ISSN 2059-9951

POST-CARBON MONOXIDE POISONING MONITORING: DECISION SUPPORT SYSTEMS AND A COMPREHENSIVE APPROACH TO LONG-TERM ASSESSMENT

Irada H. Mirzazadeh
Ministry of Science and Education of the Republic of Azerbaijan Institute of Mathematics and Mechanics
AZ 1141 Baku, **Azerbaijan**
E-mail: irada811@gmail.com

ABSTRACT

Carbon monoxide (CO) poisoning continues to pose a major global public health challenge due to its high morbidity and mortality. The often-nonspecific symptoms, along with limited access to precise diagnostic tools, complicate timely diagnosis and treatment. This article investigates how modern information technologies and advanced mathematical-statistical methods—such as time series analysis, the Mann-Whitney U-test, and biostatistical techniques—can improve the diagnosis, monitoring, and treatment decisions in CO poisoning cases. It provides an overview of the global epidemiology of CO poisoning, revealing notable regional disparities in incidence and mortality rates. A key focus is the importance of long-term monitoring in affected individuals to prevent or detect delayed complications, particularly neurological and cardiovascular sequelae. The integration of digital systems into clinical practice allows for the continuous collection and analysis of physiological and pathophysiological parameters, supporting early detection and intervention. Real-time data processing and predictive modeling facilitate individualized treatment decisions and timely therapeutic adjustments. These approaches not only enhance clinical outcomes but also reduce the long-term healthcare burden associated with CO poisoning. The article underscores the need for interdisciplinary strategies combining clinical knowledge, data science, and digital infrastructure to address the complex challenges in managing CO intoxication effectively and sustainably.

Keywords: Carbon monoxide poisoning; public health; long-term complications; monitoring; mathematical and statistical methods.

1. Introduction

The primary expectation of society from medicine is the provision of high-quality care. Despite living in the 21st century, people continue to die from preventable medical errors and delays in receiving timely treatment. It is clear that all scientific innovations must be effectively communicated to the medical community. Therefore, there is a need for sources where information can be systematically summarized and critically assessed — in other words, systematic reviews should be conducted. One approach to addressing this challenge for medical professionals is the provision of open access to leading scientific publications (e.g., through platforms such as PubMed). It is worth noting that medicine differs from other fields of knowledge in terms of the application and development of information technologies.

There are numerous challenges in medicine that require both high diagnostic accuracy and rapid emergency response. Poisoning by toxic substances is one such issue, where timely intervention plays a crucial role in determining a favorable outcome. In emergency and urgent care settings, managing such cases becomes significantly more complex, especially when the patient is in a comatose state.

CO poisoning represents a significant public health concern, with diagnosis frequently complicated by nonspecific symptoms and limited access to specialized diagnostic tools. Early detection is essential to prevent long-term complications. Prognosis largely depends on the severity of exposure and the timeliness of treatment both factors that significantly influence the risk of neurological damage and mortality.

The intensity of CO poisoning increases during the winter months due to the use of heating stoves. However, the widespread use of industrial chemicals has led to a rise in CO poisoning cases year-round.

The application of information technology in medicine is associated with the complexity of the problems to be addressed and the uncertainty surrounding many parameters. The similarity in symptoms among poisoning by fourteen toxic substances (such as aniline, atropine, barbiturates, tubazid, tranquilizers, cyanides, and others) complicates the differential diagnosis of CO poisoning. The management of such poisoning involves differential diagnosis, immediate first aid, and the selection of appropriate treatment strategies. However, recent studies have shown that CO poisoning can result in long-term consequences. For this reason, even after receiving initial treatment, patients should remain under medical supervision, which includes prolonged examinations and tests. The use of information technology facilitates patient monitoring after treatment, ensuring control over the adaptation process, minimizing unnecessary testing, verifying the reliability of results over time, and generating well-founded medical recommendations based on examination outcomes. This article presents a study focused on monitoring tasks using information technology and effective mathematical methods for more accurate resolution of issues related to CO poisoning. To this end, several mathematical statistical methods applied in monitoring will be explored, including the time series method, the mathematical methods for conducting experiments, the Mann-Whitney U-test, biostatistical methods, the Wilcoxon T-test, the Friedman test, the Kruskal-Wallis provided H-criterion and others.

2. Discussion

Epidemiology

CO poisoning is a significant global health issue, given its association with high morbidity and mortality rates [1]. According to statistics, the growth of the oil, chemical, and gas industries has led to an increased frequency of poisoning incidents involving toxic substances used in these sectors. CO is formed in various environments as a result of incomplete combustion of carbon-containing substances.

In 2021, the global mortality rate from unintentional CO poisoning was 0.366 per 100,000 population (95% uncertainty interval: 0.276–0.415), corresponding to approximately 28,900 deaths (21,700–32,800) and 1.18 million years of life lost (0.886–1.35 million). Almost 70% of deaths occurred in men (20,100 [15,800–24,000]), with the highest number of deaths in the 50–54 age group (2,210 [1,660–2,590]). The highest mortality rate was found among individuals aged 85 and older, with 1.96 deaths (1.38–2.32) per 100,000. Regionally, Eastern Europe had the highest age-standardized mortality rate, with 2.12 deaths (1.98–2.30) per 100,000 [2].

ISSN 2059-9951

The study by Mattiuzzi and Lippi (2020) in Human & Experimental Toxicology provides a detailed analysis of the global epidemiology of CO poisoning, noting that mortality rates are approximately 2.1- and 3.6-fold higher in countries with middle and middle-to-high socio-demographic index (SDI) compared to those with low-to-middle SDI [3]. In contrast, the Global Burden of Disease (GBD) Study 2021 highlights regional disparities and the complexity of the SDI-mortality relationship, with higher SDI countries (such as those in North America) showing increasing rates in recent years, likely due to factors such as drug use and housing conditions [2]. Both studies indicate a potential association between socio-demographic index and increased rates of CO poisoning.

In the United States, approximately 50,000 individuals are affected by CO poisoning annually, with a fatality rate ranging from 1% to 3% [4]. Preliminary CDC data indicate that in 2022 approximately 1,244 deaths in the United States were attributed to carbon monoxide poisoning [5]. In the United States, the majority of cases are attributed to CO exposure unrelated to fires. Notably, certain groups, including women, children under 17, the elderly, and individuals with pre-existing medical conditions, are particularly vulnerable. Low-income households often rely on alternative heating methods, which increases the risk of CO exposure [6]. Seasonal variations also impact incidence rates—during winter, the risk is heightened due to the increased use of space heaters. For example, one study emphasizes the dangers associated with using charcoal grills indoors for heat generation. Additionally, the use of gas heaters and stoves without proper ventilation has been linked to CO poisoning [5].

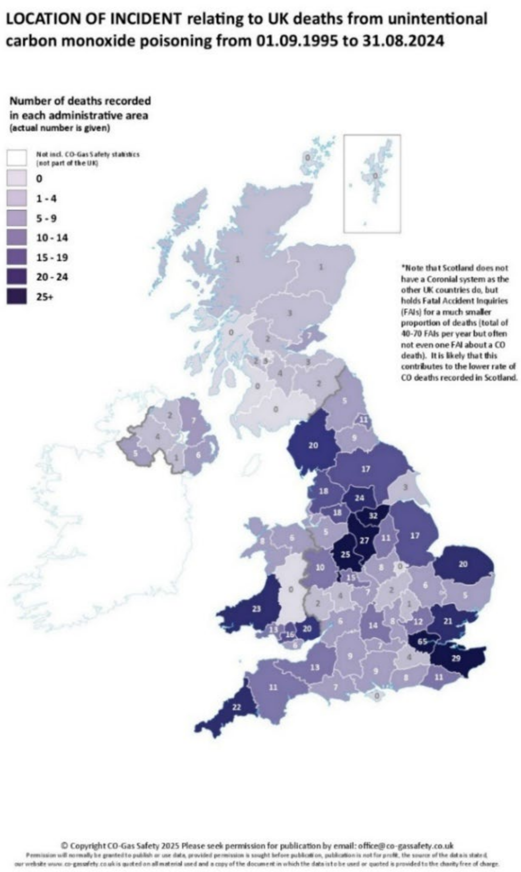

Fig. 1. Publication of 29 years of data of Deaths and Injuries from unintentional CO poisoning in the UK 1995-2024.

In the UK, the average number of unintentional CO poisoning deaths from all carbon fuels is approximately 30 per year (26.1 to be exact), although this figure drops to 8.5 when considering only the last ten years (Fig. 1). It should also be noted that, in the UK, approximately 4,000 visits to Emergency Departments occur each year due to unintentional, non-fire-related CO exposure [7, 8]. These numbers likely represent only a small fraction of the actual cases, as there is no routine CO testing for individuals who die from unexplained causes. As a result, CO-Gas Safety no longer publishes statistics on non-fatal, unintentional CO exposure, acknowledging that many cases go unreported or undiagnosed. While the data suggest a sharp decline in CO-related deaths in recent years, it can take up to three years for CO-Gas Safety to be informed of a death, usually when an investigation is carried out. Consequently, they treat such reductions with caution [9].

Similar to the UK, current statistics on CO poisoning in Germany from 2020 to 2024 are limited. However, some trends and figures can be derived from North Rhine-Westphalia, which may serve as an indicator for the entire country (Table 1).

Table 1. Hospital admissions and deaths due to CO poisoning in North Rhine-Westphalia between 2020 and 2023

Year	2020	2021	2022	2023
Hospital treatments	619	639	487	474
Number of deaths	55	60	75	73

According to the North Rhine-Westphalia Statistical Office, Information and Technology, there were 958 cases of CO poisoning treated in 2013. This indicates that the number of such cases in North Rhine-Westphalia has halved over the past ten years, showing a decrease of 50.5%. The average age of those treated in 2023 was just under 44 years. Although hospital treatments have declined, the number of deaths has remained relatively stable, with a slight increase in 2022 and 2023 [10].

According to the Initiative for the Prevention of CO poisoning, an average of approximately 3,500 patients with CO poisoning were treated annually in German hospitals over the past decade. Nearly one in six of these patients died from the poisoning (Table 2) [11].

Table 2. Number of CO poisonings (ICD-10 diagnosis) according to the Federal Health Reporting in Germany

Year	2012	2013	2014	2015	2016	2017	2018	2019
Hospital treatments	4302	3960	3764	3481	3611	3694	3438	3018
Number of deaths	582	514	594	648	640	606	629	535

CO poisoning is a significant public health concern in China, with a high disease burden. Over the past five years, 90% of CO poisoning cases in China have occurred in the northern regions. A total of 21,088 cases of acute CO poisoning were diagnosed in Shandong Province between 2019 and 2020, with the coastal cities of Qingdao and Yantai together accounting for over 3,000 cases. Jinan, the capital of Shandong Province, has a population of 10 million [12]. Among the 6,588 CO poisoning cases identified, 5,616 (85.25%) were linked to household coal heating, resulting in 180 deaths [13]. The cumulative incidence rate was 5.78 per 100,000 person-years, and the mortality rate was 0.19 per 100,000 person-years. The incidence in urban areas (6.55 per 100,000 person-years) was higher than in rural areas (5.04 per 100,000 person-years), with a statistically significant difference between the two ($P < 0.001$) [13].

According to statistical data, a slight decrease in the number of acute CO poisonings has also been observed in Azerbaijan. According to the Ministry of Healthcare of the Republic of Azerbaijan, a total of 8,751 CO poisoning cases were recorded in Baku between 2019 and 2024. Most poisoning events occur during the winter months. The majority of CO poisonings are concentrated in two age groups: 10 to 24 years and 25 to 39 years. Compared to other countries, the rate of CO poisoning in Azerbaijan was higher among females. Reliable information on CO poisonings in Baku between 2019 and 2024 is presented in Figure 2.

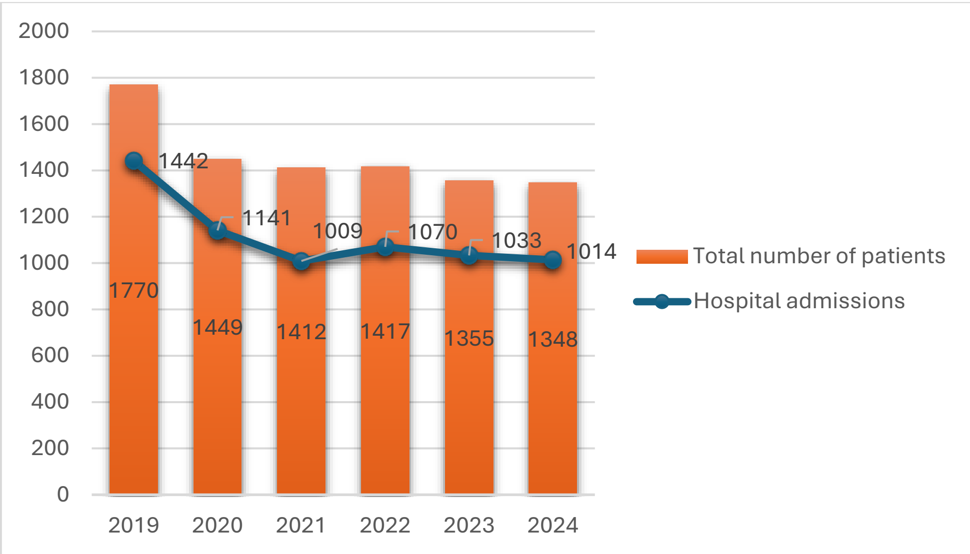

Fig. 2. Total number of patients and hospital admissions due to CO poisoning in Baku between 2019 and 2024

Complications in CO Poisoning

In addition to diagnosing CO poisoning, it is important to monitor the health of affected individuals over time. Since CO has a higher affinity for hemoglobin than oxygen, it leads to the formation of carboxyhemoglobin (COHb), thereby reducing the blood's oxygen-carrying capacity. This results in hypoxia and tissue damage. Moreover, CO can directly inhibit cellular respiration by binding to cytochrome *c* oxidase (C*c*O) in the mitochondrial electron transport chain. This suppression of oxidative phosphorylation decreases the synthesis of adenosine triphosphate (ATP) and increases reliance on anaerobic metabolism. The resulting lactic acidosis further exacerbates both cellular and systemic dysfunction [14]. CO poisoning also induces oxidative stress, triggers the release of reactive oxygen species (ROS), and activates inflammatory pathways. These mechanisms can lead to lipid peroxidation, protein degradation, and apoptosis—particularly in oxygen-sensitive organs such as the brain and heart [4, 15].

The clinical manifestations of CO poisoning range from mild symptoms to severe neurological and cardiovascular impairment, coma, or death. In most cases, symptoms resolve following normobaric or hyperbaric oxygen therapy. However, some patients continue to experience neuropsychiatric impairments or develop delayed neurological sequelae (DNS) after initial recovery, including delayed encephalopathy [16]. DNS can develop in up to 40 percent of patients 3 to 240 days after apparent recovery, encompassing a wide range of symptoms such as seizures, impaired consciousness, difficulty in concentrating, cognitive impairment, personality changes, dementia, psychosis, movement disorders (e.g., Parkinsonism), peripheral neuropathy, and even a vegetative state, which can persist for a year or longer [17]. The diagnosis of DNS is primarily based on clinical presentation and radiological findings from CT and conventional MRI. MRI and CT scans revealed that particularly vulnerable areas of the brain include the hippocampus, basal ganglia, and corpus callosum during the acute phase, while DNS is associated with significant white matter damage [18].

Acute brain injuries are accompanied by elevated biochemical markers such as neuron-specific enolase (NSE), S100β, as well as cytokines, interleukins, and growth factors in patients with loss of consciousness [20, 21]. CO poisoning also affects the dopaminergic system by increasing extracellular dopamine levels through enhanced release and inhibition of its metabolism and reuptake. This excess in dopamine can persist for several weeks and is associated with oxidative damage, apoptosis, and synaptic and nuclear cell death in the mesolimbic system, particularly in the globus pallidus [22]. Researchers have also linked oxidative metabolites of dopamine, such as reactive quinones and oxygen radicals, to the development of DNS.

Excessive dopamine production leads to striatal lesions [23]. Toxic leukoencephalopathy, characterized by demyelination and structural abnormalities in the deep white matter, has also been reported in CO poisoning, although the exact cellular targets of CO remain to be fully understood [24].

CO poisoning is closely associated with a broad spectrum of cardiac complications, including acute myocardial injury, severe necrosis, and impaired contractility. The myocardium, being extremely sensitive to oxygen deprivation, suffers hypoxic injury exacerbated by increased oxygen demand due to heightened contractility, reduced coronary reserve, and impaired cellular respiration [25]. In addition, CO induces both cellular and subcellular damage to the heart.

Acute poisoning may be accompanied by elevated cardiac biomarkers—such as troponin, creatine kinase (CK), and creatine kinase-MB (CK-MB)—as well as electrocardiographic changes ranging from NSTEMI to STEMI, despite unobstructed coronary arteries. Left ventricular dysfunction, ranging from mild to severe, has also been observed and correlates with carboxyhemoglobin (COHb) levels and duration of exposure [26]. Cases of ischemic myocardial injury following CO poisoning have been documented, including in patients with only mild intoxication [27]. This ischemic damage may be further aggravated by peripheral circulatory failure and hypotension, which reduce left ventricular output and compromise tissue oxygenation [25]. Severe cardiac decompensation due to CO exposure can result in multiple organ failure and is a major cause of death in cases of severe poisoning [28].

CO poisoning has also been associated with an increased risk of developing ischemic heart disease coronary heart disease (IHD). A large-scale study in South Korea investigated this relationship by analyzing data from 28,113 patients with CO poisoning, using a national health database. Conditional logistic regression revealed a significantly higher risk of IHD in the CO poisoning group compared to the control group (adjusted HR: 2.16; 95% CI: 1.87–2.49). The greatest risk was observed during the first two years following poisoning. Among individuals younger than 40 years, the risk was especially high (adjusted HR: 4.85; 95% CI: 3.20–7.35), and even more pronounced in those with comorbidities (HR: 10.69; 95% CI: 2.41–47.51). Notably, the elevated risk persisted for up to six years post-exposure (HR: 1.55; 95% CI: 1.27–1.89). These findings underscore a significant association between CO poisoning and the long-term risk of IHD [29].

Research into CO-induced cardiopulmonary complications in children remains limited. One reported case describes a 15-year-old boy who developed severe cardiopulmonary dysfunction without significant neuropsychiatric effects [30].

Furthermore, Fracasso et al. recently identified evidence of localized damage to the right ventricle, indicated by increased levels of fibronectin and the terminal complement complex C5b-9 [31].

Other reported cardiac effects include conduction abnormalities, atrial fibrillation, prolonged QT interval, and ventricular arrhythmias [32].

In addition, patients with CO poisoning may develop symptoms such as oliguria, anuria, and elevated serum creatinine levels, indicating acute kidney injury. The development of acute kidney injury (AKI) may progress to chronic kidney disease (CKD), which is a significant long-term complication following CO poisoning [33].

Therefore, to improve outcomes and predict complications following carbon monoxide poisoning, it is essential not only to provide timely medical care but also to monitor patients over the long term, particularly during the first two years after acute poisoning.

3. Methods

Medical monitoring refers to the systematic or continuous recording of physiological and pathophysiological parameters to assess the functional status of various organ systems in a living organism. Its primary aim is the early detection of critical changes, thereby enabling the attending physician to make an informed assessment of the patient's health status and to initiate timely, guideline-compliant therapeutic interventions [34, 35].

Clinical monitoring routinely includes imaging procedures, laboratory analyses, and measurements of vital parameters. The resulting data volumes necessitate structured processing and analysis using medical, mathematical, and statistical methodologies [36]. The principal objective of this evaluation is to distill clinically relevant information from the multitude of recorded parameters and to present it in a form that supports clinical decision-making (Fig. 4) [37]. The interpretation of such information forms a cornerstone for diagnosis, the selection of appropriate therapeutic strategies, and the evaluation of treatment outcomes.

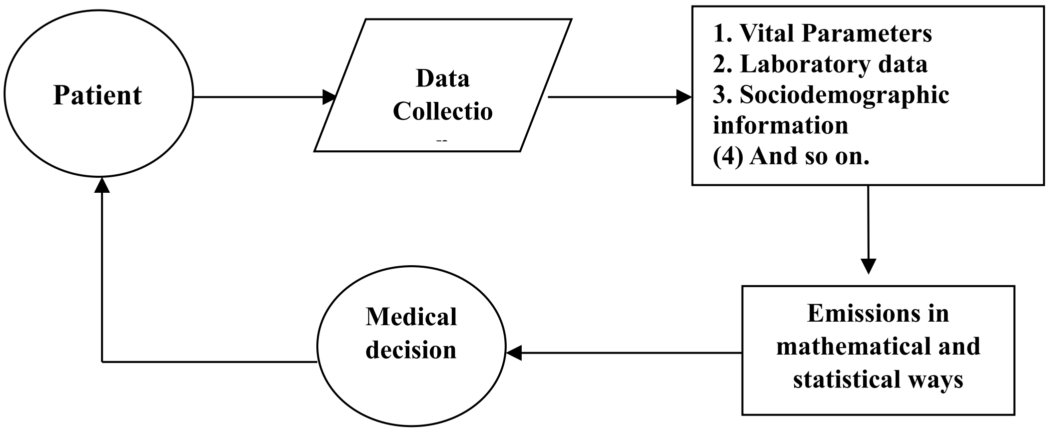

Fig. 4. Algorithm for monitoring

Simultaneously, healthcare professionals are increasingly challenged by the need to analyze and interpret complex data sets within limited time frames [38]. Human cognitive capacities are often insufficient to manage this information load effectively, particularly when critical clinical judgments must be made under pressure. Although physicians gradually develop the ability to handle large data volumes with experience, efficient information processing requires a focused reduction to the most essential parameters and their structured presentation. However, excessive data reduction may obscure relevant pathophysiological patterns and result in an incomplete representation of the patient's overall clinical status [39]. For these reasons, the application of mathematical and statistical analysis methods is gaining increasing importance. These approaches facilitate an objective, reproducible interpretation of monitoring data, identify patterns within complex datasets, and prepare the information in a manner conducive to integration into clinical decision-making processes [40, 41].

The selection of appropriate parameters and their diagnostic relevance are essential prerequisites for effective monitoring. In particular, the analysis of diverse data—such as physiological parameters, age, gender, social status, etc.—plays a crucial role. An integrated analysis of these heterogeneous data sources enables a more precise depiction of the clinical picture and supports a comprehensive assessment of the patient's health status [34, 42]. Monitoring involves the assessment of deviations from the physiological norm. This process is typically based on probabilistic models that present the treating physician with the most likely scenarios for decision-making [40, 41].

In this context, monitoring plays a significant role in predicting the complications caused by CO poisoning. The health status of poisoned individuals is observed over a certain period of time. Statistical analysis methods can be employed to address the issues that arise during monitoring.

Monitoring should begin once the patient has successfully completed inpatient treatment. Throughout the monitoring period, the CO victim's biochemical markers and functional parameters are regularly assessed at predefined intervals to track their clinical status. To compare the results of these analyses and identify those that differ most in terms of specificity, paired autocorrelation and non-parametric methods are employed. In individuals treated and monitored with these methods, changes in any symptom or group of symptoms are observed.

After treatment, changes in test results should be monitored over time to prevent complications from CO poisoning. The primary method used for this is time series analysis. The basis of time series analysis is that events in the past serve as an important indicator for future events. A time series is a sequence of data points that reflects the state at consecutive time points. In contrast to the analysis of random samples, time series are based on the observation of data at consistent time intervals.

According to time series analysis, the data consist of random noise, which makes it difficult to identify systematic components and regularly varying components. Most regular time series variables can be classified into two categories: they either have trend or seasonal components.

The trend reflects the dynamics of change. A trend consists of a general systematic linear or nonlinear component that changes regularly over time. The seasonal component repeats cyclically [43].

The use of time series for forecasting is based on the fact that the impact of certain factors on the data of the observed process in the past and present is likely to be similar in the near future.

When analyzing observations, the process is not continuous but discrete (possibly not evenly distributed over time) at specific time points. At this stage, indicators should be selected that might lead to dangerous developments in the near future (months, sometimes years).

There are no "automatic" methods for detecting trends in time series. If the trend is monotonic (either increasing or decreasing), the analysis of the series is not difficult. If the time series contains a significant error, smoothing should be applied as a filtering method first. Smoothing involves averaging the data, where non-systematic errors cancel each other out. The most common smoothing method is the moving average, where each value in the series is replaced by the simple average of m adjacent values, with m being the number of intervals. Exponential smoothing is also used to detect trends. Many monotonic time series can be described by a linear function and expressed analytically. If a nonlinear component is present, a data transformation is applied to remove it. This often involves logarithmic, exponential, or polynomial transformations. In some cases, smoothing is also performed using the least squares method. All these methods filter out noise and convert the data into a relatively smooth line or curve.

The moving average method helps detect the beginning of a new trend and provides a warning before it ends or reverses. This method allows tracking the development, which can also be considered as trend lines. However, it is not used for forecasting, as it follows the dynamics without predicting them, simply indicating the start of a new trend. When averaging indicators, their curve is smoothed, making the trend easier to recognize. A short-term moving average reflects the dynamics more accurately than calculations for longer intervals.

The moving average is defined as follows:

$$y_t \approx \frac{1}{m} \sum_{i=t-p}^{1+p} y_i \qquad (1)$$

where y_i is the value at the i-th level; **m** — the number of levels included in the smoothing intervals $(m = 2p + 1)$; y_t — the current level of the dynamic range; i — the ordinal number of the level in the smoothing interval; for odd-numbered sequences of $p – m$, the value $p = (\boldsymbol{m} – 1)/2$.

The determination of the smoothing interval depends on the change in the indicators. Therefore, for irregular, small changes in the indicators, a large smoothing interval is chosen. Conversely, when small changes need to be accounted for, the smoothing interval is smaller.

The moving average method is also used when the time series diagram consists of straight lines. In such cases, the dynamics of the indicator are not distorted. However, if the series is non-linear, applying this method will distort the indicators. In this case, exponential smoothing is employed [44].

The method of analytical smoothing of time series is used to determine the general development trend over time.

$$\hat{y}_t = f(t), \qquad (2)$$

where the theoretical value of the time series is determined by the analytical expression at time $\hat{y}_t$—t.

The theoretical values are derived from the mathematical model.

Indicating the trend of development, the following features are implemented:

- A linear function, whose graph is a straight line:
$$\hat{y}_t = a_0 + a_1 t$$
- Exponential function:
$$\hat{y}_t = a_0 * a_1^t,$$
- Exponential function second degree (parabola):
$\hat{y}_t = a_0 + a_t * t + a_2 t^2;$
- A logarithmic function:
$$\hat{y}_t = a_0 + a_t lnt$$

The calculation of the function parameters is carried out using the least squares method. In this case, the solution minimizes the sum of the squared differences between the theoretical and empirical levels of the trend:

$$\sum(\hat{y}_t - y_i)^2 \rightarrow min, \qquad (3)$$

where $\hat{y}_t$ is calculated, y_t — are the real levels.

Linear smoothing is used in cases where the absolute increments are constant.

Smoothing with an exponential function is applied when the series is geometrically invariant, i.e., when the chain coefficients of the slope are constant.

The smoothing with a second-degree exponential function is used when the dynamic series changes with constant chain increments.

Smoothing with a logarithmic function reflects the decline in the growth rate at the end of the time series period, i.e., when growth approaches zero at the final levels of the time series.

The accuracy of calculations with analytical expressions is determined as follows: The sum of the values of the empirical series must match the sum of the levels of the smoothed series. At this point, small errors may occur due to rounding of the calculated values:

$$\sum y \approx \sum \hat{y}_t \qquad (4)$$

In addition to the time series smoothing method, the autocorrelation of indicators is calculated to identify their patterns of change. The autocorrelation function helps determine whether the variation in an indicator is seasonal, increasing, or decreasing. The coefficient of determination is used to evaluate the accuracy of the trend model:

$$R^2 = \frac{\sigma_{\hat{y}}^2}{\sigma_y^2}, \qquad (5)$$

where $\sigma_{\hat{y}}^2$ is the variance of the theoretical data obtained from the trend model, and σ^2_y is the variance of the empirical data.

The trend model reliably reflects the development trend of the indicators when the coefficient of determination (R^2) is close to 1.

According to the time series method, indicators are processed in three steps: The first step involves filtering to eliminate distortions caused by seasonal or other irregular variations. The goal is to reveal the actual change in the dependent variable *y* as a result of a change in the independent variable *x*—that is, to eliminate external factors that may further affect this relationship. Among the known filtering techniques, the moving average is the most commonly used.

This method calculates the average of a specified number of values before and after a particular point in time. In doing so, long-term fluctuations are smoothed out, allowing short-term trends to be identified more clearly. However, filtering must be approached with caution, as important information may be lost due to smoothing. For this reason, it is advisable to use multiple filtering methods and confirm the results through correlation analysis.

In the second step, the forecast of the indicator is developed by selecting and constructing an appropriate regression model.

Regression analysis serves two main purposes:

- To determine whether a relationship exists between the measured parameters;
- To predict the value of the dependent variable based on the value of the independent variable.

In the context of carbon monoxide poisoning monitoring, the time series method is useful both for identifying correlations between indicators at specific points in time and for forecasting their future changes. When applying this method, changes in indicators over time are described using regression equations. A simple (one-factor) regression equation illustrates how the values of a particular indicator change throughout the observation period. The temporal variation of values leads to the formation of time series or dynamic series. These series are characterized by changes in the variable *y* (the feature of interest) depending on the independent variable *x*, with time being the dominant factor. This dependency can be expressed in the form of a regression equation.

When using the time series method, both simple and multiple regression analyses can be employed. The simple regression for a single indicator can be represented by the following equation:

$$y = a + b * x \quad (6)$$

where *a* represents the intercept (also known as the constant term), and *b* determines the slope of the regression line relative to the rectangular coordinate axis. The equations for calculating these parameters using the least squares method are as follows:

$$a * n + b \sum x = \sum y \qquad (7)$$

$$a \sum x + b \sum x^2 = \sum y * x \qquad (8)$$

The given formulas are used to determine the parameters.

$$a = y - b * x \qquad (9)$$

$$b = \frac{y * x - \bar{y} * \bar{x}}{x^2 - \bar{x}^2} \qquad (10)$$

The multivariate regression equation is used to track and predict the

$$\hat{y}_x = a + b_1 x_1 + b_2 x_2 + \ldots + b_m x_m \quad (11)$$

dynamics of changes in multiple variables simultaneously.

It is not possible to accurately test probabilities based on multivariate regression, as trends are usually more clearly detectable than these probabilities. Large trends in the values of different variables lead to significant shifts in the regression coefficients, and the direction of the regression line may change. Even the presence of an extremum in the sign values leads to a change in the result. Although it is important to monitor many indicators in the case of carbon monoxide poisoning, it has been considered more reasonable to predict each symptom individually through a univariate regression to obtain more realistic results. This has been confirmed through numerous experiments. The forecast using the regression equation is made for a specific time period after the observation period ends.

In the third step, the quality of the model is assessed.

The adequacy of a regression model is expressed by the coefficient of determination:

$$R^2 = \sum_{i=1}^{N}(\hat{y}_i - \bar{y})^2 / \sum_{i=1}^{N}(y_i - \bar{y})^2 \quad (12)$$

here, $\hat{y}_i$ - x_i is the theoretical or calculated value corresponding to y_i .

The coefficient of determination shows the degree of scatter relative to the dependent variable. A high value of R^2 indicates that the regression equation is highly adequate. The coefficient of determination allows for the use of the regression model for prediction. To determine the significance of the regression equation, Fisher's criterion is used:

$$F = \frac{R^2}{1`-R^2} * \frac{n-m-1}{m} \quad (13)$$

where R is the coefficient of determination, n is the number of observations, and m is the number of parameters in the x-variables (the number of factors in the model in linear regression).

This criterion evaluates the significance of the factor included in the regression equation. The calculated F-value is compared with the table value at n-m-1 degrees of freedom at the α-significance level. If the calculated F-value exceeds the value in the table, that is, $F \geq F_{Table}$, then the inclusion of the factor x in the model is statistically valid. If the calculated F-value is smaller than the table value, the x-indicator included in the model is not significantly important for the change in y, and its inclusion in the model is not advisable. Using the coefficient of determination, the correlation coefficient is determined as follows:

$$r = \sqrt{R^2} \quad (14)$$

The values of the coefficient of determination and the correlation coefficient range from -1 to +1. The fact that the value of the coefficient of determination is close to +1 indicates a strong relationship between y and the factor x and proves that this indicator is more important for the outcome than other additional factors. In this context, a regression model can be used to predict a specific indicator.

The indicators to be observed for monitoring in the intellectual-informational system are selected as follows:

$$x_i \in \{X\},\ i = \overline{1,n}$$

where x_i are the indicators.

For the parameters under consideration, there are generalized norm values. Based on this, there is a specific range of variation for $\forall x_i$ (in some cases, these norms differ for men and women). The upper and lower limits of the norms are y_i and z_i , respectively. Then

$$y_i < x_i < z_i$$

each x_i is observed at time $T=\{t_1, t_2, ..., t_k\}$ is the number of measurements. Then, any parameter can be described as x_i^j. Here, $i=1,2, ..., n$, $j=1,2,..., k$. Deviations below and above the norm are considered pathological:

$$x_i^j < y_i \text{ və ya } x_i^j > z_i$$

Smoothing curves and autocorrelation functions are created to observe the change of any indicator x_i^j over time $T = \{t_1, t_2, \ldots, t_k\}$. It should be noted that the numbers in the experiments performed below do not reflect the values of medical indicators. A random number generator was used. The specific k-points, which are used as observation times, represent the number of months and sometimes the number of years.

For example, the number distribution given by 36 points, the smoothing curve, the moving autocorrelation with fixed time, and the special autocorrelation function are shown. Since the price ranges of this series are large, the smoothing curve reflects a very strong up and down trend (Fig. 5a).

The specific autocorrelation function shows how the autocorrelation function represents the relationship between two random variables, but ignores the effect of the internal values of the autocorrelation. On smaller time scales, the specific autocorrelation is identical to the ordinary autocorrelation. In practice, the specific autocorrelation shows periodic dependencies more "clearly". The occurrence of autocorrelation and the specific autocorrelation function depend on the length of the time series. Autocorrelation functions more accurately reflect the model when the series is long enough. With shorter series, correlograms lose accuracy, and the calculation accuracy of autocorrelation and specific autocorrelation decreases.

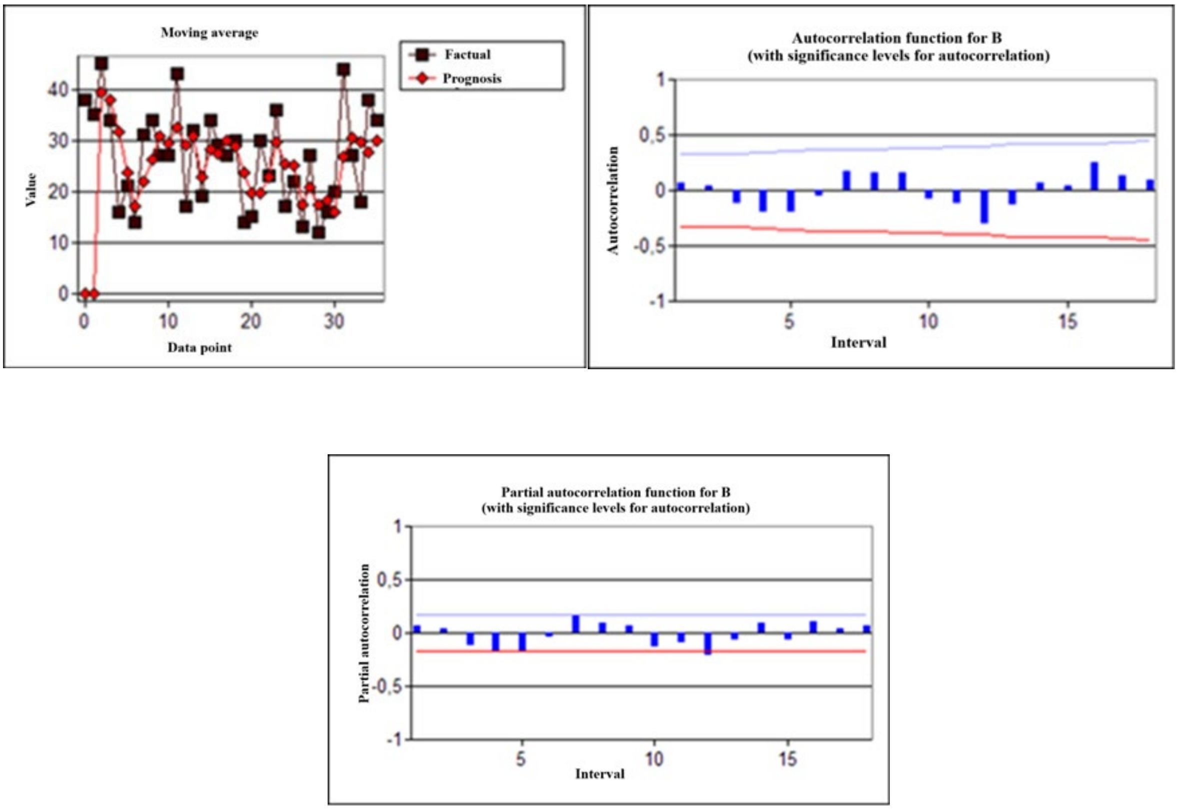

Fig.5a. Smoothing curves, autocorrelation and specific autocorrelation functions

The autocorrelation function indicates that there is no uniform trend or periodic fluctuation in the series.

The regression equation for predicting a given distribution order is as follows:

$$y=30.0175 - 0.1826*x$$

The coefficient of determination is 0.0414 and the correlation coefficient is 0.2036. This suggests that the price dispersion is high and this indicator cannot be used for forecasting. According to the Fisher criterion, this indicator is statistically not significant.

When the values of a time series change over a small interval, smoothing curves, autocorrelation, and specific autocorrelation functions are useful (Fig. 5b).

The smoothing curve of the series indicates the presence of a trend, while the autocorrelation function shows the rise and fall of prices. The regression function is:

$$y = 25.1339 + 1.666*x$$

The coefficient of determination is 0.5187 and the correlation coefficient is 0.7202. These values suggest that there is a relationship between the dependent and independent variables, and this relationship is statistically significant according to the Fisher test.

In monitoring, in addition to observing the indicator over a certain period of time, a clear difference between one or more indicators should be detected in each time interval. The Mann-Whitney test is used to evaluate the difference between independent indicators over time. The Wilcoxon test is used to assess the change in any given indicator over a certain period during the monitoring period after treatment. The Friedman test is used to evaluate the difference between repeated measurements of an indicator when it has more than two observations over time, and the Kruskal-Wallis test is used to assess the participation of any indicator in multiple measurements [43].

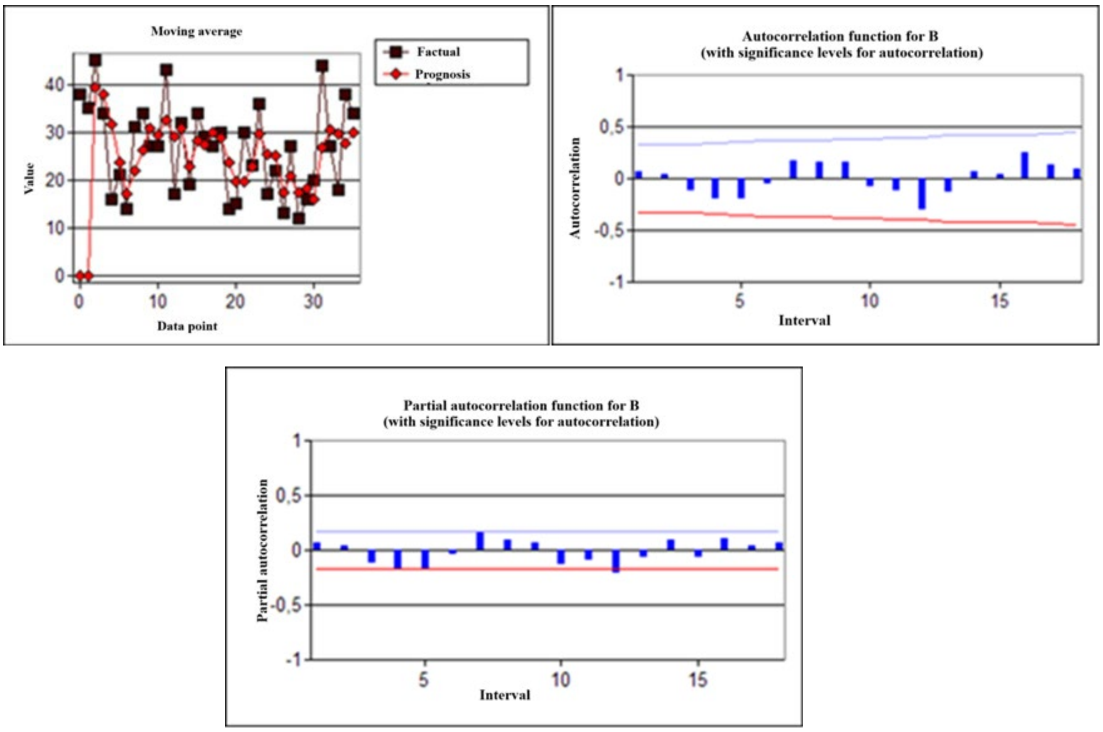

Fig. 5b. Smoothing curves, autocorrelation and specific autocorrelation functions

4. Conclusion

Carbon monoxide poisoning remains a significant health issue with serious health consequences, particularly during the winter months. The diagnosis is often challenging due to nonspecific symptoms, which complicates timely intervention. Early detection and treatment are crucial to minimize long-term complications such as neurological disorders, cardiovascular issues, and kidney damage. The use of information technology and mathematical models in monitoring CO poisoning holds great potential to improve diagnostic accuracy and patient care, especially after treatment. Long-term monitoring is necessary to detect potential complications, particularly in cases of chronic poisoning. The application of time series analysis, regression models, and statistical methods helps interpret data and make precise predictions. Improving early diagnosis, understanding the epidemiological aspects, and public education are key to reducing the incidence and mortality of this preventable condition.

References

1. Siebenmann, C.; Keiser, S.; Robach, P.; Lundby, C. CORP: The assessment of total hemoglobin mass by carbon monoxide rebreathing. J. Appl. Physiol. 2017, 123, 645–654. [CrossRef] [PubMed]
2. Moberg, Madeline E et al. Global, regional, and national mortality due to unintentional carbon monoxide poisoning, 2000–2021: results from the Global Burden of Disease Study 2021. The Lancet Public Health, Volume 8, Issue 11, e839 - e849. https://doi.org/10.1016/S2468-2667(23)00185-8
3. Mattiuzzi, C.; Lippi, G. Worldwide epidemiology of carbon monoxide poisoning. Hum. Exp. Toxicol. 2020, 39, 387–392. [CrossRef] [PubMed]
4. Rose, J.J.; Wang, L.; Xu, Q.; McTiernan, C.F.; Shiva, S.; Tejero, J.; Gladwin, M.T. Carbon monoxide Poisoning: Pathogenesis, Management, and Future Directions of Therapy. Am. J. Respir. Crit. Care Med. 2017, 195, 596–606. [CrossRef]
5. Zonta, G.; Rispoli, G.; Malagù, C.; Astolfi, M. Overview of gas sensors focusing on chemoresistive ones for cancer detection. Chemosensors 2023, 11, 519. [CrossRef]
6. Eggert, E.; Huss, F. Medical and biological factors affecting mortality in elderly residential fire victims: A narrative review of the literature. Scars Burn. Heal. 2017, 3, 2059513117707686. [CrossRef]
7. Health and Safety Executive. The cross-government group on gas safety and carbon monoxide awareness. Health and Safety Exec utive 2020. https://www.hse.gov.uk/gas/domestic/cross-governme nt-group-2021.pdf (2 January 2022, date last accessed)
8. All-Party Parliamentary carbon monoxide Group. Carbon monoxide poisoning: saving lives, advancing treatment. Policy Connect 2017.
9. Statistics of Deaths and Injuries | CO-Gas Safety
10. Kohlenmonoxid-Vergiftungen: Krankenhausbehandlungen in 2023 | Landesbetrieb IT.NRW
11. S2k guideline diagnosis and treatment of carbon monoxide poisoning. GMS German Medical Science 2021, Vol. 19, ISSN 1612-3174
12. Zhang, L. et al. Acute carbon monoxide poisoning in Shandong, China: An observational study. Chinese Medical Journal 135(13):p 1539-1544, July 5, 2022. | DOI: 10.1097/CM9.0000000000001942
13. Mingjun Li, Bing Shan, Xiumiao Peng, Huiyun Chang, Liangliang Cui. An urgent health problem of indoor air pollution: results from a 15-years carbon monoxide poisoning observed study in Jinan City. Scientifc Reports. 2023 Jan 28;13(1):1619. doi: 10.1038/s41598-023-28683-0.
14. Motterlini, R.; Foresti, R. Biological signaling by carbon monoxide and carbon monoxide-releasing molecules. Am. J. Physiol. Cell Physiol. 2017, 312, C302–C313. [CrossRef]
15. Wang, T.; Zhang, Y. Mechanisms and therapeutic targets of carbon monoxide poisoning: A focus on reactive oxygen species. Chem. Biol. Interact. 2024, 403, 111223. [CrossRef]
16. Kassa, B.D.; Yigzaw, A.A.; Kassie, Y.G.; Kedimu, M.W.; Mekuanint, Y.F.; Moges, N. Delayed neuropsychiatric sequelae due to long-term effects of carbon monoxide poisoning in Ethiopia: A case report. Toxicol. Rep. 2023, 11, 36–39. [CrossRef]
17. Yelmo-Cruz S, Dorta-González JF, Tascón-Cervera JJ. Delayed neuropsychiatric syndrome after carbon monoxide poisoning. Actas Esp Psiquiatr. 2022 Jan; 50(1):65-67. Epub 2022 Jan 1. PMID: 35103300; PMCID: PMC10803870.
18. Sung Hwa Kim, Yoonsuk Lee, Soo Kang, Jin Hui Paik, Hyun Kim, Yong Sung Cha. Derivation and Validation of a Score for Predicting Poor Neurocognitive Outcomes in Acute Carbon Monoxide Poisoning. JAMA Netw Open. 2022 May; 5(5): e2210552.
19. Jeon SB, Sohn CH, Seo DW, Oh BJ, Lim KS, Kang DW, Kim WY. Acute Brain Lesions on Magnetic Resonance Imaging and Delayed Neurological Sequelae in Carbon Monoxide Poisoning. JAMA Neurol. 2018 Apr 1;75(4):436-443. doi: 10.1001/jamaneurol.2017.4618. PMID: 29379952; PMCID: PMC5885203.

20. Park, E.J.; Min, Y.G.; Kim, G.W.; Cho, J.P.; Maeng, W.J.; Choi, S.C. Pathophysiology of brain injuries in acute carbon monoxide poisoning: A novel hypothesis. Med. Hypotheses 2014, 83, 186–189. [CrossRef]
21. Oh, S.; Choi, S.C. Acute carbon monoxide poisoning and delayed neurological sequelae: A potential neuroprotection bundle therapy. Neural Regen. Res. 2015, 10, 36–38. [PubMed]
22. Bauer, N.; Liu, D.; Nguyen, T.; Wang, B. Unraveling the Interplay of Dopamine, Carbon Monoxide, and Heme Oxygenase in Neuromodulation and Cognition. ACS Chem. Neurosci. 2024, 15, 400–407. [CrossRef] [PubMed]
23. Afzal M, Agarwal S, Elshaikh RH, Babker AMA, Choudhary RK, Prabhakar PK, Zahir F, Sah AK. Carbon Monoxide Poisoning: Diagnosis, Prognostic Factors, Treatment Strategies, and Future Perspectives. Diagnostics (Basel). 2025 Feb 27;15(5):581. doi: 10.3390/diagnostics15050581. PMID: 40075828; PMCID: PMC11899572.
24. Bandeira, G.A.; Lucato, L.T. Toxic leukoencephalopathies. Handb. Clin. Neurol. 2024, 204, 455–486.
25. Lippi, G.; Rastelli, G.; Meschi, T.; Borghi, L.; Cervellin, G. Pathophysiology, clinics, diagnosis and treatment of heart involvement in carbon monoxide poisoning. Clin. Biochem. 2012, 45, 1278–1285. [CrossRef]
26. Haliga, R.E.; Morărașu, B.C.; Șorodoc, V.; Lionte, C.; Sîrbu, O.; Stoica, A.; Ceasovschih, A.; Constantin, M.; Șorodoc, L. Rare Causes of Acute Coronary Syndrome: Carbon Monoxide Poisoning. *Life* 2022, *12*, 1158. https://doi.org/10.3390/life12081158
27. Hocagil, H.; Tanrikulu, C.S.; ¨Ulker, V.; Kaya, U.; Koca, L.; Hocagil, A.C. Asymptomatic myocardial injury in a low level of carbon monoxide poisoning. Eurasian J. Emerg. Med. 2015, 14, 91–93. [CrossRef]
28. Armandeh, M.; Bameri, B.; Baeeri, M.; Haghi-Aminjan, H.; Rahimifard, M.; Hassani, S.; Hooshangi Shayesteh, M.R.; Khalid, M.; Samadi, M.; Hosseini, R.; et al. The role of levosimendan in phosphine-induced cardiotoxicity: Evaluation of electrocardiographic, echocardiographic, and biochemical parameters. Toxicol. Mech. Methods 2021, 31, 631–643. [CrossRef]
29. Bahng, Y, Baek, K, Park, J.T., Choi, W.J., Kwak, K. Carbon Monoxide Poisoning and Developing Ischemic Heart Disease: A Nationwide Population-Based Nested Case-Control Study. Toxics 2021, 9(10), 239; https://doi.org/10.3390/toxics9100239
30. Chang-Teng Wu, Jing-Long Huang, Shao-Hsuan Hsia. Acute carbon monoxide poisoning with severe cardiopulmonary compromise: a case report. Cases Journal. 2009 Jan 14;2(1):52. doi: 10.1186/1757-1626-2-52.
31. Fracasso, T.; Pfeiffer, H.; Michaud, K.; Köhler, H.; Sauerland, C.; Schmeling, A. Immunohistochemical expression of fibronectin and C5b-9 in the myocardium in cases of carbon monoxide poisoning. Int. J. Leg. Med. 2011, 125, 377–384. [CrossRef]
32. Onvlee-Dekker IM, De Vries AC, Ten Harkel AD: Carbon monoxide poisoning mimicking long-QT induced syncope. Arch Dis Child 2007, 92:244-5.
33. Bernhard, W., & Frei, R. (2017). "Renal injury and its prevention in acute carbon monoxide poisoning." *Toxicology and Industrial Health*, 33(4), 235-245.
34. Vincent JL, Hall JB. *Oxford Textbook of Critical Care*. 2nd ed. Oxford: Oxford University Press; 2018.
35. Marik P..E. *Evidence-Based Critical Care: A Case Study Approach*. New York: Springer; 2010.
36. Riggert J, Heringlake M. Monitoring in der Intensivmedizin. In: Heringlake M, Riggert J., editors. *Intensivmedizin – Praxis und Perspektiven*. Berlin: Springer; 2014. p. 123–138.
37. Dünser M.W., Hiesmayr M., Pajk W., Schmutz R., Knotzer H. Monitoring critically ill patients: a cornerstone of intensive care. *Wien Klin Wochenschr*. 2013;125(7–8):195–206.
38. Wachter R.M. *The Digital Doctor: Hope, Hype, and Harm at the Dawn of Medicine's Computer Age*. New York: McGraw-Hill Education; 2015.
39. Roth SC, Das P, Beringer T, Rees G, Doshi P. Information overload in clinical practice – a scoping review. *BMC Med Inform Decis Mak*. 2021;21:238.
40. Johnson A.E.W., Ghassemi M.M, Nemati S., Niehaus K.E., Clifton DA, Clifford GD. Machine Learning and Decision Support in Critical Care. *Proc IEEE*. 2016;104(2):444–466.
41. Nemati S., Holder A., Razmi F., Stanley M.D., Clifford G.D., Buchman T.G. An Interpretable Machine Learning Model for Accurate Prediction of Sepsis in the ICU. *Crit Care Med*. 2018;46(4):547–553.
42. Kuehl, D., L. Hessel, et al. "The Importance of Monitoring Physiological Parameters in Intensive Care." *Intensive Care Medicine*. 2019;45(4):657-665.
43. Mirzazadeh I.Kh., Abdullayeva G.G., Naghizade H.R. Artificial intelligence in problems of diagnostics and monitoring. Lambert Academic Publishing, Germany, Saarbruecken, 2022
44. Mirzazadeh İ.H.. Poisoning with Carbon Monoxide and Importance of Monitoring of Patients after CO Poisoning. Caspian Journal of Applied Mathematics, Ecology and Economics. Volume 10, Issue 2. Baku, 2023. Pp. 19-42