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## Original Article

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# Rate of cystic echinococcosis in animals slaughtered in the slaughterhouse of Ordu province

## Abstract

**Aim:** Cystic echinococcosis (CE) is a disease that develops as a result of the larval form of *E. granulosus* settling in the internal organs of intermediate hosts such as sheep, goats, cattle, pigs and humans. The disease adversely affects both human and animal health. It has been reported that it is frequently seen in East, North East and Central Anatolia. In this study, it was aimed to detect the presence of CE in animals slaughtered between 2020-2021 in the slaughterhouse of Ordu province.

**Materials and Methods:** The internal organs of animals slaughtered in the slaughterhouse between 2020-2021 and organs with CE were brought to the parasitology laboratory and evaluated in terms of scolex.

**Results:** In the slaughterhouse, 4094 cattle were slaughtered in 2020 and 3788 in 2021, and hydatid cysts were detected in 187 cattle in 2020 and 112 in 2021. No parasites were found in sheep and goats during the study period. Lung and liver localization were detected together in 150 of 299 animals with CE. Scolex was detected in only 3 of them.

**Conclusion:** This condition was thought to be common in animals in the region. It was concluded that epidemiological studies should also be conducted in people who can be seen as a risk group in the region.

**Keywords:** Cystic echinococcosis; Animal; Ordu

## CITATION

Gemici G, Karaman U. Rate of cystic echinococcosis in animals slaughtered in the slaughterhouse of Ordu province. Int Target Med J. 2022;1(1):1-4.

## INTRODUCTION

*Echinococcus multilocularis*, *E. oligarthrus*, *E. granulosus* and *E. vogeli* species have different morphological features and the species that frequently cause disease in humans are *E. granulosus* and *E. multilocularis*. *E. granulosus* causes cystic echinococcosis (CE), and *E. multilocularis* causes alveolar echinococcosis (AE) (1).

The length of *E. granulosus* is 2-6 mm and consists of head, neck and rings. The final host in the evolution of the parasite, which is hermaphrodite, is the dog, and the intermediate hosts are mammals like cattle, buffalo antelope, goat, camel, pig, deer, horse, elephant, rabbit, squirrel, mouse, monkey, human, etc.. The parasite can settle in almost any organ and cause infection. The parasite usually grows very slowly, depending on the organ in which it is located in the intermediate host. The larva that settles in the organ forms a cyst and this cyst can reach 5-10 mm in diameter in about 5 months (1). It may cause economic losses in the country due to surgical and chemotherapeutic treatment expenses, hospital expenses, and loss of workforce in patients

with CE (1,2). It was thought that diagnosis and control programs should be done for the difficulties in diagnosis and economic losses due to the disease process. Moreover, the disease causes reductions in economic income due to carcass, infected liver and yield losses in animals such as sheep, goats and cattle (3-5).

CE, which has a wide distribution in the climate areas where there are stray dogs and animal husbandry in the world, is frequently seen in Greece, Bulgaria, every region of Asia, Australia, New Zealand, South Africa, Central and South America (6-8). It has been reported that the parasite can also be found in areas where it has been detected endemic or sporadically. It has been stated that it has never been found in Greenland and Iceland (8-12). CE spreads widely in Turkey due to reasons such as geographical structure, climate, socio-economic level, inadequacy of veterinary health organization and lack of education. The incidence of the disease varies from region to region. The regions where it is most common are Eastern Anatolia, Southeastern Anatolia and Central Anatolia (7,9,10). The epidemiology of the parasite in the source information reached is 0.7-20/100000 in humans, 5.8-82% in

cattle, 30.6-80% in sheep, 24% in goats, and 5-8.4% in pigs in countries neighboring Turkey (1-5). In Turkey, it was found to be 0.87-6/100000 in humans, 25.9% in cattle, 30.6% in sheep, 12.7% in goats and 1.4% in horses (13,14).

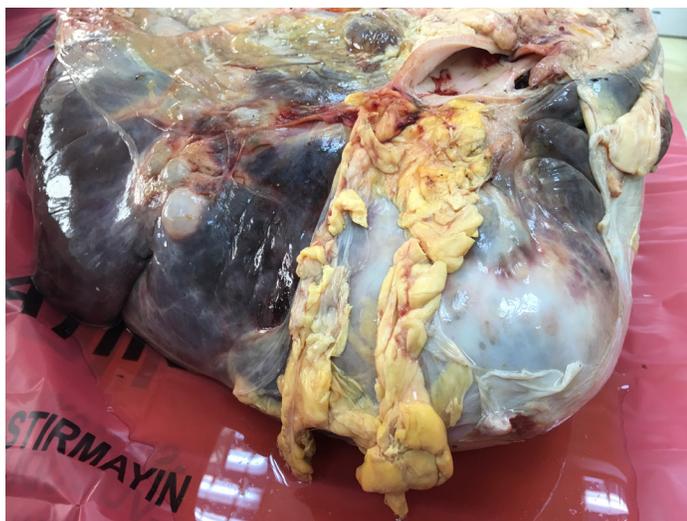
A limited number of epidemiological studies have been identified in animals and humans around Ordu province. Considering that it will contribute to the epidemiology, it is aimed to evaluate the presence of CE in bovine animals prospectively between 2020-2021 in the slaughterhouse located in the city center where there is a large number of stray dogs.

## MATERIALS AND METHODS

The organs of the animals with CE slaughtered between 2020-2021 in the central slaughterhouse of Ordu province were taken from the slaughterhouse, placed in clean bags and brought to the parasitology laboratory without waiting. Organs brought to the parasitology laboratory were evaluated for protoscoleces in the cyst fluid. Age, sex and cyst diameters in the organs with CE were also evaluated in the slaughtered animals.

## RESULTS

In the slaughterhouse, 4094 cattle were slaughtered in 2020 and 3788 in 2021, and hydatid cysts were detected in 187 cattle in 2020 and 112 in 2021. No parasites were found in sheep and goats during the study period. Hydatid cysts were detected in the lungs of 150 of 299 animals, and in the lung and liver localizations together of the others (Figure 1). Scolex was detected in only 3 of them (Figure 2).



**Figure 1.** Liver CE

In laboratory examinations, the smallest cyst diameter was 5 cm and more than one cyst was usually detected. Parasites were detected in only 7 males of 299 cattle with CE, and positivity in 297 remaining was detected in females. The youngest animal slaughtered was 1.5 years old and the oldest animal was 7 years old.



**Figure 2.** Protoscoleces obtained from CE liver

## DISCUSSION

*Echinococcus granulosus* is a member of the taenia family, and its larvae cause CE disease in intermediate hosts. It negatively affects the health of both humans and animals in the world and in Turkey. It can cause different clinical symptoms depending on the regions where the parasite is located, as well as cause death. Since it can cause structural and functional disorders by settling in the tissues of animals, it can also cause economic losses in slaughtered animals (1,8,15,16).

In studies conducted abroad in dogs that were the last host of the parasite, the lowest rate was reported by Villeneuve et al. (17) in Canada in 2015 as 0.4%. The highest rate was detected as 51.2% by Omer et al. (18) in Sudan. Studies in dogs were performed using PCR, Copro antigen and necroscopic methods (17,18). In studies conducted in Turkey, positivity between 1.0-14.0% was reported with PCR examination (19-22). In the source information reached, no study was found on dogs in Ordu province.

In the study carried out in cattle abroad, the lowest rate was found in Italy and Egypt as 0.1, and the highest rate was found in Moldova as 78.9% (23-25). In studies conducted in Turkey, CE was found at a rate of 24.0% in Erzurum (22), 6.8% in Kars (26), 38.5 in Van (27), 3.4% in Kırkkale (28) and 4.0% in Tekirdağ (29).

In previous studies in Ordu, Karaman et al. (8) reported that they encountered parasites at a rate of 4.4, while Fidan and Kapakin found parasites at a rate of 11.3 (30). In the present study, similar to Karaman et al. (8), CE was found at a rate of 4.56% in 2020 and 3.0% in 2021. The difference obtained in the studies may have resulted from the method, sample selection and regional differences. In the presented study, the lower CE detection rate compared to Fidan and Kapakin (30) may have resulted from the researcher's going to the slaughterhouse after slaughter and veterinary control.

In Sivas, 765 cattle slaughtered in three separate slaughterhouses in April and May were examined and 273 (35.7%) were reported as positive. Researchers found CE in the liver of 66 (8.6%) and in the lungs of 103 of positive animals (5). Hydatid cysts were detected in the lungs of 150 of 299 animals, and in the lung and liver localizations together of the others. Scolex was detected in only 3 of them.

In the study, going to the laboratory to bring hydatid cysts to the laboratory after veterinary control was determined as the limitation of the study.

In human studies conducted on CE in Ordu province, a study was found, the researchers took samples from butchers and farmers, whom they considered as risk groups, in that study, and they reported that they did not detect CE seropositivity. The researchers worked with 90 serum samples and attributed the negative seropositivity to the low farm animal population (31).

## CONCLUSION

In the study, it was determined that there are often sterile cysts in cattle. It was not detected in ovine animals during two-year period. Again, considering that the dogs may also be infected after the study conducted by the researchers in 2015, a project was started in dogs working in the shelter, taenia eggs were found in feces examinations and it has not yet been published. In line with these results, it was concluded that epidemiological studies should be conducted in humans as well. PCR studies are also planned for species identification in animals. It is also suggested that control studies should be planned after the epidemiology of the parasite has been determined.

**Competing interests:** The authors declare that they have no competing interest.

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**Ethical approval:** This study "Declaration of Helsinki" was conducted in accordance with the ethical principles stated.

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## Original Article

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# Retrospective analysis of lactate levels, lung involvement and treatment methods of patients with COVID-19 who applied to the emergency department

## Abstract

**Aim:** Covid 19 affects more than 6,000,000 confirmed cases. It can be asymptomatic in the case of the disease, or it can be observed in simpler symptoms such as fatigue, myalgia, fever, sore throat and dry cough that can be treated on an outpatient basis. However, in more severe cases, septic shock accompanied by dyspnea and/or hypoxemia and especially Acute Respiratory Distress Syndrome (ARDS) may develop. this condition has a high mortality. When there is hypoxemia, cellular anaerobic respiration predominates. In this case, an increase in plasma lactate levels, which is an anaerobic respiratory metabolite, occurs.

**Materials and Methods:** Patient data were accessed through the patient registration system. Age, gender, comorbidities, blood lactate levels, and lung tomography reports (Co-Rads Classification) of the patients were examined.

**Results:** 135 cases were excluded. While 43.2% (n=60) of the patients were male, 56.8% (n=19) were female. It was determined that 74.8% (n=104) patients had negative tomography and 25.2% (n=35) patients had positive tomography. When the treatment types of the patients were examined, 49.6% (n=69) were treated as outpatients, 43.2% (n=60) were treated as inpatients in the hospital ward, and 7.2% (n=6) were treated in the intensive care unit. Pulmonary involvement rates of outpatients were the least, increased in those who were treated in the ward, and the highest rate of involvement was found in those who were hospitalized in the intensive care unit. This situation was found to be statistically significant ( $p<0.001$ ). The lactate level of the patients hospitalized in the intensive care unit was found to be statistically significantly higher than the lactate level of the patients receiving outpatient treatment ( $p 0.002$ ).

**Conclusion:** In predicting the disease treatment method in patients with Covid 19; It was suggested that it should be followed in terms of blood lactate level and lung tomography involvement.

**Keywords:** Covid 19; lactate; Lung Involvement; Treatment Methods; Co-Rads Classification

## CITATION

Saribas MS. Retrospective analysis of lactate levels, lung involvement and treatment methods of patients with COVID-19 who applied to the emergency department. Int Target Med J. 2022;1(1):5-9.

## INTRODUCTION

COVID-19 disease first appeared in China in 2019. It spread very quickly and turned into a pandemic that affected the whole world in a short time. Covid 19 affects more than 200 countries, it is known that there are more than 6,000,000 confirmed cases and more than 370,000 deaths (1). It can be asymptomatic in the case of the disease, or it can be observed in simpler symptoms such as fatigue, myalgia, fever, sore throat and dry cough that can be

treated on an outpatient basis. However, in more severe cases, septic shock accompanied by dyspnea and/or hypoxemia and especially Acute Respiratory Distress Syndrome (ARDS) may develop. this condition has a high mortality (2). Cases reported as having a corads score of 3 and above were considered to have lung involvement.

Acute Respiratory Distress Syndrome (ARDS) is a clinical condition in which both lungs are affected, characterized by

sudden onset, capillary endothelial damage, diffuse pulmonary infiltration, and hypoxemia resistant to oxygen therapy. When there is hypoxemia, cellular anaerobic respiration predominates. In this case, an increase in plasma lactate levels, which is an anaerobic respiratory metabolite, occurs. It has been reported that increased plasma lactate levels are associated with high mortality in conditions such as sepsis and septic shock (3).

Another important tool for diagnosing ARDS is tomographic examination of the lung. In this examination, ARDS is investigated by considering the presence of bilateral opacities, consolidation and ground-glass opacities together with the patient's clinic (4,5).

Treatments of Covid 19 patients are planned according to their clinical status and the severity of lung tomography involvement. Accordingly, it can be done on an outpatient basis, as well as in the hospital ward or in the intensive care unit (2). In the present study, we examined the relationship between lactate levels, lung tomography findings and treatment modalities in cases diagnosed with Covid 19 in the emergency department. In this way, we aimed to contribute to the diagnosis and treatment algorithms that can be created.

## MATERIALS AND METHODS

The presented study is cross-sectional and retrospective. Before starting the study, approval was obtained from the Ethics Committee of Ordu University Faculty of Medicine (2022/36 date: 11.02.2022). As study was conducted retrospectively, the need for informed consent forms from patients was waived. The study was conducted in accordance with the Declaration of Helsinki.

Patient data were accessed through the patient registration system. Age, gender, comorbidities, blood lactate levels, and lung tomography reports of the patients were examined.

The characteristics of the study population in the study and the criteria of Lung Tomography Analysis are given below.

### Study Population

#### Inclusion Criteria

1. Applying to the emergency department between 01/07/2021 and 31/12/2021
2. 18 years or older
3. Cases with positive SARS-CoV-2 PCR analysis and whose data can be accessed from the patient information system

#### Exclusion criteria

1. Those with inconsistency in SARS-CoV-2 PCR analyzes and not diagnosed with COVID-19
2. Cases with positive SARS-CoV-2 PCR analysis but without blood test and lung tomography
3. Cases with positive SARS-CoV-2 PCR analysis but whose data could not be accessed from the patient information

system

4. Pregnant cases
5. Immunosuppressed cases
6. Patients with previous lung diseases such as asthma and COPD who developed (ARDS)

### Lung Tomography Analysis

The pulmonary tomography reports of the patients included in the study were evaluated according to the corads scoring. Accordingly, cases reported as having a corads score of 3 and above were considered to have lung involvement (6).

### Co-Rads Classification

Level	Suspicion Level	Findings
CO-RADS 0	Not evaluated	The review is technically inadequate.
CO-RADS 1	Very low	Normal or non-infectious findings (mild or severe emphysema, perifissural nodules, lung tumor or fibrosis)
CO-RADS 2	low	Typical findings for other infections (Budded branch, centrilobular pattern, lobar or segmental consolidation, cavitation)
CO-RADS 3	Medium / uncertain	Findings in both COVID-19 and other diseases (central ground glass opacities, pulmonary edema, Homogeneous, diffuse ground-glass appearance with interlobular septal thickening or pleural effusion suggestive ground glass nodules that are not centrilobular or adjacent to the visceral pleura)
CO-RADS 4	High	Suspicious / possible findings for COVID-19
CO-RADS 5	Very high	Typical findings for COVID-19 (bilateral and multifocal, including fissure, adjacent to the visceral pleura, with or without consolidation, ground glass opacities)
CO-RADS 6	Definitive diagnosis	RT-PCR** positive patient

### Statistical analysis

Data analysis was performed using SPSS v26 software. (IBM Inc., Chicago, IL, USA). Data are given in numbers and percentages. relationship between types of comorbidities and treatment settings or patient mortality.

It was investigated using the chi-square t-test. The relationship between these biomarkers and mortality was examined using the Mann-Whitney U test. Data were tested for normality using analysis first. Statistical evaluation using Kolmogorov-Smirnov test and Levene test for homogeneity of variance was considered significant when  $p < 0.05$ .

## RESULTS

In the specified date range, 274 cases were found to be Covid positive in the emergency department. However, 135 cases were excluded because they did not meet the inclusion criteria. While 43.2% (n=60) of the patients were male, 56.8% (n=19) were female.

Patients included in the study whose lung tomography reports were reported as corads 3 and above were considered positive. According to this; It was determined that 74.8% (n=104) patients had negative tomography and 25.2% (n=35) patients had positive tomography. When the treatment types of the patients were examined, 49.6% (n=69) were treated as outpatients, 43.2% (n=60) were treated as inpatients in the hospital ward, and 7.2% (n=6) were treated in the intensive care unit. was detected.

The relationship between tomography involvement and treatment of the patients was investigated. It was determined that 11.6% (n=8) of the outpatients, 30.0% (n=18) of the hospitalized patients and 90% (n=9) of the patients hospitalized in the intensive care unit had lung involvement (Table 1). Pulmonary involvement rates of outpatients were the least, increased in those who were treated in the ward, and the highest rate of involvement was found in those who were hospitalized in the intensive care unit. This situation was found to be statistically significant ( $p < 0.001$ ).

**Table 1. The relationship between the patients' Lung tomography involvement status and treatment modalities**

	CT negative		CT positive		Total	
	n	%	n	%	Number	%
Outpatient	61	88.4	8	11.6	69	100.0
Inpatient	42	78.0	18	30.0	60	100.0
Intensive care	1	10.0	9	90.0	10	100.0
Total	104	74.8	35	25.2	139	100.0

The blood lactate levels of the patients included in the study were checked. Since the lactate values did not fit the normal distribution, the median and IQR were used and the median value was 1.2 (IQR 0.9). Lactate levels and treatment modalities of the patients were compared. The lactate level of 51.1% (n=69) who received outpatient treatment was found to be  $1.30 \pm 0.78$ . The lactate level of 44.4% (n=60) of the patients who received inpatient treatment in the ward was found to be  $1.48 \pm 0.78$ . Groups were analyzed with the Student-T test. The lactate levels of the patients receiving outpatient treatment were found to be lower than those of the patients hospitalized in the ward, and the lactate levels of the patients treated in the intensive care unit were found

to be the highest. The lactate levels of the patients who received outpatient treatment and those treated in the intensive care unit were compared. The lactate level of 4.5% (n=6) of the patients who received outpatient treatment was  $1.30 \pm 0.78$ , and the lactate level of the patients who received treatment in the intensive care unit was  $2.15 \pm 1.37$ . Both groups were analyzed with the Student-T Test; The lactate level of the patients hospitalized in the intensive care unit was found to be statistically significantly higher than the lactate level of the patients receiving outpatient treatment ( $p = 0.002$ ). The lactate levels of the patients in the ward and in the ICU were examined. The lactate level of 44.4% (n=60) who received inpatient treatment in the ward was  $1.48 \pm 0.78$ , and the lactate level of the patients who received treatment was  $2.15 \pm 1.37$ . The lactate levels of the patients admitted to the intensive care unit were found to be significantly higher than the lactate levels of both outpatients and inpatients in the ward ( $p = 0.002$ ) (Table 2).

**Table 2. The relationship between the lactate levels of the patients and the treatment modalities**

	n	Laktat	
		Mean	SD
Outpatient	69	1.30	$0.78 \pm 0.9$
Inpatient	60	1.48	$0.78 \pm 0.11$
Intensive care	10	2.15	$1.37 \pm 0.43$

Lactate level and tomography involvement were compared. 77% (n=104) of the patients did not have lung involvement, and the median lactate levels were found to be  $1.29 \pm 0.72$ . Pulmonary involvement was positive in 23% (n=35) of the patients, and their lactate levels were found to be  $1.88 \pm 1.07$ . The difference between the groups was analyzed by Student's T test, and the lactate level of the patients with lung involvement was found to be higher than those without involvement ( $p < 0.001$ ).

## DISCUSSION

According to the source information reached, it has been reported that the most affected organ from covid 19 is the lung. In case of damage to the lungs; It has been reported that it may cause widespread alveolar epithelial destruction, hyaline membrane formation, capillary damage, capillary hemorrhage, alveolar septal fibrous proliferation and/or pulmonary hypertension (7). Yu et al. reported that they found the prevalence of developing pulmonary fibrosis to be higher in patients with severe clinical course (8). It was reported that different degrees of lung damage and pulmonary interstitial fibrosis were observed in the autopsies of COVID-19 patients (9). Similarly, according to the British Thoracic Society Guidelines, it has been reported that the prevalence of lung fibrosis and accompanying functional disorders increases in patients with severe disorders (10). In such cases, it is difficult to predict the severity of the disease. For this reason, different classification systems are used to assist physicians in assessing the severity of the disease. The CO-RADS classification system is more reliable in diagnosis and a more practical method

to follow the course of the disease compared to others (11). Bellini et al. reported that the CO-RADS classification is useful in diagnosing Covid 19 suspected cases and making decisions in the treatment of the disease. Bellini et al., while distinguishing between Covid 19 and other pre-diagnoses, suggested that those reported as corads 3 and above be considered positive(12). In the presented study, the CO-RADS classification system was used when evaluating suspected cases of Covid 19, and those reported as corads 3 and above were considered positive. It was determined that 74.8% (n=104) of the patients who applied to the emergency department had negative tomography and 25.2% (n=35) patients had positive tomography. When the treatment methods of the patients were examined, it was found that 49.6% (n=69) were treated as outpatients, 43.2% (n=60) were treated as an inpatient in the hospital ward and 7.2% were treated in the intensive care unit. When the pulmonary tomography involvement of the cases and the treatment modalities were examined; It was determined that 30.0% of those hospitalized in the ward and 90% of those hospitalized in the intensive care unit had lung involvement. The relationship between lung involvement and treatment modalities was found to be significant ( $p<0.001$ ).

The destruction of Covid 19 in the lungs is manifested by impaired diffusion capacity (13). Hypoxemia and anaerobic metabolism occur when diffusing capacity is impaired. Serum lactate level occurs as a product of anaerobic metabolism (14) In Covid 19 infection, hypoxemia develops and accordingly lactate levels increase. It is known that lactate level gives clues about the prognosis of infectious diseases such as in-hospital mortality (15,16). Shapiro et al. reported that mortality increased as the lactate level increased (17). Vincent et al. reported that it can be used to predict the course of the disease in various critical conditions such as sepsis, trauma, cardiac arrest and respiratory failure (18). Another study reported that blood lactate levels can be used to predict disease severity, specify specific treatments, and monitor the adequacy and timing of interventions (19). In the presented study, the presence of changes in diffusion capacity was investigated by looking at blood lactate levels in patients with Covid 19. In addition, the relationship between the change in lactate level and the treatment modalities of the patients was examined. The lactate level of the patients receiving outpatient treatment was found to be statistically significantly lower than the lactate level of the patients receiving inpatient treatment in the intensive care unit. In fact, the lactate levels of the patients who received inpatient treatment in the ward and the patient who received treatment in the intensive care unit were compared. The lactate levels of the patients hospitalized in the intensive care unit were found to be statistically significantly higher than the lactate levels of the patients hospitalized in the ward.

In addition, the relationship between blood lactate level and lung tomography involvement was examined in the presented study. Similarly, blood lactate levels of patients with lung involvement were found to be statistically significantly higher than those without lung involvement.

## CONCLUSION

It has been determined that there is a correlation between the lung tomography involvement of patients with Covid 19 and the blood lactate level. It was concluded that as the disease progresses, hypoxia develops due to lung involvement, which increases lactate.

It was determined that the blood lactate levels of patients with Covid 19, who were planned to be treated with intensive care hospitalization, increased significantly compared to the groups that were planned to be treated with outpatient or service admission. In predicting the disease treatment method in patients with Covid 19; It was suggested that it should be followed in terms of blood lactate level and lung tomography involvement.

**Competing interests:** The authors declare that they have no competing interest.

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**Ethical approval:** Before starting the study, approval was obtained from the Ethics Committee of Ordu University Faculty of Medicine (2022/36 date: 11.02.2022).

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**Original Article**

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# Green synthesis, characterization of gold nanomaterials and assessment of microbial potentials of nanoparticules using *lavandula officinalis* flower extract

**Abstract**

**Aim:** In this study, environmentally friendly synthesis of gold nanoparticles was carried out by using the extract obtained from the flowers of the lavender (*Lavandula officinalis*) plant.

**Materials and Methods:** In the metal solution used in the study, gold nanoparticles (AuNPs) were obtained by precipitation with the help of high-speed centrifugation as a result of the reduction of the ionized Au<sup>+3</sup> form by phytochemicals. Zeta potential, X-ray diffractometry, UVVis spectroscopy, transmission electron microscopy (TEM), Fourier transform scanning electron microscope (FE-SEM) and Electron for elucidation of the characterization and structure of (LO-AuNPs) synthesized with *Lavandula officinalis* extract dispersed. X-ray (EDX) device data was used.

**Results:** Antimicrobial effect of LO-AuNPs synthesized of biological origin on pathogenic strains, minimum inhibitory concentration (MIK) on gram positive bacteria (*S. aureus* and *B. subtilis*), gram negative bacteria (*E. coli* and *P. aeruginosa*) and *Candida albicans* for fungal strain determined with. The effective concentrations on *C. albicans* were determined as 0.012, 0.625, 0.5, 0.125 and 0.50 µg/ mL, respectively.

**Conclusion:** It was concluded that the synthesis obtained in the study can be used as an effective drug for these pathogens in the future.

**Keywords:** *Lavandula officinalis* flowers; LO-AuNPs; EDX; UV-vis. and XRD

**CITATION**

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**INTRODUCTION**

Nanotechnology is accepted as a molecular scale engineering branch for functional systems. Today, it encompasses all the techniques used to develop high-performance tools. The superior physicochemical properties of nanoparticles ranging

from 1 to 100 nm and the widespread use of multidisciplinary fields increase the interest in such materials (1). There are many methods used for the synthesis of metallic nanoparticles (NPs). Biological methods, which are also called green synthesis, are cheaper, less laborious, and do not contain toxic chemicals. At the same time, many researchers prefer this method because it is

environmentally friendly. (2). The efficiency of green synthesis is due to the reducing and stabilizing properties of some bioactive metabolites, such as phenolic compounds, flavonoids, aromatic compounds, carbonyl compounds, and alkaloids contained in terpenes, which are synthesized for plant stress factors. The *Lavandula officinalis* plant used in our study is a species belonging to the Lamiaceae family, which has important therapeutic properties and includes many medicinal plants. *Lavandula* species are aromatic plant species that are widely distributed in the Mediterranean region (28).

The application areas of nanomaterials obtained by green synthesis are quite wide. Nanobiotechnology, which is a multidisciplinary science, has a wide use potential in fields such as science, chemistry, computers, materials science, and electronics, in addition to its use in medicine, health, textiles, paint, agriculture, pharmacy, and industry, and is constantly developing (3,4). Gold nanoparticles (AuNPs) have uses in the pharmaceutical industry, agriculture, medical applications, electronic devices, biosensors, catalysis, and many biological applications (5).

In the present study, an environmentally friendly, easy, and low cost synthesis of LO-AuNPs was carried out by means of *Lavandula Officinalis* flower extract, which had never been used in the synthesis of gold nanoparticles before. In order to elucidate the properties and structures of LO-AuNPs synthesized by the green synthesis method, it was aimed to characterize and investigate their antimicrobial effects in terms of their usability as an alternative to biocompatible new generation antibiotic drugs with commercial value against pathogen strains.

## MATERIALS AND METHODS

### Preparation of *Lavandula officinalis* Flower Extract and Gold Solution

*Lavandula officinalis* flower was collected at the end of August in the village of Yalim in the Artuklu district of Mardin. The flowers were washed and dried at room conditions. 10 g of the pre-dried *Lavandula officinalis* flower was weighed and allowed to boil in a beaker with 100 ml of distilled water, and filtered. Afterwards, the obtained extract was stored at +4 oC to be used in experimental studies. A solution of 0.002 molar (M) concentration was prepared from Sigma-Aldrich (Germany) Tetrachloroauric (III) acid trihydrate 99 % (HAuCl<sub>4</sub>.3H<sub>2</sub>O) salt.

### Green Synthesis of LO-AuNPs from Extract of *Lavandula officinalis* Flower

Lavender (*Lavandula Officinalis*) flower extract of 70 ml was taken, 130 ml of 0.002 M HAuCl<sub>4</sub>.3H<sub>2</sub>O solution was added, and the mixture was left to react on a magnetic heater at 65 oC in a flask. At the end of 30 minutes, the color of the mixture changed to pink-red due to the reaction. Depending on the color change as a result of the synthesis of plant origin, absorbances were measured with UV-Vis spectroscopy at maximum wavelength scans.

## Structure Elucidation and Characterization of LO-AuNPs

Malvern brand Zeta Potential to determine the surface charges that affect the stability of LO-AuNPs, UV-Vis (UV 1800, Shimadzu) for maximum wavelength trspit, TEM (Jeol JEM-2100 Plus, Japan) to illuminate their morphological appearance, (FESEM) and The elemental profile of the gold nanoparticles obtained from vegetable source was determined by Electron Distributed (EDX). The crystal patterns and crystal nano sizes (Debye-Sherer's equation) of the synthesized particles were determined using the XRD device (Rigaku).

## Minimum Inhibitory Concentrations of LO-AuNPs Synthesized Using Flower Extract on Microorganisms

For the antimicrobial potential of LO-AuNPs synthesized with flower extract, minimum inhibition concentration (MIC) values were found by applying microdilution method on gram positive, gram negative and fungal strains. Gram-positive *Bacillus subtilis* ATCC11774 (*B. subtilis*) and gram-negative *Escherichia coli* ATCC25922(*E. coli*), *Pseudomonas aeruginosa* ATCC27833 (*P. aeruginosa*) pathogenic bacteria were used for the experimental study. In addition, for the anti-fungal activity of LO-AuNPs, the antifungal study on *Candida albicans* was also studied with the same method. All the microorganism strains used in the experimental work were taken from the Mardin Artuklu University Biochemistry Research Laboratory (Mardin, Turkey). The minimum inhibition concentration (MIC) used for the antimicrobial activity study was performed according to the microdilution method procedure (6).

## RESULTS

### UV-Vis Study

The extract and HAuCl<sub>4</sub> solution obtained from the previously prepared lavender flower were left in the reaction medium in a flask. It was observed that the color of the mixture turned pink-red at the end of 30 minutes at 65 oC in the magnetic stirrer. Samples were taken and wavelength scans were performed. Surface Plasma Resonance (SPR), which shows the changes in the plasma surface caused by the color change in UV-vis spectra, showed that LO-AuNPs were formed with the maximum wavelength bands of 509.32 nm. A study of biological origin showed the presence of AuNPs with a maximum wavelength of 510 nm (7). (Figure 1). *Drosera capensis* plant extract, the maximum wavelength absorbance of AuNPs depending on SPR at 515 nm in UV-vis spectra was said to be characteristic of AuNPs (8). In another study, it was observed that AuNPs nanoparticles from the *Capsicum annum* plant gave maximum absorbance at 335 nm (9). It was said that AuNPs were formed with *Phyllanthus embilica* extract with absorbances taken at the maximum wavelength at 537 nm (10).

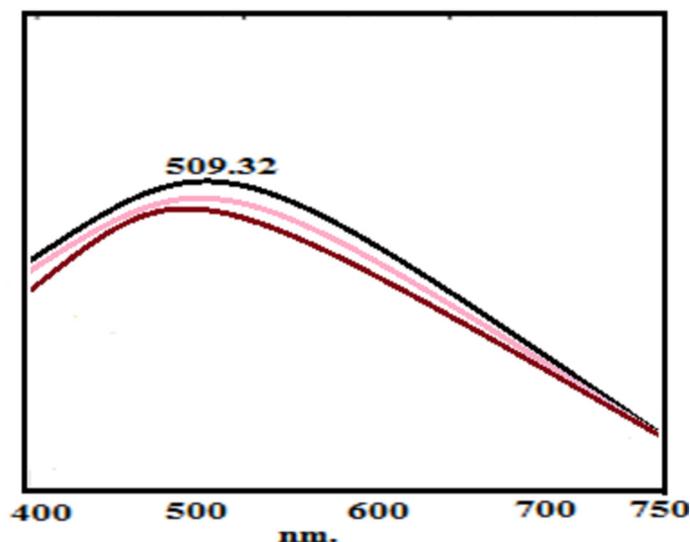


Figure 1. UV-Vis spectrum of LO-AuNPs

#### Evaluation of Xrd Data

The crystal structures of LO-AuNPs obtained by green synthesis were investigated by XRD analysis. The peaks taken at 111o, 200o, 220o, and 311o at  $2\theta$  gave the values of 38.79, 44.88, 64.33, and 76.95, respectively (Figure 2). The cubic centroid structure of the LO-AuNPs at these points was reflected on the plane. LO-AuNPs were calculated to be 24.95 nm when the crystal nano size was calculated by Debye Scherrer's (11) equation with a high peak value of 64.33. In a study, it was reported that the size of nanoparticles obtained from Croton Caudatus Geisel leaf extract was 10.75 nm (12). XRD findings in similar studies were also found to be compatible (5,13).

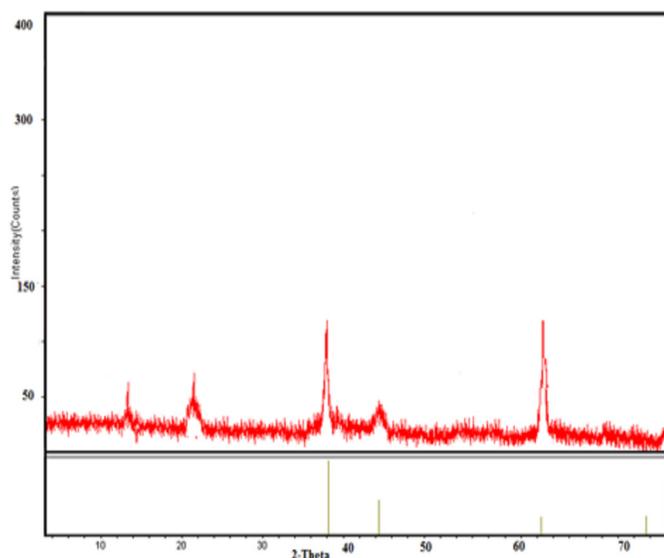


Figure 2. LO-AuNPs of XRD analysis

#### FESEM, EDX and TEM analysis data of LO-AuNPs Synthesized with Flower Extract

The morphology and particle size distribution of LO-AuNPs synthesized from biological origin were determined using TEM and FE-SEM images. As seen in Figure 3, TEM and FESEM micrographs showed that LO-AuNPs exhibited a spherical appearance and a monodisperse. EDX spectra of LO-AuNPs synthesized with flower extract at 2.435 keV showed the presence of AuNPs, with LO-AuNPs giving strong peaks (Figure 3). In their similar studies, strong gold peaks in EDX profiles indicated the presence of AuNPs (17,18).

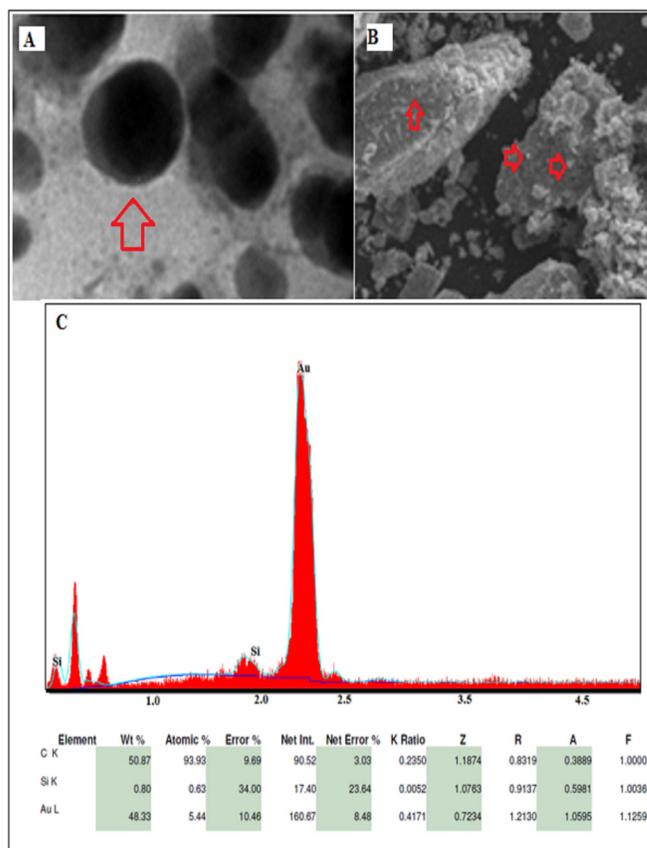
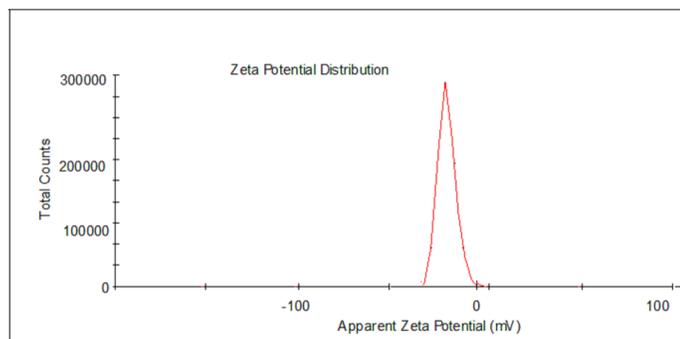


Figure 3. The synthesized particles; A. TEM, B. SEM, and C. EDX profiles

#### LO-AuNPs of zeta potential analysis

Zeta potential analysis data were used to determine the mobility, distribution and stability properties of LO-AuNPs synthesized from biological source. It was determined that LO-AuNPs have a surface charge distribution of -17.20 mV. This showed that the formed nanostructures were stable. Therefore, it was understood that biologically synthesized LO-AuNPs were stable only with negative surface charge, and exhibited monodispersity due to electrostatic repulsion between particles(14,19,20).



**Figure 4.** Zeta potential measurement diagram of LO-AuNPs

## DISCUSSION

The effects of LO-AuNPs synthesized with the extract obtained from the flower of *Lavandula officinalis* plant on pathogenic microorganisms were determined by micro-dilution technique. In this study, MIC values were determined in antibiotics and HAuCl<sub>4</sub> solution. As seen in Table 1, 0.08-1.25 µg mL<sup>-1</sup> concentrations on pathogenic strains were found to have a suppressive effect on the growth of microorganisms. MIC values of LO-AuNPs were determined as 0.31-0.16 µg mL<sup>-1</sup> on gram-positive *S. aureus* and *B. subtilis*, and 0.63-1.25 µg mL<sup>-1</sup> on gram-negative bacterial strains. These MIC values were determined to be extremely low concentrations compared to HAuCl<sub>4</sub> solution and antibiotics. The effect of LO-AuNPs on *C. albicans* yeast was 0.08 µg mL<sup>-1</sup>, which showed that they were effective at much lower concentrations than the fluconazole antibiotic and HAuCl<sub>4</sub> solution used. AuNPs interact with living organisms by electrostatic force. They cause structural and functional disorders by increasing the reactive oxygen species. They inhibit metabolic activities that are very important for the organism (such as ATP synthesis). As a result, death becomes inevitable for the organism that cannot perform its vital activities (21,22). Antimicrobial effects of *Prunus cerasifera pissardii* nigra extract and AuNPs on *B. subtilis*, *S. aureus*, *P. aeruginosa*, *E. coli*, and *C. albicans*, respectively. MIC values were determined as 0.125, 0.25, 0.5, 1.0, and 0.5 µg mL<sup>-1</sup>. had been disclosed. In other environmentally friendly synthesis studies, AuNPs were found to have antimicrobial effects (15,23–27).

## CONCLUSION

Green synthesis of LO-AuNPs formed by reduction of Au<sup>3+</sup> valence form from HAuCl<sub>4</sub> solution using lavender plant flower extract was carried out successfully. Lavender is a plant that is resistant to various climatic conditions, especially in the Mediterranean Region, and can be grown in every region. The synthesized LO-AuNPs were characterized by the results obtained by TEM, EDX, FESEM, XRD, UV-vis, and Zeta potential analysis. It was determined that they were stable with a maximum absorbance of 510 nm wavelength, a surface charge of -17.20 mV (absence of aggregation caused by attraction of different charges), exhibited a spherical morphology, and had

crystal nano dimensions of 24.95. Stability and biocompatibility of synthesized LO-AuNPs will contribute to the field of pharmacology. The properties of LO-AuNPs will be developed further and will be greatly beneficial to studies for medical applications.

**Competing interests:** The authors declare that they have no competing interest.

**Financial Disclosure:** There are no financial supports.

**Ethical approval:** Not necessary.

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## Case Report

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# Peripheral facial nerve paralysis after dental procedure

## Abstract

Peripheral facial paralysis is the loss of muscle function of part or all of the face due to mononeuropathy of the 7th cranial nerve. Its etiology is not fully known. general thought; It is known that the clinical picture develops due to compression or damage to the 7th cranial nerve for any reason. In addition, rare causes of peripheral facial paralysis include; It is also stated that peripheral facial paralysis may develop after local anesthetic agents applied for dental procedures.

In this study; A case of peripheral facial paralysis developed shortly after applying a local anesthetic with adrenaline and lidocaine to the molar tooth to perform a dental procedure is presented.

**Keywords:** Peripheral facial paralysis; local anesthetic; Dental Procedure

## CITATION

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## INTRODUCTION

Facial nerve is a nerve Which responsible for innervation of many areas of the face such as facial muscles, digastric muscle, lacrimal, submandibular and sublingual glands, anterior 2/3 of the tongue, and external auditory canal (1).

Peripheral facial paralysis (PFP) is a mononeuropathy of the 7th cranial nerve manifested by loss of muscle function of part or all of the face. Its etiology is not fully known. It is known that the clinical picture develops due to compression or damage to the 7th cranial nerve for any reason (2).

In the presented study; A case of peripheral facial paralysis developed shortly after the application of a local anesthetic with adrenaline and lidocaine to perform a dental procedure on the molar tooth is presented.

## CASE REPORT

A 40-year-old female patient was admitted to the emergency service with complaints of numbness on the right side of her face, limitation of movement and inability to close her right eye. In the patient's anamnesis; it was learned that he had pain in his right upper molar tooth for 15 days and he went to the dentist. It was learned that the dentist applied local anesthetic with adherence and lidocaine to the patient and then filled the caries with molar teeth. 30 minutes after the dental treatment, the complaints of

numbness on the right side of the face, limitation of movement, inability to close the right eye, and loss of taste in the tongue,. But gradually it progressed (Figure 1).



**Figure 1.** Case with facial paralysis

It was learned that the patient did not have any additional systemic disease, did not use drugs and had not had facial paralysis. In the examination, the general condition of the patient was good, he was conscious and cooperative. The patient was found to have stage 3 peripheral facial paralysis according to the House-Brackmann facial nerve staging. Bilateral oropharynx and tonsillar examination of the case was found naturally. No emergency pathology was detected in the neurological examination. In laboratory examinations; the white blood cell count was 9.200/mm<sup>3</sup>, hemoglobin 13.7g/dL and the platelet count was 286,000/mm<sup>3</sup>. Erythrocyte sedimentation rate (ESR) 29 mm/hr, C-reactive protein (CRP) 9.8 mg/L, aspartate aminotransferase (AST) 34 U/L, alanine aminotransferase 28 U/L, alkaline phosphatase (ALP) 52 IU/ L, gamma-glutamyl transferase (GGT) 25 U/L, total bilirubin 0.14 mg/dL, direct bilirubin 0.1 mg/dL. Prothrombin and partial thromboplastin time, international normalized ratio (INR), kidney function tests and serum electrolytes were found to be within normal limits. In addition, the central imaging of the patient was interpreted naturally. As a result of the initial evaluations, the patient was consulted to the otolaryngology clinic. The patient was diagnosed with peripheral facial paralysis after the dental procedure.

## DISCUSSION

Facial nerve palsy, depending on the mononeuropathy of the 7th cranial nerve. It is clinically referred to as the transition or permanent loss of function of some or all of the muscle functions of the face (1).

Facial nerve palsy is examined in two subgroups in terms of etiology. First etiologic origin is from the central nervous system, the second etiologic origin is from the peripheral nerve. Peripheral facial nerve palsy is the most common type of neuropathy among cranial nerve motor neuropathies. Although it has been reported that the etiology of peripheral facial paralysis, it may include trauma, viral infection, surgery, immune system disorders, inflammatory and metabolic abnormalities, it can also be idiopathic (3).

It has been reported in the literature that peripheral facial paralysis may develop after local anesthetic agents applied for dental procedures. Facial nerve damage can be caused by local anesthetic applying indirectly to the facial nerve. Besides the feeding of the facial nerve may be indirectly impaired due to the vasoconstrictor agents in the local anesthetic substance, reflex vasospasm of the external carotid artery may cause ischemia of the facial nerve or the facial nerve may be adversely affected secondary to dental infections (4). In the study of Vasconcelos et al., it was found that the needle used during the dental procedure may directly damage the facial nerve or that the needle may cause trauma to the blood vessels in the area close to the nerve and hematoma may develop. He reported that compression and fibrosis may develop in the facies nerve due to hemorrhage and this may develop in a very short time (5). In our study, similar to the literature, the approximate time was 30 minutes.

In another study, it was reported that vasoconstrictor agents in local anesthetics can indirectly cause ischemia and cause loss of function in the facial nerve and therefore peripheral facial paralysis can develop (6). In another study; It has been reported that many different local anesthetics such as articaine, lidocaine and bupivacaine can cause peripheral facial paralysis due to their neurotoxic properties (7,8). It has also been reported in the literature that dental surgery can activate especially latent viral infection. And it can cause viral infection, especially herpes simplex type 1 facial paralysis (9).

In the presented study, it was determined that there was a sudden onset of peripheral facial paralysis about half an hour after the dental procedure. After this condition was excluded by other preliminary diagnoses that would cause peripheral facial paralysis, both by physical examination, laboratory and imaging methods, peripheral facial paralysis was diagnosed after dental procedure, which is a diagnosis of exclusion. In our case, like other cases in the literature, it appeared suddenly and in a very short time like 30 minutes after the procedure, supporting the diagnosis. But is this due to the neurotoxic effect of the local anesthetic? in the destruction of the needle directly to the nerve? It is not known whether it is vascular or not.

## CONCLUSION

Dental procedures are often performed in areas adjacent to the facial nerve. Knowing the anatomical route of the facial nerve well and being careful in the procedures play a great role in reducing the situations that can cause both temporary and permanent damage to the facial nerve. However, despite all precautions, it should be kept in mind that complications related to facial nerve damage may still develop after dental procedures. Both the physician should be aware of this situation and the patient and his/her relatives should be informed that this situation may occur.

**Competing interests:** The authors declare that they have no competing interest.

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**Informed Consent:** Written consent was obtained from the patient and his parents.

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## Review Article

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# Effects of chronic exposure to lead on some organs

## Abstract

Lead is one of the most important heavy metals to threaten human health and ecological balance. Exposure to lead due to occupational necessity or for various reasons creates toxic effects on cells. There are generally three forms of lead in the environment, metallic lead, lead salt, or organic forms containing carbon. Damage caused by lead in living systems after exposure to free radicals involves two different mechanisms. Lead causes tissue and organ damage by inhibiting two important enzymes, such as delta-aminolevulinic acid dehydratase (ALAD) and glutathione reductase (GR).

Lead exposure occurs mostly through the gastrointestinal system, respiratory system, and skin. After lead is taken into the body, it binds to hemoglobin at a rate of 99% and is distributed mainly in soft tissues. Low dietary calcium content is an important factor that increases lead absorption. Lead vapor and dust reach the lungs through the respiratory tract and pass from the lungs into the blood. Respiratory exposure is very important in lead poisoning.

Lead exposure is known to increase the risk of lung infections and cancer. Lead exposure can adversely affect the nervous system, especially the central and peripheral nervous systems. Fetal lead exposure in the early stages of life has been reported to cause neurodegeneration in postnatal life.

**Keywords:** Lead; nervous system; hematological system; reproductive system; cardiovascular system

## CITATION

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## INTRODUCTION

Lead is a metal that can be found in small amounts everywhere and it is one of the most important heavy metals threatening human health and ecological balance. It can be molded easily and is resistant to corrosion, does not deteriorate like other materials and has a structure that can accumulate over time. It is a metal which can be easily processed due to low melting and is widely used in industrial life. Hence, lead can quickly be contaminated to food products and can be found in air a lot. But it is one of several substances that are not used in the human body and even a small amount of ingestion that damages the living cell (1). Exposure to lead due to occupational necessity or for various reasons creates toxic effects on cells. The lead usually enters the body through inhalation and immediately is absorbed. The severity of lead toxicity depends on factors such as number of exposures, time of exposure, route of exposure, duration of exposure, age, health status, nutrition and genetic structure of the individual. There are generally three forms of lead in environment, metallic lead, lead salt or organic form containing carbon. Organic lead is more soluble than the inorganic one and more toxic for living beings. (2,3).

Inflammation is the body's protective response to damage that may occur to living tissue by physical agents, chemical substances, and various immune reactions. Inflammation is a redox-based mechanism activated by cytokines such as NF- $\kappa$ B that regulates gene expression via inflammatory mediators. There is a strong relationship between free radicals and oxidative stress and inflammation. Both conditions are associated with endothelial dysfunction. Eventually, reactive oxygen species (ROS), lipid and protein oxidation products are released and inflammation occurs (3).

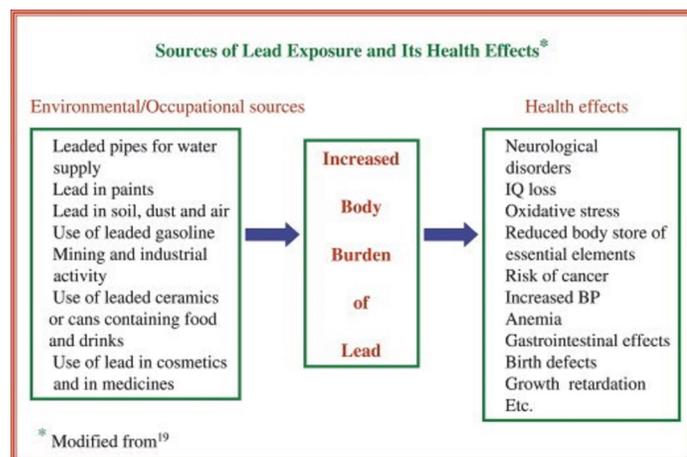
Oxidative stress is the case that the existing elements of the body's antioxidants are insufficient to neutralize different types of free radicals. As a result, the different components of the cells are greatly damaged due to oxidation. Lead toxicity has several mechanisms, oxidative stress is known as the most important mechanism. The body's antioxidant defense system is activated to neutralize the produced radical oxygen derivatives. The most effective antioxidant in cells is glutathione (GSH). Less effective ones are enzymes such as glutathione disulfide (GSSG), glutathione peroxidase (GPx), glutathione reductase (GR), superoxide dismutase (SOD) and catalase (CAT). Damage caused

by lead in living systems after exposure to free radicals involves two different mechanisms. The first of these is the formation of reactive oxygen species (ROS) such as oxygen radical (O<sub>2</sub>), peroxide (H<sub>2</sub>O<sub>2</sub>), and hydroperoxides. The other is the rapid depletion of antioxidants in the cell (4). Lead causes tissue and organ damage by inhibiting two important enzymes, such as delta-aminolevulinic acid dehydratase (ALAD) and glutathione reductase (GR) (5).

Our aim in this review is to examine the effects of lead exposure on respiratory, cardiovascular, neurological, and digestive system disorders and the role of the underlying mechanisms for these effects.

## Lead Exposure

People can be exposed to lead through food, cigarettes, paint, water, soil, air, dust, household items, clothing, occupational contact, and toys. In general, lead is taken into the body through the digestive tract, through the intestines, breathing in the lungs, through skin contact, or by ingestion directly (Figure 1) (6). Absorption of inorganic lead from the body occurs through the respiratory and gastrointestinal tracts. For adults who are occupationally exposed to lead, the most important absorption route is through the respiratory system. Lead absorption by the respiratory system depends on particle size and chemical properties. It is stated that lead, which is later included in the blood circulation, is approximately 30–40 % (7).

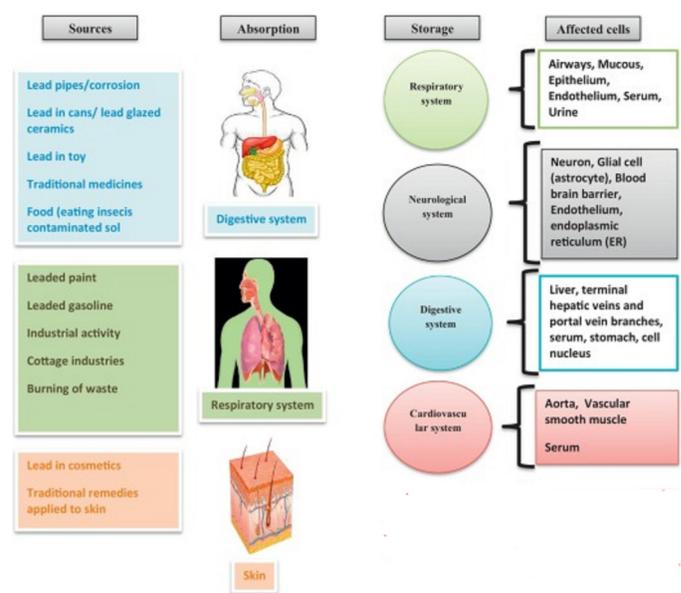


**Figure 1.** Sources of lead exposure and its health effects (8)

When lead is absorbed, it can accumulate in some organs of the body and pose a danger. This may cause some symptoms that vary according to the physiological state of the person, the exposure time and the dose taken. Lead is stored in the body, and it becomes difficult to excrete it out of the body. With this exposure, many symptoms affecting the body systems, such as neurological, haematological, gastrointestinal, cardiovascular, and renal systems, congenital disorders, and growth and development arrest are caused (9).

Lead exposure occurs mostly through the gastrointestinal system,

respiratory system, and skin. Organic lead compounds can also be taken from the skin (Figure 2). Calcium and lead compete for the same transport mechanism, and therefore, low dietary calcium content is an important factor that increases lead absorption. After lead is taken into the body, it binds to hemoglobin at a rate of 99% and is distributed mainly in soft tissues (10). The rate of excretion from the body is very slow. For this reason, it starts to be stored in various tissues in case of continued exposure. Bone tissue is the primary organ of lead storage in the body, indicating long-term cumulative lead exposure (11). Lead, which enters the circulation, first binds to red blood cells, then disperses to soft tissues, and finally passes to the bones and accumulates there. Lead can remain in the bones for 20–30 years. Returns to circulating blood through bone-to-tissue turnover.



**Figure 2.** Environmental lead, uptake, absorption, and storage in some organs by humans (3).

## The organs most affected by exposure to lead are

- 1-Respiratory system
- 2-Nervous system
- 3-Reproductive system
- 4- Hematopoietic system and
- 5- Cardiovascular system.

### 1-Respiratory system

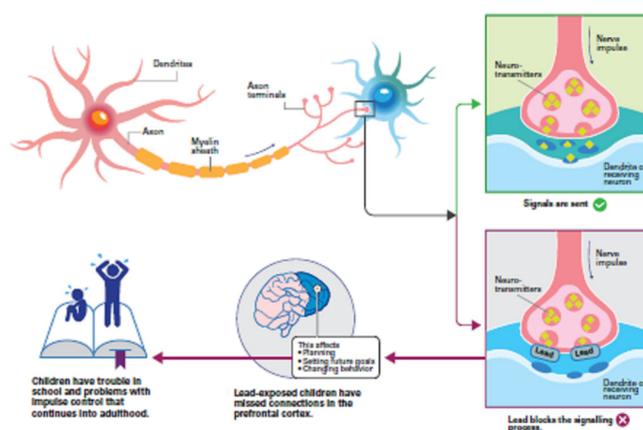
The most important entry route for lead into the organism is the respiratory system. Lead vapor and dust reach the lungs through the respiratory tract and pass from the lungs into the blood. Some of the coarse particles that cannot go down to the alveoli dissolve in the mucosa and some are thrown back. The remaining particles enter the digestive system by swallowing. Respiratory exposure is very important in lead poisoning. Because 30-40% of the lead taken passes into the blood circulation. The entry of

dust into the respiratory system varies depending on the size of the dust particles and the respiratory capacity of individuals. If the diameter of the dust particles is smaller than 1.0  $\mu\text{m}$  or with the increase in the labor force, the absorption increases as a result of rapid and deep breathing. The toxic effects of lead begin when it enters the body, mainly in the form of inhalation and then ingestion. It easily passes from the lungs into the bloodstream and is absorbed (12). Absorbed lead then binds to erythrocytes and accumulates in soft tissues such as the lungs, then the brain, liver, spleen, bone, kidneys, and muscles. The tissue in which lead accumulates the most is bone. Exposure to lead is known to increase the risk of lung infections and cancer (13).

## 2-Nervous system

Recent studies on the effects of lead on the nervous system show that exposure to lead has adverse effects on the central and peripheral nervous systems. Furthermore, fetal lead exposure in the early stages of life has been reported to cause neurodegeneration in postnatal life. The nervous system is seen as the target and the system most affected by lead. Both the central and peripheral nervous systems are affected by lead at roughly the same rate (14). The developing infant and child nervous systems are more affected by this lead exposure than the nervous systems of adults. In mild exposure, nervous system symptoms may include encephalopathy and, eventually, dullness, decreased attention, irritability, muscle weakness, headache, memory loss, and hallucinations (Figure 3). In more severe exposures, delirium, incoordination, muscle contraction, paralysis, and coma can be seen (15). Lead exposure also causes a decrease in the number of neurons, loss of neuron myelin sheath, and cessation of neuron development by interfering with neurotransmission. It is also observed that the prefrontal cortex decreases in volume in MRI performed on children. It also inhibits the development of some other neurochemicals, especially neurotransmitters (16).

Young children are 3-4 times more likely to be affected by lead exposure than adults. so that children exposed to lead at a young age carry a lifetime neurologic and cognitive risk. They are faced with the risk of multiple organ disorders, especially the brain, kidney, heart, and hematological systems, due to acute lead poisoning. According to Sanders et al., lead's ability to easily penetrate the blood-brain barrier is due to its ability to displace calcium ions. As it is known, calcium has an intracellular second messenger function and regulates cell functions. Sometimes lead replaces calcium and disrupts this regulatory function, causing disruption of intracellular biological activity (14). Even small picomolar concentrations of lead compete for binding sites with Phosphokinase C in the cerebellum. In this case, it affects the entry of calcium into the cell and into the neurons. It changes the mitochondrial structure of the cell and inhibits its cellular respiration. Therefore, this alters neuronal signaling. Eventually, an increase in neurotransmitter release occurs (Figure 3). On the other hand, in a study conducted in the USA, it was reported that lead causes hyperactivity, motor function, hand-eye coordination, behavioral disorders, and mental regression in children (17).



**Figure 3.** Lead affects the entry of calcium, a messenger, into cells and neurons. It changes the mitochondrial structure of the cell and inhibits its cellular respiration. Therefore, this modifies the neuronal signal. Eventually, an increase in neurotransmitter release occurs.

In adults, lead exposure appears to have a significant effect on the frontoparietal brain network. This causes the performance of working memory to deteriorate and the sustainability of attention to decrease. An underlying potential mechanism is that the toxic effect of lead metal ions interacting with the N-methyl-D-aspartate (NMDA) receptor in the brain causes neuronal damage in the hippocampus. It has been shown that lead disrupts the  $\text{Ca}^{2+}$  ion signaling mechanism and causes dysregulation of  $\text{Ca}^{2+}$ -sensitive pathways in the hippocampal region (18).

## 3- Reproductive system

Lead can directly affect both the male and female reproductive systems. When the blood lead level rises above 40  $\mu\text{g}/\text{dL}$  in men, changes in sperm volume and quality begin to occur. Sperm motility and morphology also begin to be affected. In women, the symptoms may be more severe than in men. Elevated lead levels can cause miscarriage, premature birth, and low birth weight in women. It causes developmental disorders in the fetus and slow development in the postnatal baby (16). Other common effects of lead in men can be listed as follows: decreased libido, chromosomal damage to sperm, infertility, prostate damage, and changes in serum androgen levels. In women, infertility, premature rupture of membranes, preeclampsia, and preterm delivery are common (15).

In another study, a decrease in gonadotropin hormone was observed among people exposed to lead, while moderate blood serum lead level caused an increase in FSH level. In accumulator workers exposed to inorganic lead, it has been determined that it causes reproductive problems, hypogonadism, and decreases in testosterone levels in the hypothalamic-pituitary-testis sequence (19).

## 4- Hematologic system

One of the systems most affected by lead toxicity is the hematopoietic system. Along with the reduction of hemoglobin

synthesis, lead also causes hemolysis of erythrocytes. Enzymes in both synthesis and synthesis are adversely affected, and acute toxicity occurs. Affected enzymes are Delta aminolevulinic acid dehydratase (ALAD), aminolevulinic acid synthetase (ALAS) and ferrochelatase enzymes. Among them, the most affected is the ALAD enzyme (20). Lead inhibits these three enzymes, causing an accumulation of heme intermediates such as protoporphyrin. As a result, it increases the fragility of cell membranes and shortens the lifespan of circulating erythrocytes, causing anemia. (1,15). Another effect of lead on the hematopoietic system is the formation of radical oxygen derivatives (ROS). ROS causes damage to erythrocyte membranes by causing oxidative stress. In addition, lead binds directly to phospholipids in the erythrocyte membrane and eventually leads to hemolysis, causing anemia (21).

### 5- Cardiovascular system

According to the World Health Organization (WHO), the most important cause of death in the world is coronary artery disease. The cause of death of 13.2% of people in the world is ischemic heart diseases (22). Many epidemiological and clinical studies have found a positive association between lead exposure and high blood pressure. Vaziri et al. studied 543 men aged 40–59 years and found a significant link between blood lead and both systolic and diastolic blood pressure (23). In another study in rats, it was reported that continuous exposure to lead causes increased chemoreceptor sensitivity. It was later shown to induce autonomic dysfunction, thereby causing disturbances in the cardiovascular system (24). The cardiovascular effects of chronic exposure to lead are not limited to elevated blood pressure and hypertension. In addition, it is closely related to the increase in diseases such as coronary heart disease, peripheral artery disease, and stroke (25).

### DISCUSSION

Lead is a metal known and used by humans since ancient times. With the industrial revolution, its use has become more widespread and its exposure has increased greatly. Lead has no biological function in the human body. In fact, when it enters the body, it accumulates and it is difficult or even impossible to excrete it out of the body. The accumulation of lead in tissues and organs is considered toxic. Lead is a free radical, so its destruction in the cell is in the form of oxidative damage or direct cell lysis.

Lead is taken into the body, usually by inhalation or food, and a small amount through the skin. As a result of entering the body in all three ways, it is included in the blood vascular system and mostly damages erythrocytes. One of the most damaged organs is the central and peripheral nervous system. The nervous system is particularly affected by lead in the fetal and childhood stages. The bone, cardiovascular system, and respiratory system are also affected by chronic lead exposure.

### CONCLUSION

Reducing chronic lead exposure, which also causes environmental

pollution, should be a target policy for public health. In order to protect the body from this destruction, it should be fed with phenolic-based and calcium-rich foods.

**Competing interests:** The authors declare that they have no competing interest.

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**Ethical approval:** Not necessary

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