

Effects of Heavy Metals on Renal Function: A Mini Review

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Abstract: This extensive study provides a synopsis of the kidney health effects of lead, cadmium, and arsenic. Kidney damage is caused by these metals. These include oxidative injury, inflammation, and structural deterioration of renal tissue. These processes involve complex molecular and cellular pathways. Metals that exhibit synergistic effects elevate the likelihood of nephrotoxicity and a decline in renal function. The function of environmental exposure and the significance of interaction effects in chronic renal diseases are illuminated by regional studies. Analyses of the response to exposure to nephrotoxic metals indicate that they induce kidney stones and severe renal complications. Strategies for stratifying populations illustrate the intricate relationship between exposure patterns and a variety of health outcomes. Due to the severe health effects of heavy metal exposure, stringent monitoring and control measures are required to mitigate health hazards. Subsequent research ought to concentrate on the cumulative impacts of heavy metals, early indicators of nephrotoxicity, and remedies based on regional exposure patterns. Each duty ought to be completed. Our results establish a fundamental basis for public health interventions aimed at safeguarding the renal well-being of a heterogeneous populace in light of the enduring peril of heavy metal exposure.

Keywords: Environmental exposure, Heavy metals, Kidney health, Nephrotoxicity, Oxidative stress, Public health.

I. INTRODUCTION

Exposure to heavy metals has emerged as a public health concern in recent times. Because it has the potential to harm vital organs, specifically the kidneys. Personal use, industrial processes, and pollution all contribute to increased heavy metal exposure. Regarding renal function, the health consequences of heavy metal ingestion are particularly worrisome. As a result of urbanisation, industrialization, and other anthropogenic environmental changes, heavy metal exposure has increased.

Arsenic, lead, and cadmium are prevalent in numerous environmental matrices [5]. Depleted in the environment are these metals. Individuals must be cognizant of the detrimental effects that these perilous substances have on kidney health, given their pervasive exposure via food, drink, and air [13].

Waste-excreting kidneys are particularly susceptible to heavy metal injury. Nephrotoxicity can result from the accumulation of heavy metals in the renal system, which induces molecular and metabolic reactions. Renal dysfunction can have detrimental effects on an individual's health due to the kidneys' responsibility of waste elimination and maintenance of electrolyte and fluid equilibrium [7].

Lead is a non-biodegradable metal and is present in nature, although in small quantities. The burning of fossil fuels, mining, manufacturing and other human activities are all contributing to the constant rise in atmospheric lead levels [13]. When exposed to higher than ideal levels, lead is harmful to human health. Youngsters are more susceptible to lead poisoning, and these verity of the poisoning worsens when they come into touch with dust that contains environmental lead [11].

The nineteenth century saw the first reports of cadmium poisoning among zinc smelters' employees. Lead and zinc-containing ores can include cadmium (Cd). Industrial workers who are exposed to Cd or people who live in highly polluted regions are often the ones that develop chronic Cd poisoning. Still utilised today include Li-Cd battery manufacturing, electroplating, and pigment synthesis (particularly in plastics, where it accounts for about 25% of global output). The people most at risk today are those who handle, assemble, and dismantle batteries, computer circuit boards, and cell phones—collectively, “electronic waste”—although it may take years of exposure before signs of chronic poisoning appear [16]. Exposure to cadmium causes damage to the glomeruli, which in leads to albuminuria and a gradual decline in the glomerular filtration rate (GFR), which ultimately leads to end-stage renal failure (Fig. 1) [12].

Because millions of people are exposed to water levels over the limit, arsenic exposure continues to be a serious public health concern. Arsenobetaine, the most common chemical in fish, is non-toxic to people, but arsenite, which is primarily found in drinking water, is extremely harmful to humans. These

compounds are found in nature as inorganic (arsenite, arsenate) or organic (arsenobetaine, arsenocholine, and arsenosugars) [14]. Arsenic is associated with formation of tumors in skin, lungs, bladder, liver and kidneys; arsenic exposure has also been recognized as a risk factor for many diseases [15].

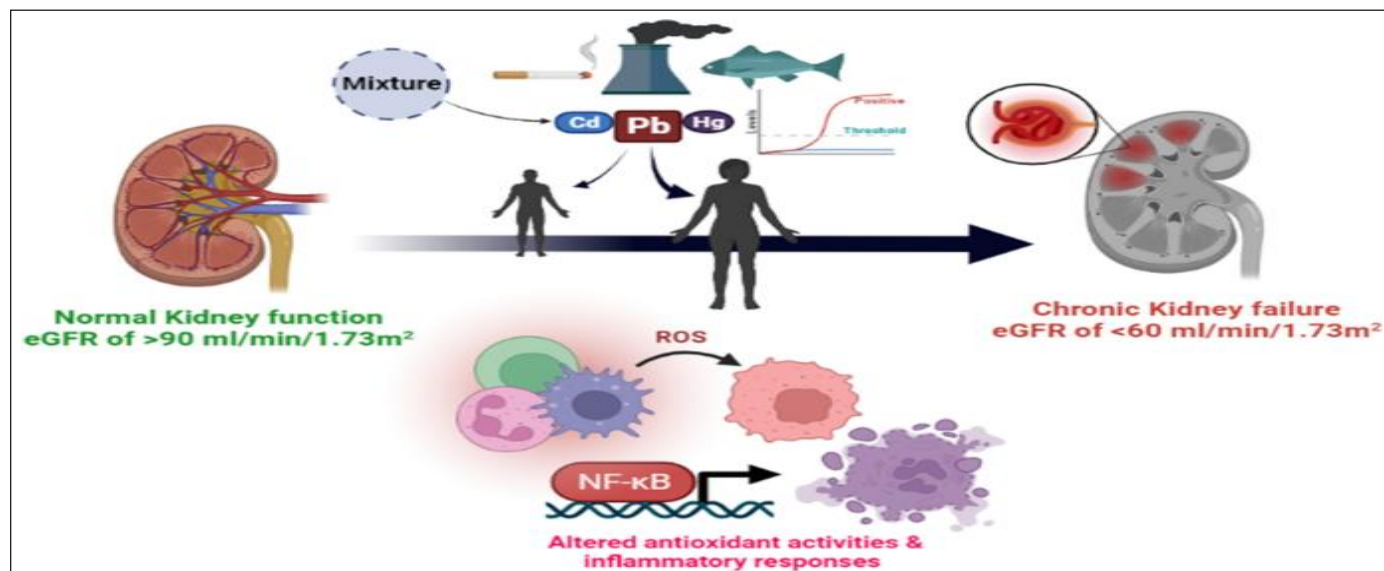


Fig. 1: Heavy Metals Affecting GFR Rate of Kidney

This study is intended to provide a synopsis of the renal function effects of lead, cadmium, and arsenic. We analysed the most recent research to assist you in comprehending how heavy metals damage the kidneys. Major research on the relationship between heavy metal intake and renal health will be examined in order to identify pathways, risk factors, and fundamental biological processes. To accomplish this, we will conduct as much research as possible. This study primarily focuses on lead, cadmium, and arsenic owing to their pervasive nature, extensively documented health hazards, and substantial societal ramifications but we have included different heavy metals which are affecting kidney in any manner. Polluted food, air, or water can lead to the accumulation of heavy metals. To develop effective preventative and management strategies, it is necessary to comprehend the effects of each heavy metal on kidney function. Understanding the effects of heavy metals on renal function is crucial for mitigating occupational and environmental hazards. This becomes more evident as the investigation progresses. This finding has the potential to impact public health policy through its ability to inspire further investigation and safeguard susceptible populations against heavy metal nephrotoxicity.

II. LITERATURE REVIEW

A. Toxic Mechanisms of Heavy Metals

Metals are substances with high electrical conductivity, malleability, and shine, which voluntarily lose their electrons to form cations. Kidney injury can be caused by heavy metals such as arsenic, chromium, lead, mercury, and cadmium via intricate biological and chemical mechanisms. These pathways must be comprehended in order to determine how metals cause kidney injury. In 2021, Author discovered that the reactivity of mercury is decreased by biological proteins and sulfhydryl groups. An imbalance in cellular redox results in physiological and oxidative stress. Mercury induces apoptosis in kidney cells through the inhibition of mitochondrial activity [1]. Renal function may be affected by the cumulative effects of these processes. Mercury-induced kidney injury, according to necessitates oxidative stress. Their research indicates that ROS and lipid peroxidation are critical. Renal injury and oxidative insult are exacerbated by diminished antioxidant defences (Fig. 2) [2].

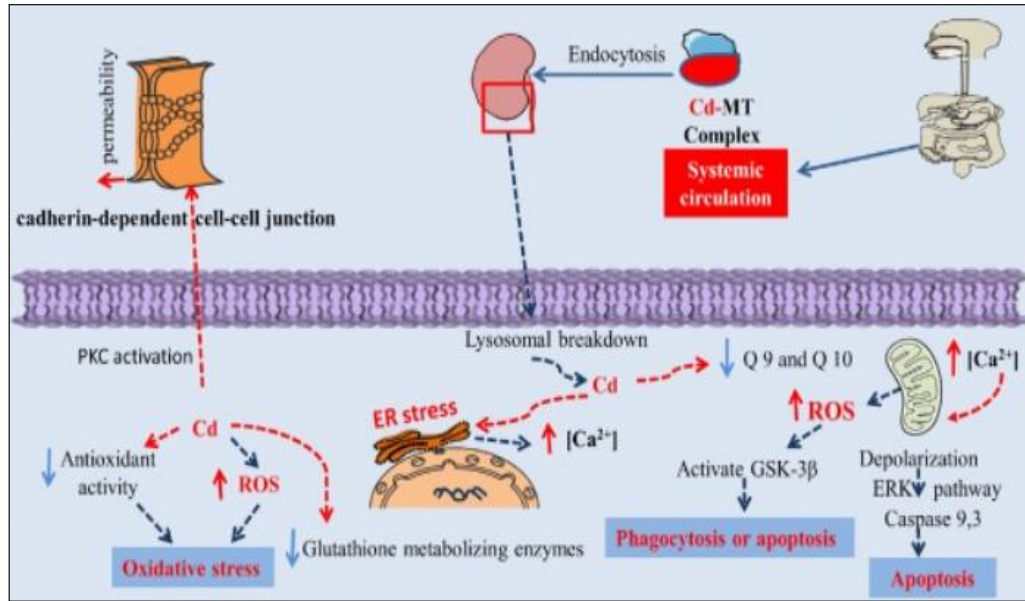


Fig. 2: Toxicodynamic of Cd-Induced Kidney Toxicity

B. Combined Exposure and Kidney Health

The combined influence of these heavy metals increased the likelihood of renal impairment. The combination of lead, cadmium, mercury, and arsenic caused kidney injury. Individual metal effects were weaker than synergistic metal effects. Author discovered that metal exposure significantly reduced kidney health indicators. The effects of synergistic relationships on kidney health are dramatic. Renal impairment was exacerbated by heavy metal accumulation, which increased the risk of renal failure. All heavy metal exposures should be monitored for renal health hazards, as demonstrated by this study. This study focus on the synergy; however, severe nephrotoxic effects remain a challenge for scientists to manage. By combining metals, scientists discovered unexpected outcomes. Potential changes may occur in biological reactivity, oxidative stress, and metal repair mechanisms [3]. The inadequate understanding of the detrimental impacts of lead, cadmium, mercury, and arsenic on kidney function carries significant implications for public health. In order to reduce heavy metal exposure among adolescents, regulatory measures and strategies must take into account the cumulative effect. Because adolescents are likely to come into contact with numerous pollutants. Author underscore the criticality of quantifying exposure to lead, cadmium, mercury, and arsenic in order to ascertain potential hazards to kidney health. For vulnerable patients to maintain renal function, a comprehensive environmental hazard mitigation and assessment plan is required. The intricate nature of heavy metal interactions is exemplified by synergistic effects [3].

C. Hazards of Heavy Metal Contamination

Researcher provides a comprehensive analysis of heavy metal contamination issues. The author emphasises dangers to the kidneys. The detrimental impact of heavy metals on renal function is a cause for concern. Author asserts that the bioaccumulation of heavy metals and their resistance to the environment present significant health hazards. It is possible for heavy metals to contaminate soil, water, and food. Lead, mercury, arsenic, and cadmium all cause kidneys damage first. This study demonstrates the effect of heavy metal toxicity on renal function. In addition to filtering contaminants, the kidneys may also accumulate heavy metals. Nephrotoxicity to heavy metals results in chronic kidney disease, renal function decline, and kidney injury. In numerous ways, heavy metals cause kidney injury, as stated by author [4]. Included are oxidative damage, inflammation, direct cellular toxicity, and disruption of the signalling system. Collectively, these mechanisms may alter the structure and function of renal tissue. Kidney disease may be induced or exacerbated by heavy metal exposure, according to one study. Chronic kidney disease can be induced and renal function deterioration slowed by even trace amounts of heavy metals. The findings of Jarup emphasise the necessity of determining the long-term effects of heavy metal exposure on renal health. Incorporating knowledge of heavy metal exposure risks into regulatory and public health strategies is vital. The negative impacts of heavy metals on human and kidney health can be mitigated through the implementation of preventive measures, vigilant surveillance, and risk assessments.

Researcher concludes with the kidney injury caused by heavy metal toxicity. The present study focusses on the complex correlation that exists between exposure to heavy metals and renal injury. This can aid public health initiatives to protect the kidneys of vulnerable populations [4].

D. Renal Oxidative Stress and Functions

Author investigates the relationship between human renal function, oxidative stress, heavy metals (mercury, lead, arsenic, and zinc), and oxidative stress. A balance between the body's ability to combat reactive oxygen species (ROS) and O₂ production constitutes oxidative stress, which is essential to comprehending how heavy metals influence renal function. Sanchez states that oxidative stress is induced by mercury, to which renal tissues are vulnerable. ROS produced by mercury surpass the antioxidant defences of the kidney. One type of mercury is distinct from another. Oxidative damage has the potential to induce lipid peroxidation, protein degradation, and cellular inactivation. Mercury-induced oxidative stress can cause structural and functional injury to the kidneys [5]. According to the investigation, lead induces oxidative stress in the kidneys. Reactive oxygen species (ROS) generated by lead cause harm to numerous cellular biological components. The effects of lead-induced oxidative stress on kidney antioxidant systems, cell mortality, and inflammation are described by author. These modifications, which are critical for renal operation, could potentially disrupt the intricate equilibrium required for renal functioning, resulting in nephrotoxicity. The detrimental impacts of arsenic on oxidative stress in the kidneys are the subject of ongoing research. Arsenic impairs mitochondrial function, redox equilibrium, and ROS production. Kidney cell mortality and inflammation result from oxidative stress induced by arsenic, leading to the development of renal failure. Zinc, an essential trace element for numerous physiological processes, is only briefly alluded to in the review regarding its potential dual function. Elevated zinc levels in the kidneys induces oxidative stress. Zinc homeostasis maintenance is vital for proper kidney function. The comprehensive investigation elucidates the intricate interplay among zinc, lead, mercury, renal oxidative stress and function, and zinc [5].

E. Regional Studies and Chronic Kidney Disease

The impact of ambient heavy metals on chronic kidney disease (CKD), a prevalent malady in Sri Lanka that lacks a definitive cause, was investigated by Author. Rice, urine, well water, lead, chromium, and cadmium were utilised in experiments. Chronic kidney disease (CKD) of unknown aetiology impacts agricultural labourers in Sri Lanka at a disproportionate rate. Scholars discovered a correlation between heavy metal concentrations in rice and well water and CKD of unknown aetiology [6]. Environmental matrices containing renally toxic lead, chromium, arsenic, and cadmium surpassed safety

limits. The concentrations of heavy metals in rice, well water, and urine exhibit a correlation with both internal body burden and environmental exposure. Deliberation is required. Author investigates the association between heavy metal exposure and the unknown aetiology of CKD. Location-specific research can identify environmental factors that contribute to chronic renal disease. The present study sheds light on the complex correlation that exists between renal health and environmental contaminants [6].

F. Chromium Exposure and Decline in Kidney Function

Chromium exposure and renal function decline were extensively studied by author [7]. The study addresses lead and cadmium consequences. The chromium exposure cohort research examined kidney damage from heavy metals. Chrome inhibits kidney function, whereas lead and cadmium worsen it, one study found. The study found that heavy metal combinations affected the kidneys more than separate exposures. Chromium exposure damage kidneys separately and substantially. Chromium, lead, and cadmium increase oxidative stress, renal inflammation, and cellular signalling, the study found. These findings explain renal function decline mechanisms. Researcher discuss chromium nephrotoxicity and the necessity of heavy metal testing in renal function evaluations. Communities exposed to chromium in the environment or at work must work together to monitor and reduce the cumulative effects of heavy metal exposure on renal function [7].

G. Nephrotoxic Metals and Kidney Stones

Researcher examined the intricate correlation between nephrotoxic metals and adult kidney stones by utilising NHANES exposure-response data. The enquiry was instigated due to the presence of mercury, arsenic, cadmium, lead, and kidney stones. A study found that these nephrotoxic medications increased the risk of kidney stones with time. Cadmium, lead, mercury, and arsenic all exhibited a dose-dependent kidney stone risk, according to an exposure-response analysis [8]. Heavy metal nephrotoxicity increases the risk of chronic kidney disease. Each characteristic was associated with kidney stones. Kidney stones may be induced by heavy metals, as stated in "The Cumulative Impact of Heavy Metals on Renal Health." Sun and colleagues advise the use of numerous nephrotoxic factors in kidney stone risk monitoring. This information is vital for public health initiatives aimed at reducing the prevalence of hazardous substances. These environmental factors that cause kidney stones are shed light on by this research. Also emphasised is the protection of metal-sensitive kidneys [8].

H. Population Stratification and Health Outcomes

Author conducted a comprehensive analysis of the demographic implications. Individual exposure patterns to mercury, lead, cadmium, and arsenic delineate individuals. Continuation of research into cardiac, renal, and pulmonary issues. The

health effects of each metal were ascertained through the implementation of extensive population stratification in accordance with exposure patterns [9]. Diverse demographic groups exhibited varying degrees of heavy metal exposure, which consequently determined their susceptibility to health complications. Arsenic, lead, cadmium, and mercury negatively impacted the respiratory, cardiovascular, and renal health of subgroups. Population-wide assessments are necessary to enhance public health and comprehend the health effects of heavy metals. Yao emphasise the significance of individual risk assessments in order to enable efficient prevention. Thus, the intricate connections between heavy metals and health problems are clarified [9].

I. Water Quality Standards and Synergic Effects

The effects of heavy metals, fluoride, and hardness on renal tissues and WHO water quality were investigated by author. The health hazards associated with coexisting water contaminants are investigated in this study. The concentrations of heavy metals and fluoride in potable water are compared to the WHO standards in this study. This comparison illustrates exposure to lead, cadmium, fluoride, and arsenic. Preexisting health conditions may be exacerbated by multiple contaminants, according to the study [10]. This study highlights the criticality of understanding the interrelationships between water quality measurements, particularly in areas afflicted with pollution. Our results indicate that regulations governing water quality should take into account the cumulative impact of multiple contaminants on renal tissues. Researcher assert that in order to consider synergistic impacts, regulatory frameworks should be revised, and water quality criteria should be aligned with actual exposure scenarios in the real world. This is essential for the benefit of public health [10].

III. CONCLUSION

It concludes that the complex relationship between exposure to lead, cadmium, and arsenic directly associated with the kidney health. Due to the oxidative stress, inflammation, and structural damage mechanisms of toxicity, renal tissues are particularly susceptible to the hazardous compounds. It is necessary to assess interaction effects due to the fact that cumulative exposure significantly amplifies nephrotoxicity. Regional inquiries have shed light on the correlation between chronic renal disorders and environmental exposure. Severe renal outcomes and kidney stones are consequences of nephrotoxic metals, according to exposure-response studies. Strategies for stratifying populations illustrate the intricate relationship between exposure patterns and a variety of health outcomes. Clearly, heavy metal exposure is detrimental to public health; therefore, it must be immediately regulated and monitored to reduce health risks. Additional research is required to investigate the synergistic effects of distinct heavy metals, early indicators of nephrotoxicity, and

the adaptability of therapeutics to diverse exposure patterns in different regions. The aforementioned findings have established the groundwork for informed public health measures aimed at protecting the kidneys of diverse populations from heavy metal-induced harm.

REFERENCES

- [1] M. Balali, K. Naseri, Z. Tahergorabi, M. R. Khazdair, and M. Sadeghi, "Toxic mechanisms of five heavy metals: Mercury, lead, chromium, cadmium, and arsenic," *Front Pharmacol.*, vol. 12, p. 643972, 2021.
- [2] M. N. Rana, J. Tangpong, and M. M. Rahman, "Toxicodynamics of lead, cadmium, mercury and arsenic-induced kidney toxicity and treatment strategy: A mini review," *Toxicology Reports*, vol. 5, pp. 704-713, 2018.
- [3] A. P. Sanders, M. J. Mazzella, A. J. Malin, G. M. Hair, S. A. Busgang, J. M. Saland, and P. Curtin, "Combined exposure to lead, cadmium, mercury, and arsenic and kidney health in adolescents age 12–19 in NHANES 2009–2014," *Environment International*, vol. 131, p. 104993, 2019.
- [4] L. Jarup, "Hazards of heavy metal contamination," *British Medical Bulletin*, vol. 68, no. 1, pp. 167-182, 2003.
- [5] T. Sanchez, "Effects of mercury, lead, arsenic and zinc to human renal oxidative stress & functions: A review," *Arch. Med.*, vol. 4, no. 2, 2003.
- [6] H. M. A. S. Herath, T. Kawakami, S. Nagasawa, Y. Serikawa, A. Motoyama, G. G. Tusara Chaminda, S. K. Weragoda, S. K. Yatigammana, and A. A. G. D. Amarasooriya, "Arsenic, cadmium, lead, and chromium in well water, rice, and human urine in Sri Lanka in relation to chronic kidney disease of unknown etiology," *Journal of Water and Health*, vol. 16, no. 2, pp. 212-222, 2018.
- [7] T. L. Tsai, C. C. Kuo, W. H. Pan, Y. T. Chung, C. Y. Chen, T. N. Wu, and S. L. Wang, "The decline in kidney function with chromium exposure is exacerbated with co-exposure to lead and cadmium," *Kidney International*, vol. 92, no. 3, pp. 710-720, 2017.
- [8] Y. Sun, Q. Zhou, and J. Zheng, "Nephrotoxic metals of cadmium, lead, mercury and arsenic and the odds of kidney stones in adults: An exposure-response analysis of NHANES 2007–2016," *Environment International*, vol. 132, pp. 105-115, 2019.
- [9] X. Yao, X. S. Xu, Y. Yang, Z. Zhu, F. Tao, and M. Yuan, "Stratification of population in NHANES 2009–2014 based on exposure pattern of lead, cadmium, mercury,

- and arsenic and their association with cardiovascular, renal and respiratory outcomes,” *Environment International*, vol. 149, p. 106410, 2021.
- [10] H. M. Wasana, G. D. Perera, P. D. Gunawardena, P. S. Fernando, and J. Bandara, “WHO water quality standards vs Synergic effect (s) of fluoride, heavy metals and hardness in drinking water on kidney tissues,” *Scientific Reports*, vol. 7, no. 1, p. 42516, 2017.
- [11] N. Loh, H.-P. Loh, L. K. Wang, and M.-H. S. Wang, “Health effects and control of toxic lead in the environment,” *Nat. Resour. Control Process.*, pp. 233-284, 2016.
- [12] Y. T. Supabhorn, A. V. David, P. Phisit, K. Tanaporn, C. G. Glenda, and S. Soisungwan, “Chronic kidney disease induced by cadmium and diabetes: A quantitative case-control study,” *Int J Mol Sci.*, vol. 24, no. 10, p. 9050, 2023.
- [13] S. Mitra, C. Arka Jyoti, T. Abu Montakim, E. Talha Bin, N. Firzan, K. Ameer, M. I. Abubakr, K. Mayeen Uddin, O. Hamid, A. Fahad, and S. Jesus Gandara, “Impact of heavy metals on the environment and human health: Novel therapeutic insights to counter the toxicity,” *J. King Saud Univ. – Sci.*, vol. 34, no. 3, p. 101865, 2022.
- [14] T. Watanabe, and S. Hirano, “Metabolism of arsenic and its toxicological relevance,” *Arch Toxicol.*, vol. 87, pp. 969-979, 2013.
- [15] C. Ferreccio, A. H. Smith, and V. Duran, “Case-control study of arsenic in drinking water and kidney cancer in uniquely exposed Northern Chile,” *Am J Epidemiol.*, vol. 178, pp. 813-818, 2013.
- [16] R. R. Mehrdad, R. R. Mehravar, K. Sohrab, and A. A. Moghadam, “Cadmium toxicity and treatment: An update,” *Caspian J Intern Med.*, vol. 8, no. 3, pp. 135-145, 2017.