Carbon monoxide poisoning: are hospital discharge rates high enough? (#85650)

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Carbon monoxide poisoning: are hospital discharge rates high enough?

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Background**:** We aimed to evaluate Carbon monoxide poisonings in Adıyaman, a southeastern city in Turkey, especially to investigate the effect of poisoning on mortality leading to new morbidities in people who survived the poisoning.

Methods : The descriptive-retrospective study evaluated all Carbon monoxide poisoning cases between 2012-2022 in the Adıyaman. For the fatality, all cases were followed up through Turkey's Death Notification System until the end of 2022. One-year health records of cases treated as inpatients in Adıyaman hospitals were analyzed for nine diagnoses. 4,395 Carbon monoxide cases, recorded over 11 years, were all noted to be accidental cases.

Results: The rate of carbon monoxide poisoning in Adıyaman was calculated as 63.2 per hundred thousand. A total of 87 (2%) of the cases died. The population's hospitalization rate was 1.71, while the mortality rate was 1.25 in a hundred thousand. Among the cases, the hospitalization rate was 2.7, and the admission to intensive care rate was 1.7. The fatality rate was 6.5% for those hospitalized and 12.2% for those admitted to the intensive care unit. The highest fatality rate was 65.5% in patients aged 65 and above. 11.8% of patients discharged from the hospital died within one year. One out of five morbidities was developed in 8.4% of cases within one year. The fatality rate of those who developed morbidities (40%) was higher than those who did not (5.5%). Being male posed a 1,886-fold risk for mortality, and each increase in age posed a 1,086-fold risk for mortality.

Conclusion: Individuals who had carbon monoxide poisoning should be followed up closely for one year after poisoning due to the possibility of the emergence of new diseases that increase the risk of mortality.

Carbon monoxide poisoning: An 11-year evaluation

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Abstract

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Conclusion: Individuals who had carbon monoxide poisoning should be followed up closely for one year after poisoning due to the possibility of the emergence of new diseases that increase the risk of mortality.

Keywords: Carbon monoxide, carbon monoxide poisoning, poisoning, unintentional poisoning, toxicity

Introduction

Carbon monoxide (CO), present in trace amounts in the air we breathe, is a colourless, tasteless, odourless, non-irritating toxic gas called the "silent killer".[1,2] It is found in the smoke formed due to the incomplete combustion of fuels Having “carbon” in their contents, such as bottled gas, natural gas, kerosene, and gasoline, especially coal and wood.[3]

Since CO cannot be detected during respiration, it causes poisoning much faster than other gases. It is most commonly caused by using items such as a stove for heating or a geyser to obtain hot water in indoor settings with insufficient ventilation.[4] Furthermore, there is a risk of CO poisoning in situations where exhaust fumes are inhaled and in environments with misplaced gasoline-powered generators, iron foundries, ice rinks where propane-powered resurfacing machines are used, and house fires.[3,5]

Casualties do not realize that they inhale high CO during poisoning. CO poisoning leads to death or permanent defect by causing damage to hypoxia-sensitive organs and tissues such as the brain and heart. Neurological damage may occur two days to 6 weeks after exposure to carbon monoxide.[5] Common symptoms include loss of consciousness, dizziness, headache, nausea, and vomiting. Less frequently seen ones are confusion, lethargy, weakness, respiratory distress, chest pain, abdominal pain, ataxia, nervousness, vision disorders, seizures, and incontinence. Ataxia, dementia, Parkinson's, lack of concentration, and abnormal behaviours are some examples of permanent neurological damage.[6]

A minimal amount of CO is also produced in the human body. CO, emerging endogenously due to haemoglobin catabolism, leads to the formation of less than 1% COHb. Endogenous CO is a neurotransmitter and regulator for other neurotransmitters and hormones.[7]

After CO enters the body with respiration, it has an affinity for haemoglobin 200 times more than oxygen, binds to haemoglobin, and forms carboxyhemoglobin (COHb). COHb leads to tissue hypoxia by reducing the oxygen-carrying capacity and oxygen release to the tissues.[3,4] At COHb levels below 5%, the physiological compensation of increased blood flow and oxygen release prevents hypoxia. This blood flow at the beginning continues until loss of consciousness due to hypotension and ischemia in the cerebral arteries. The resulting loss of consciousness might lead to delayed neurological sequelae. Unless the COHb rate in the blood exceeds 20%, there is no significant change in brain oxygenation, while any value above 51% leads to seizures, coma, severe acidosis, and eventually death.[3,8]

Anamnesis is the most valuable finding in CO poisoning since no specific finding may exist in a physical examination. Also, if a long time has passed after exposure to carbon monoxide or supplemental oxygen therapy has been given, the CO level might be misleadingly low.[9]

CO poisoning is one of the most common poisonings. The annual incidence of household CO poisoning in France's Rhône-Alpes and Auvergne regions was 2.3 per 100,000 people.[10] Mattiuzzi and Lippi found the incidence as 137 per million and the risk of death 4.6 in a worldwide epidemiological evaluation conducted in 2019. Although there was no change in the incidence of CO poisoning between 1992 and 2017, they reported that the risk of death decreased

by 36%.[2] Lisbona & Hamnett stated that deaths due to CO poisoning are more common in men than women since men are more in contact with CO.[11] Mattiuzzi & Lippi, on the other hand, argued that although there was no difference in gender in terms of incidence, the death rate due to CO poisoning in men was twice that of women.[2]

In Japan, between 2000-5000 people die annually from stoves poisoning.[12] Wood and coal stoves, geysers, and bottled gas are used frequently in Turkey. However, no record of CO poisoning has been nationwide for more than ten years. There are studies based on the data from the emergency department of one hospital or autopsy data from local forensic medicine institutes.[13,14] In a study collecting data sources was controversial; data obtained from a news agency that had been collecting the news from national and local newspapers and TV channels, the risk of death due to carbon monoxide in Turkey was found to be 0.35/100.000 between 2008 and 2017, and Adıyaman was not in the first 15 cities with the highest risk.[15] According to 2010 data, in a study conducted throughout Turkey, Adıyaman was the ninth city in the country with the highest number of cases per population.[16]

The present study investigated both the frequency and short and long-term effects of carbon monoxide poisoning in Adıyaman, a southeastern province of Turkey, where traditional heating and water heating systems are frequently used. In order to examine the long-term effects of carbon monoxide poisoning on the person, the development of neurological, cardiological, psychiatric, and endocrinological morbidities after carbon monoxide poisoning was investigated; in this way, the effect of carbon monoxide poisoning on mortality leading to the emergence of new morbidities in people who survived the poisoning was tried to be revealed.

Materials and Methods

This descriptive-retrospective study evaluated all of the 4,395 CO poisoning cases that occurred in 11 years between 2012-2022 in Adıyaman, with a population of 632,148 in Southeast Turkey. In the power analysis made concerning the study of Kavalcı et al. (21.8% of poisoning cases are CO poisoning), n = [DEFF*Np(1-p)]/ [(d2/Z21-α/2*(N-1)+p*(1-p)] It was found that at least 262 patients should be reached at 95% confidence interval.[17]

All the study data were obtained from the Adıyaman Provincial Health Directorate Main Data System, where Hospital Information Management System (HIMS) data of 8 state hospitals in the province were collected. The study was conducted between 15.12.2022 and 15.01.2023, and the researchers had no access to the names of the cases included in the study.

All patients and fatalities were the ones with the "T58- Toxic effect of carbon monoxide" classification according to the " International Classification of Diseases (ICD)-10 code" in the official records. It was not taken into consideration with which complaint the patients were brought to the hospital by themselves or others—persons not diagnosed with T58 were excluded from the study. It was also not considered whether the clinicians diagnosed CO poisoning by anamnesis or by determining the COHb level.

For the fatality, all cases were followed up through Turkey's Death Notification System until the end of 2022. One-year health records of cases treated as inpatients in Adıyaman hospitals were analyzed for nine diagnoses: cerebrovascular accident, dementia, Parkinson's,

ataxia, depression, anxiety, arrhythmia, Myocardial infarction (MI) and hypothyroidism. If any of these nine diseases were diagnosed at a date after CO poisoning, it was accepted that this morbidity occurred after poisoning. These diagnoses were not evaluated as poisoning-related morbidity if present before the poisoning.

Statistical analysis

Data analysis was performed with the SPSS 22 package program (Statistical Package for Social Sciences). In the study, descriptive data were shown as n and percentile values for categorical data, while they were shown as mean±standard deviation (Mean±SD) values for the continuous data. Chi-square analysis (Pearson Chi-square) was used to compare categorical variables between groups. The Kolmogorov-Smirnov test evaluated whether the continuous variables had a normal distribution. Mann-Whitney U-test was used to compare paired groups, and the Kruskal-Wallis test was used to compare more than two variables. Logistic regression analysis was used to calculate the mortality risk. Significant ones in the univariate analysis were included in the model for multivariate. The statistical significance level in the analysis was accepted as $p<0.05$.

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Non-interventional Clinical Research Ethics Committee of Adıyaman University (protocol code 2022/9-1 and date of 13.12.2022). Since this is a retrospective study it was not possible to obtain any verbal or written consent from the participants.

Results

A total of 4,395 carbon monoxide poisoning cases were found to occur in Adıyaman as per the examination of 11 years of data in this study. There was CO poisoning at a rate of 63.2 per hundred thousand in Adıyaman, with an annual average of 399.5 cases. All the cases in the study were accidental, with no cases of suicide or murder. All 4,395 cases, 2,546 (57.9%) female and 1,849 (42.1%) male, were included in the study. The mean age of the cases was 27.1 ± 20.1 years (min=1-max=100). While 25.2% of them resided in the city, 34.5% in the districts, and 40.3% in the towns/villages. Most cases (97.3%) were treated as outpatients, and 2.7% were treated as inpatients. The hospitalization rate per 100,000 people was found to be 1.71. According to the discharge information of 199 patients, 118 (59.3%) were discharged after being cured, 58 (29.1%) with a referral to another institution, 7 (3.5%) were with the treatment, 3(1.5%) voluntarily, and 13 (6.5%) of them died. Fifty patients among the referred ones were transferred to the hospital in Adıyaman city from the district hospitals, and other 8 (13.8%) were referred to hospitals outside of Adıyaman. Seven of 8 patients were transferred to institutions in other cities without being admitted to any hospital in Adıyaman. The only other case was transferred after he/she spent four days in the hospital's intensive care unit (ICU) in Adıyaman. The mean hospital stay of the patients was 2.6 ± 2.5 days, and 1.7% of the cases were admitted to the ICU. Moreover, the mean duration in the ICU of the patients was 2.3 ± 1.2 days. 87 (2%) of all cases died, of which 70.1% died in the hospital, 25.3% at home, and 4.6% at different

locations. The mean time from diagnosis to death was 35.5±30.7 months. When one-year health records of cases treated as inpatients in Adıyaman hospitals were analyzed for nine disease diagnoses, morbidity was detected in 10 (8.4%) of 119 cases. When these morbidities were examined in detail, only five of these nine diseases were diagnosed, which were 3 (2.5%) Cerebrovascular accidents, 3 (2.5%) Parkinson's disease, 2 (1.7%) anxiety, 1 (0.8% depression), and 1 (0.8%) arrhythmia (Table 1).

A total of 87 of the cases died. So, the death rate from carbon monoxide poisoning was calculated as 1.25 per hundred thousand for the population of Adıyaman, with 7.9 deaths annually.

The distribution of the cases according to age showed that the highest rate was between the ages of 20-39 (30.1%). The lowest rate was in the cases of 65 or above (6.1%). In the distribution of 87 cases with a fatality, the highest fatality rate was found in the 65 or above group (Figure 1).

Six (6.9%) of the cases with fatality died at the scene due to carbon monoxide poisoning, while 5 (6.2%) of the remaining 81 deaths occurred within the first month, 8 (9.9%) within the first two months, 12 (14.5%) within the first six months, and 21 (25.9%) within the first year. However, different reasons other than CO poisoning were recorded as the causes of death for these eight cases.

When the distribution of the cases according to the time of admission to the hospital was examined, 40.8% of them were found to be admitted between 00:00-08:00, 46.1% were between 08:00-16:00 and 13.1% were between 16:00-00:00. When analyzed by months, the highest poisoning rate was in January (34.2%), December (22%), and February (17%), and the lowest in August (0.2%), June (0.4%), and May (0.5%), respectively. Considering the season, the highest rate was in winter (73.3%), and the least was in Summer (1.4%) (Table 2).

The mean age of the ones who died was significantly higher than the mean age of the ones who recovered ($p<0.001$). The fatality rate of males (2.5%) was significantly higher than that of females (1.6%) ($p=0.039$). The fatality rate of inpatients (8.4%) was found to be significantly higher than that of outpatients (1.8%) ($p<0.001$). The fatality rate of those who stayed in the ICU (%12.2) was significantly higher than those who did not (1.8%) ($p<0.001$). The fatality rate of those with morbidity (40%) was significantly higher than the rate of those without any morbidity (5.5%) according to the five identified diseases ($p=0.004$). The highest fatality rate was observed in those with Parkinson's disease (66.7%), and there was a significant difference between diagnoses in terms of death ($p=0.005$) (Table 3).

The time from diagnosis to death in outpatients was significantly higher than inpatients ($p=0.009$). It was significantly lower in those staying in the intensive care unit than in those who did not ($p=0.026$) (Table 4).

According to the univariate analysis in the logistic regression analysis to calculate the mortality risk, being male increases the risk of mortality 1.559 fold (95% CI=1.019-2.385), one year increase of age increases it 1.087 fold (95% CI=1.074-1.101), receiving inpatient treatment increases it 5.003 fold (95% CI=2.520-9.932) and staying in intensive care increases it 7.532 fold

(95% CI=3.622-15.663). The ones found to be significant in the univariate analysis were used in the multivariate analysis, and being male posed a 1,886-fold (95% CI=1.187-2.996) risk for mortality. Each age increase had a 1,086-fold (95% CI=1.072-1.099) risk for it (Table 5).

Discussion

The rate of intentional CO poisoning cases is rare in Turkey. Only 0.3% of cases were found to be intentional in one study.[13] There were no intentional cases of suicide or murder in the present study as per the examination of all the cases included, which may be due to intentional cases with a fatality being transferred to the Forensic Medicine Institute for autopsy directly without being taken to the hospital, or the fact that deaths cannot be classified as CO poisoning, since the cause of death cannot be determined without an autopsy.[16]

CO poisoning rates by population show differences from country to country and by region within the same country. This difference varies according to many parameters, especially the length of the winter season, the temperature, the heating methods, and the wind intensity. Although no evidence exists that treatment makes a difference in mortality rates in different regions, it reduces long-term morbidity.[18]

In an epidemiological study conducted worldwide in 2019, CO poisoning was found to be 13.7 per hundred thousand.[2] The rate was 14 per hundred thousand in 10,154 cases in Turkey in 2010 and 4.3 per hundred thousand for accidental cases in Ankara and its surrounding 15 cities between 2001-2011.[16] In a study conducted in Iran, the rate was reported as 38.91 per hundred thousand.[19] In the present study, it was found to be 63.2 per hundred thousand, much higher than the data in the literature. In some of the villages and districts with lower economic income in Turkey, there is no natural gas. Even if it is available, the only way of heating is traditional wood and coal stoves in most of the houses. Geysers working with gas bottles are used to heat water in the bathrooms.

Therefore, the incidence of CO poisoning in rural areas was higher than the urban areas. Most of the CO poisoning cases (¾) in the present study were found to reside in rural areas outside the urban areas, supporting the study of Uysal.[14] Adıyaman is in the Southeast region of Turkey, which has the lowest socioeconomic level. Although natural gas usage rates are increasing daily, wood and coal stoves are still used frequently, especially in rural areas. In the study of Metin et al. in 2010, the highest number of CO poisoning cases according to the population occurred in Kilis, also a southeastern city, with 199.80 cases per hundred thousand.[16] The rate in Adıyaman, according to the population, was determined as 36.60 cases per hundred thousand. Although Adıyaman was the 11th city with the highest number of cases, with 216 cases, and the ninth city according to the population, we can not fully explain the incidence of CO poisoning in Turkey was only 14 cases per hundred thousand. Many factors, such as climate and socioeconomic and education levels among 81 cities, might be the reasons for significant differences in incidence between the cities.

Furthermore, Metin et al. reported that there were 10,154 CO poisoning cases in 2010 even though the rate of natural gas use was much lower, while they noted that there were no deaths in eight of the 20 cities with the highest number of cases.[16] Adıyaman was one of these

eight cities. In this study, the annual mean number of fatalities was 7.9. Metin et al. reported only 39 deaths in 12 of the 20 cities with the highest cases. Besides the authors' statement of this particular study that they had suspicions of a deficiency in the number of deaths, we think there might have been a deficiency in the number of cases along with the number of deaths in the study of Metin et al. Accordingly, CO poisoning in Turkey in 2010 should have been higher. However, in some years, the winter season is colder or warmer, and the number of days when the wind is intense changes. These changes might have an impact on the number of CO poisonings. The 11-year data in the present study, different from the studies with 1-year data, eliminates the possibility of a random cold or hot year.

Most deaths occur during the cold and windy days of winter, including in temperate climates such as Taiwan. The wind causes the smoke to recoil from the stove chimney, causing a decrease in ventilation.[14] A study conducted in Bursa, located northwest of Turkey, showed that 64.6% of the cases occurred in the winter season.[13] A study in France determined that 84% of poisonings occurred in the autumn-winter seasons (between October and March).[10] In the present study, 73.2% of the poisonings occurred in the winter season, in December, January, and February, and 7.4% in September, October, and November, which were in the autumn.

In their epidemiological study, Mattiuzzi & Lippi determined that the incidence of CO poisoning had two definite peaks between the ages of 0-14 (31% of all cases) and those between the ages of 20-39 (34% of all cases).[2] Both groups had the highest incidence of poisoning in the present study, with 34.9% between 0-14 years old and 30.1% between 20-39 years old. Similar to other cities in the Southeastern region of Turkey, Adıyaman, with a high fertility rate, has a high young population. The high rate of young population in the city might be why most cases of CO poisoning occur in the younger population. In this study, the least poisoning rate was 6.1% for those 65 or above. However, this group had the highest fatality rate, and the mean age of cases was 27.1 years.

The hospitalization rate for accidental CO poisoning cases between 2001 and 2010 for the entire population in England was 0.49/100,000. In addition, the incidence of cases and hospitalization rates in rural areas was higher than in urban areas.[20] In this study, the hospitalization rate per population was higher (1.71/100,000) than in England. However, in the study covering the cases between 2002 and 2016, the mean number of annual accidental CO poisonings in England was 107.8, whereas this number was 399.5 in Adıyaman. The higher hospitalization rate in Adıyaman compared to England might be related to the number of cases rather than the severity or clinician preference.

However, the present study’s data covers all the hospitals in Adıyaman, including the small-scale hospitals in its districts. The hospitalization status of the seven patients transferred directly to other cities without being hospitalized in Adıyaman could not be determined. If the data could be accessed, patients who were transferred to hospitals outside the city with better facilities would increase the rate of hospitalization and intensive care because of their critical situation. However, none of those eight patients transferred out of the city died. Regarding nine

diseases identified, one of the ten patients diagnosed (anxiety) in Adıyaman hospitals was one of the patients transferred out of the city.

A total of 3,500 people died from carbon monoxide poisoning between 1968 and 1998 in the United States, where 50,000 people are believed to visit the emergency services annually with complaints of carbon monoxide poisoning. According to current data from the Centers for Disease Control and Prevention, approximately 438 people in the United States die annually due to poisoning unrelated to fire and accidental CO2 poisoning.[21]

In a study worldwide, the risk of death from CO poisoning was found to be 0.46 per hundred thousand, while it was 0.35 per hundred thousand in a study conducted across Turkey.[2,15] In the present study, 87 of 4,395 CO poisoning cases in 11 years died, and the mortality rate in Adıyaman was 1.25 per hundred thousand.

According to the data from the Forensic Medicine Institute in Ankara, a total of 380 people, 203 in Ankara and 177 in 15 cities reporting to this institute, died between 2001-2011 due to carbon monoxide poisoning.[14] In their study published in 2010, Akkose et al. reported that the fatality rate due to carbon monoxide poisoning in patients admitted to the hospital ranged from 2.6% to 9.8% in the literature.[13] However, in Iran, Nazari et al. reported in their study, also published in 2010, that 346 people died of 3,078 CO poisonings in Northwest Iran between 2003 and 2008, so the fatality rate was 11.24%.[22] In a study conducted in China, the fatality rate was 2.5% in hospital admissions and 14.3% in those admitted to the ICUs.[23] In Turkey, the fatality rate was 3.3 in 305 patients who visited the emergency department of a hospital in Bursa.[13] In France, this rate was 3-5% and 9.5% in Iran.[10,19] In the present study, the fatality rate was 6.5% in hospital admissions and 12.2% in ICU patients.

Hampson & Weaver stated that deaths from CO poisoning were more common in older adults.[18] In their study, Mattiuzzi & Lippi argued that the risk of death from carbon monoxide poisoning was high in older adults and infants, and the risk increased with age.[2] In the present study, the highest death rate was seen in people aged 65 or above, with 65.5%. However, unlike Mattiuzzi & Lippi's finding, only 1.1% of deaths were children aged between 0 and 5 years, despite accounting for 10.7% of all the cases in the present study. The mean age of the ones who died was significantly higher than the mean age of the ones who survived. In the multivariate analysis of age, gender, treatment method, and ICU admission criteria, each age increase had a 1,086-fold risk for mortality.

After asymptomatic days or weeks following exposure to CO, the effects of chronic neurological damage begin to appear. Due to the aggravation of existing chronic diseases or new diseases triggered by the poisoning, the risk of death becomes high, especially in the first month, within 1-6 months, and 6-12 months afterwards. In the study of Huang et al., 1.93% of the patients followed up between 1999 and 2010 died during the follow-up, and the death rate was 5.24 times higher than the control group.[24]

The complaint-free period after poisoning leads to false reporting of these sequelae and deaths caused by these sequelae with another diagnosis unrelated to carbon monoxide poisoning. After carbon monoxide poisoning, 6 (6.9%) of the cases died at the scene, while 5 (6.2%) of the

remaining 81 deaths occurred within the first month, 8 (9.9%) in the first two months, and 12 (14.5%) in the first six months. Furthermore, 21 (25.9%) died within one year. However, the causes of death were recorded for reasons other than CO poisoning. The mean time from the diagnosis of poisoning to death was three years (35.5 ± 30.7 months).

Eichhorn et al. stated that delayed neurological damage due to CO poisoning reveals itself in the form of ataxia, dementia, Parkinson's disease, lack of concentration, and abnormal behaviours.[6] Delayed neurological damage is between 15% and 40%.[25] Increased risk of neuropsychiatric sequelae, arrhythmia, MI, coronary artery disease, heart failure, hypothyroidism, diabetes mellitus, and hypertension was detected in the follow-up period after CO poisoning.[26-29] In the present study, the health data of 119 hospitalized patients in Adıyaman hospitals were scanned for one year for cerebrovascular accident, dementia, Parkinson's disease, ataxia, depression, anxiety, MI, arrhythmia and hypothyroidism, and at least one of these diseases was detected in 10 (8.4%) patients. Three (2.5%) patients were diagnosed with cerebrovascular accident (CVA), three (2.5%) with Parkinson's disease, one (0.8%) with depression, two (1.7%) with anxiety, and one (0.8%) with arrhythmia. The fatality rate of those with morbidity (40%) was significantly higher than those without (5.5%). The highest number of deaths occurred in those with Parkinson's disease, with 66.7%. The mechanisms by which CO poisoning paves the way for developing diseases that cause mortality should be clarified by further studies.

In one study, the mortality due to carbon monoxide poisoning in the general population was twice as high in men as in women. This difference was attributed to the shorter COHb elimination times in women than in men. Because of the short elimination period, women could tolerate carbon monoxide better.[29] Similarly, in the present study, the fatality rate of males (2.5%) was significantly higher than that of females (1.6%), and according to multivariate analysis, being male posed a 1,886-fold risk for mortality. We think that it would be helpful to examine the effect of gender on fatality in CO poisoning with other studies to be conducted in the future.

Stove-related poisoning occurs, especially at night. In cases where the piping setting of the stove, especially in windy weather, cannot provide good ventilation, CO gas leaks into the room from the incompletely burned wood and coal. Households who do not realize that the stove has been fully lit or not at night while asleep are exposed to the harmful effects of carbon monoxide. We did not find any study in the literature comparing the time of the day of their admission to the hospital due to CO poisoning. In the present study, 40.8% of the cases were admitted to the hospital between 00-08 hours and 46.1% between 08-18 hours. Surprisingly, 40.8% of them visited the hospital before 8 am. Individuals who get up early for morning prayers or things to do in their villages may have survived due to not being further exposed to Carbon monoxide and have ensured that their household members were admitted to the hospital with them.

Conclusions

Although almost all CO poisoning can be prevented with simple precautions, it is still a severe cause of death in regions of Turkey where traditional heating and water heating methods are used. The present study showed that 11.8% of patients discharged from the hospital died within one year because CO poisoning increases the possibility of new diseases (8.4% of cases) with an unclear mechanism that increases mortality risk. Since morbidities cerebrovascular accident, ataxia, dementia, Parkinson's, depression, anxiety, and arrhythmia leading to death might occur weeks or months after poisoning, people diagnosed with CO poisoning should be followed up closely for about one year. Furthermore, clinicians should consider CO poisoning in the aetiology of sudden neurologic, cardiologic, psychiatric, and endocrinologic disorders. In addition, the present study showed that women and the elderly have a greater risk of mortality from CO poisoning, and 29.9% of deaths occurred outside the hospitals, indicating that CO poisoning is a multidisciplinary health problem that concerns many institutions.

Acknowledgements

We acknowledge the support given by the IT staff of Adiyaman Provincial Health Directorate İsmail Turhan and Yaşar Dikici during the data collection process.

References

1. Byard RW. Carbon monoxide-the silent killer. *Forensic Sci. Med. Pathol* 2019;15:1-2.

2. Mattiuzzi C, Lippi G. Worldwide epidemiology of carbon monoxide poisoning. *Human & Experimental Toxicology* 2020;39(4):387-392.

3. Bleecker ML. Carbon monoxide intoxication. *Handb Clin Neurol* 2015;131:191-203.

4. İncekaya Y, Feyizi H, Bayraktar S, Ali İ, Topuz C, Karacalar S, et al. Carbon Monoxide Poisoning and Hyperbaric Oxygen Therapy. *Okmeydanı Tıp Dergisi* 2017;33(2):114-118.

5. Hampson NB, Kramer CC, Dunford RG, Norkool DM. Carbon monoxide poisoning from indoor burning of charcoal briquets. *Jama*, 1994;271(1):52-53.

6. Eichhorn L, Thudium M, Jüttner B. The Diagnosis and Treatment of Carbon Monoxide Poisoning. *Dtsch Arztebl Int*. 2018; 115(51-52):863–870.

7. Verma A, Hırsch DJ, Glatt CE, Ronnett GV, Snyder SH. Carbon Monoxide: a Putative Neural Messenger. *Science.* 1993;259(5093):381-384.

8. Lo CP, Chen SY, Lee KW, Chen WL, Chen CY, Hsueh CJ, et al. Brain Injury After Acute Carbon Monoxide Poisoning: Early and Late Complications. *American Journal of Roentgenology* 2007;189: W205-W211.

9. Hampson NB, Hauff NM. Carboxyhemoglobin levels in carbon monoxide poisoning: do they correlate with the clinical picture? *The American Journal of Emergency Medicine* 2008;26(6):665-669.

10. Sam-Laï NF, Saviuc P, Danel V. Carbon monoxide poisoning monitoring network: a five-year experience of household poisonings in two French regions. *Journal of toxicology, Clinical Toxicology* 2003;41(4):349–53.

11. Forés C, Hamnett HJ. Epidemiological Study of Carbon Monoxide Deaths in Scotland 2007–2016. *Journal of Forensic Sciences* 2018;63(6):1776-1782

12.Kinoshita H, Türkan H, Vucinic S, Naqvi S, Bedair R, Rezaee R, et al. Carbon monoxide poisoning. *Toxicology Reports*. 2020;7:169-173.

13. Akkose S, Turkmen N, Bulut M, Akgoz S, Iscimen R, Eren B. An analysis of carbon monoxide poisoning cases in Bursa, Turkey. *East Mediterr Health J* 2010;16(1):101–6.

14. Uysal C, Celik S, Duzgun Altuntas A, Kandemir E, Kaya M, Karapirli M, et al. Carbon monoxide-related deaths in Ankara between 2001 and 2011. *Inhal Toxicol* 2013;25(2):102–6.

15. Can G, Sayili U, Sayman ÖA, Kuyumcu ÖF, Yilmaz D, Esen E, et al. Mapping of carbon monoxide related death risk in Turkey: a ten-year analysis based on news agency records. *BMC Public Health* 2019;19:9.

16. Metin S, Yıldız Ş, Çakmak T, Demirbaş Ş. Frequency of Carbon Monoxide Poisoning in Turkey in 2010. *TAF Prev Med Bull* 2011; 10(5): 587-592.

17. Hampson NB, Weaver LK. Carbon monoxide poisoning: a new incidence for an old disease. *Undersea Hyperb Med* 2007;34(3):163-7.

18. Hosseininejad SM, Aminiahidashti H, Khatir IG, Ghasempouri SG, Jabbari A, Khandashpour M. Carbon monoxide poisoning in Iran during 1999–2016: A systematic review and meta-analysis. *Journal of Forensic and Legal Medicine* 2018;53:87-96.

19. Roca-Barceló A, Crabbe H, Ghosh R, Freni-Sterrantino A, Fletcher T, Leonardi G, et al. Temporal trends and demographic risk factors for hospital admissions due to carbon monoxide poisoning in England. *Preventive Medicine* 2020;136:106104.

20. Liao WC, Cheng WC, Wu BR, Chen WC, Chen CY, Chen CH, et al. Outcome and prognostic factors of patients treated in the intensive care unit for carbon monoxide poisoning. *Journal of the Formosan Medical Association* 2019;118(4):821-827.

21. CDC. https://www.cdc.gov/nceh/multimedia/infographics/carbon_monoxide.html. Updated 2020 Accessed on January 2023.

22. Nazari J, Dianat I, Stedmon A. Unintentional carbon monoxide poisoning in Northwest Iran: A 5-year study. *Journal of Forensic and Legal Medicine* 2010;17(7):388-391.

23. Huang CC, Chung MH, Weng SF, et al. Long-term prognosis of patients with carbon monoxide poisoning: a nationwide cohort study. *PLOS ONE* 2014;9:e105503.

24. Rose JJ, Wang L, Xu Q, McTiernan CF, Shiva S, Tejero J, et al. Carbon Monoxide Poisoning: Pathogenesis, Management, and Future Directions of Therapy. *American Journal of Respiratory and Critical Care Medicine* 2017;195(5):596-606.

25. Han S, Choi S, Nah S, Lee SU, Cho YS, WoonnKim G, et al. Cox regression model of prognostic factors for delayed neuropsychiatric sequelae in patients with acute carbon monoxide poisoning: A prospective observational study. *NeuroToxicology* 2021;82:63-68.

26. Lee FY, Chen WK, Lin CL, Kao CH. Carbon monoxide poisoning and subsequent cardiovascular disease risk. *Medicine (Baltimore)* 2015;94:e624.

27. Huang CC, Ho CH, Chen YC, Hsu CC, Lin HJ, Su SB, et al. Increased risk for hypothyroidism associated with carbon monoxide poisoning: a nationwide population-based cohort study. *Scientific Reports* 2019;9(1):1-8.

28. Huang CC, Chung MH, Weng SF, Chien CC, Lin SJ, Lin HJ, et al. Long-Term Prognosis of Patients with Carbon Monoxide Poisoning: A Nationwide Cohort Study. *Plos One* 2014;9(8):e105503

29. Zavorsky GS, Tesler J, Rucker J, et al. Rates of carbon monoxide elimination in males and females. *Physiol Rep* 2014; 2(12): e12237.

Table 1(on next page)

Characteristics of carbon monoxide poisoning cases

The table shows the age, gender, and place of residence of cases that were evaluated. Also, it contains information about the prognosis of the cases.

1 **Table 1.** Characteristics of carbon monoxide poisoning cases

		Number	%
Age (years), Mean ± SD		27.1 ± 20.1	
Gender	Female	2546	57.9
	Male	1849	42.1
Area of residence	City	1106	25.2
	District	1516	34.5
	Town / Village	1773	40.3
Type of treatment	Outpatient	4276	97.3
	Inpatient	119	2.7
Type of discharge	Cured	118	59.3
	Referred	58	29.1
	Treated	7	3.5
	Death	13	6.5
	Voluntary	3	1.5
Duration of hospital stay (days), Mean ± SD		2.6 ± 2.5	
Admitted to the ICU	Yes	74	1.7
	No	4321	98.3
ICU stay (days), Mean ± SD		2.3 ± 1.2	
Exitus	Yes	87	2.0
	No	4308	98.0
Place of death	Hospital	61	70.1
	Home	22	25.3
	Other	4	4.6
Time from diagnosis to death (months), Mean ± SD		35.5 ± 30.7	
Morbidity presence	Yes	10	8.4
	No	109	91.6
	Cerebrovascular accident	3	2.5
	Parkinson's disease	3	2.5
	Depression	1	.8
	Anxiety	2	1.7
	Arrhythmia	1	.8
	None	109	91.6

2

Table 2(on next page)

Temporal distribution of CO poisoning patients' admissions to hospital

Data shows the distribution of cases by hours of the day and by months of the year.

Table 2. Temporal distribution of CO poisoning patients' admissions to hospital

		Number	%
Hour	00:00:00--07: 59:59	1795	40.8
	08:00:00--15: 59:59	2026	46.1
	16:00:00--23: 59:59	574	13.1
Month	January	1504	34.2
	February	749	17.0
	March	632	14.4
	April	139	3.2
	May	21	.5
	June	16	.4
	July	36	.8
	August	9	.2
	September	25	.6
	October	52	1.2
	November	244	5.6
	December	968	22.0
Season	Spring	792	18.0
	Summer	61	1.4
	Autumn	321	7.3
	Winter	3221	73.3

Table 3(on next page)

Comparison of exitus presence according to various parameters

Data shows the exitus presence according to various parameters. The p-value is bold if the analysis was significant.

Table 3. Comparison of Exitus presence according to various parameters

		Exitus presence		No Exitus		P
		Number	%	Number	%	
Age (years), Mean ± SD		65.5 ± 22.1		26.4 ± 19.3		**<0.001***
Gender	Female	41	1.6	2505	98.4	**0.039****
	Male	46	2.5	1803	97.5	
Area of residence	City	25	2.3	1081	97.7	0.121**
	District	21	1.4	1495	98.6	
	Town / Village	41	2.3	1732	97.7	
Type of treatment	Outpatient	77	1.8	4199	98.2	**<0.001****
	Inpatient	10	8.4	109	91.6	
Type of discharge	Cured	3	2.5	115	97.5	0.072**
	Referred	6	10.3	52	89.7	
	Treated	1	14.3	6	85.7	
	Death	0	0	3	100.0	
Staying in the ICU	Yes	9	12.2	65	87.8	**<0.001****
	No	78	1.8	4243	98.2	
Morbidity presence	Yes	4	40.0	6	60.0	**0.004****
	No	6	5.5	103	94.5	
Diagnoses received within one year after hospitalization	Cerebrovascular	1	33.3	2	66.7	**0.005****
	Parkinson's Disease	2	66.7	1	33.3	
	Depression	0	.0	1	100.0	
	Anxiety	1	50.0	1	50.0	
	Arrhythmia	0	0	1	100.0	
	None	6	5.5	103	94.5	
Duration of hospital stay (days), Mean ±		3.0 ± 1.7		2.6 ± 2.5		0.256*
Duration of ICU stay (days), Mean ± SD		2.3 ± 1.0		2.3 ± 1.2		0.685*

*Mann Whitney U test, **Chi-square analysis was applied.

Table 4(on next page)

Comparison of the time from diagnosis to death according to various parameters

Data shows the time from diagnosis to death according to various parameters. The p-value is bold if the analysis was significant.

Table 4. Comparison of the time from diagnosis to death according to various parameters

		Time from diagnosis to death (months)	P
		Mean ± SD	
Gender	Female	36.3 ± 34.6	0.862*
	Male	34.7 ± 27.1	
Area of residence	City	32.2 ± 30.0	0.068**
	District	47.9 ± 29.4	
	Town / Village	31.1 ± 30.8	
Type of treatment	Outpatient	37.8 ± 30.3	**0.009***
	Inpatient	17.2 ± 29.2	
Type of discharge	Cured	30.7 ± 30.6	0.149**
	Referred	6.0 ± 7.9	
	Treated	15.0 ±-	
Staying in the ICU	Yes	19.0 ± 30.4	**0.026***
	No	37.4 ± 30.4	
Place of death	Hospital	34.0 ± 30.3	0.468**
	Home	36.1 ± 30.9	
	Other	54.8 ± 38.0	

*Mann Whitney U test, **Kruskal Wallis test was applied.

Table 5(on next page)

Logistic regression analysis of the presence of mortality

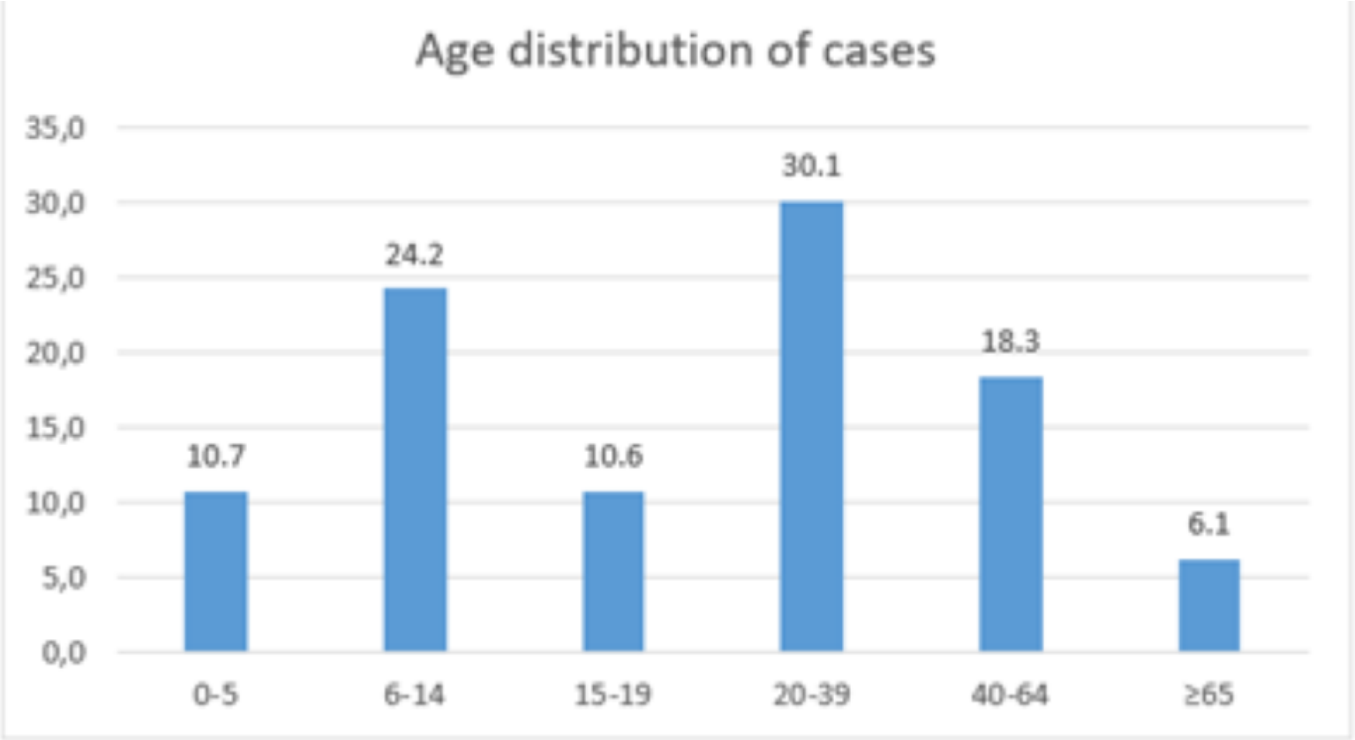
The p-value is bold if the analysis was significant.

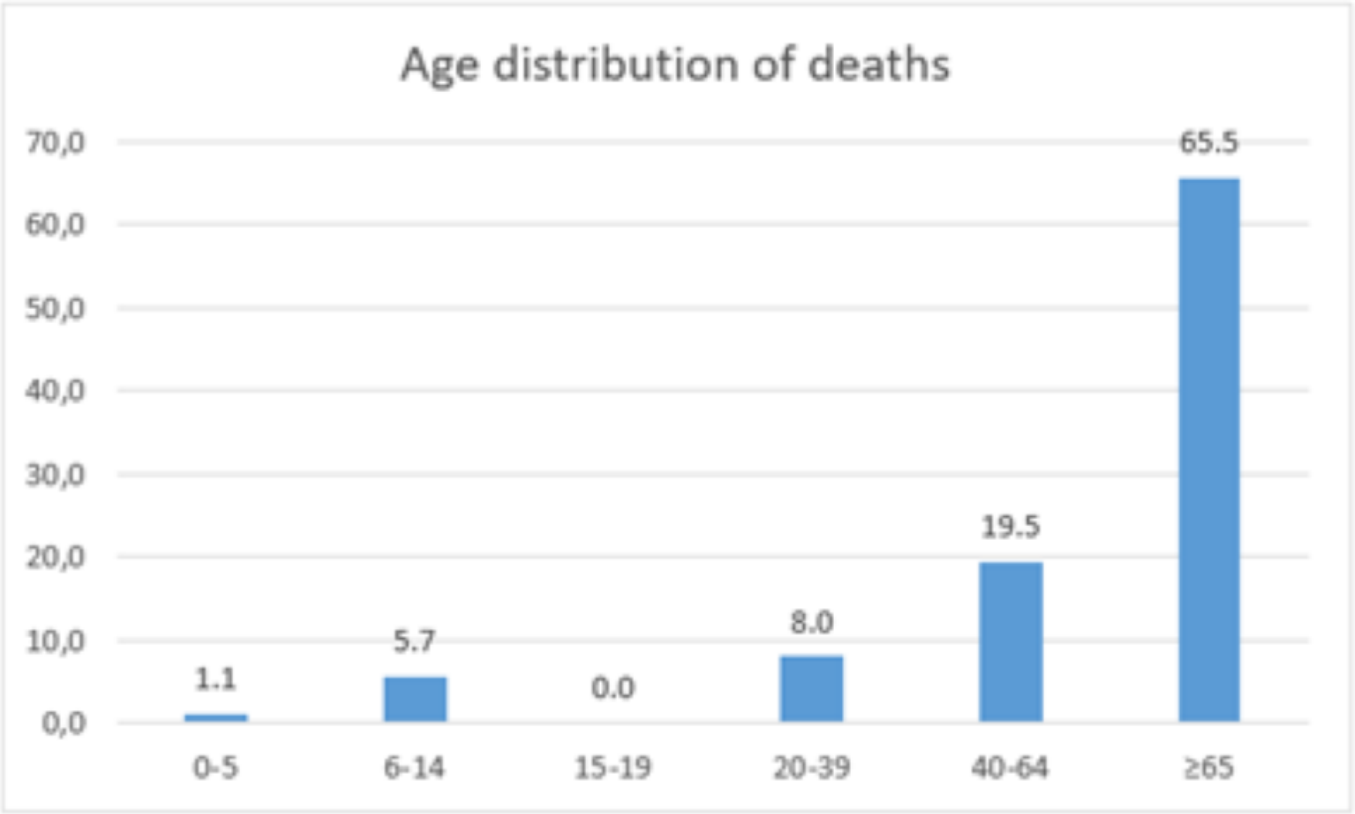
Table 5. Logistic regression analysis of the presence of mortality

	Univariate				Multivariate			
	B	p	OR	%95 GA	B	p	OR	%95 GA
Gender (ref = female)	444	**0.041**	1.559	1.019-2.385	634	**0.007**	1.886	1.187-2.996
Age	084	**<0.001**	1.087	1.074-1.101	082	**0.001**	1.086	1.072-1.099
Type of treatment (ref=outpatient)	1.610	**<0.001**	5.003	2.520-9.932	138	0.897	1.148	141-9.338
ICU (ref=non-staying)	2.019	**<0.001**	7.532	3.622-15.663	586	0.607	1.797	193-16.754

Figure 1

Distribution of cases and deaths by age


Age distribution of cases
35,0
30,0
25,0
20,0
15,0
10,0
5,0
0,0
10.7
24.2
10.6
30.1
18.3
6.1
0-5
6-14
15-19
20-39
40-64
≥65


Age distribution of deaths
70,0
60,0
50,0
40,0
30,0
20,0
10,0
0,0
1.1
5.7
0.0
8.0
19.5
65.5
0-5
6-14
15-19
20-39
40-64
≥65