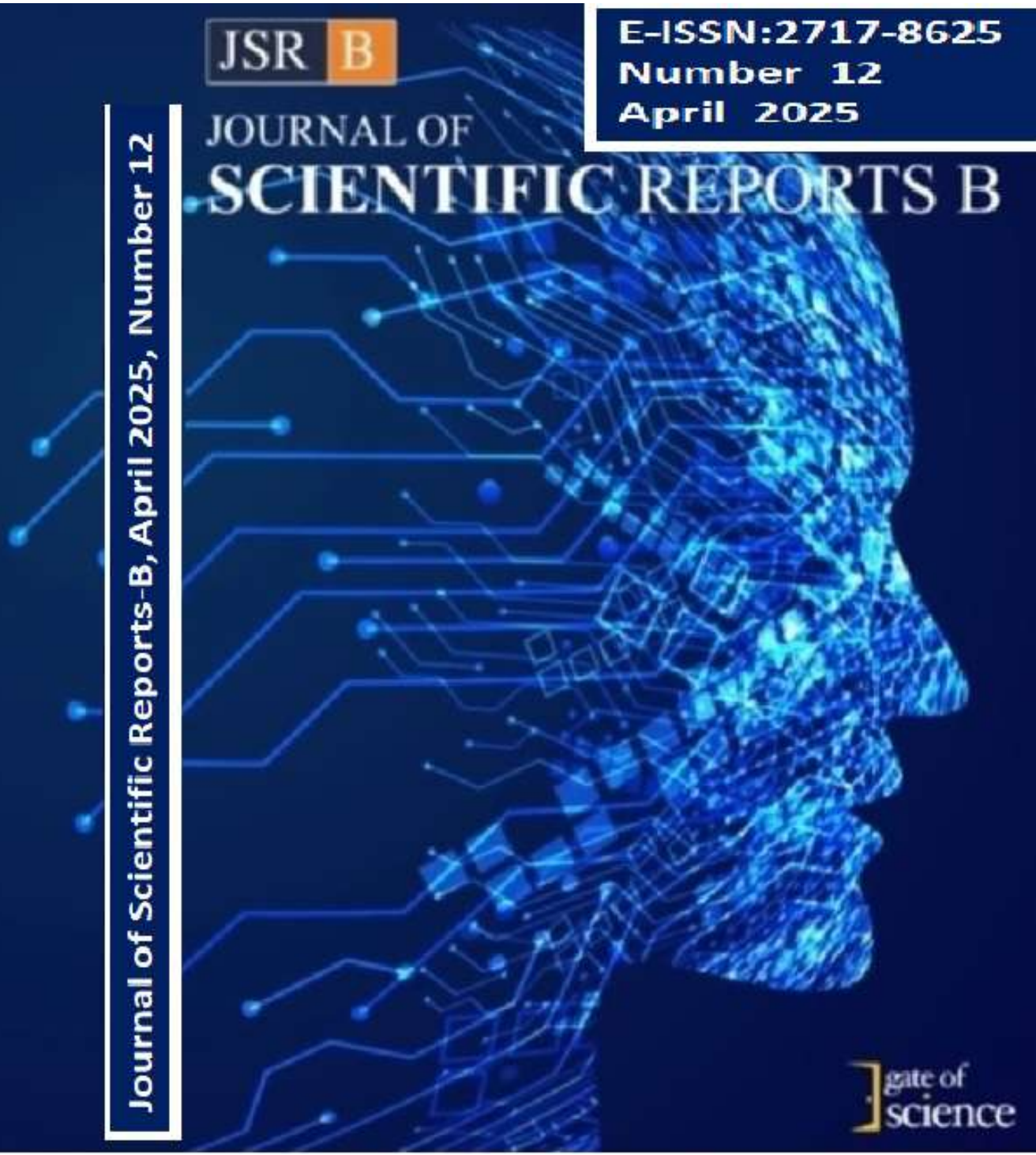
JSR B

E-ISSN:2717-8625
Number 12
April 2025

JOURNAL OF SCIENTIFIC REPORTS B

Journal of Scientific Reports-B, April 2025, Number 12



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Institute of Graduate Studies

Journal of Scientific
Reports-B
E-ISSN: 2717-8625

Number 12, April 2025

JSR B
Journal of Scientific Reports

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Journal of Scientific Reports-B was separated from Journal of Science and Technology of Dumlupınar University which started its publication life in 2000 and is a international peer-reviewed journal published regularly third times a year in April, August and December. The language of the journal is English. Articles submitted to the journal are evaluated by at least two referees who are experts in the subject and selected by the editorial board. All articles submitted to the journal are evaluated by the double-blind method. Articles submitted to our journal for review should not be previously published, accepted for publication and in the process of being evaluated for publication in another journal. All responsibility for the articles published in the journal belongs to the author(s).

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JSR B
Journal of Scientific Reports

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JOURNAL OF SCIENTIFIC REPORTS-B

E-ISSN: 2717-8625

CONTENTS

RESEARCH ARTICLES

Contents lists available at *Dergipark*

Journal of Scientific Reports-B

journal homepage: *https://dergipark.org.tr/en/pub/jsrb*

E-ISSN: 2717-8625 ***Number 12, April 2025***

RESEARCH ARTICLE

Receive Date: 24.04.2025 *Accepted Date: 30.04.2025*

Performance of machine learning methods on breast cancer prediction

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Abstract

In the last 50 years, the effect of cancer disease on the annual number of deaths has increased significantly. This has led to an increase in research on early detection and diagnosis of cancer. Early diagnosis of cancer increases the chance of surviving the disease and reduces the possibility of recurrence of the disease. The technological advances in artificial intelligence and machine learning are used to analyse patient data, while at the same time reducing the likelihood of developing diseases. In this paper, 7 different machine learning algorithms commonly used in the literature are used for breast cancer diagnosis. These are: Logistic Regression (LR), K-Nearest Neighbours (KNN), Support Vector Machines (SVM), Radial Basis Function (RBF) Kernel, Naive Bayes, Decision Tree (DT), and Random Forest (RF) algorithms. In our study, two separate datasets were used for breast cancer diagnosis. In the first dataset, Random Forest, SVM (RBF), and SVM (Linear) algorithms had the highest accuracy value of 96.5, while the K-Nearest Neighbours algorithm had the highest sensitivity value of 98.8, and the decision tree algorithm had the highest specificity value of 98.1. The K-Nearest Neighbour algorithm was also found to be the fastest algorithm, with 1.03 seconds. In the second dataset with different data, the K-Nearest Neighbours algorithm reached the highest accuracy value of 97.7 and was observed to be the second fastest algorithm with 1.48 seconds after the Gaussian Naive Bayes algorithm with 1.14 seconds.

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Keywords: Machine learning, classification algorithms, artificial intelligence, breast cancer prediction.

1. Introduction

The second most common cause of cancer-related deaths among women is breast cancer. The risk of breast cancer death for a woman is around 1 in 43, or 2.3% [1]. This study compares a number of machine learning methods for data analysis and breast cancer prediction early detection.

1.1. Breast Cancer

Breast cancer is a cancer of the breast and surrounding tissue. It is more common in women after skin cancer, but it can also affect men. After skin cancer, it is considered the most dangerous cancer in women's lives [2]. The funding of scientific research to develop treatments and early detection, as well as media coverage to increase awareness of breast cancer, have enhanced the diagnosis and treatment of the disease. According to the American Cancer Society, women will experience 49,290 new instances of ductal carcinoma in situ (DCIS) and 281,550 new cases of invasive breast cancer in 2021. The lifetime risk of breast cancer is 13% for women, and between 2010 and 2022, the annual death rate from breast cancer dropped by 1.2% [1].

1.2. Artificial Intelligence and Machine Learning

Artificial intelligence is the attempt to simulate human intelligence through devices, and in most cases, the device used is a computer. Artificial intelligence relies on three cognitive abilities to emulate human intelligence: learning, reasoning, and self-correction (learning from mistakes). Artificial intelligence works by analysing data and creating rules for analysing that data to derive a possible benefit from it. Machine learning: The term machine learning emerged when scientists wanted to know about the ability of computers to learn from data [3].

Machine learning is tested by inputting new data and testing its ability to reach correct results, and the computer learns from previous data [4]. After the technological revolution, the increasing impact of artificial intelligence (AI) and the importance of machine learning (ML) and artificial intelligence in our lives are having a pioneering way, especially in the treatment and diagnosis of diseases. Advances in machine learning have helped diagnose diseases by using large data sets to detect diseases early, especially in chronic diseases such as cancer [5].

1.3. Disease Identification

The machine learning method allows us to create models relating multiple variables to a disease. Machine learning algorithms analyse data, identify correlations between variables, and display the results. Clinicians now have access to vast amounts of data, including clinical symptoms, biochemical assays, and imaging device outputs, all of which are incorporated into machine learning models. There are several valuable data types to make an accurate medical diagnosis using machine learning, such as disease, environmental, and genetic data. It also has many benefits in research on risk factors and increases the efficiency of diagnosis [6-7].

2. Literature Review

In Jacob and Ramanai’s study, they compared the performance of various classification algorithms. The best algorithms were random forest and decision trees with 100% accuracy [8].

Abyan Farid Agharib compared six machine learning algorithms to analyze data of breast cancer patients to help diagnose the disease. Algorithms used: Linear regression, multilayer perception, nearest neighborhood, search,

softmax regression, support vector machine. Algorithms are compared based on their test accuracy, sensitivity, and specificity values. All algorithms showed a success of more than 90%, and the best result of the MLP algorithm showed an accuracy of 99.04% [9].

Sengar and others compared two machine learning algorithms. Using the Wisconsin diagnostic dataset, the same dataset we used in this paper, they compared the test accuracy of the logistic regression algorithm and the decision tree algorithm. Both algorithms showed more than 90% success results, showing the superiority of the decision tree algorithm with a 100% accuracy rate [10].

Jain and others used five classification algorithms to classify the type of breast cancer, K-Nearest Neighbor, Logistic Regression, Random Forest, SVM, and Decision Tree. With 96.52% and 98% eloquent effectiveness, Logistic Regression and K-Nearest Neighbor were the best indicators [11].

Ojha and Goel used a total of eight algorithms, four of which are classification algorithms: KNN, SVM, Naive Bayes, and C5.0, which is the algorithm used in data mining as a decision tree classifier that can be employed to generate a decision. Four of them are clustering algorithms, which are K-means, Expectation Maximization, Partitioning around Medoids, and Fuzzy c-means. C5.0 and SVM classifiers were the best prediction algorithms with an accuracy of 0.813, while the fuzzy mean clustering algorithms came out worse with an accuracy of 0.3711 [12].

In Özkan and Gündüz's study, they utilize the Breast Cancer Database, the exhibition of AI calculations in anticipating the shot at endurance following bosom malignant growth was investigated Surveillance Epidemiology and End Result (SEER). The algorithms used: Naive Bayes, J48 algorithm is used to classify different applications and performs accurate results of the classification, SVM and Multiobjective and Evolutionary Fuzzy Classifier (MEFC), the J48 algorithm showed a success rate of 93.02 and a speed of 84.39 seconds, which is considered the second fastest algorithm used [13].

In Kıyan and Yildirim's study, they tested diagnosing breast cancer using structural neural networks' performance, comparing the accuracy of different structural neural networks. Radial Basis Functions, Probabilistic Neural Networks, Generalized Regression Neural Networks (GRNN), The RBF and PNN structures showed the highest rate with 100% training accuracy. The GRNN structure test result showed the highest accuracy rate of 98.8%.

Based on the overall findings, GRNN appears to be the best neural network model for WBCD data classification [14].

Hazra and others' study showed that the Naive Bayes algorithm produces the highest accuracy with an average of 97.3978% with only five dominant features and a time of 0.102023 ms, which is the fastest algorithm comparing the other two classifiers (Support Vector Machine and Ensemble) [15].

Abdulla and others compared five machine learning algorithms. The SVM algorithm achieved the highest accuracy rate of 97% when combined with other algorithms such as Random Forest, Naive Bayes, and KNN. Convolutional neural networks (CNNs) the Deep Learning algorithm has reached 98% accuracy [16].

Shravya and others focused on creating prescient models to accomplish a decent rate utilizing regulated AI techniques. As a result of the comparison of three algorithms, k-nearest neighbor, logistic regression and SVM, the SVM algorithm gave the best result for breast cancer prediction with the highest accuracy rate of 92.7% [17].

Al-Azzam and Shatnawi compared the effectiveness and accuracy of supervised learning (SL) and semi-supervised learning (SSL) algorithms for breast cancer detection. SSL requires less data and is less expensive than SL. As a result of this study, SSL algorithms are almost as accurate as SL algorithms, where the predictions were correct for all malignant and benign tumours with a rate between 91% and 98%. KNN algorithms (SL = 98.4% & SSL = 97.4%) and logistic regression (SL = 97% & SSL = 98.4%) produced the best result. It is possible to replace supervised learning algorithms with semi-supervised learning algorithms [18].

Darwich and Islam provide suggestions for further study after weighing the advantages and drawbacks of every machine learning technique and dataset [19-20].

3. Material and Method

3.1. Machine Learning Classification

Logistic Regression is a fundamental classification method and is one of the quickest and uncomplicated classifications, and is convenient for interpreting results. It can apply to multiclass problems since it is a binary classification algorithm [21].

One kind of supervised machine learning technique is the K-Nearest Neighbors algorithm. KNN can handle challenging classification tasks and is simple to implement. Considering that there is no exceptional training phase, it is a lazy learning algorithm. It is a nonparametric learning algorithm, meaning that it has no prior knowledge or assumption about the underlying data. KNN algorithm needs more memory and more time to scan all data points [22]. Support vector machines outperform other classifiers like logistic regression and decision trees in terms of accuracy. Gene classification, handwriting recognition, facial identification, intrusion detection, email categorization, news articles, and web pages are just a few of the many uses for it. SVM is an algorithm with rather straightforward ideas. An SVM classifier is also referred to as a different classifier since it uses the hyperplane with the largest margin to separate the data points. Performance is improved by linear SVM training, which is quicker than non-linear ones (such as the RBF kernel) [23-25].

Naive Bayes is the simplest and fastest classification algorithm suitable for a large portion of data. A naive Bayes classifier is used in spam filtering, text classification, and recommendation systems. The classifier trains the model on a particular dataset and measures its functioning in the learning phase, and performance is evaluated based on various criteria such as accuracy, error, and recall [26].

An internal node's decision tree property, in which each leaf node indicates the outcome and the branch reflects a decision rule and a tree structure resembling a flowchart. This framework, which resembles a flowchart, aids in decision-making. Similar to a flowchart diagram, visualization readily imitates human-level thought processes. Decision trees are, therefore, simple to comprehend and analyze. Compared to the neural network algorithm, the training period is quicker. It is a non-parametric or distribution-independent approach that is independent of assumptions about probability distributions. High-dimensional data can be accurately processed by decision trees [27-28].

A supervised learning technique used for regression analysis or classification is called random forests. In contrast to other algorithms, it is versatile and simple to use. Random data samples are used to make the decision; each tree is estimated, and the best outcome is chosen by voting. It can be used for many things, such as feature selection and image rating. The choice is based on a divide-and-conquer strategy and uses a tree-clustering method (randomly partitioned data set) [29].

3.2. Datasets

The first dataset, named the Diagnostic Wisconsin Breast Cancer Database, contains information about breast cancer patients, determining whether their cancer diagnosis is malignant or benign, as prepared by researchers at the University of Wisconsin with expertise in databases and general surgery [30]. This dataset is widely used in breast cancer diagnosis using machine learning and statistical analysis techniques. The dataset consists of 569 samples in total. Of these samples, 212 represent malignant tumours (Malignant - M) and 357 represent benign tumours (Benign - B). The dataset contains 30 numerical features for each sample, in addition to 1 target variable (diagnosis) and 1 ID column containing the patient identification number.

The second dataset, named the Original Wisconsin Breast Cancer Database, is also a widely used dataset for breast cancer diagnosis [31]. The dataset, containing 699 samples in total, consists of 10 columns, each with 9 numerical features and 1 class label (benign or malignant). The features include morphological measurements

obtained from microscopic images of cells. Each feature is rated on a scale from 1 to 10. The class label indicates whether the tumour is benign or malignant.

3.3. Evaluation Metrics

Three evaluation metrics were used to compare the performance of the algorithms: accuracy, sensitivity, and specificity. Accuracy is one of the evaluation measures used to evaluate a classification model's overall performance. The ratio of projected samples to total samples is known as accuracy. When the distribution of classes is balanced, it is ideal [32]. Sensitivity indicates how accurately the model predicts examples belonging to the positive class. This metric expresses the rate at which the model correctly recognizes examples belonging to the positive class. It is especially used in applications where correctly detecting examples belonging to the positive class is important [33]. The rate at which the model accurately identifies instances from the negative class is known as specificity. This indicator demonstrates how well the model forecasts instances from the negative class. In applications where accurately identifying examples from the negative class is crucial, it is particularly utilized [33].

4. Results

As a result of pre-processing the breast cancer data set from the first database, a data set consisting of 30 traits and class values contains 18240 records. The second database provides ten items and 6990 record-classification assessments. We did the experiments and described them in the Jupyter notebook using the Python programming language. We separated the dataset into 75% for training and 25% for testing. In the first dataset, the number of records in the training set is 13680, and the amount of data used in the test set is 4560. In the second dataset, the number of records in the training set is 5243, and the amount of data used in the test set is 1748. The data set was analyzed using logistic regression, K-Nearest Neighbors, Naive Bayes, decision tree, random forest, and SVM. Each of the algorithms gave results with different success rates. In the first database, SVM Linear, SVM RBG, and random forests achieved an equal accuracy rate of 96.5%. The algorithm with the lowest rate was the Naive Bayes calculation with a pace of 92.3%. In the second database, K-Nearest Neighbor had the highest accuracy rate of 97.7%, and the algorithm with the lowest accuracy rate was the Decision Tree Classifier algorithm with 93.7%. Algorithms' run times vary widely in the application. We take the average of running seven algorithms. The fastest learning algorithm for the first database is the K-Nearest Neighbor algorithm with 1.03 seconds, and the slowest algorithm is the Random Forest Classifier algorithm with 33.43 seconds. The Gaussian Naive Bayes algorithm is the fastest in the second database with 1.14 seconds, and the logistic regression algorithm is the slowest with 16.67 seconds. In the following table, you can see the success rates of the algorithms and the average timing for each algorithm.

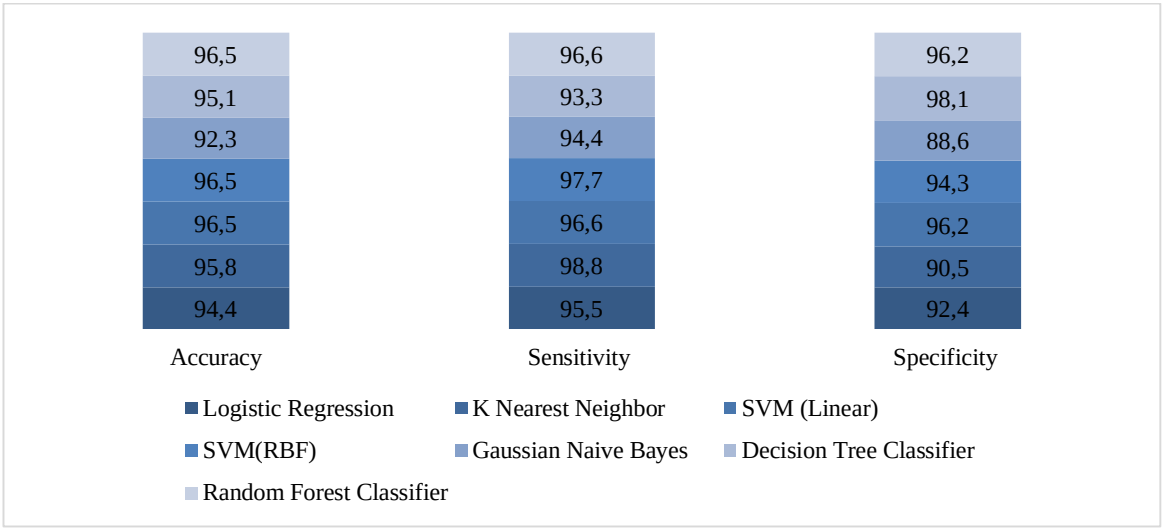

Fig. 1. Evaluation results for the first dataset.

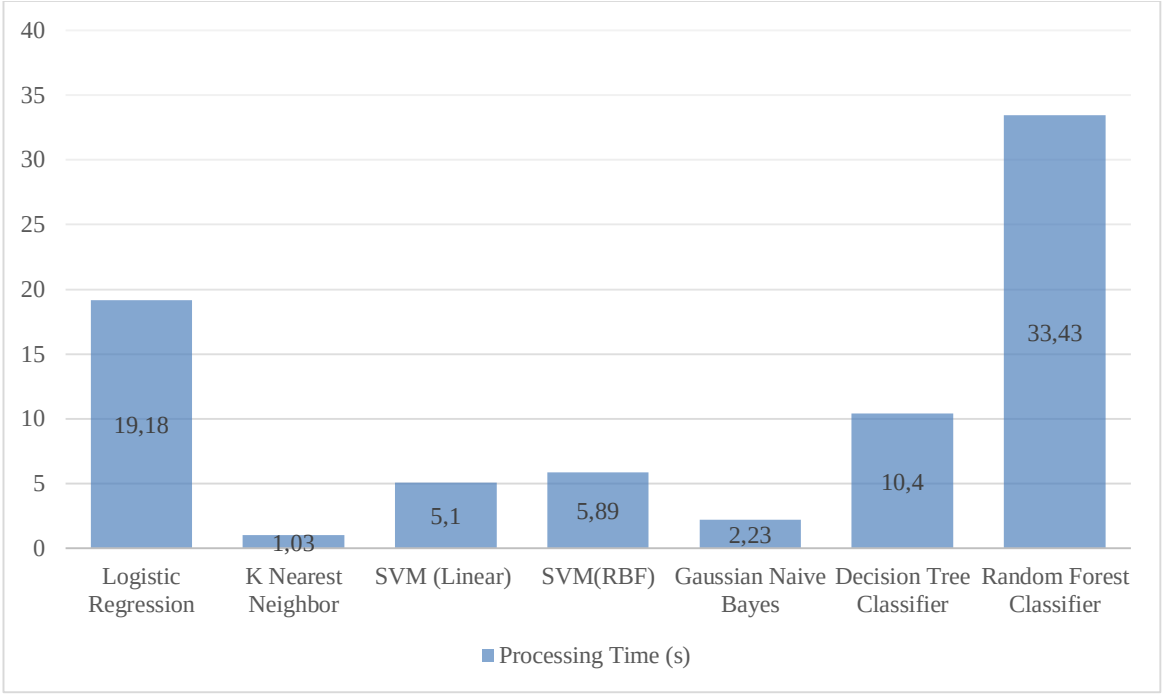

Fig. 2. Processing time results for the first dataset.

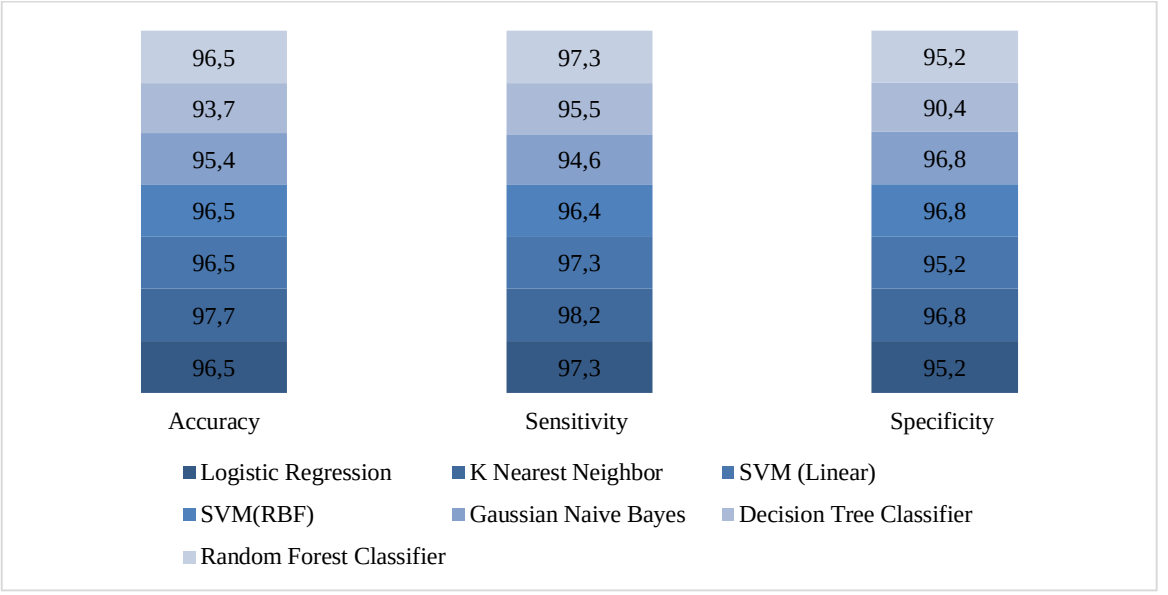

Fig. 3. Evaluation results for the second dataset.

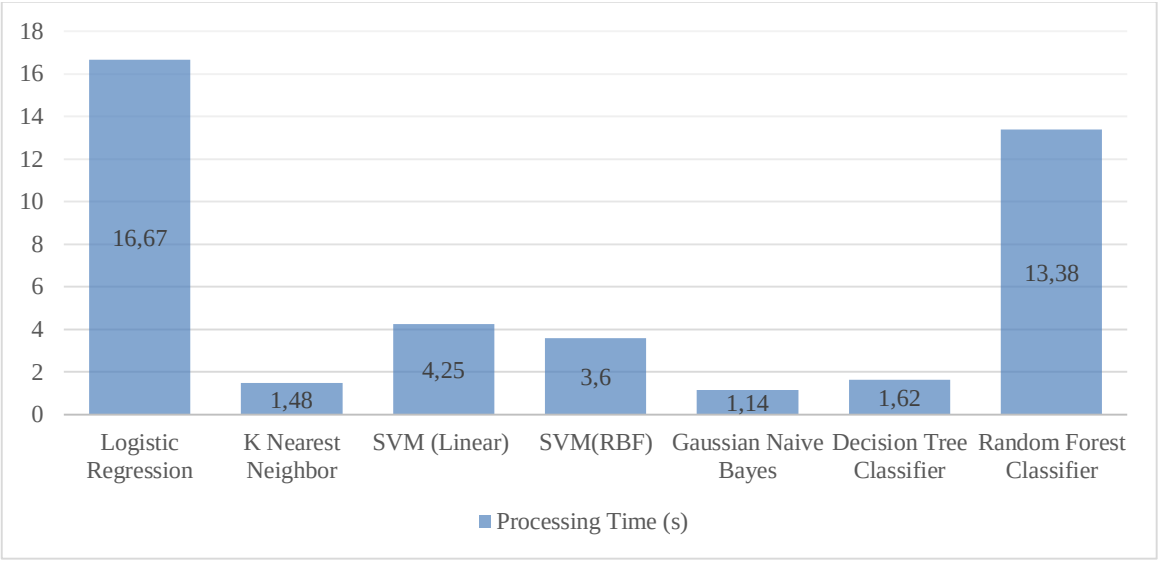

Fig. 4. Processing time results for the second dataset.

4. Conclusion

Breast cancer early detection is necessary to reduce mortality and increase the likelihood of recovery. This paper aims to apply the classification algorithms that can help identify breast cancer characteristics, clean the data, and identify traits that can help predict breast cancer. As a result of this study, the first data set, we found that the linear and non-linear SVM algorithms and the random forest algorithms nearby to the highest accuracy of 96.5%. For the second dataset, we found that the K-Nearest Neighbors algorithm achieved the highest accuracy of 97.7%. With this result, we conclude that it is possible to predict the likelihood of developing breast cancer using artificial intelligence and early detection, which helps in treatment and early prevention.

Acknowledgements

This study did not receive any dedicated funding from public, commercial, or non-profit organizations.

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Contents lists available at *Dergipark*

Journal of Scientific Reports-B

journal homepage: *https://dergipark.org.tr/en/pub/jsrb*

E-ISSN: 2717-8625 ***Number 12, April 2025***

RESEARCH ARTICLE

Receive Date: 14.02.2025 *Accepted Date: 29.04.2025*

Covid-19 Impact on Blood Sugar Levels and Renal Function Deterioration: A Comparative Study

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Abstract

COVID-19 is an infectious disease triggered by the SARS-CoV-2 virus. Its first emergence was documented in December 2019 in Wuhan, China, leading to a global spread and a pandemic declaration. COVID-19 symptoms usually include fever, cough, headache, fatigue, respiratory problems, and loss of sensation. Diabetes is a medical condition characterized by insufficient insulin production from the pancreas. According to previous studies, there is a two-way relationship between diabetes and Covid-19. On the one hand, it was found that diabetes leads to a fourfold increase in the risk of infection with Covid-19 in the average person. On the other hand, infection with Covid-19 can cause diabetes in patients who do not have diabetes. Renal dysfunction is a condition in which the kidneys are unable to remove waste macromolecules from the blood serum and require medical support. According to previous studies, more than one-third of patients infected with COVID-19 had acute renal dysfunction, and 15% of those infected are known to be on dialysis. Samples were collected from patients, which numbered 160 samples, the number of normal samples was 60, and the number of abnormal samples was 60. The following analyses were performed for all samples (PCR. Ferriten, LDH, D.Dimer, S.Creatinine, B. Urea, Albumin, S, Glucose). In Covid 19, the following three analyses were chosen to diagnose the presence of the virus in the body: PCR, Ferriten, LDH, and D.Dimer. In diabetes mellitus, the following analyses were selected for this disease. These analyses are among the most accurate analyses for diagnosing diabetes which is: S, Glucose. In renal failure, the three most important analyses were chosen to diagnose the efficiency of the work and functions of the kidneys creatinine,

B.UREA, and Albumin. When samples were tested by Independent T-test regarding ferritin, LDH D-dimer, and FBS, there were no significant differences between samples that were affected by COVID-19 and samples that were not infected by COVID-19. While Creatinine, Urea, and Albumin, there are significant differences between samples that are affected by COVID-19 and samples that are not infected by COVID-19. Thus, there is a relationship between Covid 19, diabetes, and kidney function impairment, and this relationship whenever there is a strong infection with the Covid 19 virus may result in kidney function impairment or diabetes.

Keywords: COVID-19; Renal Function; Diabetes; PCR; CRP; LDH; D-dimer.

1. Introduction

The global public health emergency known as severe acute respiratory syndrome COVID-19 is caused by the coronavirus 2 (SARS-CoV-2) virus. The first symptoms of COVID-19 are known to have appeared in December 2019 in Wuhan, Hubei province, China. Since the first outbreak of COVID-19 pneumonia, it has spread rapidly and has been reported in several regions beyond China [1]. First, a group of viruses must exhibit distinctive characteristics to be classified under the family Coronaviridae of the order Nidovirales. Within this family, Coranaviruses are non-segmented, enveloped, positive RNA viruses in the coronaviridae family of the order Nidovirales. The International Committee on Taxonomy of Viruses is the primary body charged with classifying the virus family and all known viruses [2]–[4].

The coronavirus team, including COVID-19, a member of the virus family that we have recently encountered, is causing outbreaks affecting public health in East Asia and the Middle East. The first patient admissions of Severe Acute Respiratory Syndrome (SARS) in 2002 and Middle East Respiratory Syndrome (MERS) in 2012 have seen widespread public outbreaks, as well as the emergence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in recent years, leading to the declaration of a global pandemic that continues to affect numerous countries and regions [5], [6]. SARS-CoV-2 is a highly virulent public health problem, transmitted through contact between individuals, as well as through contaminated objects and airborne atmospheric transmission. It is worth noting that personal protective equipment (PPE) could also serve as a source of airborne infections [7], [8]. As previously mentioned, the person-to-person transmission of SARS-CoV-2 primarily occurs through respiratory droplets generated when a patient coughs, sneezes, talks, or sings. Typically, these droplets have a limited range of about six feet (almost two meters) and linger in the air for a brief duration. Nevertheless, SARS-CoV-2 remains viable and contagious in smaller droplets (less than five microns in diameter), capable of remaining suspended in the air for up to three hours [9], [10].

Diabetes mellitus encompasses a group of disorders, including autoimmune, metabolic, and genetic factors, all characterized by elevated blood glucose levels (hyperglycemia). The approach to measuring plasma glucose and the criteria for defining normal or abnormal levels have undergone various revisions in recent decades. Diabetes mellitus is classified into four main categories: type 1 diabetes, type 2 diabetes, various specific types, and gestational diabetes. Type 1 diabetes usually involves impaired pancreatic beta-cells, often due to autoimmune inflammatory mechanisms. Autoimmune markers in serum include antibodies to insulin, tyrosine phosphatases IA-2 and IA-2b, zinc transporter ZnT8, islet cell autoantibodies, and antibodies to glutamic acid decarboxylase (GAD). Although the rate of development might vary, this damaging process typically culminates in absolute insulin insufficiency, which is defined by undetectable levels of plasma C-peptide [11], [12].

Diabetes mellitus is a common coexisting condition and contributes to a more unfavorable prognosis in individuals with COVID-19. Certainly, when examining instances of pneumonia with unidentified origins documented in Wuhan and individuals with a history of exposure to the Huanan seafood market before January 1, 2020, it was observed that

20% of these cases were associated with diabetes. Data from Italy indicates that over two-thirds of individuals with COVID-19 who did not survive had a history of diabetes [13]

To sum up, diabetes is a common comorbidity, a risk element, and an independent prognostic factor among individuals with COVID-19 [14–17]. Strong evidence supporting the adverse impact of diabetes in COVID-19 patients is further supported by two meta-analyses. In individuals with COVID-19, the prevalence of diabetes is twice as high in severe/ICU cases compared to non-severe/non-ICU cases [18].

Certainly, the identification of diabetes in a group of patients with COVID-19 infection revealed a subset of individuals facing a 2.26-fold elevated risk of encountering unfavorable disease outcomes, as reported in analyses by [19]. Furthermore, individuals with obesity and/or glucose intolerance appear to be particularly susceptible to COVID-19 [20]. Diabetes is associated with an increased risk of COVID-19 infection and worse outcomes, including hospitalization and death Individuals with diabetes, both Type 1 and Type 2, have a higher risk of contracting COVID-19 compared to those without diabetes. Insulin treatment is associated with a greater risk of COVID-19 infection compared to non-insulin drugs or no treatment. Poor glycemic control, as indicated by higher hemoglobin A1c levels, is also associated with an increased risk of COVID-19 infection. Diabetes, especially when poorly controlled, is a risk factor for severe COVID-19 outcomes [1], [21], [22].

The phrase renal failure indicates the kidneys' incapacity to carry out the excretory function, resulting in the accumulation of nitrogenous waste products in the blood [23]. There are two forms of kidney function impairment: acute and chronic renal failure. The term used when a patient requires renal replacement therapy is end-stage renal disease (ESRD).

Acute renal failure (ARF) is a clinical syndrome characterized by a swift decrease in glomerular filtration function, disruptions in water and electrolyte balance, and the rapid accumulation of nitrogen wastes in the body [24] [25].

Recently, the term acute kidney injury (AKI) has been used instead of acute renal failure (ARF) because AKI encompasses the complete clinical spectrum from a minor elevation in serum creatinine to evident renal [26].

A determined glomerular filtration rate (GFR) of less than 60 milliliters per minute (or 1.73 millimeters) or excessively increased blood creatinine for more than three months are the hallmarks of chronic renal disease (CKD), Chronic renal failure (CRF), also known as chronic kidney disease, is characterized by a gradual deterioration in renal structure and function, eventually necessitating kidney transplantation therapy [27]. People with multiple sclerosis, especially those on immunosuppressants or immunomodulators, are more at risk for serious symptoms of SARS-CoV-2 infection and COVID-19 sequelae [28]. Research has sought to determine which MS patients are more vulnerable to SARS-CoV-2 infection, analyze the relationship between SARS-CoV-2 and MS, and assess the immune system's reaction to SARS-CoV-2 infection and vaccinations [29].

In COVID-19, kidney disease has been documented, with AKI observed in over 20% of severely ill or deceased patients, a proportion consistently reported in studies conducted in China, Italy and the United States [30], [31]. It is noteworthy that AKI, proteinuria, and hematuria have been individually linked to an increased risk of mortality in individuals with COVID-19 [32]. The occurrence of pre-existing chronic kidney disease was markedly higher among those experiencing severe COVID-19 disease [33].

According to tissue cell immunohistochemistry analyses, ACE2 appears to be absent in renal endothelial cells. However, a study using single-cell analysis confirmed the presence of ACE2 and TMPRSS2 expression in human renal endothelial cells [5]. Recently, viral particles were observed in the endothelial cells of glomerular capillary loops in a COVID-19 patient using electron microscopy [34]. Histopathological analysis of the kidney of the patient with COVID-19 showed the presence of inflammation or endothelial tissue damage even in the absence of interstitial inflammatory infiltrates [35],[36].

Although there have been studies conducted on the impact of COVID-19 on diabetes and renal disease separately, there has not been any research on their combined effect in the same patient [37]. Therefore, our study aims to investigate the effect of COVID-19 on both diabetes and renal function in the same patient. We will analyze the data

to determine the correlation between the two conditions and how they may exacerbate each other in COVID-19 patients [38].

The samples were chosen from the Middle Euphrates region of Iraq, where 60 healthy samples were taken from individuals who were not infected with the COVID-19 virus and did not exhibit any symptoms of infection, and 60 abnormal samples were taken from individuals who were positively identified as having the virus and displaying symptoms of the illness. Males and females between the ages of 15 and 70 were chosen, and all 120 samples underwent the following analyses. The tests included (PCR, CRP, Ferritin, LDH, D. Dimers, Creatinine B. UREA, Albumin, and Glucose).

2.Material and Method

2.1.Collection of blood

Venous blood is drawn from the arm using a sterile syringe. The arm should be warm and the person should be in a comfortable position. A compressive bandage is applied gently, the skin is cleaned with alcohol, and then a needle is inserted into the vein to draw 5-10 ml of blood. After withdrawing the needle, the blood is placed in a test tube for separation.

2.2.Collecting samples for PCR analysis

as follows: 1. Blood test. 2. Nasal swabs. Nonetheless, nose swabs were utilized in this investigation, and there are three ways to collect nasal swabs: Frontal Nasal Swab: To perform this, place the swab in the front of your nostrils and hold it there for ten to fifteen seconds. Mid Nasal Swab: Here, the swab is inserted until resistance is felt, then it is rotated for 15 seconds before being withdrawn. This process is repeated in the second nostril. Oropharyngeal Nasal Swab: In this method, the swab is inserted into the nostril, reaching the nasopharynx or the back of the throat, and then rotated before being withdrawn. All specimens to be tested are infectious body fluids and must therefore be handled under the requirements of laboratory biosafety rules.

2.3. Polymerase chain reaction (pcr) test

Turn the 96-well plate upside down so that the liquid that sticks to the sealing film and the well walls falls to the bottom of the plate. To use, let them stand for three to five minutes. every part included in the package. In a 96-well plate, mix. After removing the sealing film, add 200 µL of sample and 15 µL of Proteinase K in succession to Extraction Reagent II in the 96-well plate. As directed, load plates into the instrument; once loaded, close the door. Select the program after turning on the nucleic acid extraction device. Launch the extraction software; it will take around 12 minutes. When finished, remove the 96-well plate.

2.4. Ferritin test

Transfer 30 µL of sample to a tube with detection buffer, mix thoroughly, and immediately pipette 75 µL of the mixture into a sample well on the cartridge. Insert the cartridge into an i-Chamber or incubator at 25 °C for 10 minutes. After incubation, scan the cartridge immediately using the instrument for ichroma™ tests. The normal range for women is 20-250 ng/mL and for men is 30-350 ng/mL, with a working range of 10-1,000 ng/mL.

2.5. C-reactive protein (CRP) test

In summary, the process involves adding undiluted serum and control samples to a slide and then adding CRP latex reagent to each sample. Agglutination is observed within 3 minutes, with positive results indicating a CRP concentration > 6 mg/l and negative results indicating a CRP concentration < 6 mg/l or no CRP present.

2.6. Elevated lactate dehydrogenase (ldh) test

Pipette the reagents into a 1 cm long thermostat cuvette and bring the reagent media to 37°C 1000 µL after allowing the samples to stand at room temperature, then add the collected sample. Once the media is calibrated, collect 20 µL of sample, mix, and add again for measurement. Record the first absorbance at 340 nm (or 334 nm) after 30 seconds, then record the absorbance again after 1 minute and 2 minutes. Obtain results by calculating the change in absorbance per minute (Abs/min.). Calculations: LDH activity (IU/L) = (ΔAbs/min)Assay / (ΔAbs/min)Calibrator × Calibrator Activity. Normal Range Adult LDH activity: at 37° C: 200-400 IU/L (SFBC method).

2.7. D-dimer test

The process involves taking 150 µL of detector diluent and adding it to the detector tube containing a granule to form the detection buffer, then adding 10 µL of sample and mixing it thoroughly. After that, 75 µL of the sample mixture is dispensed into the sample well of the cartridge, which is then left at room temperature for 12 minutes. The cartridge is then scanned immediately using the instrument for ichroma™ tests, and the test result is read on the display screen. The normal range for the test is 500 ng/mL, with a working range of 50-10,000 ng/mL. It's important to ensure the cartridge is scanned immediately after incubation to avoid inaccurate results.

2.8. Creatinine blood test

Measuring against air at rising absorbance, measure mercury at wavelength 492 nm (490-510 nm), optical path (1 cm), and temperature 25°C/37°C. The cuvette and reagents should be heated to the appropriate temperature (±0.5°C) and maintained there during the test. Procedure for Assay Sample/STD 100 ul and working reagent 1000 ul are collected from the first tube, and Sample/STD 200 ul and working reagent 2000 ul are obtained from the second tube. When the mixing process begins, start the timer. Read the absorbance value A after 30 seconds, followed by the absorbance value A2 after 2 minutes. The keratin blood test's normal serum range is 0.5 _ 0.9 mg/dl for women and 0.6 _ 1.1 mg/dl for males (Eq.1).

$$A2\_ A1 = AA \text{ sample or } AA \text{ STD.} / \text{ Calculations } C = 2.0 \text{ X } \Delta A \text{ sample} / \Delta A \text{ STD [mg/dl].} \quad (1)$$

2.9. Albumin blood test

The sample to be measured is specific at a wavelength of 546 nm. The measurement is taken against the reagent blank at a cuvette length of 1 cm, temperature 20-25°C. Three tubes were taken into the Test Procedure and a Blank (Albumin Reagent 1000 µL, Standard 0 µL, Sample 0 µL) was taken in the first tube. Standard (Albumin Reagent 1000 µL, Standard 10 µL, Sample 0 µL) was taken in the second tube. Mix the sample (Albumin Reagent 1000 µL, Standard 0 µL, Sample 10 µL), mix and incubate at 20-25°C for 5 minutes. Measure the absorbance of the sample (As) and standard (Astd) against the reagent blank within 30 minutes.

Calculation Serum Albumin (g/dL) = ΔA sample /ΔA standard X 4 (Std.conc.) Normal Range serum albumin 3.8_5.1g/Dl

2.10. Blood urea nitrogen (bun) test

For the BUN test, optimum conditions for temperature (20-25°C or 37°C), wavelength (570-600 nm, 546 nm) 578 nm for Hg, Path 1 cm, and reagent should be provided. For each series, just one reagent blank is needed. Assay Methodology Sample/STD 0 µl, Enzyme reagent (R1) 1000 µl are placed in the first tube, and Sample/STD 10 µl and Enzyme reagent (R1) 1000 µl are placed in the second tube. After mixing and incubating for 5 minutes at 20–25°C or 3 minutes at 37°C, add 1000 µl of RGT2/R2 to each of the two tubes that came before it. Combine, then let it sit for 10 minutes at 20–25°C or 5 minutes at 37°C. Within 60 minutes, compare the absorbance of the sample (As ample) and the STD (ASD) to the reagent blank. Worksheets C = urea

2.11. Fasting blood sugar (fbs) test

For sample measurement, set the wavelength to 505 nm (490-550), temperature to 37°C/15-25°C, and cuvette length to 1 cm. Zero the instrument cavity with distilled water and then place the sample in the cuvette. Three tubes are taken for the test procedure. The first tube is blank (WR(ml) 1.0, standard grade 1.2(ul) 0 ul, sample (ul) 0 ul); the second tube is standard (WR(ml) 1.0, standard grade 1.2(ul) 10 ul, sample (ul) 0 ul); the third tube is sample (R(ml) 1.0, standard grade 1.2(ul) 0 ul, sample (ul) 10 ul). Mix the sample before placing it in the instrument and incubate for 10 minutes at 37°C or 20 minutes at room temperature (15-25°C). Read the absorbance (A) of the samples and standard against the blank. However, the color in the sample is stable for at least 30 minutes. Normal Range Serum or plasma should be 60_110 mg/dL, 3.33_6.10 mmol/L. Calculations (A) Sample - (A) Blank / A) Standard- (A) Blank x 100 (Standard conc.) = mg/dL glucose in the sample,

3.Sample Grouping

A total of 120 samples were collected and divided into two groups. The first group consisted of 60 samples infected with Corona virus and the second group consisted of 60 samples not infected with Corona virus. The following analyzes were performed on the samples; PCR test (Polymerase Chain Reaction Test), Ferritin test, Dimer Neo test, LDH test (Lactate dehydrogenase test), CRP test (C reactive protein), Creatinine Blood test, Blood Urea test, Glucose test.

4.Statistics Analysis

We carried out the statistical study based on patient tests transcribed in the form of an Excel table. To test the normality of the data, we used the Kolmogorov-Smirnov test and an independent t-test to compare the two groups (COVID and non-COVID). The chosen threshold of statistical significance was $p < 0.05$.

5.Results and Discussion

A total of 120 samples were tested using PCR and CRP for COVID-19, with negative results being placed in the non-COVID-19 group and positive results being placed in the COVID-19 group

5.1. Descriptive statistics

The mean and standard deviation values of the minimum, maximum test analyses for the groups without COVID-19 are given in table 1.

Table 1. Descriptive statistics, and values for Non-COVID groups.

Test Name	Minimum	Maximum	Mean	Std. Deviation
Ferritin Test	108.00	213.00	195.7833	19.45276
D.DIMER Test	108.00	213.00	96.13333	8.784552
LDH Test	108.00	213.00	242.3333	18.10952
ALBUMIN Test	3.40	5.40	4.355	0.595299
S.CREATININE Test	108.00	213.00	0.839333	0.186828
B.UREA Test	8.00	24.00	17.835	4.527012
FBS Test	80.00	125.00	99.4667	10.67147

The mean and standard deviation values of the minimum, maximum test analyzes for COVID-19 are given in table 2.

Table 2. The Descriptive statistics, and values for COVID groups.

Test Name	Minimum	Maximum	Mean	Std. Deviation
Ferritin Test	391.00	433.00	412.5932	10.99382
D.DIMER Test	391.00	433.00	617.5254	11.28876

LDH Test	391.00	433.00	524.6441	13.15677
ALBUMIN Test	2.40	8.90	4.040678	1.268901
S.CREATININE Test	391.00	433.00	1.978305	5.643343
B.UREA Test	59.00	901.00	76.28367	9.657102
FBS Test	145.00	208.00	183.5085	13.52771

A total of 120 samples were tested using PCR and CRP for COVID-19, with negative results being placed in the non-COVID-19 group and positive results being placed in the COVID-19 group. Subsequently, all samples were tested for LDH, Ferritin, and D-dimer, which, in contrast to the non-COVID-19 group, demonstrated an increase in the COVID-19 group. The diabetes test indicated that samples in the COVID-19 group had a higher mean value than those in the non-COVID-19 group. In terms of renal function tests, Creatinine and Urea increased, whereas the COVID-19 group's mean albumin levels dropped in comparison to the non-COVID-19 group. When samples were tested by Independent T-test regarding ferritin, LDH D-dimer, and FBS, there were no significant differences between samples that were affected by COVID-19 and samples that were not infected by COVID-19. While Creatinine, Urea, and Albumin, there are significant differences between samples that are affected by COVID-19 and samples that are not infected by COVID-19 (Figures 1,2 and 3).

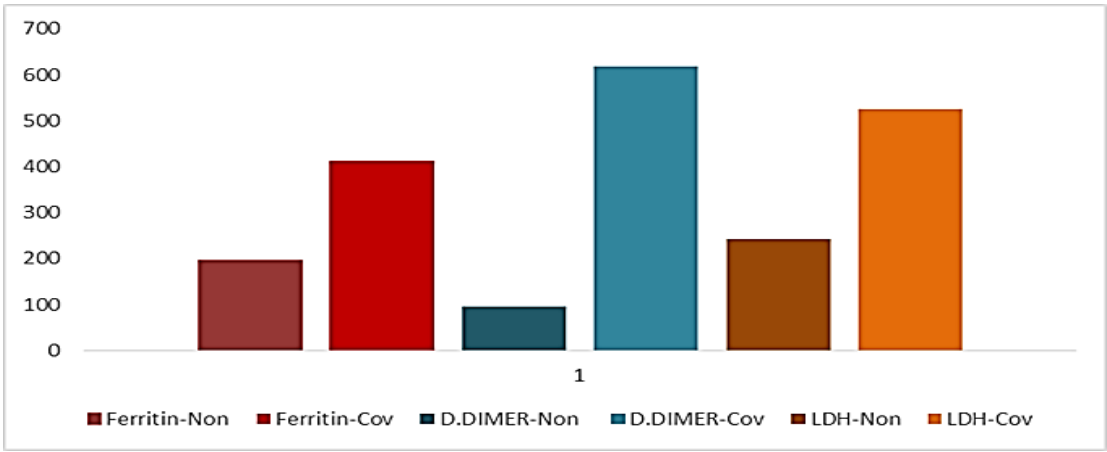

Fig. 1. The bar chart represents the non-significant increase in ferritin, LDH, and D-dimer levels in the COVID-19 group when compared to the non-COVID-19 group.

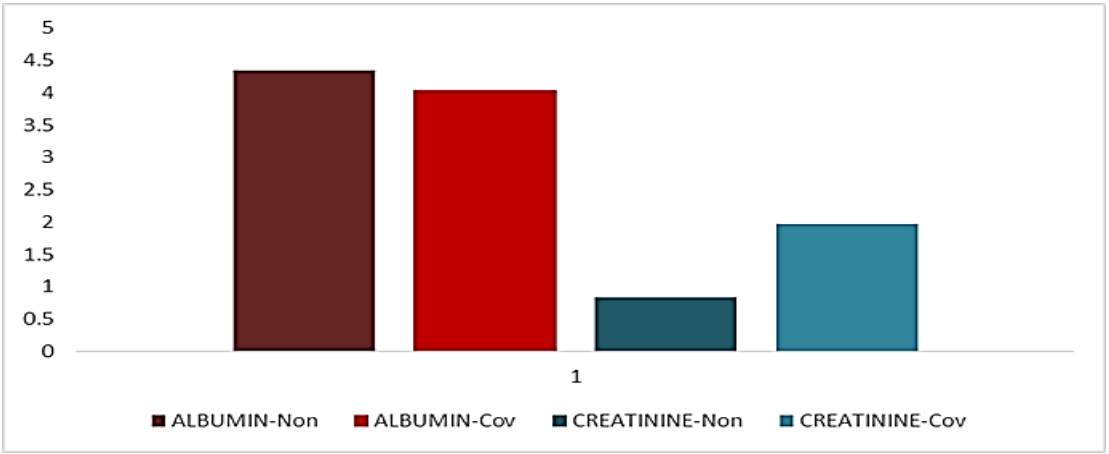

Fig. 2. The bar chart represents a significant increase in Creatinine, while Albumin appears significant decrease in levels in the COVID-19 group when compared to the non-COVID-19 group.

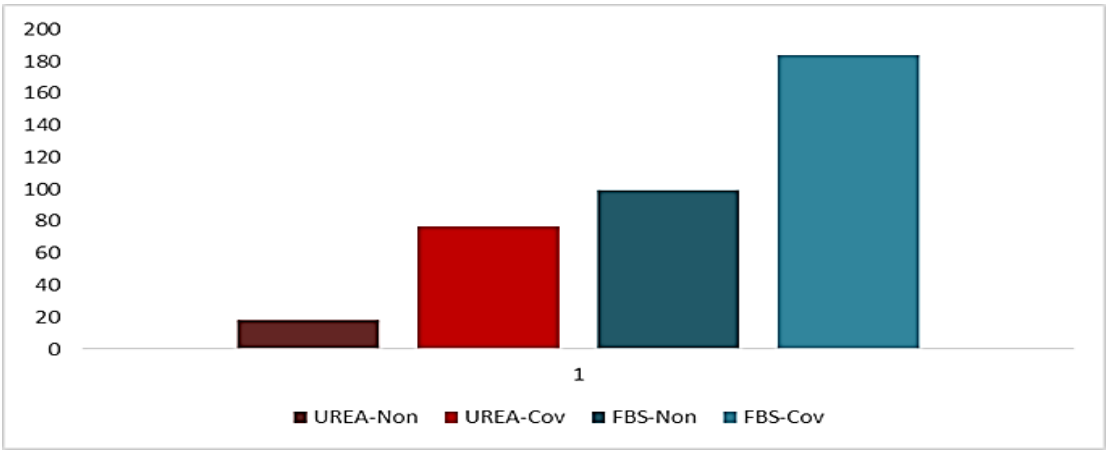

Fig. 3. The bar chart represents a significant increase in Urea while FBS appears non-significant levels in the COVID-19 group when compared to the non-COVID-19 group.

5.2. Polymerase Chain Reaction (PCR) and C-reactive Protein (CRP) Technique

PCR and CRP tests appear to aid in the early diagnosis and management of COVID-19, which is crucial in preventing the spread of the disease. In addition, the collected body fluid results provide evidence that PCR and CRP are effective testing and diagnostic tools for identifying COVID-19 cases. The findings highlight the importance of common tests that can be established to accurately identify and isolate infected individuals in the context of a

pandemic. PCR and CRP assays are diagnostic and in addition to investigating their efficacy in different populations and disease settings, there is a need for further research to explore the potential of new emerging potential diseases.

5.3. Ferritin Test

The test kits show that ferritin levels are elevated in individuals with the disease, but there is no statistical difference compared to patients without COVID-19. The results clearly show that a systematic review did not lead to significant results when compared to patients without elevated ferritin levels. The increase in ferritin levels may be due to cytokine storm and secondary hemophagocytic lymphohistiocytosis. The findings are similar to previous meta-analysis and meta-regression analysis studies [39], [40].

5.4. D-dimer Test

Tests have shown an increase in D-dimer levels in COVID-19 patients, but there is no statistically significant difference compared to patients without COVID-19. Tests have shown that D-dimer levels are commonly elevated in COVID-19 patients. The test results corroborate each other, suggesting that COVID-19 may be a useful tool in determining mortality risk, given the risk of disease transmission [7]. Increased D-dimer levels in COVID-19 patients are known to have several clinical implications, including its role in disease progression, its ability to guide in monitoring the course of treatment. These results suggest that elevated D-dimer levels may be associated with more severe COVID-19 outcomes such as death and syndrome in individuals suffering from COVID-19. Near future studies suggest that D-dimer levels, when used in combination with other testing factors, may help predict favorable COVID-19 outcomes [41].

5.5. Elevated Lactate Dehydrogenase (LDH)

The research findings reveal that among COVID-19 carrier individuals, there was a significant increase in Elevated Lactate Dehydrogenase (LDH) levels among those whose disease course did not progress. In addition, individuals without COVID-19 did not show a statistically significant increase in LDH levels compared to COVID-19 carriers, consistent with findings from previous studies. In addition, recent studies show that LDH levels in the blood of a patient with COVID-19 are an independent risk factor for the severity of COVID-19 and mortality in the population. Therefore, it suggests that a high LDH/Lymphocyte ratio is an independent risk factor for population mortality in COVID-19 patients. This finding demonstrates the potential use of LDH/lymphocyte ratio as a valuable diagnostic tool and prognostic marker in the clinical management of COVID-19 [42], [43].

5.6. Albumin Blood (ALB)

Tests show that serum albumin levels are significantly higher in patients with non-severe COVID-19 than in patients without COVID-19. A study by Gulam Rabbani and Saeyoung Nate Ahn reveals that low serum albumin levels are associated with an increased risk of severe COVID-19 and mortality. This is due to albumin's role in protecting the lungs from inflammation [44– 46].

5.7. Creatinine Blood

The test kit performed reveals that the Creatinine levels of individuals with COVID-19 are significantly higher than those who do not carry the virus. This difference is statistically significant compared to other test kits. The explanation

for high creatinine is a sign of November muscle damage. The results are in line with previous research by Deniz Ok MD et al. Blood urea nitrogen (BUN) levels of COVID-19 patients have been found to be significantly higher. The increased risk of death and the severity of the disease appear to be strongly associated with high Creatinine levels. High Creatinine values indicate acute kidney injury caused by COVID-19 treatment or the virus itself. This study is also in line with his study, which suggests that an increase in creatinine is the first presentation of coronavirus disease 2019 (COVID-19). Therefore, the increase in keratin levels can be caused by various factors, including rhabdomyolysis, injuries, certain medications, and cardiovascular disease [47– 49]

5.8. Blood Urea Nitrogen (BUN)

In our study, urea levels were significantly increased in COVID-19 patients, and the difference was statistically significant compared to patients without COVID-19. These findings are consistent with previous studies Fesih Ok MD et al., 2020 We found that blood urea nitrogen (BUN) levels were significantly higher in COVID-19 patients. Elevated BUN levels were positively associated with increased disease severity and risk of death. Elevated blood urea nitrogen (BUN) levels may be a sign of acute kidney injury caused by the virus or by the treatments used to treat COVID-19 [50].

Additionally, a study found that BUN levels were significantly higher in the deceased group compared to the survivor group. Specific BUN threshold values can be used to identify patients at high risk and initiate appropriate therapeutic interventions early [51].

5.9. Fasting Blood Sugar (FBS)

A significant increase is observed in glucose level studies conducted on non-severe COVID-19 patients. This increase gives statistically significant results, that is, the probability of it being due to chance is quite low. In cases of COVID-19, the increased glucose level in combination with diabetes disease is of importance in past, present and future studies. Therefore, he suggests that high blood sugar levels pose a risk factor along with severe cases of COVID-19. In October, an increase in glucose levels is also associated with an increased risk of COVID-19 complications, such as acute respiratory syndrome (ARDS) and respiratory failure. There are several possible explanations for high blood sugar in people with COVID-19. The first possibility is that infection with the COVID-19 virus can damage the cells of the pancreas that produce insulin. This can lead to a decrease in insulin production, and as a result, high blood sugar levels are observed. Another possibility is that, on the contrary, infection with the COVID-19 virus can lead to the release of insulin from the pancreas. This can lead to a decrease in blood sugar levels, which in turn leads to an increase in the production of glucose from the liver [52]. In addition, this study by Zohair Jamil Gazzaz confirms the high blood sugar studies in the tests for the 2021 COVID-19 cases.

6.Conclusion

Various studies are being proposed against the COVID-19 virus, disease markers, monitored methods, infection risks and high plasma levels. Also as a result of this study, it is known that COVID-19 patients have higher LDH, Ferritin, D-dimer and diabetes markers, as well as kidney dysfunction compared to non-COVID-19 patients. Along with these findings, the symptoms encountered in COVID-19 cases cause various organ and tissue damage. In addition, it shows that it can damage many organs and systems, including the kidneys and pancreas, leading to potential long-term health consequences. Therefore, it is very important to monitor various biomarkers such as LDH, Ferritin December, D-dimer, BUN and glucose in COVID-19 patients, to perform their tests at regular intervals and to develop appropriate treatment methods.

Acknowledgements

The authors dedicated this publication to the 100th anniversary of the Republic of Türkiye. As scientists raised by Türkiye, they are proud to be citizens of this country.

Author Contribution

Hussein Ali Mashkoor Shubbar, Ebru Halvacı, Nour Elhouda Tiri, Aysenur Aygun, Nihal Yigir Ertas, Saadet Celikozlu; wrote, edited, drew figures and developed the article. Fatih Sen; supervisor and responsible person.

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Contents lists available at *Dergipark*

Journal of Scientific Reports-B

journal homepage: *https://dergipark.org.tr/en/pub/jsrb*

E-ISSN: 2717-8625 ***Number 12, April 2025***

RESEARCH ARTICLE

Receive Date: 09.04.2025 *Accepted Date: 30.04.2025*

Investigation of the correlation between Endocan, Interleukin-10, and biochemical parameters in Iraqi patients with cardiovascular diseases

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Abstract

The correlation between biomarkers endocan and interleukin-10 (IL-10) in patients with various cardiovascular diseases—angina pectoris, ischemic heart disease, and myocardial infarction—is examined in this work. There were 200 participants overall, 50 in each of the three disease groups and a control group of fifty healthy people. Along with other factors including renal function, glucose metabolism, and lipid profile, the study gauged serum levels of endocan and IL-10. With myocardial infarction patients showing the highest levels, results revealed that all patient groups had notably greater levels of endocan and IL-10 than healthy controls. With greater blood urea and serum creatinine levels than those with ischemic heart disease and angina pectoris, the study revealed that patients with myocardial infarction demonstrated notably impaired renal function. Along with a poorer lipid profile comprising increased total cholesterol, triglycerides, and low-density lipoprotein (LDL) levels, individuals with myocardial infarction also had higher fasting glucose and hemoglobin A1c levels. By comparison, the healthy control group had the lowest levels of these biomarkers and indicators. The results imply that levels of endocan and IL-10 could be markers of the degree and progression of cardiovascular disease. Particularly those with myocardial infarction showed more marked metabolic and renal abnormalities than those with ischemic heart disease or angina pectoris, so highlighting the possible use of these biomarkers in tracking disease severity and supporting clinical management of cardiovascular diseases.

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Keywords: Angina pectoris; ischemic heart disease; myocardial infarction; endocan and Interleukin-10.

1. Introduction

CVD refers to a range of disorders affecting the heart and blood vessels, and leads to serious conditions such as angina pectoris, ischemic heart disease, myocardial infarction, and death. According to the World Health Organization, CVD remains the leading cause of death globally. The process of atherosclerosis development starts during childhood and is one of the factors contributing to determining CVD events such as coronary artery disease or stroke later in life [1], [2]. As the disease progresses, it manifests through a combination of metabolic derangements, oxidative status imbalance, and endothelial dysfunction, and these events are avenues to a more complex spectrum of CVD. Since CVD is one of the most common diseases leading to morbidity and mortality worldwide, prevention of its occurrence, as well as timely detection, are important for healthcare [3], [4]. Classification of CVDs is diverse, but in general the clinical presentation is always subtle and insidious with few exceptions. Point of CVD presentation may start early with mild dyspnea, chest discomfort, fatigue in addition to mental health concerns [5], [6]. Other than chest pain or sudden death, these could include, an uneven pulse rate, low blood pressure and peripheral atherosclerosis. The modern model of reconstructive bilitative system includes clinical methods along with diagnostic modalities like echocardiography and coronary imaging, of course clinical examination is still of great importance [7], [8].

Cardio vascular disease contributes to the number of deaths around the world. Cardiovascular conditions account for nearly 31 percent of deaths on an annual basis. Apart from obesity and diabetes, it is also correlated with obesity and other diseases associated with one's way of living [9]. Such conditions affect both men and women across the globe and more than 17 million people were considered to have been affected in 2004 alone. Additionally, more than 23 million are expected to be affected by the year 2030 [10], [11]. Chest pain, fatigue, shortness of breath, and dizziness are just a few symptoms that might appear as the condition progresses. This illness, along with many others, is often asymptomatic for a long-time making diagnosis very difficult. To improve such a situation, the need for early diagnosis cannot be overstated as it can help minimize the risk of further complications. Adopting a range of diagnostic tests such as ultrasound, electrocardiograms, computed tomography, and magnetic resonance would allow medical practitioners to identify the diseases [12], [13]. When it comes down to Prevention, one must take into consideration controlling diabetes, high blood pressure, smoking, and sedentary lifestyles in conjunction with a proper and healthy diet as well as exercise. People suffering from these diseases, on the other hand, will have to modify their ways of living alongside routine medical checkups in order to reduce the chance for further invocations [14], [15]. Your heart disease risk is significantly reduced by simply altering your way of life, adopting a healthier diet, maintaining minimal intake of saturated fats, performing mild exercises like walking on a daily basis, using the mindfulness technique in its lifestyle [16], [17].

2. Materials and Methods

2.1.1 Equipment and analytical devices

The equipment and analytical devices utilized within the study are listed in (Table 1).

Table 1. Equipment and analytical devices utilized throughout the study.

Equipments and analytical devices	Company-Origin
Biochemistry analyzer	Mindray-China
Centrifuge device	Hettich-Germany

ELISA system	Mindray-China
Immunofluorescence analyzer	Boditech-South Korea
Incubator	ESCO-Lithuania
Multichannel pipette	Thermo Scientific- Germany
Pipette	Thermo Scientific- Germany
Printer	Canon-Taiwan
Refrigerator	LG- South Korea
Tips	IMC-China
Water path	Memmert-Germany

2.1.2 Kits

The study used specific kits, including those for measuring Endocan and Interleukin-10 (from Mybiosource, USA), as well as kits for evaluating HbA1c, blood glucose, serum creatinine, blood urea, and other lipid markers (from Mindray, China).

2.2 Methods

2.2.1 Participants

The kits utilized within the study are listed in (Table 2.).

Table 2. Kits utilized in the study.

No	Kit	Company-Origin
1	Endocan	Mybiosource-USA
2	Interleukin-10	Mybiosource-USA
3	HbA1c, Blood glucose, Blood urea, Serum creatinine, TC, TG, and HDL	Mindray-China

2.2.2 Samples collection

Blood samples were collected from each participant. Five millilitres were divided into two tubes: 3 mL in a gel tube for serum separation (processed by centrifugation), and 2 mL in an EDTA tube for HbA1c evaluation. The serum was stored at -20°C for further analysis.

2.2.3 Human endocan

The Human Endocan levels were measured using a sandwich ELISA method. Anti-Human Endocan antibodies were pre-coated onto a 96-well plate, and biotin-labeled detection antibodies were used. After adding the specimen and performing a series of wash steps, HRP-Streptavidin was added, followed by a substrate solution to generate a color change. The concentration of Human Endocan was determined by measuring the optical density at 450 nm (Figure 1).

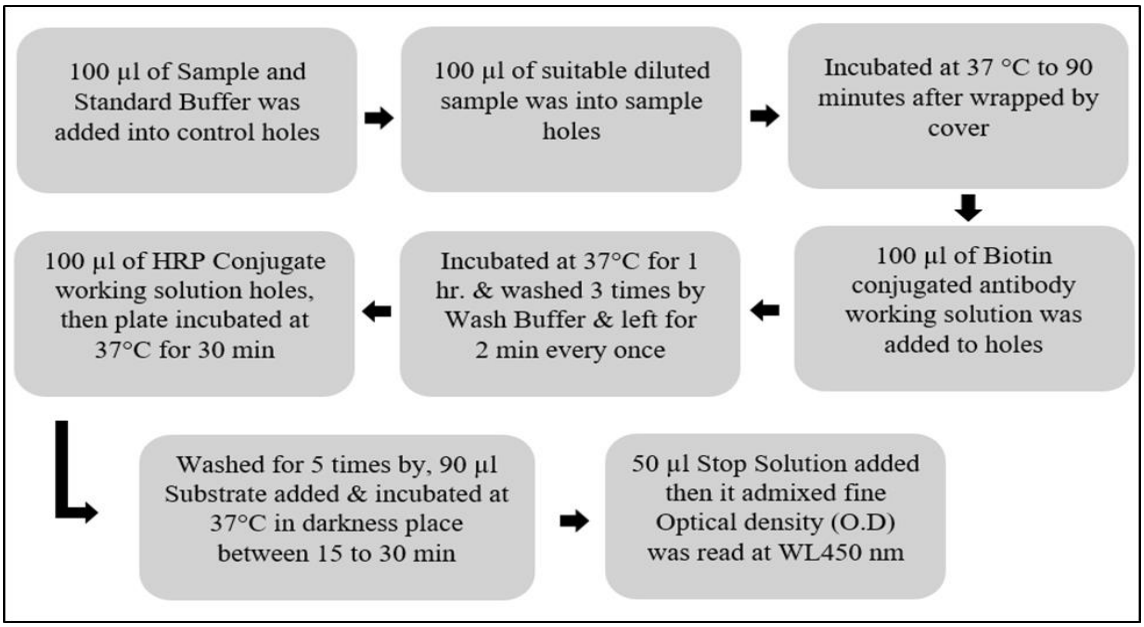

Fig.1. Diagram of endocan assay.

2.2.4 Human interleukin-10

The concentration of Human Interleukin-10 was measured using a sandwich ELISA method. Anti-Human Interleukin-10 antibodies were pre-coated onto a 96-well plate, and biotin-labeled detection antibodies were used. After incubation and washing, HRP-Streptavidin was added to initiate a color change, which was measured at 450

nm. The optical density of the yellow color produced was proportional to the concentration of Interleukin-10 in the sample (Figure 2).

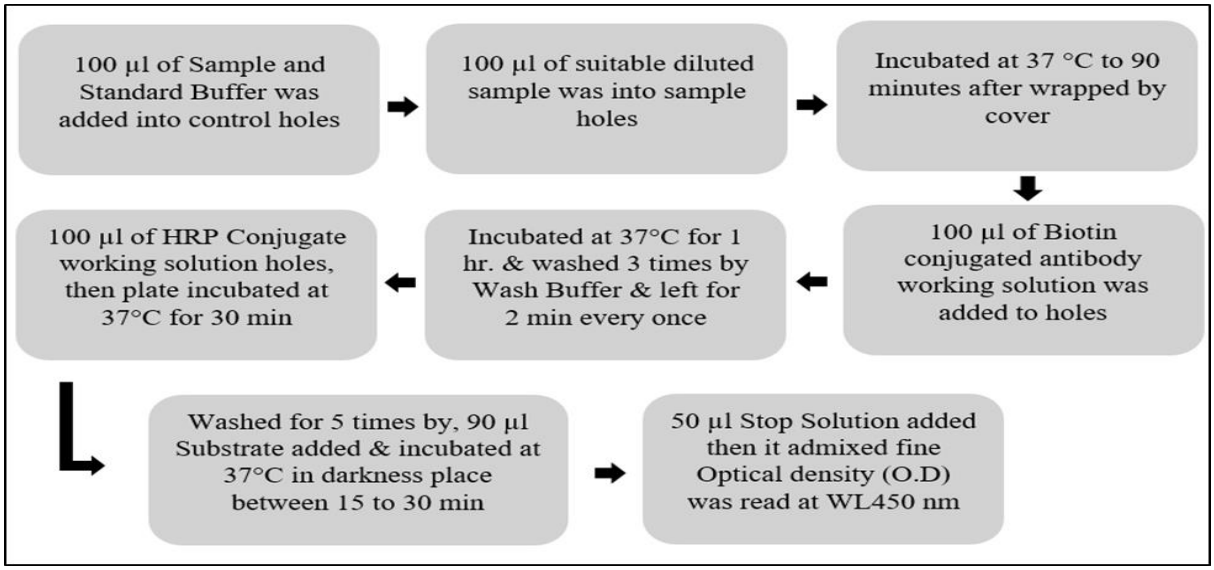

Fig. 2. Diagram of Interleukin-10.

2.2.5 Serum creatinine

Serum creatinine was measured using a colorimetric reaction with alkaline picrate. The creatinine in the sample reacts with picrate, and the color change is measured kinetically at a wavelength of 490 nm. The analysis was performed automatically using a biochemistry analyzer.

2.2.6 Blood urea

Blood urea levels were measured using an enzymatic and colorimetric method where urease breaks down urea into ammonium ions, which then form a blue-green complex with chloride and salicylate. The results were automatically obtained using a biochemistry analyzer.

2.2.7 Blood glucose

Blood glucose was measured using the Trinder method, where glucose is oxidized to gluconic acid and hydrogen peroxide by glucose oxidase. The peroxide reacts with 4-amino-antipyrine and chloro-4-phenol to produce a red-colored compound, which is measured at 500 nm using a biochemistry analyzer.

2.2.8 HbA1c

The HbA1c test uses a sandwich method to detect immune complexes formed between the antigen in the reagent and the sample. The intensity of fluorescence generated by these complexes is proportional to the percentage of glycated hemoglobin in the blood, and results were obtained automatically using a biochemistry analyzer.

2.2.9 Total Cholesterol

Total cholesterol levels were measured through an enzyme-catalyzed hydrolysis and oxidation process. The product, quinone-imine, is synthesized by peroxidase from 4-amino-antipyrine and phenol, and the concentration is determined using a biochemistry analyzer.

2.2.10 Triglycerides

Triglycerides were measured by breaking down lipoproteins using lipolysis enzymes. The resulting compound, quinone imine, was formed by peroxidase and hydrogen peroxide reacting with 4-amino antipyrine and 4-chlorophenol. Results were obtained automatically using a biochemistry analyzer.

2.2.11 High-density lipoprotein

High-Density Lipoprotein (HDL) was measured using a homogeneous method without centrifugation. Specific antibodies bound to HDL cholesterol, allowing selective measurement of HDL-cholesterol through an enzymatic test, and the results were obtained automatically using a biochemistry analyzer.

2.2.12 Low-density lipoprotein and very low-density lipoprotein

Low-Density Lipoprotein (LDL) and Very Low-Density Lipoprotein (VLDL) were calculated using the formulas: LDL = TC - HDL - VLDL and VLDL = TG/5.

2.3 Statistical analysis

The statistical analysis was performed using SPSS 21.0 and Microsoft Excel 2013. Numerical data were presented as mean and standard deviation, and the independent sample t-test was used for group comparisons. Categorical data were analyzed using the chi-square test, with statistical significance set at $p \leq 0.05$.

3. Results and Discussion

3.1 Demographic characteristics of the study groups

3.1.1 Age of study population

This study included 200 participants divided into four groups with a mean age of 49.88±6.14 for the healthy control, 55.32±6.39 for angina pectoris patients, 52.30±6.32 for ischemic heart disease patients, and 53.28±6.37 for myocardial infarction patients. Statistically significant age differences ($p < 0.001$) were found across the groups. Cardiovascular diseases like ischemic heart disease, myocardial infarction, and angina pectoris predominantly affect individuals over 50, especially in Iraq, and are often associated with factors such as atherosclerosis, hypertension, diabetes, and smoking. Age-related endothelial dysfunction, chronic inflammation, and oxidative stress also contribute to increased cardiovascular risk, underscoring the importance of managing these risk factors to prevent disease progression in older adults (Figure 3).

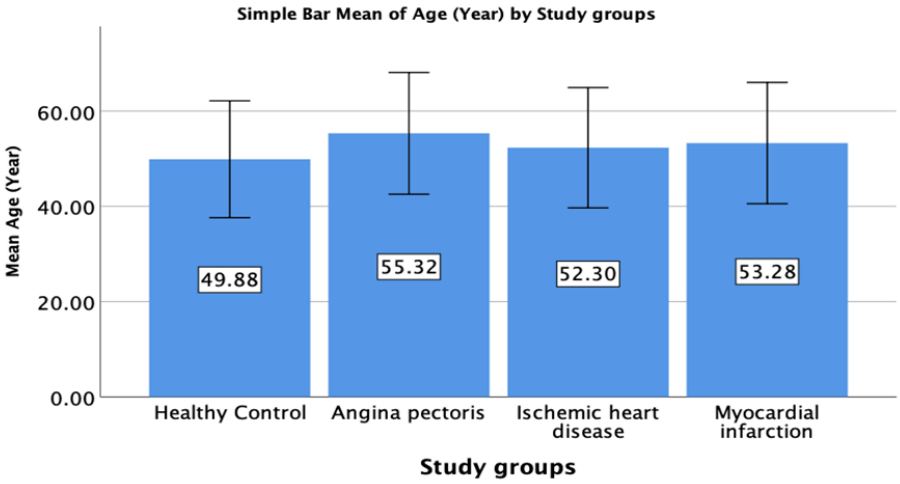

Fig. 3. Age distribution across all study groups' population.

3.1.2. Distribution of study population groups according to sex

The study observed a higher prevalence of males in the groups with ischemic heart disease, myocardial infarction, and the control group, while an equal distribution of sexes was seen in the angina pectoris group. However, there were no statistically significant sex differences across the groups (p-value 0.287). Cardiovascular disease characteristics vary notably between men and women due to biological, hormonal, and lifestyle differences. Men are generally more susceptible to these conditions, partly due to the protective effects of estrogen in premenopausal women, which helps maintain vascular health and reduces atherosclerosis risk. Testosterone, linked to risk factors like smoking and obesity, may also play a role. Additional factors influencing sex-based differences in cardiovascular disease include anatomical variations, lifestyle choices, and responses to stress, with men often at higher risk due to lifestyle patterns, larger heart size, and higher smoking rates (Table 3)

Table 3. Study population groups stratified according to sex distribution.

		Study groups			
		Healthy Control	Angina pectoris	Ischemic heart disease	Myocardial infarction
Sex	Female	20	25	23	16
		40.00%	50.00%	46.00%	32.00%
	Male	30	25	27	34
		60.00%	50.00%	54.00%	68.00%
Total		50	50	50	50
p-value				0.287	

3.2 Endocan serum levels of study groups

The study revealed that endocan serum levels were significantly elevated in all patient groups compared to the healthy control group, with the highest levels observed in myocardial infarction patients (2.14±0.19 ng/ml), followed by ischemic heart disease (1.72±0.19 ng/ml) and angina pectoris patients (1.2±0.15 ng/ml), and the lowest in the control group (0.76±0.17 ng/ml), with high statistical significance (p-value <0.001). Endocan, a vascular endothelial proteoglycan, has become a critical biomarker in cardiovascular disorders due to its involvement in inflammation, endothelial dysfunction, and plaque development. Elevated endocan levels indicate systemic inflammation, which accelerates atherosclerosis and myocardial infarction risks. Endocan's influence on endothelial function—such as impaired vasodilation and increased vascular permeability supports its role in advancing ischemic heart disease. Furthermore, high endocan levels correlate with plaque instability, linked to myocardial infarction and unstable angina. This study aligns with prior research, reinforcing endocan as a marker for cardiovascular disease diagnosis, prognosis, and as a potential therapeutic target. Further research is essential to clarify its therapeutic applicability and mechanisms in cardiovascular disease management (Figure 4).

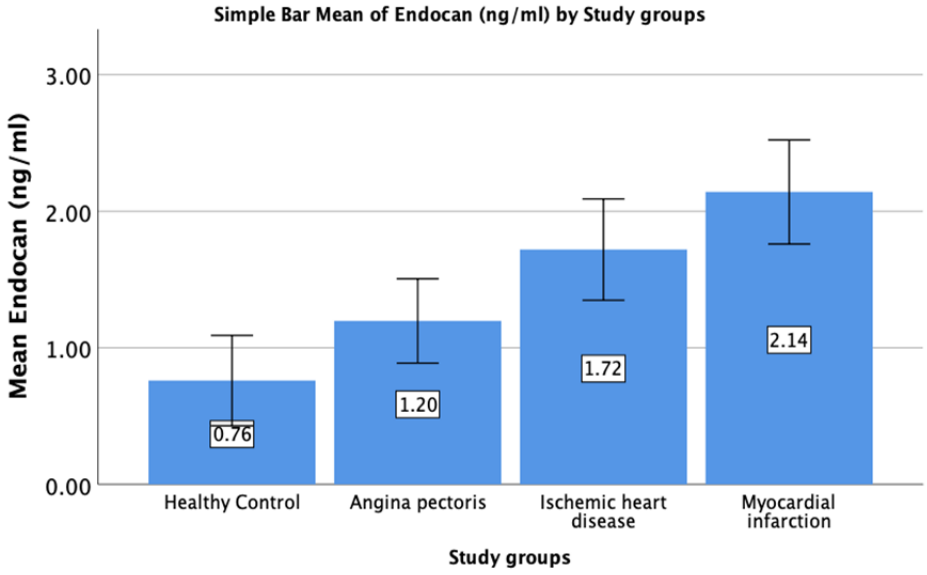

Fig. 4. Endocan serum levels between study populations.

3.3 Interleukin-10 (IL-10) serum levels of study groups

This study revealed that IL-10 serum levels were significantly higher in all patient groups compared to the healthy control group (Figure 5). Myocardial infarction patients showed the highest IL-10 levels (57.01±8.15 pg/ml), followed by ischemic heart disease patients (46.19±7.61 pg/ml) and angina pectoris patients (40.69±6.93 pg/ml), with the lowest levels found in the healthy control group (1.96±0.4 pg/ml). These results were statistically significant (p-value <0.001). IL-10 is an acid-labile anti-inflammatory cytokine that plays a crucial role in regulating and suppressing inflammation, especially following cardiac events. Its timing in the re-perfused myocardium after post ischemia owing to modified macrophage activity greatly reduces the influence plastic changes exert on the matrix and aids in tissue repair. In athero-sclerosis, for instance, greater IL-10 levels occur in cardiovascular patients owing to tissue damage

and inflammation and IL-10 is secreted for mitigating the inflammation. The present findings support other findings in the course of this research in which it was demonstrated that CAD was associated with an increase in serum IL-10 and it was shown that IL-10 decreased T-cell and macrophage responses and angiogenesis. The study of the function of IL-10 in these patients may provide the basis for development of novel strategies to treat IL-10 mediated cardiovascular diseases associated with inflammation.

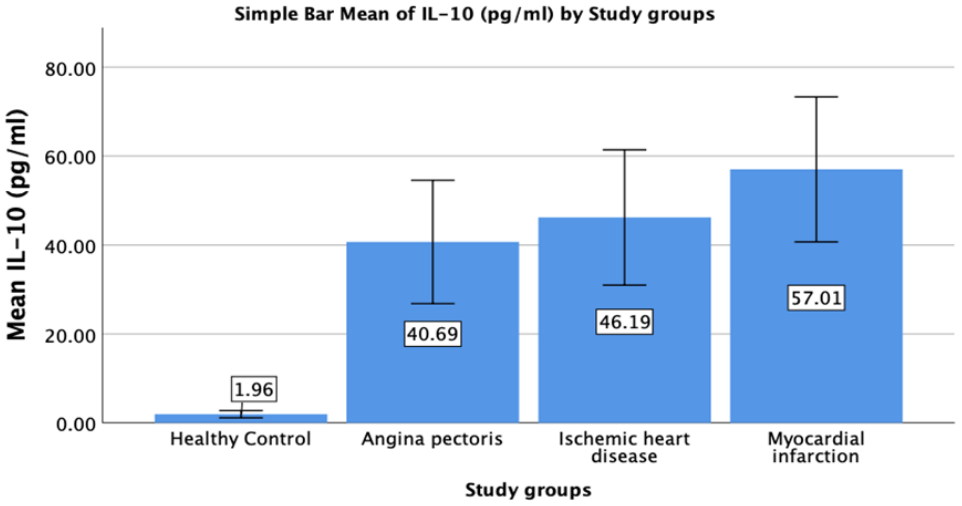

Fig. 5. IL-10 serum levels between study populations.

3. 4 Renal functions

3.4.1 Blood urea concentration of study groups

In contrast to the control group, whose blood urea mean levels averaged 22.72±2.09 mg/dL, those suffering from myocardial infarction, ischemic heart disease, and angina pectoris had significantly higher levels: 33.02±5.59 mg/dL, 30.42±3.83 mg/dL, and 27.28±2.63 mg/dL respectively. Blood urea concentration differences across the mentioned study groups are also very statistically significant (p-value <0.001), as is shown in figure 6.

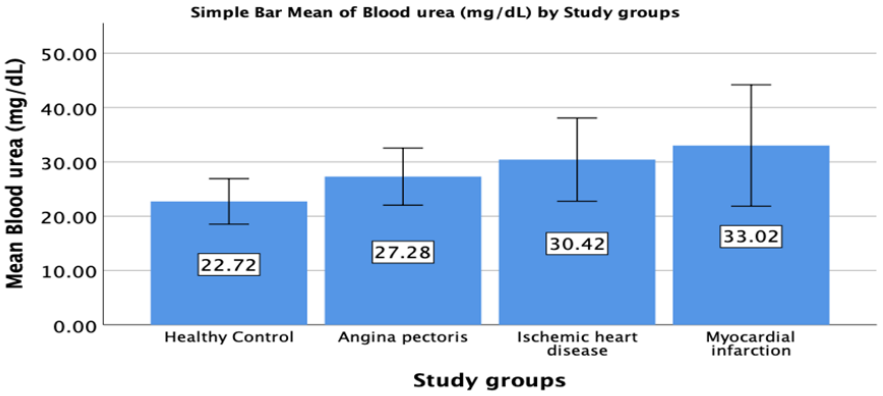

Fig. 6. Comparisons of blood urea concentration between study groups.

3.4.2 Creatinine serum concentration of study groups

This study showed that serum creatinine levels were significantly higher in patients with myocardial infarction (0.9±0.12 mg/dL), ischemic heart disease (0.88±0.09 mg/dL), and angina pectoris (0.79±0.09 mg/dL) than in the healthy control group (0.71±0.1 mg/dL), with a highly significant difference (p-value <0.001). Elevated blood urea and creatinine levels in cardiovascular patients suggest potential renal impairment, which may result from factors like acute kidney injury, reduced renal perfusion, infections, atherosclerosis, and hypertension. These renal function indicators highlight the importance of monitoring kidney health in patients with cardiovascular diseases to prevent further deterioration (Figure 7).

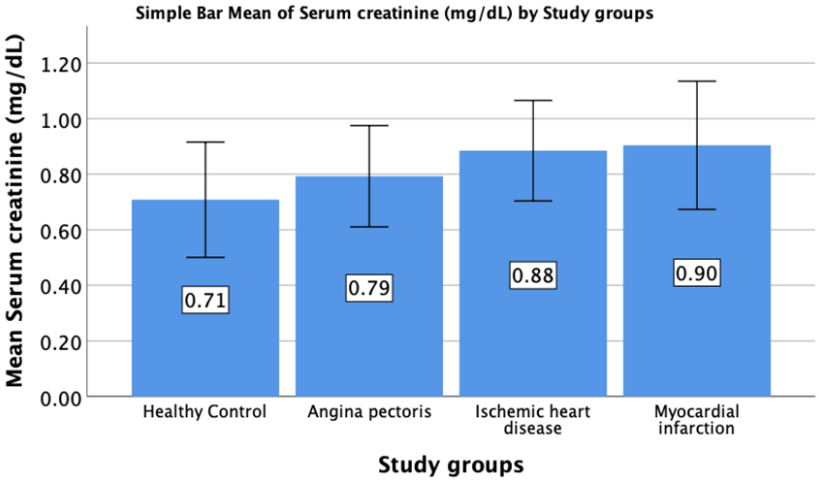

Fig. 7. Comparisons of creatinine serum concentration between study groups.

3.5 Blood glucose indices

3.5.1 Fasting blood glucose of the study groups

The mean serum fasting glucose levels were significantly higher in patients with myocardial infarction (130.12±22.18 mg/dL) compared to those with ischemic heart disease (125.46±24.65 mg/dL) and angina pectoris (111.64±13.51 mg/dL) (Figure 8). All patient groups exhibited elevated serum fasting glucose levels compared to healthy controls (90.04±5.24 mg/dL). These disparities were statistically significant (p-value <0.001) across all groups.

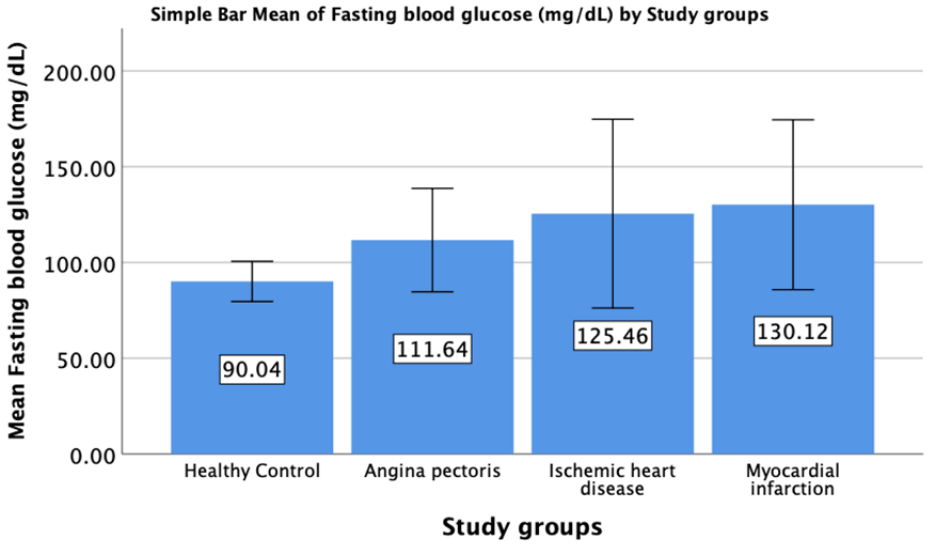

Fig. 8. Comparisons of fasting glucose serum levels between study groups.

3.5.2 Hemoglobin A1c (HbA1c) blood concentration of the study groups

The study found significantly higher HbA1c blood concentrations in patients with myocardial infarction (6.37±0.61%), ischemic heart disease (6.19±0.71%), and angina pectoris (6.05±0.53%) compared to the healthy control group (5.21±0.34%), with a statistically significant difference (p-value <0.001). These elevated HbA1c levels indicate impaired glucose metabolism, a known risk factor for cardiovascular diseases. Diabetes and cardiovascular diseases are closely linked, with diabetes increasing the prevalence of coronary heart disease and stroke. Elevated glucose levels contribute to endothelial damage, inflammation, and increased clotting, further exacerbating cardiovascular risk. Understanding the relationship between HbA1c and cardiovascular conditions can aid in better prevention and treatment strategies (Figure 9).

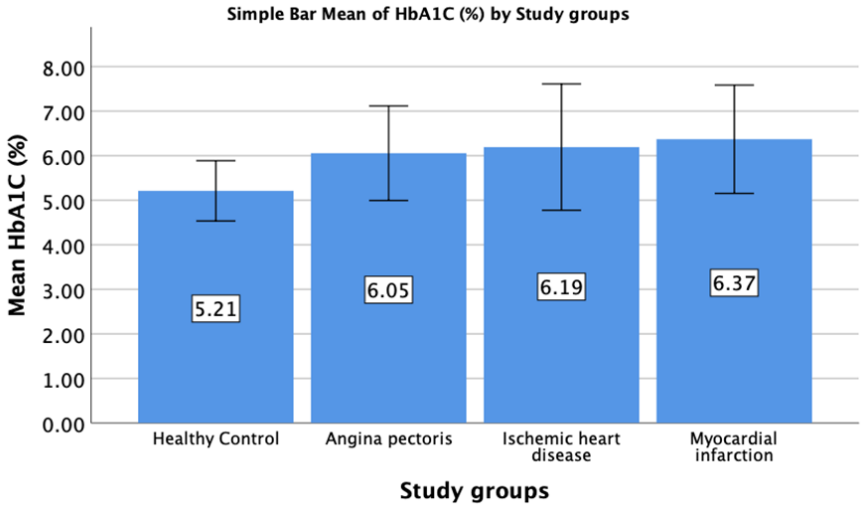

Fig. 9. Comparisons of HbA1c blood concentrations between study groups.

3.6 Lipid profile

3.6.1 Total cholesterol (TCL) of the study groups

All patient groups showed elevated TCL compared to the healthy control group (Figure 10). Additionally, the myocardial infarction patients exhibit higher TCL concentrations (172.60±22.13 mg/dL) than ischemic heart disease (132.7±18.56 mg/dL) and angina pectoris patients (111.08±16.97 mg/dL), while, the healthy control group showed lower TCL concentration (92.64±15.53 mg/dL).

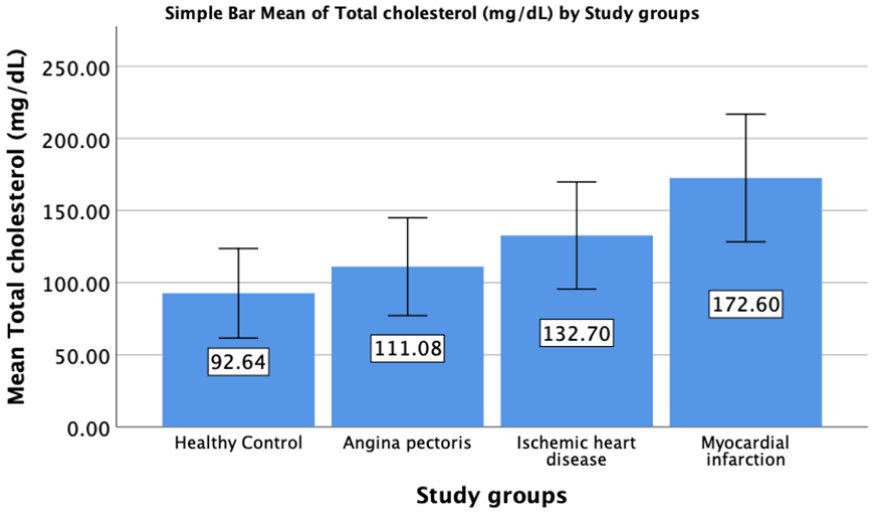

Fig. 10. Comparisons of total cholesterol concentrations between study groups.

3.6.2 Triglyceride (TG) of the study groups

All patient groups exhibited elevated TG levels compared to the healthy control group (Figure 11). Notably, myocardial infarction patients displayed the highest TG concentrations (239.46±40.94 mg/dL), surpassing those observed in ischemic heart disease (179.62±42.97 mg/dL) and angina pectoris patients (119.4±41.08 mg/dL). Conversely, the healthy control group exhibited significantly lower TG levels (39.28±24.21 mg/dL).

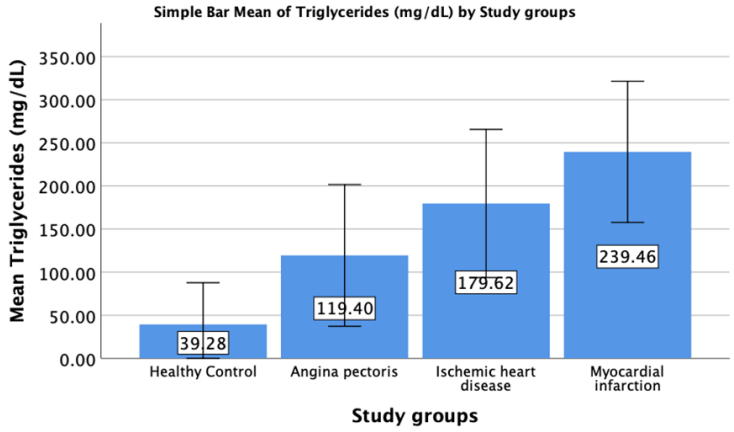

Fig. 11. Comparisons of triglyceride concentrations between study groups

3.6.3 High-density lipoprotein (HDL) of the study groups

The data presented in figure 12 revealed that patients with myocardial infraction exhibited lower HDL concentrations (27.96±5.7 mg/dL) than all study groups, followed by ischemic heart disease patients (29.48±5.8 mg/dL) and angina pectoris patients (30.92±5.78 mg/dL). In contrast, the healthy control individuals showed higher HDL concentrations (42±5.77 mg/dL) than all patient groups.

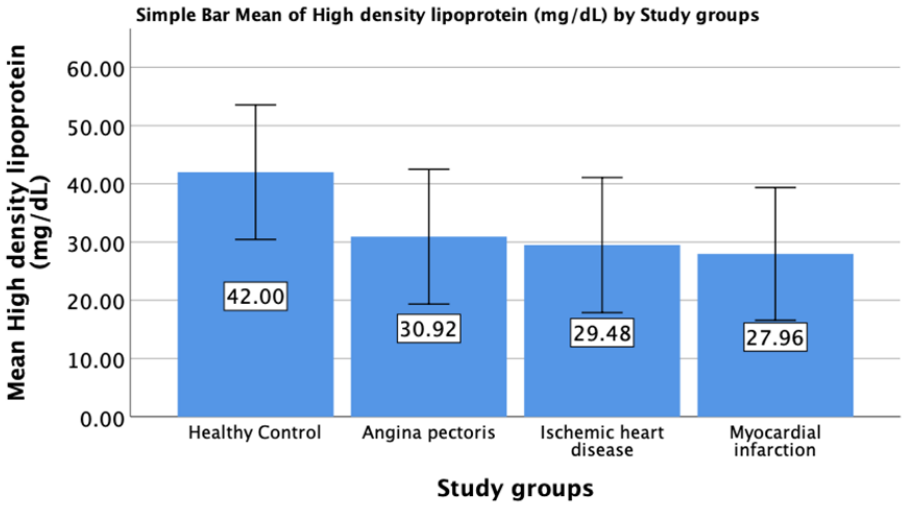

Fig. 12. Comparisons of high-density lipoprotein concentrations between study groups.

3.6.4 Low-density lipoprotein (LDL)

All patient cohorts had increased LDL levels compared to the healthy control group (Figure 13). Furthermore, patients with myocardial infarction have elevated LDL levels (96.75±22.14 mg/dL) compared to those with ischemic heart disease (67.3±20.38 mg/dL) and angina pectoris (56.28±20.64 mg/dL). Meanwhile, the healthy control group has a reduced LDL concentration (42.78±18.31 mg/dL).

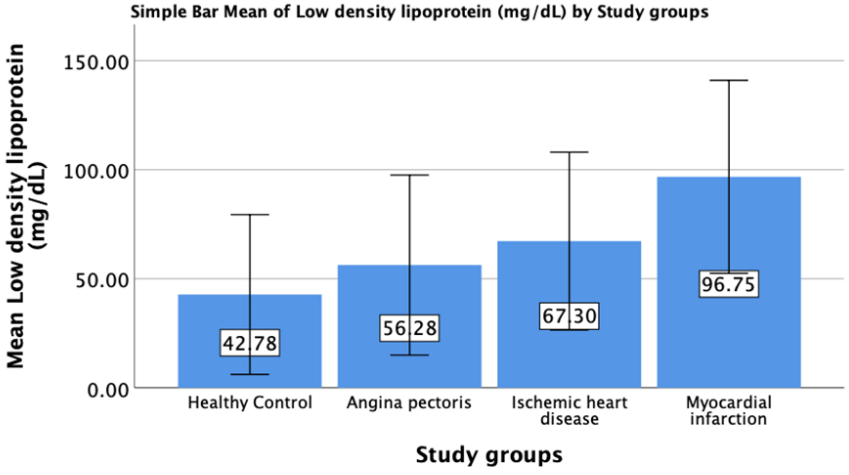

Fig. 13. Comparisons of low-density lipoprotein concentrations between study groups.

3.6.5 Very low-density lipoprotein (VLDL)

All patient groups exhibited elevated VLDL levels compared to the healthy control group. Notably, myocardial infarction patients displayed the highest VLDL concentrations (47.89±8.19 mg/dL), surpassing those observed in ischemic heart disease (35.92±8.59 mg/dL) and angina pectoris patients (23.88±8.22 mg/dL). Conversely, the healthy control group exhibited significantly lower VLDL levels (7.86±4.84 mg/dL) (Figure 14).

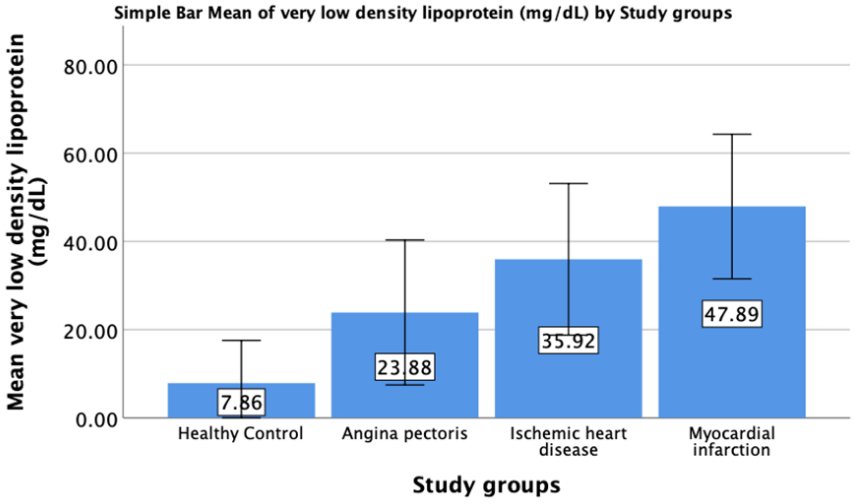

Fig. 14. Comparisons of very low-density lipoprotein concentrations between study groups.

Dyslipidemia, characterized by abnormal lipid levels such as increased total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG), along with decreased high-density lipoprotein cholesterol (HDL-C), is a major risk factor for cardiovascular and cerebrovascular diseases, including stroke and myocardial infarction. The study found elevated cholesterol levels and decreased HDL-C in patients, which aligns with the established link between high cholesterol, atherosclerosis, and cardiovascular disease. Elevated LDL-C and triglycerides contribute to plaque formation in arteries, promoting inflammation and narrowing blood vessels, increasing the risk of cardiovascular events.

4. Conclusions

Patients over 50 are more susceptible to cardiovascular diseases, with age-related factors like arterial stiffening and heart muscle weakening playing key roles. Older males have a higher incidence of ischemic heart disease and angina, likely due to hormonal, genetic, and lifestyle factors. Higher endocan levels in patients highlight its role as a proinflammatory biomarker in cardiovascular disease. Increased IL-10 levels reflect the body's anti-inflammatory response in cardiovascular conditions. Elevated blood urea, creatinine, glucose, HbA1c, and abnormal lipid profiles indicate kidney dysfunction, dysglycemia, and dyslipidemia, all contributing significantly to cardiovascular disease risk.

Author Contribution

Ghadah Azeez Khaleefah, Youssra Al-Hilaly, Rayane Mahious, Ebru Halvacı; wrote, edited, drew figures and developed the article. Fatih Sen; supervisor and responsible person.

Acknowledgments

The authors dedicated this publication to the 100th anniversary of the Republic of Türkiye. As scientists raised by Türkiye, they are proud to be citizens of this country.

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