ARSENIC IN DRINKING WATER IN PAKISTAN AND ASSOCIATED HEALTH RISKS

Mehwish Niazi.
MSc (Zoology) University of Sargodha Sub-Campus Mianwali, Pakistan.

This paper first reviews the arsenic nature, and its mobilization in environment. Arsenic is a significant element of earth crust and also in a human body. General sources of arsenic are air, food, cigarette smoke and beverages. Being soluble in water it exists in ionic forms and affects the humans who consume arsenic contaminated water. Its effects are severe and long lasting. Pakistan is one of those countries where most of the ground water is contaminated with arsenic. Different organizations such as World Health Organization, International Agency for Research in Oncology & International Agency for Research in Cancer and the United States Environmental Protection Agency has set up the maximum permissible value of arsenic in drinking water for various countries. IARC has ranked arsenic a group 1 human carcinogen which causes lung, bladder and urinary cancers. In Punjab (Pakistan) 20% of population is exposed to over 10 µg/L in drinking water and 3% of population is exposed to over 50 µg/L and in Sindh 36% of population is exposed to arsenic via drinking water. In Punjab and Sindh drinking water is contaminated with arsenic above the permissible value defined by World Health Organization (WHO), while KPK is less affected. Baluchistan is almost safe from arsenicism.

Introduction:

Being universal element arsenic is present in abundance in earth’s crust and positioned as 20th in earth’s crust, 14th in seawater and characterized as 12th abundant element in human body. (Khan and Ho, 2011). Various natural processes such as weathering reaction, biological activities, anthropogenic activities and volcanic emanations are involved in mobilization of arsenic in environment (Toor and Tahir, 2008). Earth crust contains high level of arsenic due to which arsenic can easily leach in to the underground water (Kaltreider et al., 2001).

Water is most fundamental element in life like oxygen without it we could die in few days. More than two thirds of human body is comprised of water; brain consists of 95 % water while 82 % and 90 % water exists in blood and lungs (Tareen et al., 2013). As Arsenic is soluble in water it subsists in two primary forms: arsenite (As+3) and arsenate (As+5). Both these forms are toxic and have severe and long lasting effects to a wide variety of organisms including humans also (Abbas and Cheema, 2015).

General sources of organic or inorganic arsenic exposure are air, food and beverages and fundamental source is drinking water. International Agency for Research on Cancer (IARC) classified arsenic as human carcinogen of skin
and lung, and it is attributed to cancer of digestive and urinary systems also (Chen; 1992). Humans are exposed to arsenic via inhalation of dust particles and by ingestion through drinking water (Rich et al., 1996).

It is reported that arsenic concentration in well waters ranges from 0.01 to 1.82 mg/L, which is approximately 0.5 mg/L (Pershagen, 1981). It is reported that at some places in Punjab and Sindh province the level of arsenic in drinking water is beyond the acceptable limit defined by World health organization (WHO) which is (10 μg/L) (Khattak et al., 2016). Arsenic is exposed to human population via ingestion of arsenic contaminated water, foods, drugs, smoking, it exerts serious and prolonged effects on health (Singh et al., 2006).

Endothelial cell dysfunction, inflammation and angiogenesis are associated with cognitive dysfunction and these are proposed mechanisms which cause Alzheimer’s disease (Bryant et al., 2011). Epidemiological studies are conducted in different areas of the world, which revealed that arsenic exposure influences human health severely it causes cancers of liver, lung, bladder, kidneys and also cause skin cancers include hyperkeratosis and hyperpigmentation and it is also associated with neurological disorders such as amnesia and peripheral neuropathy, diabetes and arteriosclerosis (Raschid-Sally, 2000).

**Regional Status of Arsenic Exposure in Pakistan**

It is difficult to quantify the people who are subjected to arsenic poisoning especially in those areas where geochemical resources are limited. Estimations are extensive and based on four principles; (1) Frequency of recently documented cases of arsenicosis (2) Probability of ingested concentrations surpassing 50 μg/L (3) Number of people living in arsenic exposed areas (4) Liable aptitude of region to mitigate/remediate against arsenic contamination (Thakur et al., 2010).

**Table No 1:- National level survey for Arsenic Contamination.**

| Province     | Total samples (No.) | Arsenic conc. >10 μg/L | Arsenic conc. >50 μg/L | References       |
|--------------|---------------------|------------------------|------------------------|------------------|
|              | Field | Lab | Field | Lab | Field | Lab |                    |
| Punjab       | 31,693 | 4,611 | 32.5 | 31.4 | 10.0 | 9.0 | Ramay et al., 2007 |
| Sindh        | 67,556 | 4,825 | 24.0 | 36.0 | 7.8  | 17.0 | Ramay et al., 2007 |
| KPK          | 1,560  | 156  | 0.30  | 22.0 | 0.0  | 0.6  | Ahmed et al., 2004 |
| Baluchistan  | 619    | 71   | 1.30  | 1.40 | 0.0  | 0.0  | Ahmed et al., 2004 |

**Table - 1**

It is commonly observed from this table that water of Punjab and Sindh is affected from arsenic and Khyber Pakhtunkhwa (KPK) is less affected. Baluchistan is almost safe from arsenicism.

**Punjab Province**

Most populated province of Pakistan is Punjab where drinking water sources have been reported to contain Arsenic concentration above the safe limit defined by WHO and 20% of population is exposed to Arsenic (Bahadar et al., 2014).

| District   | No. of Samples | Source | Arsenic conc. | Ref           |
|------------|----------------|--------|---------------|---------------|
| Layyah     | 250            | Ground water | 0-150 μg/L   | Soomro et al., 2011 |
| Faisalabad | 64             | Ground water | 9 μg/L       | Hussain et al., 2016 |
| Sheikhupura| -              | Hand pump | 65-70 μg/L   | Abbas et al., 2014 |
| Multan     | 75             | Ground water | >50 μg/L    | Haqras, 2013   |
| Muzaffargarh| 49            | Shallow water and ground water | >50 μg/L | Naqvi et al., 2013 |
| Rahim Yar Khan | -          | Rotor pump | >20 μg/L   | Mahar et al., 2015 |

**Table - 2**
Sindh Province
Epidemiological investigations are conducted in Sindh to expose the severe health effects of arsenic. Their findings revealed that 61-73 % population is exposed to severe and prolonged effects of arsenic on human population residing on the bank of Manchar Lake (Kazi et al., 2009). The general population of 30 to 40 % living in Bobak village near Manchar Lake are exposed to high levels of arsenic, which cause several dermal diseases such as skin lesions and rough skin with black dots (Arain et al., 2009).

**Table - 3**

| District   | Study Area       | Source                                | Total No of samples | No of samples showing arsenic | Arsenic conc. | Ref          |
|------------|------------------|---------------------------------------|---------------------|-------------------------------|---------------|--------------|
| Thatta     | Ghulamula        | Ground water                          | 75                  | 10                            | 81 µg/L       | Arain et al., 2014 |
|            |                  |                                       |                     | 11                            | 81 µg/L       |              |
|            |                  |                                       |                     | 12                            | 45 µg/L       |              |
|            |                  |                                       |                     | 13                            | 90 µg/L       |              |
|            |                  |                                       |                     | 14                            | 76 µg/L       |              |
|            |                  |                                       |                     | 15                            | 63 µg/L       |              |
| Khairpur   |                  | Tube wells, hand pumps and dug wells   | 45                  | 30                            | <10 µg/L      | Arain et al., 2006 |
|            |                  |                                       |                     | 9                             | 25-50 µg/L    |              |
|            |                  |                                       |                     | 6                             | 100-250 µg/L  |              |
| Tando Allah Yar | Hand pumps, electric pumps, open wells and dug wells | 107                  | 82                      | 10 µg/L                      | Majidano et al., 2010 |
|            |                  |                                       |                     | 37                            | 200 µg/L      |              |
|            |                  |                                       |                     | 60                            | 100 µg/L      |              |
| Matiari    | Pumps and Motor pumps |                                         | 85                  | 22                            | 50 µg/L       | Uqaili, 2016 |
|            |                  |                                       |                     | 18                            | 20 µg/L       |              |

**Table - 4**

| District   | Source                  | Arsenic conc | Ref          |
|------------|-------------------------|--------------|--------------|
| Mardan     | Ground water, Tap water | >10 micro g/L| Khattak et al., 2016 |
| Sawat      | Ground water, shallow water | 0.2 micro g/L | Alam et al., 2008 |

**Health Problems with Arsenic in Drinking Water**
Arsenic in drinking water is ranked as a known human carcinogen by International Agency for Research of Oncology (IARO) and it cause skin, bladder and lung cancer (Memon et al., 2014). Most of the human population is exposed to arsenic through ingestion, inhalation and through skin contact. Chronic respiratory diseases are caused by most of the lung carcinogens but few studies revealed that the population exposed to arsenic has non-malignant respiratory effects, but few studies reported high-risk assessment (Ehrenstein et al., 2005). Lung tumors, which are caused by arsenic exposure, show different genetic and epigenetic modifications when compared with the studies on individuals, which were living in arsenic free environment. Only inorganic arsenic is not involved in molecular alterations in arsenic -induced tumors but the product which are produced in arsenic metabolism play major role in such alterations (Hubax et al., 2013). It is estimated that the rate of mortality from lung cancer by consuming arsenic contaminated water is higher than that of lung bladder and kidney cancers including cardiovascular diseases (Smith et al., 2009).

Exposure of Arsine (AsH3) causes anemia due to massive intravascular hemolysis. Changes in sodium and potassium levels act as earliest indicators of erythrocytes impairment (Chabowska et al., 2002). It is reported that arsenic-induced apoptosis is induced as a result of over expression of BCR-ABL gene in human lymphoblast cells. Arsenic as a tumor causing agent and it is selective in inducing apoptosis in promyelocytic leukemia cells. It is studied that arsenic induces modifications in other signaling pathways via apoptosis (Tchounwou et al., 2003).
Arsenic was characterized as a first chemical agent, which cause liver disease in humans. Chronic exposures of arsenic over periods of months and years cause accumulation of arsenic in liver and badly affect the hepatic system (Clarkson et al., 1991). Hyperkeratosis, hyper pigmentation and respiratory complications due to ingestion of arsenic in drinking water stimulate changes in hormonal and mucosal immune response (Luqueno et al., 2013). The chronic arsenic exposure cause skin de pigmentation which results in white spots that looks like rain drops, this condition is medically described as leukomelanosis (Singh and Kumar; 2012). It is estimated that high arsenic exposure via drinking water into young children aged less than 20 years (RR=10.6, 95% CI 2.9-39.2, p<0.001) suffered from liver cancer and become target of mortality (Tantry et al., 2015). When arsenic is present in arsenate and arsenite ionic form these ions replaces the phosphate ions and thiol group in cell and disrupt the normal functioning of cells (Shahid et al., 2015). High levels of arsenic ingested by pregnant women exerts serious effects on reproductive and developmental systems, arsenic can cross the placental barrier and cause miscarriages, low-birth weight deliveries, and neonatal and postnatal mortalities (Lubin et al., 2007). Arsenic may affect internal organs, impair their normal functioning without causing any visible external symptoms, and become difficult to recognize. Hair, nails, urine and blood can be indicators of arsenic exposure before the external appearances (Petrusevski et al., 2007). Arsenic affects children at higher rates because the symptoms are difficult to recognize at early (Bhatia et al., 2014).

| System                  | Effects                                                                 | Ref                   |
|-------------------------|-------------------------------------------------------------------------|-----------------------|
| Cardiovascular system   | Myocardial depolarization and cardiac arrhythmias, hypertension and atherosclerosis. | McCarty et al., 2011 |
| Blood forming System    | Intravascular hemolysis, Erythrocytes impairment and anemia.            | Pakulska et al., 2006 |
| Respiratory system      | Lung tumors and bronchial epithelial cell malignant transformation.      | Wang et al., 2011     |
| Nervous system          | Polyneuropathy, EEG abnormalities and, in extreme cases, hallucinations, disorientation and agitation. | Rodri et al., 2003   |
| Dermal system           | Melanosis (diffuse and spotted), keratosis of palm and sole (spotted or diffuse), leukomelanosis (rain drop pigmentation), and hyperkeratosis. | Khan et al., 2003   |
| Renal system            | Protein urea, oliguria, mitochondrial damage in tubular cells           | Saha et al., 1998     |
| Hepatic system          | Liver enlargement and hepatic fibrosis                                  | Guhamazumder, 2008   |

Table - 5

Role of Metabolism of Arsenic in its Toxicity
Two main types of reactions take place in Arsenic metabolism: (a) Pentavalent arsenic goes reduction reactions and convert into trivalent arsenic and (b) In oxidation reaction. These trivalent forms of arsenic are successively methylated to form mono, di and trimethylated products by using S-adenosyl methionine which act as methyl donor and glutathione (GSH) act as a co-factor (Pritchard, 2007). After ingestion, transition from blood into tissues arsenate undergoes reduction reaction and reduced to arsenite. In Liver, arsenic undergoes methylation reaction and methylated to form mono-methylated arsenic acid (MMAV), which further reduced to form mono-methyl arsenous.
acid (MMA III). This is converted into dimethyl-arsenic acid (DMA V) through a series of methylation reactions. In this process of methylation, some reactive oxygen species (ROS) are formed (Lee et al., 2010). Arsenic metabolism is followed by methylation process because methylated arsenic is excreted fast and easily than inorganic arsenic (Rossman, 2003).

Figure 2 showing the metabolism of arsenic in which arsenate is reduced to arsenite and methylated to form pentavalent and trivalent forms of arsenic, dimethyl arsenic acid and dimethyl arsenuous acid and trimethyl oxide are also generated. Enzymes involved in reaction are GSH, reduced glutathione; GSTO1, glutathione S-transferase omega-1; SAM, Sadenosylmethione; SAH, S-adenosylhomocysteine; AS3MT, arsenic methyltransferase(Cyt 19) (Ebele, 2009).

Worldwide Extent of Arsenic Problems
The maximum acceptable levels of dissolved arsenic in drinking water are 0.01mg/l and 0.05mg/l according to the World Health Organization and the United States Environmental Protection Agency, respectively. Several countries in the world have identified excess amount arsenic in drinking water including Argentina, Bangladesh, Chile, China, Hungary, India, Japan, Mexico, Mongolia, Poland, Taiwan, and the United States (Khalequzzaman et al., 2005). Most of the countries have found that their waters are contaminated with arsenic due to mining wastes; countries included Korea, Poland and Brazil. It is estimated in 2001 that approximately 130 million people are exposed to arsenic concentrations beyond the 50 μ g L−1 (Halem et al., 2009).

Table 6: Showing three Arsenic affected countries with Maximum approved parameter for Arsenic concentration in drinking water defined by WHO.

| Countries   | Maximum Approved parameter | References             |
|-------------|-----------------------------|------------------------|
| Pakistan    | 50 μ g L−1                  | Rahman et al., 2009    |
| Bangladesh  | 50 μ g L−1                  | Naidu et al., 2006     |
| USA         | 10 μ g L−1                  | Shakoor et al., 2015   |

Table – 6

In 1988, the EPA documented that continuing ingestion of arsenic 50 μ g /L-1 results in skin cancer rate of 1 in 400 in US, in 1992 EPA assessed that mortality risk of internal cancer is approximately 1.3 in 100 at 50 μ g/L. In 1999, NRC reported that overall cancer mortality risk is approximately 1 in 100 at 50 μg/L (Talibi et al.). IARC have been classified arsenic as a group 1 human carcinogen and toxic agent which also cause a wide variety of other diseases except cancer and almost every part of internal system of human body is disturbed through arsenic (Naujokas et al., 2012). Most of the ground and surface water of Pakistan has exceeded the level of heavy metals defined by WHO (Gilani et al., 2013). According to a British Geological Survey study in 1998 on shallow tube-wells in 61 of the 64 districts in Bangladesh, 46% of the samples were above 0.010 mg/L and 27% were above 0.050 mg/L. When combined with the estimated 1999 population, it was estimated that the number of people exposed to arsenic concentrations above 0.05 mg/l is 28-35 million and the number of those exposed to more than 0.01 mg/l is 46-57 million (BGS, 2000). The US EPA suggested that by lowering the arsenic standard from 50 to 10 μ g/L could reduce
the mortality rate which is due to skin, lung and bladder cancers and from heart diseases (Kapaj et al., 2006).

**Conclusion:**
It is derived that Arsenic is an element, which is hazardous to health mainly in ionic form in water. It influences human health mainly by the consumption of water. There are many countries in the world where drinking water has exceeded the maximum permissible level of arsenic defined by World Health Organization (WHO). Arsenic is a toxicant as well as a potent carcinogen which causes the lungs, urinary and bladder cancers. Pakistan is affected with arsenicism specifically Punjab and Sindh provinces. Drinking water of Lyayh and Faisalabad districts of Punjab is badly affected. Ground water of Khairpur and Thatta (Sindh) have maximum concentration of Arsenic. KPK is less affected and Baluchistan has shown no arsenic concentration in experimental water samples.

**Abbreviations:**
- WHO: World Health Organization
- EPA: Environmental Protection Agency
- NRC: Nature Reviews Cancer
- IARC: International Agency for Research in Cancer
- IARO: International Agency for Research in Oncology

**References:**
1. Arain, M.B, Kazi, T.G, Baig, J.A., Jamali,M.K., Afridi, H.I., Jalbani. N., Sarfraz, R.A., Shah, A.Q., & Kandhro, G.A. (2009). Respiratory effects in people exposed to arsenic via the drinking water and tobacco smoking in southern part of Pakistan. *Journal of Sci Environment*, 407,524-5530.
2. Arain, G. M., Aslam, M., Limajidano, S., & Khuwawar, M. Y. (2007). A preliminary study on the Arsenic contamination of underground water of Matiari and Khairpur Districts, Sindh, Pakistan. *Journal. Chem. Soc. Pak.*, 29(5).
3. Akhtar, M. M., Zhonghua, T., Sissou, Z., & Mohamadi, B. (2015). Assess arsenic distribution in groundwater applying GIS in capital of Punjab, Pakistan. *Journal of Nat. Hazards Earth Syst. Sci.*, 3, 2119–2147.
4. Abbas, M., & Cheema, K.J. (2015). Arsenic levels in drinking water and associated health risk in district Shiekhupura .Pakistan. *Journal of Anim. Plant Sci*, 25 (3 supp 2), 719– 724.
5. Abbas, M., & Cheema, K.J. (2014). Correlation Studies of Arsenic Level in Drinking Water and hair Samples of Females in District Sheikhupura. Pakistan *International journal of current microbiology and applied sciences*, 3 (8), 1077-1085.
6. Aslam, S., Ahmed, S., & Bangash, F.K. (2008). Drinking water quality of Sawat District, *Journal of Chem. Soc. Pak.*, 30 (1).
7. Ahmad, T., Kahlown, M.A., Tahir, A., & Rashid, H. (2004). Arsenic Emerging Issue: Experiences from Pakistan, 30th WEDC International Conference, Vientiane, Lao PDR.
8. Bahadar, H., Mostafalou, S., & Abdollahi, M. (2014). Growing burden of diabetes in Pakistan and the possible role of arsenic and pesticides. *Journal of Diabetes & Metabolic Disorders*, 13 (1), 117.
9. Bhatia,S., Balamurugan, G., & Baranwal, A. (2014) High arsenic contamination in drinking water hand-pumps in Khap Tola, West Champaran, Bihar, India. 2 (49).
10. Chabowska, A.S., Juchiewicz, J. A., & Ryszard.(2002). Some aspects of Arsenic toxicity and carcinogenicity in living organisms with special regards to its influence on cardiovascular system, blood and bone marrow. *International Journal of occupational Medicine and environmental health*, 15(2), 101-116.
11. Chen, C.-J., Chen, C.W., Wu, M.-M., & Kuo, T.-L. (1992). Cancer potential in liver, lung, bladder and kidney due to ingested inorganic arsenic in drinking water. *Br. J. Cancer*, 66, 888-892.
12. Lee, C. H., Liao, W. T., & Yu, H. S. (2010). Mechanisms and Immune Dysregulation in Arsenic Skin Carcinogenesis. *Journal of Cancer Therapy*, 1, 76-86.
13. Clarkon, T. W. (1991). Inorganic and organometallic pesticides. Handbook of pesticide Toxicology. *Academic press, San Diego*, 545-552.
14. Ebele,O. S. Mechanisms of arsenic toxicity and carcinogenesis. (2009). *African Journal of Biochemistry Research*, 3 (5), 232-237.
15. Gilani, S. R., Mahmood, Z., Hussain, M., Baig, Y., Abbas, Z., & Batool, S. (2013). A Study of Drinking Water of Industrial Area of Sheikhupura with Special Concern to Arsenic, Manganese and Chromium. *Pak. J. Engg. & Appl. Sci*, v 13, p 118-126.
16. GuhaMazumder, D. N. (2008). Chronic arsenic toxicity & human health. *Indian Journal of Med Res*, 128, 436-447.

17. Halem, D., van Bakker, S. A., Amy, G. L., & Dijk, J. C. van (2009). Arsenic in drinking water: a worldwide water quality concern for water supply companies. *Journal of Drinking Water Eng. Sci*, 2, 29-34.

18. Hubaux, R., Daiana D Becker-Santos, Katey SS Enfield, Rowbotham, D., Lam, S., Wan L Lam, & Victor D Martinez. (2013). Molecular features in arsenic-induced lung tumors.

19. Hagh, M.A. (2013). Water quality assessment and hydrochemical characteristics of groundwater in Punjab, Pakistan. *IJRRAS*, 161 (2).

20. Hussain, Y., Dilawar, A., FidaUllah, S., Akhter, G., Martinez-Carvajal, H., Hussain, M.B., & Aslam, A. Q. (2016). Modelling the spatial distribution of arsenic and its correlation with public health, central Indus basin, *Pakistan. Journal of Geoscience and Environment Protection*, 4, 18-25.

21. Kazi, T.G., Arain, M.B., Jamali, M.K., Jalbani, N., Afridi, H.I., Sarfraz, R.A., Baig, J.A., & Shah, A.Q. (2009). *Ecotox Environ Safety*, 72, 301–309.

22. Khan, M.M.H., Sakauchi, F., Sonoda, T., Washio, M., & Muri, M. (2003). Magnitude of Arsenic Toxicity in Tube-well Drinking water in Bangladesh and its adverse effects on human health including cancer, Evidence from the view of literature. *Jour Asian Pacific cancer*, 4, 7-14.

23. Khan, M. A., & Yuh-Shan Ho. (2011). Arsenic in Drinking Water: A Review on Toxicological Effects, Mechanism of Accumulation and Remediation. *Asian journal of Chem*, 23 (5), 1889-1901.

24. Kaltenreider, R.C., Davis, M.A., Lariviere, P. J., & Hamilton, W. J. (2001). Arsenic Alters the Function of the Glucocorticoid Receptor as a Transcription factor. *Journal of Environ Health Perspect*, 109, 245–25.

25. Khattak, S. A., Polya, A., Ali, L., & Shah, M. T. (2016). Arsenic exposure assessment from ground water sources in Peshawar Basin of Khyber Pakhtunkhwa, Pakistan, *Journal of Himalayan Earth Sciences*, 49 (1), 68-76.

26. Kapaj, S., Peterson, H., Liber, K., & Bhattacharya, P. (2006). Human health effects from chronic arsenic poisoning arsenic poisoning: a review. *Journal of Environmental Science and Health Part A*, 41, 2399–2428.

27. Luqueño, F.F., Valdez, F.L., Melo, P.G., Suárez, S.L., González, E. N. A., Martínez, I. A., Guiller no, G. M. S., Martínez, H. G., Mendoza, H.R., Garza, A. M. A & Velázquez, P. I (2013). Heavy metal pollution in drinking water - a global risk for human health: A review. *African journal of environmental science and technology*, 7(7), 567-584.

28. Lubin, H.J., Beane, L. E., Freeman, Cantor, K.P. (2007). Inorganic Arsenic in Drinking Water: An Evolving Public Health Concern. *Oxford Journals*, 99 (12).

29. Memon, A. R., Jalbani, R.A., Shaikh, T. A. (2014). Arsenicosis is one of the Predisposing Factor of Carcinoma of Lung in Non-Smokers. *Rep Opinion*, 6(2), 71-74.

30. Mukharjee, A., Sengupta, M. K., Hossain, M.A., Ahmed, S., Das, B., Lodh, B. D. N., Rahman, M., & Chakrabort, D. (2006). Arsenic Contamination in Groundwater: A Global Perspective with Emphasis on the Arsenic Asian Scenario. *Journal of Health Popul Nutr*, 24(2), 142-163. dcsaoesju@vsnl.com.

31. McCarty, K.M., ThiHanH., & Kim, K.W. (2011). Arsenic geochemistry and human health in South East Asia. *Journal of Environ Health Perspect*, 26(1), 71–78.

32. Mohsin, M., Safdar, S., Asghar, F., & Jamal, F (2013). Assessment of Drinking Water Quality and its Impact on Residents Health in Bahawalpur City. *International Journal of Humanities and Social Science*, 3 (15).

33. Mahar, M.T., Khuwawar, M.Y., Jahangir, T. M., & Ahmad, M. (2015). Determination of Arsenic contents in ground water of District Rahim Yar Khan Southern Punjab, Pakistan. *Arab Journal of Geosci.*

34. Majidano, S.A., Arain, G.M., & Khuwawar, Y. M. (2010). Arsenic levels in ground water of Sindh Pakistan Arsenic in Geo sphere and Human diseases-Jean-Bundschuh and Bhattacharya (eds).

35. Md.Khalequzzamamn., Farouqi, F., & Mitra, A. (2005). Assessment of Arsenic contamination in ground water and health problems in Bangladesh. *International journal of environmental health and public research*, 2 (2), 204-213.

36. Naidu, R., Smith, E., Owens, G., Bhattacharya, P., & Nadeem, P. (2006). Arsenic around the world—an overview. In Managing Arsenic in the Environment: From Soil to Human Health; *CSIRO publishing: Victoria, Australia*, 3–31.

37. Naqvi, M. S., Taneez, M., & Khan, N. (2013). Physiochemical analysis of drinking water of Dhokelhaimal (Mohra Fatima) GujjarKhan. *Pakistan International Journal of Advanced Scientific and Technical Research*, 6 (3).

38. Naujokas, F.M., Anderson, B., Ahsan, H., Aposthi, H.V., Graziano, J.H., Khalequzzaman, Md., Faruque, S.F.M, & Mitra, A.K. (2005). Assessment of Arsenic Contamination of Groundwater and Health Problems in
Bangladesh. Int. J. Environ. Res. Public Health, 2(2), 204–213.

39. Ehrenstein, O.V., Guha Mazumder, D.N., Yuan, Y., Samanta, S., Balmes, J., Sil, A., Ghosh, N., Smith, M.H., Haque, R., Purushothamam, R., Lahir, S., Das, S., & Allan H. Smith. (2006). Decrements in Lung Function Related to Arsenic in Drinking Water in West Bengal, India. 162 (6).

40. Pakulska, D., & Czerzek, S. (2006). Hazardous Effects of Arsenic: A Short review. International Journal of Occupational Medicine and Environmental Health

41. Pershagen, G. (1981). The Carcinogenicity of Arsenic. Journal of Environmental Health Perspectives, 40, 93-100.

42. Pritchard, J. D. (2007). Inorganic arsenic toxicological overview, Version 2, 1-10.

43. Petrusheski, B., Sharma, S., Schippers, J. C., & Shordt, K. (2007). Arsenic in drinking water; thematic overview paper, IRC International Water and Sanitation Centre.

44. Rahman, M.M., Naidu, R., Bhattacharya, P. (2009). Arsenic contamination in groundwater in the Southeast Asia region. Environ. Geochem. Health, 31, 9–21.

45. Raschid-Sally, L. (2000). Arsenic contamination of groundwater in Bangladesh. Colombo, Sri Lanka, International Water Management Institute.

46. Rossman, T. G. Mechanism of arsenic carcinogenesis: an integrated approach Mutation Research. (2003). 533, 37–65.

47. Ramay, M. I., Ahmad, T., Shipin, O. V., Kadushkin, A., & Jazeph, D. (2007). Arsenic contamination of ground water and its mitigation in the province of Punjab (Pakistan) in the light of situation in South East Asia. A survey report.

48. Rondri, V.M., Jimenez-Capdeville, M.E., Giordano, M. (2003). The effects of arsenic exposure on the nervous system. 145 (1), 1-18.

49. Smith, A. H., Rich, H. C., Bates, M. N., Goeden, H. M., Picciotto, I.H., Duggan, H. M., Wood, R., Kosnett, M. J., & Smith, M. T. (1992). Cancer Risks from Arsenic in Drinking. Journal of Water Environmental Health Perspectives, 97, 259-267.

50. Saha, J.C., Dikshit., A. K., Bandyopadhyay, M., & Saha, K.C. A review of Arsenic Poisoning and its effects on human health. Department of Civil Engineering Indian Institute of Technology, Kharagpur-721302, India.

51. Shakoor, M. B., Niazi., N.K., Bibi, I., Rahman, M. M., Naidu, R., Dong, Z., Shahid, M., & Arshad, M. (2011). Unraveling Health Risk and Speciation of Arsenic from Groundwater in Rural Areas of Punjab, Pakistan, Int. J. Environ. Res. Public Health, 12, 12371-12390. www.mdpi.com/journal/ijerph.

52. Singh, M.K., & Kumar, A. (2012). A global problem of arsenic in drinking water and its mitigation— a review. IJAET, 3 (1), 196-203.

53. Shahid, N., Shahid, M., Siddique, H.F., Bakht, G., & Shah, G.M. (2015). Assessing drinking water quality in Punjab, Pakistan. Polish Journal of Environmental Studies, 24 (6).

54. Singh N., Kumar, D., & Sahu, A.P. (2007) Arsenic in the environment Effects on human health and possible prevention. Journal of Environmental Biology, 28(2), 359-36.

55. Soomro, Z. A., Dr. Khokhar, M. I. A., Hussain, W., and Hussain, M. (2011). Drinking water quality challenges in Pakistan, Pakistan Council of Research in Water Resources, Lahore – Pakistan.

56. Tareen, A. K., Sultan, I. A., Khan, M. W., & Dr. Khan, A. (2013). Determination of heavy metals found in different sizes of tube wells of district Pishin Baluchistan, Pakistan. Asian Journal of Science and Technology.

57. Talibi, A., Kemper, K., Minatullah, K., Foster, S., & Tinhof, A. An overview of current operational responses to the Arsenic issues in south and East Asia. A Technical report, Version 2.

58. Thompson, C., & William A. Suk. (2013). The Broad Scope of Health Effects from Chronic Arsenic Exposure: Update on a Worldwide Public Health Problem. Journal of Environ. Health. Perspect, 121(3).

59. Tantry, B. A., Shrivastava, D., Taheer, I., & Tantry, M. N. (2015). Mechanisms of Action and Related Health Effects Journal of Environmental and analytical toxicology, 5 (6), 2161-0525.

60. Toor, I. A., Tahir, S. N. A. (2009). Study of Arsenic Concentration Levels in Pakistani Drinking Water. Journal of Environ. Study, 18 (5), 907-912.

61. Thakur, J.K., Thakur, R. K., Ramanathan, A. L., Kumar, M., & Singh, S.K. (2010). Arsenic Contamination of Groundwater in Nepal—an Overview. 3, 1-20.

62. Tchouwou, P. B., Patiolla, A., & Jose A. Centeno. (2003). Carcinogenic and Systemic Health Effects Associated with Arsenic Exposure—A Critical Review. By Society of Toxicologic Pathology, 31, 575–588.

63. Uqaili, A. A. (2016). Arsenic contamination in groundwater sources of district Matiari. International Journal of Chemical and Environmental Engineering, 3 (4).
64. Wang, Z., Zhao, Y., Smith, E., Gregory J. Goodall., Paul A. Drew., Brabletz, T., & Yang.C. (2011). Reversal and prevention of arsenic-induced human bronchial epithelial cell malignant transformation by micro RNA, *Jour. Toxi sci Advance Access*, 1-41.