GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 7-8 (364-365) Июль-Август 2025

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

GEORGIAN MEDICAL NEWS
NO 7-8 (364-365) 2025

Содержание:

GEORGIAN MEDICAL NEWS
No 7-8 (364-365) 2025

PATTERNS OF ACETYLCHOLINESTERASE AND BUTYRYLCHOLINESTERASE ACTIVITY IN COMMON CARDIOVASCULAR PHENOTYPES

Arkam Thabit Al Neama*, Musab Mohammed Khalaf, Ahmed A.J. Mahmood.

College of Pharmacy, University of Mosul, Mosul, Iraq.

Abstract.

Background: Cardiovascular disease (CVD) is characterized by autonomic nervous system imbalance and chronic low-grade inflammation, processes reflected by the activity of blood cholinesterase enzymes—acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). Given this link, the study set out to determine whether blood AChE and BChE activities differ among patients with common cardiovascular conditions (hypertension, ischemic heart disease, heart failure, and isolated dyslipidemia) compared to healthy individuals, and whether these enzymes levels correlate with disease severity or control status.

Methods: Plasma BChE and erythrocyte AChE activities were measured in 298 adults (age 30–55 years) between December 2024 and May 2025. The patients were divided to group with either hypertension (HTN), or with ischemic heart disease (IHD), or with heart failure (HF), or with isolated dyslipidemia (DLIP), alongside with 30 healthy controls. Each patient was further classified as controlled or uncontrolled (based on achieving guideline blood pressure or disease targets) and as uncomplicated or complicated (depending on the presence of co-morbid conditions). Cholinesterase activity was quantified using an electrometric assay. Group comparisons were performed with Student's t-tests, using a significance threshold of $\alpha = 0.05$.

Results: Patients with poorly controlled hypertension and co-morbid complications showed the greatest reductions in cholinesterase activity: their mean BChE was 1.05 ± 0.17 and AChE 0.92 ± 0.12, significantly lower than in healthy controls (1.16 ± 0.14 and 0.98 ± 0.01, respectively; $p < 0.05$). Heart failure cases had uniformly low enzyme levels regardless of disease control status, with BChE ranging 0.93–0.98 and AChE 0.83–0.86. In IHD, cholinesterase patterns were heterogeneous: only the extreme subgroups (those who were controlled without complications and those uncontrolled with complications) had activities significantly different from controls, indicating intermediate values in other IHD patients. In contrast, individuals with isolated dyslipidemia exhibited elevated cholinesterase levels (BChE 1.22 ± 0.11; AChE 1.08 ± 0.07) relative to controls. Notably, neither the class of medications used, polypharmacy (multiple concurrent drugs), nor the presence of additional co-morbidities had any independent effect on AChE or BChE levels.

Conclusion: Declining blood cholinesterase activity correlates with worsening cardiovascular status: it progressively decreases with poorer control of hypertension and reaches the lowest levels in heart failure, whereas isolated dyslipidemia is associated with higher cholinesterase activity, with IHD patients showing intermediate changes. Routine measurement of plasma and erythrocyte cholinesterase could thus serve as a simple, inexpensive indicator of autonomic/inflammatory stress in CVD and help refine risk stratification if interpreted in the context of the patient's lipid profile. Larger prospective multicenter studies are warranted to validate these findings and to establish prognostic cutoff values for cholinesterase activity in cardiovascular risk assessment.

Key words. Acetylcholinesterase, butyrylcholinesterase, cardiovascular disease, cholinesterase.

Introduction.

Cardiovascular diseases (CVDs) are the leading global cause of death, responsible for an estimated 17.9 million deaths annually, and this toll is projected to rise to 23.6 million by 2030 [1,2]. CVD is a broad term that includes various disorders of the heart and vascular system. Among its most prevalent forms are hypertension [3], ischemic heart disease (IHD)—which results from restricted blood flow to the myocardium—and heart failure (HF), a condition marked by the heart's inability to pump sufficient blood to meet metabolic demands [4].

Emerging evidence points to inflammation and oxidative stress as central contributors to vascular dysfunction in CVD, exacerbating endothelial damage and atherosclerosis. The findings from the last 5 years indicate that inflammatory mechanisms contribute to the pathophysiology of hypertension [5]. Moreover, the presence of renal and vascular inflammation may exacerbate oxidative stress and compromise endothelial function, thereby promoting the progression of atherosclerosis [6].

The cholinesterase (ChE) enzyme family includes only two members: acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). Both enzymes have numerous physiological functions depending on their localization and time of expression [7]. Because the parasympathetic neurotransmitter acetylcholine (ACh) has a very short half-life and is highly unstable and challenging to measure in the bloodstream, its homologous hydrolyzing enzymes—AChE and BChE—can serve as indirect indicators [8]. BChE is the major ACh-hydrolyzing enzyme in the circulatory system [9]. By breaking down ACh, these enzymes provide a surrogate measure of parasympathetic function. This method thus offers a practical alternative to direct ACh measurement.

The cholinergic anti-inflammatory pathway is mediated by the vagus nerve and ACh, which interacts with the alpha-7 subtype of nicotinic acetylcholine receptor on immune cells to suppress inflammation. This pathway is closely linked to the

activity of ChE enzymes [10]. Accumulating evidence suggests that altered ChE activity may reflect systemic inflammation and metabolic alterations commonly associated with hypertension [11], heart failure [12,13], and ischemic heart conditions. These changes could serve as useful biomarkers for disease diagnosis, prognosis, and treatment monitoring.

Despite growing interest in ChEs, their clinical utility as biomarkers for differentiating cardiovascular phenotypes—such as controlled vs. uncontrolled hypertension, IHD, and HF—remains underexplored. This study aims to evaluate plasma ChE activity across different CVD subgroups to explore its potential diagnostic and prognostic value.

Materials and Methods.

Study design and setting: This cross-sectional study conducted in Duhok City (Iraq) was approved by The Postgraduate Studies Committee at the College of Pharmacy-University of Mosul and the institutional ethics committee of the Duhok Directorate General of Health approved the study protocol (Reference number 27112024-10-3). All the patients signed the informed consent form. the study excluded patients with conditions associated with decreased levels of ChE, i.e., liver disease (hepatitis, cirrhosis, and malignancy), malignancies, chronic renal failure, nephrotic syndrome, and toxic goiter, were excluded from the study. A total of 298 subjects were enrolled and subdivided into

I. **Hypertension (HTN) Group:** This group included 111 patients, further subdivided into four subgroups based on blood pressure control and the presence or absence of complications:
1. Uncontrolled HTN with complications: 29 patients
2. Controlled HTN with complications: 32 patients
3. Uncontrolled HTN without complications: 25 patients
4. Controlled HTN without complications: 25 patients

II. **Ischemic Heart Disease (IHD) Group:** This group consisted of 112 patients, subdivided into
1. Uncontrolled IHD with complications: 25 patients
2. Controlled IHD with complications: 37 patients
3. Controlled IHD without complications: 25 patients
4. Uncontrolled IHD without complications: 25 patients

III. **Heart Failure (HF) Group:** Comprised of 50 patients, divided into
1. Uncontrolled HF with complications: 25 patients
2. Controlled HF with complications: 25 patients

Each patient will be categorized as "controlled" or "uncontrolled" based on whether their disease indicators (e.g. blood pressure in hypertension, cardiac biomarkers in IHD or HF) meet current clinical targets and further classified as 'uncomplicated' or 'complicated' depending on the presence of one or more comorbid conditions. In addition to the above, the isolated dyslipidemia (DLIP) group will be compared to an apparently healthy control group.

Blood Sampling, Processing, and Storage:

A 5 mL of fasting venous blood sample was collected from participants by venipuncture with aseptic precautions. The blood samples were collected in an EDTA tube and centrifuged at 3000 rpm for 10 min. Then the plasma and RBC were separated and deeply frozen at –20°C until the analysis. Lipid measured based on manufacturer instruction with kit supplied by Roche cobas, (Germany).

Electrometric assay of ChE activity:

The experimental procedure began by creating a reaction mixture in a 10 ml beaker. This mixture comprised 3 ml of distilled water, 0.2 ml of either plasma or erythrocytes, and 3 ml of a barbital-phosphate buffer, which had a pH of 8.1 [14]. The initial pH of this prepared mixture (pH1) was recorded using a pH meter equipped with a glass electrode. Next, 0.1 ml of a 7.5% aqueous acetylcholine solution was added. The reaction mixture was then incubated at 37°C in a water bath for 20 minutes. Following incubation, the final pH (pH2) of the mixture was measured. Enzyme activity was then determined as the change in pH over 20 minutes (ΔpH / 20 min.), calculated by subtracting the ΔpH of a blank from the observed ΔpH [15,16].

ChE activity (ΔpH/20 min.) = (pH1-pH2)-ΔpH of blank

The blank, which served as a control, was prepared identically to the reaction mixture but notably lacked the blood aliquot (plasma or erythrocytes). The barbital-phosphate buffer solution itself was formulated by dissolving 1.24 g of sodium barbital, 0.163 g of potassium dihydrogen phosphate, and 35.07 g of sodium chloride in one liter of distilled water, with its pH meticulously adjusted to 8.1 using 0.5 N HCl.

Statistical analysis: Data expressed as mean and standard deviation. Minitab18 program and sigma plot 12.5 were used to conduct statistical analysis using ANOVA (One-way analysis of variance) test with post-hoc Turkey's test to determine significant group at p value of less than 0.05.

Results.

HTN group:

The hypertension group contained 111 patients hypertensive patients (controlled, uncontrolled, or complicated). Human plasma and erythrocyte ChE activity were tested in all of them, and they were subdivided into four groups based on their clinical diagnoses (Table 1).

To further differentiate the results and rule out the influence of other conditions in complicated cases, each complicated subgroup from Table 1 was subclassified. This subclassification was based on whether patients had single or multiple complicated diseases, and their plasma and RBC ChEs levels were then compared with the control group. This step aims to clarify if these comorbid diseases affect ChEs levels. Table 2 presents the complicated disease groups, organized according to the distribution of ChE levels for the mean of both plasma and RBC ChE.

The results presented in Table 2 indicate that no specific complicated diseases, whether alone or in combination, affect both ChE levels. All complicated diseases that demonstrated significant differences in ChE levels compared to the control group also showed no significant differences in other cases, regardless of whether they occurred alone or in combination, and across both controlled and uncontrolled groups. This suggests that complicated diseases in hypertensive patients have no direct effect on ChE levels. Instead, any correlation is solely with the severity and poor control of hypertension, as previously noted in Table 1.

IHD Group:

The IHD group contained 112 patients, they included controlled, uncontrolled, or complicated cases. Human plasma and erythrocyte ChE activity were also tested in all of them, and they were subdivided into four groups based on their clinical diagnoses, as in the HTN group (Table 3).

To account for the potential influence of other conditions in complicated cases, each complicated subgroup from Table 7 was further broken down. This subclassification considered whether patients presented with a single complicating disease or multiple, and their plasma and RBC ChE levels were subsequently compared to the control group. Much like the HTN group analysis, this step aims to clarify if these co-occurring diseases impact ChE levels. Table 4 details these complicated disease groups, arranged by the distribution of their mean plasma and RBC ChE levels.

Heart Failure (HF) group:

The HF group includes 50 patients HF patients (controlled, uncontrolled, with both being complicated). Human plasma and erythrocyte ChE activity were tested in all of them, and they were subdivided into two groups based on their clinical diagnoses (Table 5).

To further refine these results and, as previously done for the HTN and IHD groups, to account for the potential influence of other conditions in complicated cases, each complicated subgroup from Table 5 was further categorized. This subclassification was determined by whether patients suffered from a single complicating disease or multiple, and their ChE levels were subsequently compared against the control group. Table 6 details these complicated disease groups, arranged according to the distribution of their mean plasma and RBC ChE levels.

Dyslipidemia group (DLIP):

Hyperlipidemia (DLIP) is highly related to cardiac diseases, as both conditions can cause or worsen each other's morbidity. In many cases, DLIP may be associated with cardiac diseases without being diagnosed by a physician or known by the patients. Numerous research papers indicate the association of dyslipidemia states with the ChE enzyme. Thus, this DLIP group was initiated to eliminate or cancel the effect of DLIP on ChEs in all the aforementioned cardiac disease groups (if it existed and wasn't diagnosed). The DLIP group contained hyperlipidemic patients diagnosed with only hyperlipidemia, without any complicated or associated diseases. Hyperlipidemia, including high total cholesterol (TC), high total triglyceride (TG), high low-density lipoprotein cholesterol (LDL-C), and lowered high-density lipoprotein cholesterol (HDL-C), all of which may be present either individually or in various combinations Human plasma and erythrocyte cholinesterase activity were tested for this group (Table 7).

To further differentiate the correlations of this group with ChE levels, the raw results for this group were arranged based on their ChE ranges and compared with the control group. This step will also provide a clear understanding of the distributions of the ChE levels within this group, highlighting their significant deviations (either above or below) from the control group. Table 8 presents the ranged data according to the distribution of mean plasma and RBC ChE levels.

Discussion.

In hypertension, the results demonstrated a decrease in plasma ChEs (BChE) that is less pronounced than the decrease observed in RBC ChE (AChE). A significant decrease appeared in the RBCs groups (with the exception of the controlled uncomplicated group), while the uncontrolled uncomplicated group was the only group to show a significant decrease in RBC plasma ChEs compared to the control group. The complicated, uncontrolled group exhibited the lowest results in both ChE types. This suggests a correlation between ChEs activity and the progression of hypertension. Specifically, more uncontrolled and complicated hypertensive patients will have lower AChE, while BChE will be less affected. Research by de Carvalho Correa et al. (2008) indicated a decrease in RBC ChE in uncomplicated hypertensive patients. Specifically, their study of 20 hypertensive individuals showed significantly reduced erythrocyte AChE activity when compared to healthy controls, suggesting that HTN is associated with impaired peripheral cholinergic function [17].

However, other studies offer a different perspective. Tangvarasittichai et al. (2014) reported that elevated BChE co-occurred with a higher prevalence of HTN in abdominally obese subjects [18]. Another study similarly described elevated BChE activity as accompanying arterial HTN and mirroring an underlying low-grade inflammatory state [18]. Mahmoud et al. (2013) further supported this in a cross-sectional cohort

Table 1. *Plasma and RBC ChEs levels in hypertensive groups.*

Group	No of Cases	SBP ± SD	DBP± SD	Δ pH/20 min	
				Plasma ChE ± SD	RBC ChE ± SD
Controlled Hypertensive patients uncomplicated	25	124±9.13	77.8±5.79	1.13±0.12	0.97 ± 0.13
Uncontrolled Hypertensive patients uncomplicated	25	143±13.07	94.4 ±5.83	1.14±0.16	0.94 ± 0.09*
Controlled Hypertensive patients complicated	32	121.9 ± 13.15	75.3 ±7.25	1.06±0.18	0.93 ± 0.16*
Uncontrolled Hypertensive patients complicated	29	147 ± 12.49	93.4 ± 6.39	1.05±0.17*	0.92 ± 0.12*
Control group		-------		1.16± 0.14	0.98 ± 0.014

Reading repetition frequency = 2-3/sample, ChE values are means ± SD. *Significantly different from the respective control group, P<0.05 using ANOVA (One-way analysis of variance) test with post-hoc Turkey's test to determine significant group at p value of less than 0.05.

Table 2. *Plasma and RBC ChE controlled and uncontrolled complicated hypertensive patients.*

Diseases in the controlled complicated Hypertensive			
Diseases	**No of Cases**	**Δ pH/20 min**	
		Plasma ChE ± SD	**Erythrocyte ChE ± SD**
DM	5	1.1 ± 0.14	0.89 ± 0.08
DM and hyperlipidemic	2	1.07 ± 0.26	0.86 ± 0.06
DM, hyperlipdedmic and IHD	7	1.09 ± 0.11	0.96 ± 0.22
Hyperlipdedmic	12	1.17 ± 0.17	0.81 ± 0.06
Hyperlipdedmic and IHD	2	0.87 ± 0.37 *	0.96 ± 0.01
IHD	4	0.87 ± 0.18 *	0.87 ± 0.14
Diseases in the uncontrolled complicated Hypertensive			
Drugs	**No of Cases**	**Δ pH/20 min**	
		Plasma ChE ± SD	**Erythrocyte ChE ± SD**
DM	6	1.08 ± 0.05	0.96 ± 0.15
DM and IHD	4	0.95 ± 0.17	0.93 ± 0.05
DM, hyperlipidemic and IHD	6	1.05 ± 0.15 *	0.97 ± 0.11
Hyperlipidemic	3	1.03 ± 0.07	0.8 ± 0.04 *
hyperlipidemic and IHD	8	1.13 ± 0.16	0.97 ± 0.15
IHD	2	0.85 ± 0.42 *	0.98 ± 0.1
Control group		**1.16 ± 0.14**	**0.98 ± 0.014**
Reading repetition frequency = 2-3/sample, ChE values are means ± SD *Significantly different from the respective control group, P<0.05 using ANOVA (One-way analysis of variance) test with post-hoc Turkey's test to determine significant group at p value of less than 0.05.			

Table 3. *Plasma and RBC ChEs levels in ischemic heart disease subgroups.*

Group	**No of Cases**	**Δ pH/20 min**	
		Plasma ChE ± SD	**RBC ChE ± SD**
Controlled IHD patients uncomplicated	25	0.97 ± 0.11 *	0.93 ± 0.13 *
Uncontrolled IHD patients uncomplicated	25	1.18 ± 0.2	1.02 ± 0.11
Controlled IHD patients complicated	37	1.05 ± 0.17	0.97 ± 0.14
Uncontrolled IHD patients complicated	25	1.02 ± 0.2 *	0.93 ± 0.2 *
Control group		1.16 ± 0.14	0.98 ± 0.014
Reading repetition frequency = 2-3/sample, ChE values are means ± SD *Significantly different from the respective control group, P<0.05 using ANOVA (One-way analysis of variance) test with post-hoc Turkey's test to determine significant group at p value of less than 0.05.			

Table 4. *Plasma and RBC ChE mean for controlled and uncontrolled IHD patients.*

Diseases in the controlled complicated IHD			
Diseases	**No of Cases**	**Δ pH/20 min**	
		Plasma ChE ± SD	**Erythrocyte ChE ± SD**
DM	4	0.94 ± 0.14 *	0.97 ± 0.04
DM and HTN	6	1.05 ± 0.09	0.98 ± 0.21
DM and hyperlipidemic	8	1.12 ± 0.14	0.98 ± 0.11
HTN	4	1.07 ± 0.20	0.85 ± 0.06 *
hyperlipidemic	4	1.11 ± 0.26	0.97 ± 0.10
hyperlipidemic and HTN	11	1.01 ± 0.20	0.99 ± 0.16
Diseases in the uncontrolled complicated IHD			
Drugs	**No of Cases**	**Δ pH/20 min**	
		Plasma ChE ± SD	**Erythrocyte ChE ± SD**
DM	7	1.20 ± 0.13	0.98 ± 0.22
DM and HTN	6	0.96 ± 0.08 *	0.93 ± 0.24 *
HF	3	0.63 ± 0.08 *	1.05 ± 0.14
HTN	6	1.11 ± 0.21	0.95 ± 0.19
hyperlipidemic	3	1.20 ± 0.19	0.90 ± 0.19
Control group		1.16 ± 0.14	0.98 ± 0.014
Reading repetition frequency = 2-3/sample, ChE values are means ± SD *Significantly different from the respective control group, P<0.05 using ANOVA (One-way analysis of variance) test with post-hoc Turkey's test to determine significant group at p value of less than 0.05.			

Table 5. *The subdivision of the HF groups with their plasma and RBC ChEs levels.*

Group	**No of Cases**	**Δ pH/20 min**	
		Plasma ChE ± SD	**RBC ChE ± SD**
Controlled HF patients complicated	25	0.93 ± 0.2 *	0.86 ± 0.21 *
Uncontrolled HF patients complicated	25	0.98 ± 0.18 *	0.83 ± 0.08 *
Control group		1.16 ± 0.14	0.98 ± 0.014
Reading repetition frequency = 2-3/sample, ChE values are means ± SD. *Significantly different from the respective control group, P<0.05 using ANOVA (One-way analysis of variance) test with post-hoc Turkey's test to determine significant group at p value of less than 0.05.			

Table 6. *Plasma and RBC ChE for controlled and uncontrolled with complicated HF patients.*

Diseases in the controlled complicated HF			
Diseases	**No of Cases**	**Δ pH/20 min**	
		Plasma ChE ± SD	**Erythrocyte ChE ± SD**
DM	7	0.91 ± 0.2 *	0.76 ± 0.22 *
DM and HTN	5	0.91 ± 0.27 *	0.78 ± 0.24 *
DM and hyperlipedmic	6	1.02 ± 0.18	0.97 ± 0.18
HTN	7	0.95 ± 0.18 *	0.97 ± 0.21
Diseases in the uncontrolled complicated HF			
Drugs	**No of Cases**	**Δ pH/20 min**	
		Plasma ChE ± SD	**Erythrocyte ChE ± SD**
DM	6	0.99 ± 0.26 *	0.87 ± 0.1 *
DM and HTN	7	0.86 ± 0.15 *	0.82 ± 0.06 *
HTN	9	1.05 ± 0.13	0.88 ± 0.09 *
Hyperlipidemic	3	0.99 ± 0.09	0.81 ± 0.11 *
Control group		**1.16 ± 0.14**	**0.98 ± 0.014**
Reading repetition frequency =2-3 /sample, ChE values are means ± SD *Significantly different from the respective control group, P<0.05 using ANOVA (One-way analysis of variance) test with post-hoc Turkey's test to determine significant group at p value of less than 0.05.			

Table 7. *Hypercholesterolemia group with their mean plasma and RBC ChE levels.*

Group	**TC**	**TG**	**LDL-C**	**HDL-C**	**No of Cases**	**Δ pH/20 min**	
						Plasma ChE ± SD	**RBC ChE ± SD**
Dyslipidemia patients	279	250	150	38.5	25	1.22 ± 1.11*	1.08 ± 0.07 *
Control group					25	1.16 ± 0.14	0.98 ± 0.014
ChE values are means ± SE *Significantly different from the respective control group, P<0.05 using ANOVA (One-way analysis of variance) test with post-hoc Turkey's test to determine significant group at p value of less than 0.05.							

Table 8. *Distribution of plasma and erythrocyte ChE activity across ranges in dyslipidemia patients.*

ChE Range	**No of Cases**	**Plasma ChE ± SD Δ pH/20 min**	**ChE Range**	**No of Cases**	**RBC ChE ± SD Δ pH/20 min**
1.0 - 1.1	4	1.08 ± 0.02	0.9 - 1.0	2	0.98 ± 0.00
1.1 - 1.2	5	1.13 ± 0.03	1.0 - 1.1	14	1.04 ± 0.03 *
1.2 - 1.3	10	1.22 ± 0.02 *	1.1 - 1.2	9	1.13 ± 0.04 *
1.3 - 1.5	6	1.38 ± 0.06 *			
Control group		1.16 ± 0.14			0.98 ± 0.014
Reading repetition frequency = 2-3 /sample, ChE values are means ± SD *Significantly different from the respective control group, P<0.05 using ANOVA (One-way analysis of variance) test with post-hoc Turkey's test to determine significant group at p value of less than 0.05.					

of 50 hypertensive patients and 20 normotensive controls, demonstrating a link between higher BChE activity, blood pressure status, and increased triglyceride and total cholesterol levels, reinforcing BChE's role in tracking systemic inflammation [19]. Expanding on this, Sidhu et al. (2020) observed significantly higher ChE concentrations in 30 patients with isolated systolic HTN (ISH) compared to 30 matched controls, with a clear stepwise rise in activity corresponding to increasing high-sensitivity C-reactive protein (hs-CRP) [20]. It is crucial to consider that these studies, which found elevated ChE levels, often included participants with additional inflammatory factors or diseases, such as obesity and hyperlipidemia, which could be the primary cause of the increased ChE activity.

For further differentiation and a more precise discussion of the

results, each subgroup from Table 1 was subclassified according to their ChE ranges and the hypertensive drugs used by each patient in the subclasses. These subclasses were then compared with the controlled group. This step will provide a clear idea about the differences in ChEs levels and their numbers within each group, highlighting their significant deviations from the control group (either above or below it).

The results indicated that no specific complicated diseases, whether alone or in combination, affect both ChE levels. All complicated diseases that demonstrated significant differences in ChE levels compared to the control group also showed no significant differences in other cases, regardless of whether they occurred alone or in combination, and across both controlled and uncontrolled groups. This suggests that complicated diseases in hypertensive patients have no direct effect on ChE levels. Instead, any correlation is solely with the severity and poor control of hypertension, as previously noted in Table 1.

The IHD groups present a different picture compared to the HTN groups. Here, both the controlled uncomplicated group and the uncontrolled complicated group exhibited significantly reduced ChE levels when compared to the control group. This might primarily indicate that the severity of IHD does not directly correlate with an increase or decrease in either of the ChE enzymes. Interestingly, the uncontrolled uncomplicated group had a mean ChE value higher than the control group, although this elevation was not statistically significant.

The lower ChE values in the uncontrolled IHD complicated group are consistent with a study by Shenhar-Tsarfaty et al. (2020), which observed that participants undergoing angiography for Acute Coronary Syndrome (ACS) had lower AChE levels than those with stable angina [21]. A similar trend of low ChE activity was also evident in the controlled, uncomplicated IHD group. These results align with Goliasch et al.'s (2012) findings, where lower serum ChE levels were strongly associated with long-term outcomes in individuals with established coronary artery disease (CAD), a link that was even more pronounced in patients with stable IHD than in those with ACS.

A cross-sectional study by Kocabaş et al. (2016) evaluated BChE levels in a cohort of 85 patients diagnosed with acute myocardial infarction (AMI). The study determined that serum BChE levels were statistically significantly lower in AMI patients ($p<0.001$). Additionally, a moderate negative correlation was identified between BChE activity and the occurrence of AMI ($r=-0.363$, $p<0.001$). Receiver Operating Characteristic (ROC) curve analysis further indicated that BChE possessed discriminatory power in differentiating AMI patients from healthy controls, achieving a sensitivity of 51.2% and a specificity of 84.4% [22].

In contrast to the studies mentioned previously, research by Mito et al. (2021) involving 559 patients with stable CAD found that ChE levels significantly influenced myocardial ischemia. This retrospective study reported that higher ChE levels were associated with a higher BMI, dyslipidemia, and younger age. For myocardial ischemia, a ChE level of 286 IU/L yielded a specificity of 0.599 and a sensitivity of 0.658. Elevated serum ChE was identified as an independent risk factor for myocardial ischemia in CAD patients [23].

The data presented suggest that specific complicated diseases, whether singularly present or in combination, do not directly influence both ChE levels. Interestingly, complicated diseases that exhibited significant differences in ChE levels when compared to the control group in certain scenarios did not maintain these significant differences in other cases, irrespective of whether they appeared alone or in combination, and across both controlled and uncontrolled patient groups. Analogous to findings in the HTN group, this implies that complicated diseases in IHD patients do not have a direct impact on ChE levels.

Supporting a more nuanced interpretation, Sun (2016) examined the relationship between BChE activity and cardiac function in patients with Acute Myocardial Infarction (AMI). This study revealed that BChE activity was higher in patients demonstrating better cardiac function, and conversely, low BChE activity was an independent predictor of mortality. However, the predictive significance of BChE activity diminished once cardiac function was factored into the analysis. The authors therefore propose that the prognostic utility of BChE in AMI might be tied to its relationship with cardiac function [24]. Consequently, the observed correlation between ChE levels and IHD may be transient, potentially disappearing once cardiac function normalizes.

The results revealed a significant decrease in both plasma ChEs (BChE) and RBC ChE (AChE). This observation presents a stark contrast to the patterns seen in the HTN and IHD groups, strongly suggesting a direct correlation between ChE activity and the progression of HF. While only the uncontrolled HTN groups showed a significant ChE reduction, which pointed to disease severity and inadequate management. However, in HF, even though both sets of groups were complicated, they all showed significant ChE decreases, regardless of control status. This evidence strongly associates diminished ChE levels with HF.

These findings are consistent with numerous studies identifying low ChE as a marker of malnutrition in HF and a powerful predictor of outcomes. Specifically, low serum ChEs are recognized as an independent prognostic factor for mortality [25-29]

The results indicated that no specific complicated diseases, whether singularly or in combination, directly affect both ChE levels. Interestingly, complicated diseases that initially showed significant differences in ChE levels compared to the control group did not consistently maintain these differences in other cases, irrespective of their isolated or combined occurrence, or the patient's controlled or uncontrolled status. This suggests that complicated diseases in HF patients have no direct impact on ChE levels.

Instead, any observed correlation is solely with the severity and poor control of HF. This correlation resembles the pattern seen in the HTN groups but is more pronounced and stronger in HF, significantly affecting ChE levels. This differs from the IHD groups, where no strong correlation with decreased ChE enzymes was observed.

It is worth noting that the correlation between HF and ChE levels was more evident than in the HTN groups. This is supported by the fact that most disease groups in Table 16

showed significant differences from the control group, whereas in the HTN groups, only a few diseases significantly differed from the control. This distinction can be attributed to the greater severity, morbidity, and multi-systemic impact of HF compared to HTN. These findings align with established mechanistic links between HF, systemic inflammation, hepatic synthetic impairment, and autonomic dysfunction, all of which are known to downregulate ChEs.

Researchers have consistently identified low ChEs as a marker of malnutrition in HF and a powerful predictor of outcomes. For instance, studies in chronic HF populations have demonstrated that low serum ChEs are an independent prognostic factor for mortality [29]. A 2015 Japanese cohort study showed that patients whose serum ChE (primarily BChE) experienced a significant decline had markedly higher all-cause and cardiac mortality over a median 2-year follow-up, even after multivariable adjustment [25]. Subsequent larger registries and multicenter analyses, such as PURSUIT-HFpEF (2020), have further confirmed the independent prognostic value of low BChE in both acute and chronic heart failure settings [26].

Furthermore, other research highlights the utility of ChEs as a biomarker in acute decompensated HF. In acute HF admissions, serum ChE levels upon admission inversely correlate with congestion severity and the risk of short-term adverse outcomes. Patients presenting with notably low BChE activity tend to face a greater risk of early mortality or readmission [27]. This corroborates our study's results, where uncontrolled HF patients were hospitalized due to worsening HF symptoms, such as ascites and difficulty breathing. This makes plasma ChEs (BChE) a promising candidate for risk stratification upon hospital admission for HF, potentially aiding in the identification of patients who would benefit from advanced therapies. The underlying reason for this utility could be that BChE dynamically reflects nutritional and inflammatory status, which are critical determinants of HF patient survival, sometimes more effectively than traditional markers [30].

The results showed elevated plasma and RBC ChE activity compared to the control group. This elevation in both ChEs contrasts with the results observed in the CVD groups, all of which showed reduced and significantly reduced ChE levels. This observed elevation is consistent with many previous studies. In 2005, a large epidemiological and cross-sectional investigation revealed positive correlations between BChE activity and total cholesterol [31]. These observations are echoed in groups with abdominal obesity [32].

Another study by Stojanov et al. in 2011 investigated the association of serum BChE activity with risk factors for CAD in a cross-sectional population of 1512 healthy young individuals aged 18-25. Results showed higher BChE activity was associated with total cholesterol [33]. Additionally, according to Vallianou et al. (2014), the relationship between BChE and lipid levels was assessed in a cross-sectional study involving 490 healthy adults as indicators of cardiovascular disease development. Results showed that total cholesterol was positively associated with serum BChE activity [34].

The results indicated a significant correlation between hyperlipidemia and both types of ChEs. Nearly all ChE ranges were elevated compared to the control group. It's worth noting that this elevation contrasts with the reduced ChE levels observed in all CVD groups. This phenomenon suggests that the presence of a hyperlipidemic state will cause an elevation in ChE levels. If ChE levels are already decreased by another cause (like CVD or other morbidities), and hyperlipidemia is underlying or associated, it will cause ChE levels to rise, potentially bringing them near or even above the normal range. This is clearly visible in the previous complicated groups, where no significant reduction in ChEs was observed, or levels were near the control group, whenever hyperlipidemia was present (alone or with other diseases).

The results of this study indicate a significant reduction in ChEs with poorly controlled HTN and HF. The relationship is less clear in IHD. This discrepancy may be attributed to the disease duration. HTN and HF often involve prolonged treatment periods, with fluctuating states of control depending on medication adherence, correct dosages, and patient coordination. Over these extended periods, the disease can vary, leading to poor control that affects various bodily systems, including ChEs. In contrast, periods of uncontrolled or morbid IHD are typically shorter, thereby reducing their impact on ChEs. Therefore, further follow-up studies are needed across all cardiac disease types and stages in different community sections to fully understand the link between these enzymes and these diseases.

Conclusion.

Circulating cholinesterase (ChE) activity emerged as a simple, inexpensive indicator of autonomic, inflammatory, and metabolic stress across common cardiovascular disorders. Levels fell progressively in poorly controlled hypertension and were lowest in heart failure, whereas stable ischemic heart disease showed intermediate, condition-specific variations, and isolated hyperlipidemia drove ChE upward. Medication class had no consistent effect. Routine plasma/erythrocyte ChE measurement—interpreted alongside the lipid profile—could improve bedside risk evaluation, especially in resource-limited settings, but confirmation in larger, prospective cohorts is still needed.

REFERENCES

1. World Health Organization. Cardiovascular diseases (CVDs): fact sheet. Geneva: WHO; 2023.

2. Alonso A, Aparicio FH, Benjamin EJ, et al. Heart disease and stroke statistics—2021 update. Circulation. 2021;2021:e00.

3. Poznyak AV, Sadykhov NK, Kartuesov AG, et al. Hypertension as a risk factor for atherosclerosis: Cardiovascular risk assessment. Frontiers in cardiovascular medicine. 2022;9:959285.

4. Schwinger RH. Pathophysiology of heart failure. Cardiovascular diagnosis and therapy. 2021;11:263.

5. Aboukhater D, Morad B, Nasrallah N, et al. Inflammation and hypertension: Underlying mechanisms and emerging understandings. Journal of cellular physiology. 2023;238:1148-59.

6. Montecucco F, Pende A, Quercioli A, et al. Inflammation in the pathophysiology of essential hypertension. J Nephrol. 2011;24:23-34.

7. Silman I. The multiple biological roles of the cholinesterases. Progress in biophysics and molecular biology. 2021;162:41-56.
8. Mahmood AA, Khalaf MM, Zainal AA. Cholinesterases activities in diabetic and hyperlipidemic patient. Executive Editor. 2020;11:875.
9. Sridhar GR. Butyrylcholinesterase, variants and metabolic syndrome. Adipobiology. 2018;9:19-27.
10. Zouali M. Pharmacological and electroceutical targeting of the cholinergic anti-inflammatory pathway in autoimmune diseases. Pharmaceuticals. 2023;16:1089.
11. Garrido-Urbani S, Meguenani M, Montecucco F, et al. Immunological aspects of atherosclerosis. InSeminars in immunopathology. Berlin/Heidelberg: Springer Berlin Heidelberg. 2014;36:73-91.
12. Adamo L, RochaResende C, Prabhu SD, et al. Reappraising the role of inflammation in heart failure. Nat Rev Cardiol. 2020;17:269-285.
13. Jankowska E, Ponikowski P, Piepoli M, et al. Autonomic imbalance and immune activation in chronic heart failure—pathophysiological links. Cardiovasc Res. 2006;70:434-445.
14. Mahmood AA. In vitro inhibition of human blood cholinesterases and protection against chlorpyriphos (organophosphate) by weak anticholinesterase drugs. Iraqi Journal of Pharmacy. 2011;11:18-29.
15. Ahmed OA, Mohammad FK. A simplified electrometric technique for rapid measurement of human blood cholinesterase activity. Internet J Toxicol. 2005;2.
16. Mahmood AA, Zainal AA, Khalaf MM. Cholinesterase activity in non-alcoholic-fatty liver disease in diabetic patients taking oral antidiabetic drugs. Current Topics in Pharmacology. 2021;25:43-51.
17. de Carvalho Corrêa M, Maldonado P, da Rosa CS, et al. Oxidative stress and erythrocyte acetylcholinesterase (AChE) in hypertensive and ischemic patients of both acute and chronic stages. Biomedicine & pharmacotherapy. 2008;62:317-24.
18. Tangvarasittichai S, Pongthaisong S, Meemark S, et al. Abdominal obesity associated with elevated serum butyrylcholinesterase activity, insulin resistance and reduced highdensity lipoproteincholesterol levels. Indian J Clin Biochem. 2015;30:275-280.
19. Mahmoud AA, Moghazy HM, Nor El-Din AKA. Serum leptin level and butyrylcholinesterase enzyme activity in essential hypertension patients. Journal of Applied Sciences Research. 2013;9:294-297.
20. Sidhu W, Bhatia L, Vohra K. Serum cholinesterase level as a marker of systemic lowgrade inflammation in isolated systolic hypertension: a crosssectional study. Eur J Med Health Sci. 2020;2:1-6.
21. Shenhar-Tsarfaty S, Brzezinski RY, Waiskopf N, et al. Blood acetylcholinesterase activity is associated with increased 10 year all-cause mortality following coronary angiography. Atherosclerosis. 2020;313:144-149.
22. Kocabaş R, Erenler AK, Yetim M, et al. Butyrylcholinesterase as an additional marker in the diagnostic network of acute myocardial infarction. Laboratoriums Medizin. 2016;40:147-152.
23. Mito T, Takemoto M, Antoku Y, et al. Influence of serum cholinesterase levels on patients suspected of having stable coronary artery disease. Internal Medicine. 2021;60:1145-1150.
24. Sun L, Qi X, Tan Q, et al. Low serum butyrylcholinesterase activity as a prognostic marker of mortality associates with poor cardiac function in acute myocardial infarction. Clin Lab. 2016;62:1101-1108.
25. Sato T, Yamauchi H, Suzuki S, et al. Serum cholinesterase is an important prognostic factor in chronic heart failure. Heart and vessels. 2015;30:204-210.
26. Seo M, Yamada T, Tamaki S, et al. Prognostic significance of serum cholinesterase level in patients with acute decompensated heart failure with preserved ejection fraction: insights from the PURSUIT-HFpEF registry. Journal of the American Heart Association. 2020;9:e014100.
27. Shiba M, Kato T, Morimoto T, et al. Serum cholinesterase as a prognostic biomarker for acute heart failure. European Heart Journal Acute Cardiovascular Care. 2021;10:335-42.
28. Doi T, Nakata T, Tsuzuki T, et al. Decreased cholinesterase level combined with renal dysfunction and sympathetic denervation associated with increased cardiac mortality in systolic heart failure. Frontiers in Cardiovascular Medicine. 2023;10:1131282.
29. Yamashita M, Kamiya K, Hamazaki N, et al. Predictive value of cholinesterase in patients with heart failure: A new blood biochemical marker of undernutrition. Nutrition, Metabolism and Cardiovascular Diseases. 2023;33:1914-22.
30. Oda E. Associations between serum cholinesterase and incident hyperLDLcholesterolemia, hypertriglyceridemia and hypoHDLcholesterolemia, as well as changes in lipid levels in a healthscreening population. Atherosclerosis. 2015;241:1-5.
31. Randell EW, Mathews MS, Zhang H, et al. Relationship between serum butyrylcholinesterase and the metabolic syndrome. Clin Biochem. 2005;38:799-805.
32. Shenhar-Tsarfaty S, Sherf-Dagan S, Berman G, et al. Obesity-related acetylcholinesterase elevation is reversed following laparoscopic sleeve gastrectomy. International Journal of Obesity. 2019;43:297-305.
33. Stojanov M, Stefanović A, Džingalašević G, et al. Butyrylcholinesterase activity in young men and women: association with cardiovascular risk factors. Clin Biochem. 2011;44:623-626.
34. Vallianou NG, Evangelopoulos AA, Bountziouka V, et al. Association of butyrylcholinesterase with cardiometabolic risk factors among apparently healthy adults. Journal of Cardiovascular Medicine. 2014;15:377-83.