts and inadequate development of new water reservoirs (Ullah *et al*., 2009) leading to severe water shortages across various sectors. Per-capita water availability in Pakistan has dwindled from 5000 cubic meters in 1951 to 1100 cubic meters per annum (WB-SCEA, 2006). The water quality in major cities of Pakistan, including Kasur, Peshawar, Lahore, Sialkot, Gujarat, Rawalpindi, Faisalabad, Karachi and Sheikhupura, has worsened due to the discharge of untreated domestic and industrial effluents, as well as the unregulated use of fertilizers, pesticides and insecticides (Perveen, 2023; Bhutta *et al*., 2002). The particular concern among water contaminants are heavy metals, which pose significant health risks due to their high toxicity even at low concentrations. These metals, derived from both natural sources such as mineral erosion, ore leaching and volcanic activity and anthropogenic sources such as solid waste deposition and industrial and domestic discharge (Gautam *et al*., 2016) which are non-biodegradable elements (Ali *et al*., 2021). Heavy metals, characterized by a specific density exceeding 5 g/cm^3 (Klöckner *et al*., 2019) which exhibit mutagenic, cytotoxic and carcinogenic effects in animals (Masindi and Muedi, 2018).

Lead, a soft heavy metal with a gray colour (Jayakumar *et al*., 2021; ATSDR, 2000), has been utilized since ancient times for various purposes such as jewelry, water pipes, drinking vessels and statue construction due to its malleability, corrosion resistance and low melting point (De Keersmaecker *et al*., 2018). Romans even used lead to sweeten wine and it was extensively employed in pigments for cosmetics, paints and ceramics. In the 20th century, lead saw increased usage, particularly in gasoline as an anti-knocking agent, with its peak consumption occurring in the mid-1970s in the United States, where around 200,000 tonnes of lead were used (Reddy and Braun, 2010). However, the release of lead into the environment through vehicle exhaust contaminated air, soil and dust, with traces even detected in remote areas such as polar ice caps due to vehicular emissions (Marx and McGowan, 2010).

Lead exhibits toxicity to various organ systems including the cardiovascular, peripheral nervous, central nervous, reproductive, renal and hematological systems, as well as affecting red blood cells (Collin *et al*., 2021). It can also impact the brains of fetuses and infants, with even low levels of exposure (10-20 µg/dL) leading to intelligence loss, short attention spans and behavioural disruptions (Singh *et al*., 2018). Despite previous assumptions of safety at low levels of exposure (Paul and Gupta, 2018) and lead is now considered a potential carcinogen by the International Agency for Research on Cancer (IARC) which based on animal data and limited human evidence (Krewski *et al*., 2019). The World Health Organization (WHO) estimates that lead exposure contributes to 0.6% of the worldwide disease burden (World Health Organization, 2009), with Africa facing significant ecological risks due to lead exposure (Carrington *et al*., 2019).

Lead compounds have been studied for their potential in targeting specific proteins, such as thioredoxin glutathione reductase which is for the treatment of diseases like schistosomiasis (Lyu *et al*., 2020). Additionally, lead monoxide and arsenic trioxide have been found to react readily, producing particulate matter with high arsenic content, with sulphur dioxide and oxygen levels influencing the formation of lead arsenite versus lead arsenate (Yao *et al*., 2020). This review aims to elucidate the biological effects of lead, highlighting its toxicity to various systems and organs including cardiovascular, nervous, digestive, hematopoietic, reproductive, skeletal, immunological, hepatic and renal systems (Assi *et al*., 2016). By discussing exposure routes and mechanisms of action, this review seeks to contribute to a better understanding of lead toxicity, aiding in the development of solutions for lead contamination, its consequences, and potential treatments. Moreover, this review is to underscore the complexity of drinking water contamination due to lead, with a particular emphasis on various case studies across different regions of Pakistan. As such, this review will examine lead contamination in both groundwater and surface water sources, providing a comprehensive analysis of the issue.

Sources of lead exposure. Naturally, lead is found in the environment primarily as lead sulphide (galena) (Rahman and Singh, 2019) but its widespread presence in the environment is largely attributed to human activities. Lead is a significant component of airborne particulate matter, with industrial coal and oil combustion contributing an estimated 450 million/Kg annually and natural sources contributing around 30 million/Kg annually (Remonsellez *et al*., 2017). Lead contamination in water arises when water flows through antiquated pipelines containing lead solder or brass fixtures containing lead elements. Lead arsenate is used as a pesticide, contributes to the addition of arsenic to the environment, while lead chromate serves as a yellow pigment in fiber dyeing processes (Sungur and Gulmez, 2015). The slow deposition of exhaust fumes from lead-containing petrol on soil and water bodies leads to its ingress into drinking water (Tabelin *et al*., 2018) with decreased pH levels in water further facilitating lead generation (Cullen and McAlister, 2017).

Lead contamination in roadside soil is associated with road traffic density, as well as activities such as leaded gasoline plumbing, metal working (Kekeba, 2019) and lead paints, ceramics (Abbaszade *et al*., 2022) and e-scrap reprocessing (Obeng-Gyasi, 2022). Additionally, peeling or chipping of timeworn lead-based paint, particularly during renovations of old homes, poses a risk of lead exposure (Laker *et al*., 2016). Additionally, lead is recognized as one of the hazardous components found in airborne particulate matter, with an estimated annual emission rate of 450 million/Kg from industrial coal and oil combustion, along with an extra 30 million/Kg annually from natural origins (Meena *et al*., 2022). Workers and young children are identified as the two populations at the highest risk of lead exposure, both in industrially developed and developing nations. Various worker populations, including smelters, battery and ceramics manufacturers, ship breakers and construction workers which are present at risk of occupational lead exposure, primarily through inhalation. The implementation of industrial-level standards to limit airborne lead at workplaces has contributed to reductions in blood lead levels and exposure (Harrison, 2012). However, the persistence of lead exposure remains a significant issue in developing countries. Furthermore, alternative medicines, increasingly popular in advanced nations and are identified as sources of lead. Despite being believed to be harmless and self-administered without medical supervision, such remedies can be contaminated with heavy metals like lead, leading to non-occupational exposure (Bi *et al*., 2020).

Lead exposure and entry pathways within living organisms. Lead, as a non-biodegradable element, pervades the environment through air, food, soil and water. It can infiltrate the body through ingestion, inhalation and skin contact with organic lead compounds. Particles smaller than 1 micron can penetrate the alveoli and be fully absorbed, while larger particles are retained in the airways and eventually cleared through mucociliary action and swallowing, leading to gastrointestinal absorption. As it has been elaborated in Fig. 1 that there are different exposure pathways for lead contamination, through air, food, soil and water which enter the human body by ingestion, inhalation and skin contact (Shahid *et al*., 2021). Following absorption, the destiny of lead in the body relies on factors such as the individual's nutritional status, health and age. It acts as a cumulative toxicant, primarily accumulating in bones and teeth which is more than 95% of stored lead residing in bones, where it undergoes continuous exchange with blood and soft tissues. Lead has a half-life of approximately 36 days within blood, 40 days within soft tissues and 20 to 30 years within bones (Das *et al*., 2021; Munawer, 2018). Exposure pathways to lead differ across various life stages as indicated in Fig. 1 (Li *et al*., 2019).

Throughout pregnancy, the embryo and fetus face potential exposure risks through transplacental transmission, stemming from either maternal occupational exposure or lead released from maternal bones during gestation (Dutta *et al*., 2022; Chen *et al*., 2014). In infancy, breast milk may serve as a conduit for lead exposure during lactation, as lead is transferred from maternal bones to milk. In childhood, ingestion and oral exploratory behaviour represent the main sources of lead exposure (Dórea, 2019). In adulthood, approximately 90% of lead poisoning cases in adults are associated with workplace inhalation of lead, which can be present in particulate or vapour form. Lead vapors are generated during high-temperature processes

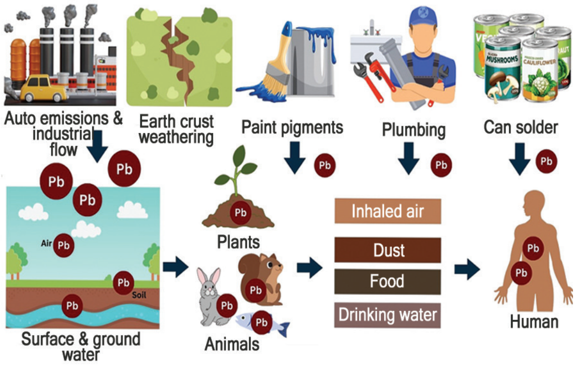

Fig. 1. Exposure pathways of Lead causing lead poisoning in living beings (Das *et al*., 2021).

such as lead smelting or burning lead-painted steel (Reuben, 2018). In old age, Lead transfer from bones becomes a significant source of exposure, especially in individuals with past occupational exposure. In women, lead mobilization occurs during bone demineralization at menopause, while in men, it occurs throughout the aging process. Substantial release of lead from bone reservoirs is linked to hypertension, cardiovascular diseases, and diminished cognitive function (Olufemi *et al*., 2022; Braun *et al*., 2021; Reuben *et al*., 2019).

Symptoms and consequences of lead poisoning. Lead poisoning can often go unnoticed due to the absence of obvious symptoms, despite even low concentrations of lead being harmful to both humans and aquatic life. Lead tends to build up in the human body *via* the food chain, resulting in a range of health problems (Mohmand *et al*., 2015). One significant waterborne disease caused by lead is lead poisoning or plumbism, with other notable diseases including fluorosis and dental caries (Wright *et al*., 2021). Ingestion of lead results in its absorption in the gastrointestinal tract, leading to long term effects of plumbism such as wrist drop and the appearance of a distinct blue line at the junction of the gums and teeth (Little and Albers, 2015).

Lead predominantly enters the body through ingestion and absorption in the gastrointestinal tract, as well as inhalation *via* the respiratory tract. Prior to being stored in bones, the kidneys and liver are identified as potential sites of lead toxicity (Grant, 2020). Depending on the degree of exposure, lead can induce various biological effects, such as decreased hemoglobin synthesis, disruption of neuro-behavioural and psychological functions, peripheral neuropathy, cardiovascular impacts, kidney tubular damage, reproductive problems, abdominal discomfort, headaches, hypertension, irritability, nerve impairment, stomach cancer, lung cancer, coma and mortality (Boskabady *et al*., 2020; Natasha *et al*., 2020). Thus, lead affects various organs and systems, including the nervous, digestive, hematopoietic, cardiovascular, reproductive, immunological, skeletal and renal systems as Fig. 2 elaborating it completely (Akepe *et al*., 2022). Lead can also replace calcium in the bone, leading to long-term effects, and can affect calcium metabolism and vitamin D levels (Ciosek *et al*., 2021). Additionally, lead exposure can elevate uric acid levels due to reduced excretion rates by the kidneys (Dermience *et al*., 2015).

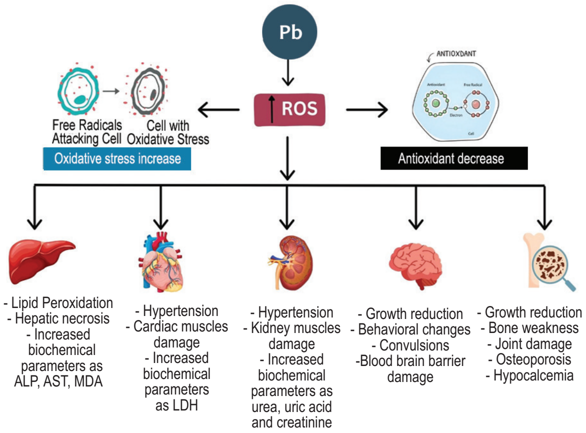

Fig. 2. Lead poisoning caused oxidant-antioxidant imbalance which further make path for various tissue damage in human and animals (Mohmand *et al*., 2015).

Effect on growth and development. Lead poisoning not only causes neurological impairment, diminished intelligence, learning disabilities and coordination issues but also has been linked to criminal activities and anti-social behavior in children (Santa Maria *et al*., 2019). Children face heightened vulnerability to lead due to elevated gastrointestinal absorption and the permeable nature of the blood brain barrier, which can induce neurotoxic effects even at minimal exposure levels. Lead exposure in children may manifest as behavioural instability, memory impairment and anemia (Ortega *et al*., 2021). Even exposure to reduced levels of lead can precipitate miscarriage, stunted growth and low birth weight (Rădulescu and Lundgren, 2019). Children absorb lead primarily through ingestion, with their proximity to the ground posing a higher risk. Sources of lead exposure for children include soil, drinking water, vinyl miniblinds, ceramics, lead-containing paints, painted glass structures, industrial discharge, lead brought into the home from work sites and toys (Yu *et al*., 2021). Lead serves no physiological role but is present in nearly all biological systems, while it can be absorbed through various pathways, ingestion of contaminated food remains the primary route of lead toxicity in children (Shadab and Afzal, 2021). Children face a greater likelihood of lead exposure compared to adults, attributed to their elevated rates of inhalation and heightened intestinal absorption.

Intense and high dose lead exposure leads to acute poisoning marked by colic, anemia, and central nervous system depression, potentially escalating to coma, seizures and mortality. Yet, recent studies indicate that even minimal blood lead levels, lacking evident symptoms, can influence diverse organs (De Carvalho Machado and Dinis-Oliveira, 2023). Toxic effects at low lead levels during prenatal and childhood stages can result in brain and nervous system impairment, along with repercussions on the immune, reproductive and cardiovascular systems. Recent studies suggest that neurobehavioral impairment can occur at blood lead levels as low as 5 μg/dL or even lower, indicating that brain damage can occur at any threshold of blood lead level (Boskabady *et al*., 2018; Flora and Agrawal, 2017). The Blood Lead Level (BLL) presents a notable health hazard, particularly in children, emphasizing the importance of regular monitoring to minimize lead exposure as much as possible (Charkiewicz and Backstrand, 2020). A study was conducted to evaluate blood lead levels among school aged children in Egypt. Four hundred children aged 6-12 years were selected from two regions in Egypt and one industrial and one urban. Comprehensive questionnaires regarding sources of lead exposure, school routines and any lifestyle variances were collected (Shvachiy *et al*., 2020). In the urban area of Egypt (Dokki), the average blood lead level was 5.45 ± 3.90 μg/dL, whereas in the industrial area (Helwan), it was 10.37 ± 7.94 μg/dL. A notable correlation was found between children displaying abnormal behaviour and paleness and blood lead levels = 10μg/dL. Residents of the industrial area, individuals with unhealthy lifestyle habits and those residing in environments with elevated exposure were at heightened risk of having blood lead levels = 10 μg/dL (AbuShady *et al*., 2017).

Effect on nervous system and behavioural response. The adverse effects of lead on the central nervous system have been observed in epidemiological studies (Babadjouni *et al*., 2017). In children, lead's impact on the CNS can result in diminished cognitive functions, aggressiveness and involvement in criminal activities (Sampson and Winter, 2018). The secondary consequence of childhood lead exposure manifests as an economic burden on affected individuals (Gaze *et al*., 2024). The intellectual abilities of young individuals may subsequently influence their educational attainment and future occupational opportunities. Furthermore, there is a correlation between decreased academic performance and the likelihood of engaging in criminal behavior (Mason *et al*., 2014). Environmental lead exposure plays a significant role in limiting the full potential of young individuals' lives (Shiek *et al*., 2021). Chronic lead exposure leads to neurological disorders characterized by antisocial behaviour such as aggressiveness. A study was conducted to investigate the association between lead exposure and aggressiveness during mid-adolescence in Johannesburg, south Africa. The sample consisted of 508 males and 578 females aged 14-15 years, spanning from birth to early adulthood. Blood samples were collected at age 13 to measure blood lead levels. The youth self-report questionnaire was used to assess aggression, encompassing various aspects including violent behaviour, substance abuse, rule-breaking, social problems, cognitive complaints, anxiety disorders, depression, mood disorders and impulsivity (Lee *et al*., 2022). Principal component analysis was employed to derive composite variables from the original aggression measures and associations between blood lead levels and dimensions of primary and secondary aggression were examined during mid-adolescence. Relationships between aggression, sex and socio-demographic factors were also explored. Blood Lead levels ranged from 1 to 28 μg/dL, with 72% of males and 47.7% of females having blood lead levels ≥5 μg/dL. In males, a positive association was found between direct aggression and blood lead levels, while a negative association was observed with indirect aggression. Maternal education level and age at birth were negatively associated with direct violent behavior during mid-adolescence (Nkomo *et al*., 2018).

Effect on enzyme activities. Lead, as a divalent cation, establishes robust bonds with sulfhydryl groups found on proteins. Its detrimental effects largely stem from its ability to distort enzymes and structural proteins, although it impacts numerous other targets. Lead disrupts the development of the endogenous opiate system (Lanphear *et al*., 2019) and can induce toxicity by directly hindering various enzyme activities (Virgolini and Aschner, 2021) or displacing essential metal ions from metallo-enzymes. Lead can catalytically cleave the ribophosphate backbone of tRNA at specific sites without necessitating a threshold proof (Giegé and Eriani, 2021).

Lead's capacity to mimic or *via* with calcium significantly contributes to many of its toxic properties. At picomolar levels, lead competes with calcium for binding sites on cerebellar phosphokinase C, impacting neuronal signaling (Virgolini and Aschner, 2021) and it hampers calcium entry into cells (Grant, 2020). Mitochondria absorb lead, leading to swelling and distortion of mitochondrial cristae. This results in uncoupled energy metabolism, inhibition of cell respiration, and altered calcium kinetics (Han *et al*., 2021). Lead exerts a dual effect on neurotransmitter release: it boosts spontaneous neurotransmitter release while dampening stimulated release (Liu *et al*., 2024).

Considerable attention has been focused on lead's impact on the synthetic pathway of heme, affecting various stages. Delta aminolevulinic acid dehydratase is particularly vulnerable to lead inhibition, leading to increased levels of circulating aminolevulinic acid (ALA). ALA acts as a weak agonist of gamma aminobutyric acid (GABA), resulting in decreased GABA release through presynaptic inhibition (Shiek *et al*., 2021). The heightened presence of ALA contributes to the behavioural symptoms observed in patients with porphyria and potentially in cases of lead toxicity. Lead demonstrates diverse effects on the central nervous system (CNS), influencing immature astrocytes, disrupting myelin formation and compromising the integrity of the blood-brain barrier (AbuShady *et al*., 2017). Lead also interferes with collagen synthesis and affects vessel permeability, resulting in brain edema and hemorrhage at sufficiently high doses (Sampson and Winter, 2018). Lead toxicity induces oxidative stress, leading to the production of reactive oxygen species (ROS) such as hydroperoxides and hydrogen peroxide, while also reducing antioxidant levels and GSH levels (Gaze *et al*., 2024). Glutathione (GSH) serves as a crucial antioxidant defense mechanism, existing in both reduced (GSH) and oxidized (GSSG) forms at the cellular level. Under normal conditions, most glutathione exists in its reduced form but oxidative stress can lead to an increase in the concentration of the oxidized form, contributing to oxidative stress (Gaze *et al*., 2024).

Effect on hormonal and reproductive system. Decreased sperm counts and a higher incidence of morphologically abnormal sperm were noted in males with substantial (74.5 mg/dL lead in blood) and moderate exposure (52.8 mg/dL lead in blood) to lead (Nkomo *et al*., 2018; Kaveri, 2017). These findings were reinforced by studies conducted in the United States and Italy, which observed a decline in sperm count among individuals exposed to lead at concentrations exceeding 60 mg/dL in blood (Perrelli *et al*., 2022). The impact of lead on male reproductive function at lower exposure levels remains uncertain (Kargar-Shouroki *et al*., 2023). Human studies have predominantly investigated semen quality, endocrine function and birth rates in individuals exposed to lead at workplace environments, revealing that exposure to inorganic lead levels surpassing 40 mg/dL in the blood compromised male reproductive function by diminishing sperm count, volume and density, or by altering sperm motility and morphology. However, no significant effects on endocrine profiles were observed (Al Sukaiti *et al*., 2023). In females, experimental evidence indicates that lead is detrimental to reproductive function at high doses (Saganuwan, 2022).

Exposure of male rats to lead acetate resulted in mean serum blood values of 30 pg/dL ± 5 μg/dL. Upon exposure to naloxone (ng/mL), serum luteinizing hormone (LH) levels were found to increase to 500 ± 70% in the control group, while in lead-treated animals, it was lower at 80 ± 10% (Büsselberg, 2016). Injection of LH (ng/dL) resulted in testosterone levels rising to 700 ± 230%, whereas in lead-treated rats, it was higher at 1200 ± 200%. Similarly, upon injection of gonadotropin-releasing hormone (GnRH) (ng/mL), serum LH levels increased to 100 ± 35%, whereas in lead-treated rats, it rose significantly to 900 ± 380%. These results clearly illustrate the effects of lead exposure on hormonal levels and reproductive function (Al Sukaiti, *et al*., 2023).

Effect on development and pregnancy. Neurodevelopmental effects from prenatal and early childhood exposures to even low levels of lead have been noted and may represent the most significant endpoint for lead toxicity (Bellinger *et al*., 2018). Fetuses of exposed females are at high risk for adverse effects of lead, although the specific mechanisms of lead toxicity during the prenatal period are not fully understood, especially at low exposure concentrations. Some evidence suggests that lead stored in bone throughout one's lifetime may be mobilized during pregnancy, particularly in females who smoke or have low calcium intake (Gundacker *et al*., 2021). Lead has long been known to readily cross the placenta (Virgolini and Aschner, 2021). Reports of pregnant women occupationally exposed to high concentrations of lead in England, Hungary and other countries in the early part of the 20th century documented increases in spontaneous abortions, stillbirths, premature births and neonatal deaths compared to non-exposed mothers (Babadjouni *et al*., 2017). Lower exposure studies have found varied associations with birth weight and prematurity. As given in Fig. 3 that lead have serious concern for pregnancy and developmental toxicity. There was a higher incidence of spontaneous abortion among females who had experienced childhood lead poisoning themselves but only some studies have demonstrated associations with lower concentrations of lead, such as those found in the general population in many urban areas worldwide. The results were mixed, with some studies suggesting an association and others showing no association (De Carvalho Machado and Dinis-Oliveira, 2023).

Methodological issues in these studies, particularly regarding exposure assessment, hinder analysis (Lee *et al*., 2022). Once blood lead levels reach moderate levels, there is an increased risk of spontaneous abortion. Clinical reports describe an elevated incidence of spontaneous abortion among female employees as well as the wives of male lead workers (Boskabady *et al*., 2020). Epidemiological and clinical studies are needed to evaluate potential associations between lead exposure in early childhood and chronic neurological disorders such as Parkinson's disease, amyotrophic lateral sclerosis, and dementia (Natasha *et al*., 2020).

Lead as carcinogenic agent. The EPA categorizes lead as a probable carcinogen in human and aquatic animals (WHO, 2010), while also causing other non-carcinogenic diseases in humans (Flora and Agrawal, 2017). Carcinogenesis results from a combination of these complex interactions. Lead cations facilitate the addition of nucleotides in the daughter strand of DNA, produced in laboratories from polynucleotide templates using DNA polymerases of microbial origin (Boskabady *et al*., 2018). The International Agency for Research on Cancer evaluation has classified inorganic lead compounds as carcinogenic to humans, whereas organic lead compounds are not classified as carcinogenic to humans. Lead exhibits mutagenic properties to some extent but it also interferes with DNA repair in vitro and interacts with other mutagens. Several cytogenetic studies of exposed workers have shown increases in chromosome abnormalities or sister chromatid exchanges, with some observations showing positive exposure-response trends. There have been eight reports of cancer mortality or occurrence among highly exposed workers, most of whom were lead smelter or battery exposed workers (Rãdulescu and Lundgren, 2019).

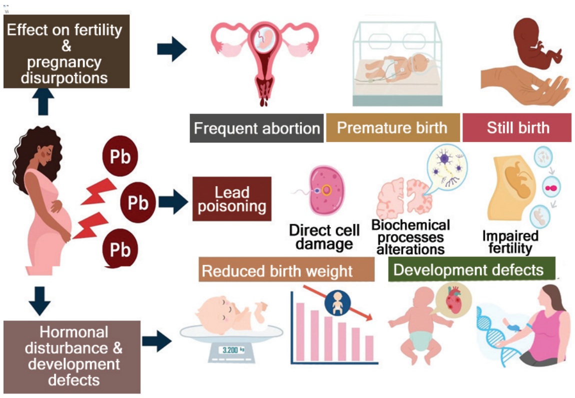

Fig. 3. Lead influences over pregnancy, fertility and development within living beings (Gundacker *et al*., 2021).

Effect on cardiovascular system. Lead poisoning can result in anemia, characterized by reduced red blood cell (RBC) lifespan and diminished hemoglobin production (Sani and Amanabo, 2021). Lead can abbreviate the lifespan of RBCs by hindering sodium-potassium ATPase and pyrimidine-5’ nucleotidase, disrupting RBC membrane stability through alterations in energy metabolism (Kshirsagar *et al*., 2016) and reducing hemoglobin production by inhibiting specific enzymes in the biosynthetic pathway such as ALAD, ferrochelatase and coproporphyrinogen oxidase (Alwaleedi, 2016). Inhibition of ferrochelatase leads to reduced hemoglobin synthesis and an increase in protoporphyrin. Erythrocyte protoporphyrin binds with zinc at the iron-binding site, forming ZPP (Slota *et al*., 2021). Elevated blood pressure stands out as perhaps the most sensitive health effect observed in lead poisoning. Several epidemiological studies have established a notable association between increased blood pressure and lead accumulation in the body (Saganuwan, 2022).

Lead poisoning can result in anemia, marked by decreased red blood cell (RBC) longevity and reduced hemoglobin production (Kargar-Shouroki *et al*., 2023). Lead can shorten the lifespan of RBCs by inhibiting enzymes like sodium-potassium ATPase and pyrimidine-5′ nucleotidase, disrupting RBC membrane stability through alterations in energy metabolism (Shiek *et al*., 2021). Additionally, lead hampers heme production by blocking enzymes in the biosynthetic pathway, including ALAD, ferrochelatase and coproporphyrinogen oxidase (Saganuwan, 2022). The inhibition of ferrochelatase results in decreased heme synthesis and an elevation in protoporphyrin levels. Protoporphyrin within erythrocytes forms complexes with zinc at sites typically occupied by iron, forming ZPP (Kargar-Shouroki *et al*., 2023).

High blood lead levels present a significant health hazard, particularly in children, emphasizing the importance of regular monitoring to mitigate lead exposure (Büsselberg, 2016). A study examining blood lead levels in school-going children in Egypt involved 400 children aged 6-12 years from two regions, industrial and urban. Detailed questionnaires on sources of lead exposure, school routines, and any interactive variations were collected. In the urban area of Egypt (Dokki), the mean blood lead level was 5.45 ± 3.90 µg/dL, while in the industrial area (Helwan), it was 10.37 ± 7.94 µg/dL. A notable association was found between children displaying atypical behaviour and pallor with blood lead levels ≥ 10 µg/dL. Residents of the industrial area, individuals with poor health habits and those residing in environments with higher exposure faced a heightened risk of having blood lead levels ≥ 10 µg/dL (AbuShady *et al*., 2017). Elevated blood pressure is a highly sensitive health effect observed in lead poisoning (Büsselberg, 2016). A case study conducted in Kosovo from 1985 to 1998 in the mining town of Mitrovica and the control town of Prishtina, involving 101 individuals including pregnant females, revealed high blood lead levels in the mining town compared to the control town, leading to hypertension among exposed individuals (Pashko *et al*., 2018).

Outbred male rats were repeatedly injected intraperitoneally with sub-lethal doses of lead acetate and cadmium chloride three times a week for six weeks. The animals exhibited clear signs of subchronic intoxication, characterized by various indices, with an increase in DNA fragmentation coefficient indicating genotoxicity (Lee *et al*., 2022). The effects of lead and cadmium on blood pressure were opposite to each other. Lead-exposed rats showed an increase in systolic, diastolic and mean arterial pressure, along with a decrease in heart rate. This arterial hypertension was associated with systemic increase in resistance to blood flow and reduced blood flow. Additionally, hypertrophy in left ventricular cardiomyocytes was observed, with mean thickness greater compared to the control group (Klinova *et al*., 2020).

Renal damage and hepatoxicity by lead. Exposure to lead acetate in rats resulted in renal tissue damage characterized by shifts in oxidative and antioxidative equilibrium. This includes a decrease in antioxidant proteins such as glutathione, glutathione reductase, glutathione peroxidase, catalase and superoxide dismutase, alongside an elevation in oxidants like lipid peroxidation and nitric oxide. Moreover, an increase in kidney inflammatory markers, such as tumor necrosis factor-alpha, interleukin-1 beta and nuclear factor kappa B, is observed, associated with the upregulation of inducible nitric oxide synthase. Additionally, impairment of apoptotic-regulating proteins is also evident (Abdel-Daim *et al*., 2020).

Liver damage resulting from heavy metals, including lead toxicity, encompasses various effects. The accumulation of lead in liver cells disrupts molecules in the membrane, leading to integrity loss and tissue damage. Exposure to lead increases the generation of reactive oxygen species (ROS) in hepatocytes. Although lead itself does not directly generate free oxygen radicals, the process of lipid peroxidation induced by lead contributes to ROS generation. Prominent radicals involved in oxidative stress caused by lead in the liver include superoxide, hydroxyl, peroxyl, alkoxyl, singlet oxygen and hydrogen peroxide (Dong *et al*., 2019; Singh *et al*., 2018; Hasanein *et al*., 2017). Reduction in intracellular antioxidant radicals contributes to lead-induced hepatotoxicity by inhibiting enzymes such as glutathione reductase and glutathione peroxidase and reducing levels of different antioxidants such as malondialdehyde and superoxide dismutase (Almasmoum *et al*., 2019). Lead disrupts gene transcription, affecting NOX2 and CYP2E1 among others. Lead toxicity induces various additional changes, including DNA hypomethylation and hypermethylation, mitochondrial stress leading to alterations in the electron-transport chain, activation of the IRE1-JNK pathway, and endoplasmic reticulum stress. It also leads to nuclear pyknosis, inflammation, overexpression of NF-κB, variation in the expression of CYP7A1 genes and HMGR, resulting in alterations in cholesterol metabolism and hepatocytic necrosis. Furthermore, lead toxicity dysregulates both pro-inflammatory and anti-inflammatory cytokines (Renu *et al*., 2021).

Possible treatment of lead poisoning using natural sources. Various bio-protectants have been investigated for their potential therapeutic effects in alleviating lead toxicity in rats. These include apple pectin (1 g/Kg in fodder), sodium glutamate (160 mg/rat: 1.5% drink instead of water), N-Acetylcysteine (30 mg in fodder), Vitamin C (3.0 mg in fodder), Vitamin E (0.27 mg in fodder), Vitamin D3 (1.78 mcg in fodder), Vitamin A (35.2 mg in fodder), Vitamin B1 (0.04 mg in fodder), Vitamin B2 (0.04 mg in fodder), Vitamin B6 (0.04 mg in fodder), rutin (1.4 mg/rat in fodder), selenium (1.38 mcg in fodder), omega^{-3} rich polyunsaturated fatty acids (13.3 mg in fodder), iodine (4.1 mcg in fodder), calcium (160 mg in fodder), iron (0.38 mg in fodder) and magnesium (2.08 mg in fodder). Administration of these bioprotectants demonstrated promising morphometric indices of kidney cells, suggesting a reduction in nephrotoxicity induced by lead exposure (Abdel-Daim *et al*., 2020).

Additionally, extracts from *Moringa oleifera* were found to alleviate the toxicity induced by lead acetate in rats. Treatment with *Moringa* extracts resulted in the restoration of redox homeostasis, inhibited inflammatory responses, and reduced apoptotic responses in kidney tissue (Abdel-Daim *et al*., 2020). Xanthones derived from the tropical fruit *Garcinia mangostana* have extensive pharmacologic attributes and have shown protective effects against lead-induced chronic kidney damage. This protective mechanism is attributed to the activation of Nrf-2 and modulation of the NF-kB and MAPK pathways (Rana *et al*., 2020). Furthermore, garlic and vitamins C and E have demonstrated therapeutic roles against lead-induced toxicity in various organs (Mumtaz *et al*., 2020). Similarly, studies by Rana *et al*. (2018) have indicated that plants and plant-derived compounds can mitigate the nephrotoxic effects of lead, cadmium, mercury and arsenic. Moreover, a system-based logic model for reducing lead exposure through consumer products and drinking water has been proposed, which may guide further actions to address lead toxicity (Pfadenhauer *et al*., 2016).

Lead contamination in soil, water and crops. The presence of lead significantly impacts groundwater quality, as reported by Khan *et al*. (2016). Heavy metals, including lead, accumulate in surface soils due to wastewater irrigation, resulting in decreased retention capacity over time (Singh *et al*., 2018). This process can lead to the release of lead into groundwater and soil solutions, subsequently absorbed by plants and entering the food chain, posing health risks to humans (Slota *et al*., 2021). Lead accumulation occurs not only in soil and crops but also in groundwater and organisms (Flora and Agrawal, 2017). Moreover, industrial and urban wastewater, often discharged untreated into rivers and the Arabian sea, contains toxic metals such as mercury, cadmium, chromium, lead, arsenic and zinc, as highlighted in studies on effluent, river and seawater quality (Education for Environment and Biodiversity in Pakistan).

According to various guidelines, standard values for lead concentration in water vary, the World Health Organization (WHO) recommends a limit of 0.01 mg/L or 10 µg/L, while the US Environmental Protection Agency (EPA) guidelines suggest no detectable lead in drinking water. Additionally, the National Environmental Quality Standards (NEQS) guidelines for drinking water set a limit of 0.05 mg/L for lead. For air quality, WHO guidelines for Europe recommend an annual average limit of 0.5 µg/m^3. The European Economic Community (EEC) allows a maximum permissible limit of 50-300 mg/Kg of lead in soil. In coastal areas of Pakistan, elevated levels of lead have been detected in sediment samples, with concentrations reaching 121 mg/Kg in coastal sediments of the Arabian sea near urban Karachi and 49.5 mg/Kg in the surface sediments of the Lyari river. Regarding vegetable contamination, the European Union sets permissible limits of 0.1 to 0.3 mg/Kg for lead. In Pakistan, lead concentrations in various plant species have been observed to range between 0.03-44 mg/Kg, with the highest concentrations recorded in M. sylvestris from Gilgit.

Another study found average lead concentrations of 27.49 mg/Kg and 15.58 mg/kg in the edible and leafy parts of vegetables, respectively. A significant portion (83%) of the vegetable specimens exceeded the safety threshold set by the European Union. Regarding groundwater quality in Pakistan, a comprehensive study showed that 1% of groundwater samples exceeded the standard limit for lead set by the World Health Organization. Individual research studies have reported maximum lead concentrations in groundwater of 70.2 mg/L in Charsada, 0.81 mg/L in Punjab (Sialkot) and 2 mg/L in Sindh (Karachi). Lead contamination in Pakistan raises significant concerns, as highlighted by case studies presented in Table 1.

Possible natural techniques for lead removal in drinking water. Several standardized techniques are available for eliminating heavy metal pollutants from wastewater, including precipitation, electroplating, chemical coagulation, ion exchange, membrane separation and electro-kinetics (Devi *et al*., 2021). However, these methods often involve high operational costs. In recent years, increasing environmental awareness in both public and regulatory spheres have emphasized the need for treating industrial effluents. Many studies

Table 1. Case studies of lead contamination in drinking water of Pakistan

Sample type	Location	Amount of lead	Source of contamination	Reference
Tubewell water of Korangi (n=4)	Korangi, Karachi	Industrial effluents cause 0.24 mg/L of lead in tubewell water of Korangi. Mahmood *et al*. (1998) reported the levels of Lead was slightly above the WHO guidelines for drinking water in groundwater of Korangi industrial area in Karachi with amount of 30 µg/L	Industrial effluents	(Amin *et al*., 2013; Mahmood *et al*., 1998)
Surface water	Various sites of river Ravi (n=5)	0.0004–0.0017 mg/L of lead	-	(Tariq *et al*., 1994)
Sample of groundwater (Wells)	Three town's (Mian Khail, Mer Ahmad Khail and Gari Banurian)	Concentration of lead was higher in Mian Khail town. Lead was within the allowable limits set by the Pakistan Environmental Protection Agency (PAK EPA) and WHO guidelines.	Sewage seepage to water reservoirs by rainwater runoff to wells	(Muhammad *et al*., 2017; Iqbal *et al*., 2014; Khan *et al*., 2008)
	drinking water sources (wells) of Kohat city of Pakistan			
Soil sample of various depth	Village of Quetta named as Killi shahozai, situated in south-west direction of Quetta	Within the 0-15cm soil depth of wastewater-irrigated area, Lead accumulated at the surface with concentration of 19.7 mg/Kg of soil, while at the depth of 15-90cm of soil, concentration reduced to 8.2 mg/Kg of soil. While in freshwater irrigated area, no accumulation of Lead at surface observed. The observed value was 7.9 mg/Kg of soil at 0-90cm soil depth; which is lower as compared to wastewater-irrigated area. Level of Lead was within the EEC-MP limits.	Untreated wastewater irrigation	(Khalil and Kakar, 2011)
Samples of fish from river Ravi	Two sites selected for study: site A was Head Balloki at the river Ravi and B was fish farms at Manawan for comparison	The lead's amount was high in the eatable fishes of site B in comparison to site A's edible and non-edible fishes. *Labeo rohita* was containing highest level of 4.40 µg/g. non-edible fishes of site A have shown intermediate level. While the lowest level found in *C. fasciata* (1.9 µg/g)	-	(Nawaz *et al*., 2010)
Ground water	Urban areas of Karachi	Lead was present within the WHO permissible limits with mean concentration of 0.006 mg/L in pre-monsoon period and 0.0065 mg/L in post-monsoon period.	Infiltration cause storm water to mobilize migrates and accumulates in groundwater. So, samples analysed before and after the monsoon.	(Zubair *et al*., 2008)
Ground water	Other areas of Karachi	Various spots in Karachi identified having 2 mg/L of lead.	Domestic, industrial, and commercial wastewater leaching to groundwater.	(Chilton *et al*., 2001; Rahman *et al*., 1997)
21 vegetables (n=210) collected from fields of farmers in Sindh and Karachi	Karachi	Maximum concentration was present in leafy vegetables (coriander) (0.15 µg/g) and minimum concentration in root and tubers (0.001 µg/g). (Parveen *et al*., 2003) identified the same trend of occurrence of Lead within the vegetables. Concentration of Lead was within the allowable range (0.2 µg/g)	Disposal of unprocessed domestic and industrial effluents and unskilled use of fertilizer, pesticide and insecticides	(Abbasi *et al*., 2015; Bhutta *et al*., 2002)

Different depths was selected within the 3 km of each side of Hudiara (n=33)	Hudiara industrial drain of Lahore, Pakistan; lies within the Indus plain	Amount of lead were not in detectable range at Hudiara. Lahore's agrochemicals and domestic waste leach down cause 0.003-0.26 mg/L of lead in water.	Agrochemicals and domestic waste leach down	(Sultana *et al*., 2014: Khattak *et al*., 2012; Farooqi *et al*., 2007)
Samples of water and fishes	Water bodies belonging to the Indus river from the northern sites of Gilgit-Baltistan to the lower regions of Sindh	Water bodies contaminated with the lead at significant quantity. At Jamshoro site, lead was observed in fresh water fishes	-	(Arain *et al*., 2007; SAFWCO, 2003)
Well water	Multan (n=3) and Muzaffargarh (n=49)	No evidence of lead	Natural geogenic source in Multan and in Muzaffargarh, natural hydrothermal volcanism and oxidation of minerals	(Nickson *et al*., 2005)
Groundwater	Nowshera; Amangarh Industrial Estate (AIE) is the area with a lot of paper, textile, ceramics, tanneries, and ghee industries.	Lead levels were <0.02–0.3 mg/L in the study region with maximum levels (0.3 mg/L) in dug well water in the AIE region. Groundwater may have greater levels of Pb contamination than surface water.	Plumbing, industrial sewage; agricultural practices and local geology	(Sardar *et al*., 2015)
Surface water of Bara River (n=9) and canal water (n=9)	Nowshera district, Akbarpura	0.34-0.43 mg/L of lead found at Canal water and 0.43-0.62 mg/L was recorded at Bara river	Industrial effluents	(Nazif *et al*., 2006)
Groundwater	Islamabad and Rawalpindi	90% of children with 1-5 years in Rawalpindi detected to have 10 µg/dl Ï ¹ of lead in blood.	Polluted drinking water due to disposal of unprocessed domestic and industrial effluents and unskilled use of fertilizer, pesticide and insecticides	(Sabiha *et al*., 2008; Bhutta *et al*., 2002)
Groundwater and air sample	Sialkot	Amount of Lead in water supply of Sialkot (n=25) was in the range of 0.11-0.81 mg/L. Amount of lead was found in the air of Sialkot.	Leather, surgical instrument and tanneries waste	(Abbasi, *et al*., 2015: Ullah *et al*., 2009)
Two normally grown vegetables: Okra and Brinjal were examine. 30 soil samples, 60 vegetable samples and 30 irrigation water samples taken	Three selected sites of Multan were Kot Abdul Fateh, Hamroot and Mozu Alamgir; given the wastewater, tube-well and underground water in respective manner.	All the samples of soil, vegetables and irrigation water polluted with lead with range exceeding the maximum residual limits (MRLs). Lead was highly accumulated in both of the vegetables.	Irrigation water of sewage sources	(Randhawa *et al*., 2014)

Groundwater	Bahawalpur	Lead was present within the permissible limits of WHO standard (0.01 mg/L) with mean concentration below 0.01 mg/L in 20 ground water samples taken from different parts of the city.	-	(Mehmood *et al*., 2012)
Groundwater (n=32)	DG Khan	No evidence of lead	Natural geogenic sources and agrochemicals leachdown	(Malana and khosa, 2011)
Tubewell and dug-wells of Hayatabad; soil and vegetables	Hayatabad and other areas of Peshawar	Lead was present in urban and rural drinking water; soil and vegetables. Mahmood *et al*., 1990 found levels of Lead upto 9 µg/L in tubewell water. Pharmaceutical, textile and oil industrial waste cause 0.2-0.97 mg/L of lead in water, while glass rubber, plastic and textile industries waste cause 0.3-1.11 mg/L of lead in water source (Jan *et al*., 2009).	Pharmaceutical, textile and oil industrial waste; glass rubber, plastic, and textile industries waste	(Khan *et al*., 2016; Waqas 2014; Khan *et al.,* 2013; Jan *et al*., 2009; Tariq *et al*., 2006; Mahmood *et al*., 1990)
Shallow wells (n=13) and deep wells (n=3) near Palosi drain Peshawar; surface water (n=4)	Palosi drain Peshawar	Shallow wells near Palosi drain Peshawar have 0.27-0.38 mg/L of Lead and while deep wells near Palosi drain Peshawar have 0.49 mg/L of lead, while in surface water, 0.34 mg/L of lead observed	Industrial effluent discharge and dissolution of naturally occurring rocks	(Ilyas and Sarwar, 2003)
Drinking water of Narangi and tubewells in Gadoon (n=3)	Gadoon Amazai Industrial Estate (GAIE) Swabi, and Narangi	Drinking water in Narangi and the surrounding regions of Swabi district showed that the physical parameters were within permissible limits greater for chemical parameters than the WHO limits: Pb and nitrite concentrations. Swabi's textile and leather industries waste cause 0.21- 1.20 mg/L of lead in water.	Industrial effluents	(Nasrullah *et al*., 2006; Tariq *et al*., 2015)
Groundwater	Sheikhupura	The concentration of lead in water samples was 0.03 to 9.76ppb.	Disposal of unprocessed domestic and industrial effluents and unskilled use of fertilizer, pesticide and insecticides	(Hassan, 2014)
Water samples	Jamber Khurd, union council of Tehsil Pattoki in district Kasur of Punjab.	Amount of Lead in 91 samples was containing 0.1-0.35 mg/L which is fit for usage, 73 samples was containing 0.36-0.70 mg/L which is marginally fit, while 36 samples was containing 0.71-1.05 mg/L which is unfit for use. In other study, 68 well-water samples from residential area of Kasur analysed. 0.003-0.26 mg/L of Lead detected. Kasur's sugar, glazed pottery, embroidery and textile industries cause 0.11 mg/L of lead in water.	Unprocessed effluents of industries into water bodies	(Ashraf *et al*., 2010; Tariq *et al*., 2008)
Water samples of tube wells of various depths	Pishin, located in the North West of Balochistan	Lead was present in all 50 freshwater samples but in amount 0.001 mg/L to 0.0078 mg/L below the recommended values. Its contents were present at almost equally in all depths of tube wells.	-	(Tareen *et al*., 2014)

Soil samples taken from various sites at eastern, western and southern sides of the produced water ponds of industry	Fateh Jang Sadqal oil and gas field, near Rawalpindi Islamabad.	The wastewater of industry emitted into the ponds 1km away near residential site. The surplus amount of water flow out into the stream. Amount of lead in all directions from ponds found to exceed the limit of reference soil	By seepage, wastewater make its way into the soil.	(Khan *et al*., 2015)
Tubewell water	Hasanabdal	0.03 mg/L of lead in water observed.	Improper disposal of domestic and industrial waste	(Lone *et al*., 2003)
Well water (n=8)	Charsadda and Risalpur, KPK	Natural geogenic sources and industrial waste leach down cause 0.33 mg/L of lead in water. Agrochemical use in agricultural lands and industrial waste (paper, sugar and leather) cause 70.2 mg/L of lead in water.	Natural geogenic sources, industrial waste leach down, agrochemical use in agricultural lands	(Khan *et al*., 2013; Midrar ul haq and Hajikhan Punu, 2005)
Groundwater	Chakera, Faisalabad	0.12 mg/L of lead in water	Textile, dyeing, and thread industries waste leach down	(Mahmood and Maqbool, 2006)
Water sample	Haripur	0.001 mg/L of lead in water	Fertilizer, chemicals and oil manufacturing industries waste	(Sial *et al*., 2006)
Water sample	Gujranwala	Electrical machines, furniture, and pharmaceutical industrial waste cause 0.09-0.35 mg/L of lead in water	Electrical machines, furniture, and pharmaceutical industrial waste	(Khan *et al*., 2013)
Water sample	Kohistan region, Gilgit Baltistan	0.04 mg/l of Lead found in water. Lead concentration was below permissible level of Lead (50–300mg/kg) in soil on which European Union (Radojevic and Bashkin, 2006) applies sewage sludge. The exception to the case was higher amount of Lead (103000mg/kg) at the contaminated soil involved in mining actions with mean reference soil value of 70 mg/kg at Kohistan region, Gilgit Baltistan.	Natural presence of mafic and ultramafic rocks and anthropogenic activities	(Muhammad *et al*., 2011; Radojevic and Bashkin, 2006)
Water sample	Buner	1.2 mg/L	Industrial effluents	(Khan *et al*., 2012)
Water sample	Swat	0.07 mg/L	Natural presence of mafic and ultramafic rocks and mining activities	(Khan *et al*., 2013)
Water sample	Kilasaifullah	Presence of natural minerals and fluvial setting cause 0.02- 0.06 mg/L of lead in water.	Natural minerals and fluvial setting	(Umar *et al*., 2013)
Groundwater	Hattar Industrial Estate (KPK)	Many groundwater samples surpassed the standard value with amount of 0.26 mg/L. Samples from three textile sectors situated in Hattar Industrial Estate, KPK, recorded the largest Pb contamination (2.34 mg/L).	Industrial effluents	(Manzoor *et al*., 2006)

Water sample	Pearl valley of Azad Jammu Kashmir	Dissolved amount of lead in samples obtained from was 1.8-4.7 mg/L. Comparison with WHO reference value guidelines has shown that the amount of lead was 46% greater in water samples obtained from the well at Kharick II in South of Azad Jammu and Kashmir.	-	(WHO, 2011; Javaid *et al*., 2008)
Water sample	Tharparker	No evidence of Lead	Natural geogenic sources and high rate of evapotranspiration	(Chellaney *et al*., 2013)
Water sample	Mailsi	0.02-0.16 mg/L	Natural geological and climatic factors	(Rasool *et al*., 2016)
Surface water	Tarbela reservoir	0.107 mg/L	-	(Ashraf *et al*., 1991)
~~Surface water~~	~~Chashma reservoir~~	~~0.058 mg/L~~	~~-~~	~~(Ashraf *et al*., 1991)~~
Surface water	Lloyd reservoir	0.107 mg/L	-	(Ashraf *et al*., 1991)
Surface water	Different sites of KPK (n=16)	0.02-0.38 mg/L	-	(Midrar-Ul-Haq *et al*., 2005)
Surface water	Malir river, Karachi (n=8)	0.09-0.32 mg/L	Disposal of unprocessed domestic and industrial effluents	(Midrar-Ul-Haq *et al.,* 2005; Bhutta *et al*., 2002)
Surface water	Kalarkahar lake, Chakwal	0.01-0.30 mg/L	-	(Raza *et al*., 2007)
Surface water	Manchar lake (n=9) and Sehwan (n=3) Jamshoro, Sindh	0.004–0.0096 mg/L at Sehwan and 0.0057–0.014 mg/L of lead at Manchar lake	Fertilizers leaching in agricultural lands	(Mastoi *et al*., 2008; Arain *et al*., 2007)
Groundwater	Basin of Zhob river	0.02-0.06 mg/L	-	(Umar *et al*., 2009)
Groundwater	Taluka daur, Nawabshah, Sindh (n = 38)	0.006–0.053 mg/L	-	(Majidano and Khuhawar, 2009)
Surface water	Kabul river, Peshawar	0.52 mg/L	-	(Ullah *et al*., 2009)
Surface water	Phulali canal, Hyderabad (n = 6)	0.026 mg/L	-	(Wattoo *et al*., 2006)
Surface water	Warsak dam	0.009 mg/L	-	(Yousafzal *et al*., 2008)

have been conducted to identify cost-effective approaches for removing contaminants from wastewater (AbuShady *et al*., 2017). The adsorption process for removing heavy metal ions from solution has gained significant attention. Natural materials, either abundantly available or derived from agricultural activities, serve as low cost adsorbents due to their widespread availability and eco-friendly nature. Numerous studies have explored the utilization of agricultural products for removing heavy metal ions, emphasizing their cost-effectiveness and efficiency (Devi *et al*., 2021). Adsorption techniques have emerged as highly efficient and attractive due to their cost-effectiveness and enhanced efficacy in eliminating heavy metal ions from wastewater. Various physico-chemical techniques have been proposed for the removal of these pollutants from industrial effluents. Adsorption, extensively employed in the industrial sector for water and wastewater treatment, is recognized as an effective method for purification and separation. Urgent action is required to ensure the safe supply of drinking water, starting with the establishment of quality standards mandated under the Pakistan Environment Protection Act, 1997. Adsorption stands out as a remarkably efficient method for purifying and separating lead in industrial sectors, particularly in water and wastewater treatment (Sani and Amanabo, 2021).

Various inexpensive natural adsorbents, including ores, rocks, plant straw and dried aquatic plants which have demonstrated efficacy in treating water contaminated with heavy metals (Dong *et al*., 2019). Coagulants such as alum, often used in conjunction with ferric chloride, have been utilized for wastewater treatment. Lime and sodium carbonate are commonly employed alkalis for environmental management, particularly in wastewater treatment (Abdel-Daim *et al*., 2020). Pyrolusite has been investigated for its capacity to adsorb Pb, Zn and Mg ions from aqueous solutions (Dong *et al*., 2019), while zeolites have proven effective in removing heavy metals from wastewater (Singh *et al*., 2018). Activated carbons derived from date pits and methods involving ferrite and chelating resin have shown potential in adsorbing heavy metal ions from polluted water (Renu *et al*., 2021). Research has explored the potential of clay surfaces for adsorbing Pb(II), with kaolinite and alumina utilized for the removal of Pb(II) from water and incinerated lubricating oil (Sani and Amanabo, 2021). Coffee has also been examined for its capability to remove heavy metals like lead, copper, mercury, cadmium and zinc from drinking water (Hasanein *et al*., 2017).

Agricultural by-products have been investigated as potential adsorbents for heavy metals due to their selectivity for metal ions (Boskabady *et al*., 2018). Materials such as banana and orange peels, activated carbon, tea residues, eggshells, mineral blends, rice husks, nut shells, maize cobs, coconut husk fibres, natural bentonite, clay aggregates, bamboo dust, fly ash, zeolite and modified hollow fibers have been employed for managing industrial waste (Boskabady *et al*., 2018). Furthermore, rice straw and sugarcane bagasse have been examined as adsorbents for metal ions in aqueous solutions (Ashraf *et al*., 2010). These adsorbents aim to effectively remove higher concentrations of toxic metal ions in shorter time frames (Hannachi *et al*., 2010). It is imperative to take proactive measures by formulating necessary strategies to ensure the safe provision of drinking water to the population. Establishing drinking water quality standards is crucial, with enforcement mandated under the Pakistan Environment Protection Act, 1997.

In urban areas, ensuring a consistent water supply, rather than intermittent and it is crucial to mitigate contamination risks. Oversight agencies responsible for public water supply in urban regions must conduct regular monitoring of water quality to ensure its safety. Existing laboratories need upgrades in terms of staffing and equipment. Prioritizing the monitoring of urban shallow groundwater is necessary and as it is mainly used by private suppliers. In rural areas, monitoring of shallow groundwater is necessary to assess the impacts of fertilizer and pesticide use (Sani and Amanabo, 2021). Addressing the illegal disposal of industrial effluents into groundwater through soakage pits is essential and research centers should develop cost-effective water treatment technologies. Mass media campaigns should be utilized to raise awareness about the importance of safe drinking water, particularly for vulnerable populations prone to water contamination (Maimoona *et al*., 2017).

Water quality standards such as the National Environmental Quality Standards (NEQS) should be enforced for large industrial sites that discharge significant volumes of wastewater into rivers. The Pakistan Environment Department must implement strict measures to prevent industrial units from discharging effluents directly into rivers and drains without proper treatment.

It is essential to develop appropriate drainage systems to mitigate the risks of leakage, overflow and wastewater accumulation in drains (Ashraf *et al*., 2010). Establishing comprehensive monitoring networks in both urban and rural areas is necessary to ensure accurate assessments of water quality, enabling appropriate management of treatment plants where required. Decentralizing power from the national to the local level is crucial for maintaining groundwater quality locally. Provincial drinking water guidelines should empower Tehsil Management Authorities (TMAs) to monitor and maintain water quality at the local level, delegating control and resources to union council-level sites to improve management of water quality in rural and isolated areas. This approach should provide comprehensive information and address research concerns related to water quality-associated health hazards (Maimoona *et al.,* 2017).

In urban areas, renovating aging water supply infrastructure proves effective, while the installation of central filtration plants in water storage tanks presents a cost-efficient solution. Increasing the allocation of funds for the proper operation of filtration plants, regular water quality checks and personnel training is paramount (Maimoona *et al*., 2017). Measures should be implemented to prevent industrial effluent dumping into water sources, with industries mandated to adhere to effluent release standards. Establishing central waste processing plants near industrial areas emerges as an economically feasible option. It is imperative to prevent cross-contamination by maintaining a distance between sewage and drinking water pipelines. Educating farmers about safe pesticide use and appropriate fertilizer application is necessary to reduce the contribution of agricultural activities to water pollution (Azizullah *et al*., 2011).

Conclusion and future perspectives. Lead is classified as a xenobiotic due to its lack of utility in the body and significant toxicity even at low levels. Elevated concentrations of lead pose severe risks to livestock, humans, and plants, making it a major environmental concern. Its water solubility exacerbates its environmental impact, leading to contamination of groundwater and other water sources. Given the pervasive nature of lead contamination and its detrimental health effects, effective source control measures are crucial for mitigating the issue. Understanding the mechanisms of lead exposure and toxicity can aid in identifying and targeting sources of contamination more efficiently. Future perspectives in addressing lead toxicity involve the development and implementation of innovative remediation technologies and regulatory measures. Nanotechnology, bioremediation and phytoremediation offer promising approaches for removing lead from the environment. Additionally, promoting public awareness, education and community engagement initiatives can help prevent lead exposure and mitigate its adverse effects. Furthermore, ongoing research efforts should focus on biomonitoring, surveillance and risk assessment to better understand the extent of lead contamination and its impact on human health and the environment. Collaborative interdisciplinary approaches involving scientists, policymakers and community stakeholders will be essential for developing comprehensive strategies to address lead toxicity effectively.

The existing literature reveals several critical aspects of lead contamination in groundwater, soil and crops, along with its subsequent implications for human health. However, there are notable research gaps that warrant further investigation. One significant research gap lies in the need for comprehensive studies to assess the extent and distribution of lead contamination in various regions of Pakistan, while some studies have focused on specific areas, there is a lack of nationwide assessments to provide a holistic understanding of the problem. Such studies could help identify hotspots of contamination and inform targeted mitigation strategies. Additionally, there is a need for longitudinal studies to evaluate the long-term effects of lead exposure on human health, while existing research highlights the immediate health risks associated with lead contamination, longitudinal studies tracking exposed populations over time could provide valuable insights into the chronic health effects and potential disease outcomes associated with sustained lead exposure. Furthermore, there is limited research on effective remediation strategies for reducing lead contamination in soil and groundwater. Developing and evaluating novel remediation techniques tailored to the local context could help mitigate the environmental and health risks posed by lead contamination. Overall, addressing these research gaps is essential for developing evidence-based policies and interventions to mitigate lead contamination and protect public health in Pakistan.

Conflict of Interest. The authors declare that they have no conflict of interest.

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