

The Relationship of Heavy Metals With Lung Cancer: A Systematic Review

Hubungan Logam Berat Dengan Kanker Paru: Sebuah Tinjauan Sistematis

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Abstract. General Background: Heavy metals such as lead, cadmium, nickel, and copper are known environmental pollutants with established toxic effects on human health. **Specific Background:** These elements have been identified as significant contributors to various diseases, with emerging evidence suggesting their role in promoting cancer, particularly lung cancer. **Knowledge Gap:** Although numerous studies have investigated the relationship between heavy metals and lung cancer, a comprehensive understanding of the impact of various metal concentrations on cancer development and progression remains underexplored. **Aims:** This systematic review aims to consolidate and analyze the existing literature on the effects of heavy metal exposure on lung cancer, focusing on different biological samples such as plasma, urine, nails, and hair. **Results:** The review identified consistent evidence linking increased levels of heavy metals with higher risks of lung cancer. Studies highlighted the role of metals like cadmium, chromium, and nickel in not only promoting cancer growth but also in impacting the efficacy of cancer treatment. The findings suggest that exposure to these metals, often from environmental and industrial sources, is a critical risk factor for lung cancer. **Novelty:** This review uniquely synthesizes data from diverse biological samples, providing a holistic view of how heavy metal exposure influences lung cancer. **Implications:** The study underscores the importance of monitoring and regulating heavy metal exposure to reduce the incidence of lung cancer. It also emphasizes the need for further research to develop targeted strategies for mitigating the risks associated with heavy metal-induced carcinogenesis.

Keywords – Heavy Metals, Lung Cancer, Cadmium, Carcinogenesis, Toxic Exposure

Abstrak. Latar Belakang Umum: Logam berat seperti timbal, kadmium, nikel, dan tembaga merupakan polutan lingkungan yang diketahui memiliki efek toksik yang nyata terhadap kesehatan manusia. **Latar Belakang Khusus:** Unsur-unsur ini telah diidentifikasi sebagai kontributor signifikan terhadap berbagai penyakit, dengan bukti yang muncul menunjukkan peran mereka dalam mendorong kanker, khususnya kanker paru-paru. **Kesenjangan Pengetahuan:** Meskipun banyak penelitian telah menyelidiki hubungan antara logam berat dan kanker paru-paru, pemahaman yang komprehensif tentang dampak berbagai konsentrasi logam pada perkembangan dan progresi kanker masih belum dieksplorasi. **Tujuan:** Tinjauan sistematis ini bertujuan untuk mengonsolidasikan dan menganalisis literatur yang ada tentang dampak paparan logam berat pada kanker paru-paru, dengan fokus pada berbagai sampel biologis seperti plasma, urin, kuku, dan rambut. **Hasil:** Tinjauan tersebut mengidentifikasi bukti konsisten yang menghubungkan peningkatan kadar logam berat dengan risiko kanker paru-paru yang lebih tinggi. Penelitian menyoroti peran logam seperti kadmium, kromium, dan nikel tidak hanya dalam mendorong pertumbuhan kanker tetapi juga dalam memengaruhi kemanjuran pengobatan kanker. Temuan tersebut menunjukkan bahwa paparan logam ini, yang sering kali berasal dari sumber lingkungan dan industri, merupakan faktor risiko penting untuk kanker paru-paru. **Kebaruan:** Tinjauan ini secara unik mensintesis data dari berbagai sampel biologis, memberikan pandangan holistik tentang bagaimana paparan logam berat memengaruhi kanker paru-paru. **Implikasi:** Studi ini menggarisbawahi pentingnya pemantauan dan pengaturan paparan logam berat untuk mengurangi kejadian kanker paru-paru. Studi ini juga menekankan perlunya penelitian lebih lanjut untuk mengembangkan strategi yang tepat guna mengurangi risiko yang terkait dengan karsinogenesis yang disebabkan oleh logam berat.

Kata Kunci – Logam Berat, Kanker Paru, Kadmium, Karsinogenesis, Paparan Racun

I. INTRODUCTION

Cancer of lung is a common malignant tumor that can be refer to many factors such as circumferential pollution and heredity, and increased levels of heavy elements in human body play basic role in growing the danger of lung

cancer[1]. Emissions of heavy metals from their various sources (natural and industrial) are one of the largest environmental pollutants, which leads to an increase in their concentration in the atmosphere. It includes a large group such as cadmium, mercury, nickel, lead, etc. [2]. Heavy elements are not a rare occurrence for humans, as they are existent in crust of earth are also existent in each part of the circumference [3]. Furthermore, heavy elements have several applications in technological, agricultural, domestic and medical. This has led to the absorption of these heavy elements in humans raising concerns in their effect on general health [4]. Although not widely understood, toxicity from the cumulating of heavy elements has been as these elements can effect on human healthy and cause many conditions such as decrease in the human body's metabolism and development many diseases such different of type cancer [5], [6]. The toxicity of metals has long been investigated and studied for its effects on human health [7]. Unessential elements such as cadmium, mercury, nickel and lead are essentially noxious and that is not have any biological role and actually do a toxic damage on each the body organ at consumed low quantity [8]. Heavy elements caused cellular damage and it is related to different properties, such as oxidation states, solubility, and soft-solid nature, which can affect their species in biological systems [9]. The IARC has classified some heavy elements, such as Pb, Ni, and Cd, as carcinogenic substances that affect the human body in general [10].

This review aims to study the effect of heavy elements in cancer of lung and its development, by briefing the latest studies with repeated exposure to elements as a risk factor for humans..

II. RESULT AND DISCUSSION

RESULT

Table (1): shows the type, levels of heavy elements and it is effect on different biological samples for our systematic review.

Table (1): Heavy elements and it is effect on different biological samples

| Heavy elements | Samples | Heavy elements levels | Effect | References |
|--|-----------------|---|--|----------------------------------|
| Hg, Cr, Ni, Cu, and Zn | Soil | Increase of heavy elements levels | Cancer of lung | Huang et al. (2013) |
| Cd | Urine | Increase of cd level | Cancer of lung in the area adjacent to the industrial zone | Lee et al. (2022) |
| Cd | Blood | Decrease of Cd level | Improving the health condition of patients suffering from lung cancer | S. Pietrzak et al. (2021) |
| Co, Cr, Pb | Lung tissue | Accumulation of heavy elements levels | Cancer of lung | M. Scimeca et al. (2014) |
| Se and Cd | Blood serum | Increase of Cd level | Cancer of lung | K. Zhang et al., (2023) |
| Pb, Cd, Ni, As, Be and Cr | Lung tissue | Increase of heavy elements levels in lung cancer patients | Increase of lung cancer with tobacco, cadmium and lead increases | G. De Palma et al, (2008) |
| Cr | Blood | Increase of Cr level | Increase of Cr with lung cancer patients | P. Baszuk et al. (2020) |
| Mg, Cu and Zn | Lung tissue | Increase of Mg, Cu and Zn | Pathogenesis of lung cancer caused by metals | Ł. J. Binkowski et al., (2020) |
| Ni, Co, Fe, Br, Co, and Fe | Lung tissue | Increase of heavy element levels | Cancer of lung development | R. Chiba et al. (2019) |
| Ca, Na, Mg, Pb K, Fe, Zn, Cu, Li, Cd, Sr, Mn, Co, Ni, and Cr | Nails and scalp | Statistically significant different in lung cancer patients | Lung cancer cases have a significant impact on mineral balance in humans | Qayyum, et. al. (2014) |
| Cd | Blood | Statistically significant increase in lung cancer patients | Increased cadmium concentration may be a sign of lung cancer | M. R. Lener et al. (2021) |
| Mg, Co, Ba and Mo | Blood | Statistically significant increase in lung cancer people | Accumulation of heavy elements levels in the blood of lung cancer people | S. A. Abduljaleel, et al. (2022) |

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|-------------------|--------------|--|---|----------------------------|
| Mg, Co, Ba and Mo | Blood serum | Statistically significant increase in lung cancer patients | Lung cancer patients have a significantly lower body mass index | A. Sadat et al. (2008) |
| Cu and Zn | Blood serum | Increase in lung cancer patients | Cancer of lung | J. Lin, et al. (2022) |
| Cu and Zn | Blood plasma | Increase of Cu in blood of lung cancer people | Cancer of lung | L.-L. Zhang, et al. (2009) |

elements by soil on lung cancer. The results indicate that there is a statistically significant relationship between exposure to chromium, copper, mercury, nickel, and zinc and the probability of developing squamous cell carcinoma of the lung [11]. A 2022 study was also conducted by Lee et al. In Yunlin County on lung cancer patients to compare cadmium levels in urine samples between the population and workers in the petrochemical industrial park, the participants working in the petrochemical industrial park had a relatively higher concentration than the population and were more develop lung cancer. In industrial areas, cadmium accumulation led to lung cancer risk[12]. Sandra Pietrzak et. al. By studying the effect of cadmium levels over different time periods on lung cancer patients in Poland, between January 2011 and November 2012, the results show that lowering the concentration of cadmium in the blood leads to an improvement in the health condition of patients suffering from lung cancer [13]. M. Scimeca, et. al. By studying the effect of heavy metals in many industrialized countries on lung tumors, 45 samples were recorded, including 15 cases of lung cancer (malignant tumor), 15 benign lung tumors, and 15 control healthy. It was concluded in this study that heavy elements such as Co, Pb, and Cr bioaccumulate in malignant tumors. In fact, a increase presence of bioaccumulated heavy metals led to lung cancers compared to benign tumors and control tissues[14]. Selenium and cadmium concentrations were measured by Kai Zhang et. al. In blood serum samples from 86 cases of patients with lung cancer and 105 controls, Se may be represent protective of cancer and effect pathogenic of Cd [15]. G. De Palma et al. By studying the beryllium, arsenic, cadmium, chromium, lead, and nickel levels in patients with lung tissue cancer, a number of healthy people were also included as a control group. This study showed that the heavy element levels in people with lung cancer are higher than in control people [16]. P. Baszuk et al. By studying the chromium level in many samples of blood for cancer of lung and comparing them with healthy people, the result was levels of chromium is higher in cancer of lung compared to control people. The study also showed that the developing lung cancer increases with increasing levels of chromium in the blood [17]. The relationship between magnesium, copper, and zinc concentrations in cancer of lung patients and without cancer of lung living in industrial settings was studied by Ł. J. Binkowski et. al., the results indicate that the accumulation of magnesium, copper and zinc may be led to the tumor growth and therefore the data obtained may have an impact in metal-induced lung cancer [18]. R. Chiba et al studied the relationship between concentrations of heavy elements in the cancer of tissue of lung and healthy people as a control group. Co, Fe, Zn, Ni, Br and Cu concentrations in cancer of lung were much higher than the concentrations of the control group[19]. M. A. Qayyum, et. al. Compare the levels of heavy elements in lung cancer people in nails and scalp hair with healthy people as a control group, it was found that the of Mg, Na, Ca, Fe, Zn, K, Sr, Cu, Li, Mn, Co, Cr, Ni, Pb and Cd concentrations is higher in nails and hair in cancer people according to control group. The study revealed reciprocal differences in the levels of minerals found in nails and scalp hair in cancer and control, indicating that lung cancer cases had a significant impact on mineral balance in humans [20]. M. R. Lener et al. By measuring cadmium concentrations in the lung cancer people blood before chemotherapy, the effect of smoking habit on lung cancer patients was also studied. The study indicates that the cadmium level in the blood may be a sign of the occurrence of lung cancer. They added to this that the level of cadmium decreases when quitting smoking [21]. S. A. Abduljaleel, et al. determined the levels of some heavy elements for patients suffering from lung cancer according to the control people. The results found absorb increase in the of Ba, Co, Mg, and Mo concentrations blood of cancer group. It is also shown that the concentrations of all heavy elements in the blood accumulated at high levels in the smokers blood compared to non-smokers, which indicates accumulate of heavy elements in lung [22]. A. Sadat et al. By determining the Ba, Co, Mg, and Mo levels in lung cancer serum patients and comparing them with healthy volunteers of the same age and gender. The results show there are lower body mass index of cancer of lung group had a significantly, and the elements level in cancer of lung blood serum patients were higher compared to controls. [23] J. Lin, et al. By studying the effect of Zn and Cu in 50 blood serum samples on lung cancer people and comparing them with 20 patients suffering from non-tumor lung diseases as a control group. Copper concentration blood serum patients was higher than in the control. However, there was no difference in the serum zinc levels between the two groups [24]. The concentrations of Cu and Zn were determined by L.-L. Zhang, et al. in blood plasm in people

with cancer of lung with group of healthy. The result shows that copper increased and zinc decreased in blood plasma patients [25].

III. CONCLUSION

In this study, and according to the databases reviewed, it was found that different types of elements exposure in peripheral lead to stimulate of oxidative stress. Thus, High levels elements may be risk case of many malignant diseases, especially lung cancer. Conclusion of a systematic review showed that the different types elements toxicity depends on the method of heavy elements exposure, the dose, as well as age, gender, nutritional status, through inhalation, eating contaminated food, and drinking. These factors have many serious effects on health of human. Some elements are also necessary for the human to maintain life, such as iron, zinc, copper, and to a lesser extent chromium, these elements can be harmful to the organism when their quantity exceeds threshold limits

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