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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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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.

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PARADOXICAL ELEVATION OF PLATELET INDICES IN SUDANESE PATIENTS WITH CHRONIC HEPATITIS B: A CROSS-SECTIONAL ANALYSIS

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Abstract.

Background: Chronic hepatitis B virus (HBV) infection is highly prevalent in Sudan. Platelet indices serve as potential non-invasive markers for liver disease severity, yet limited data exist for Sudanese populations.

Objective: To evaluate platelet indices in Sudanese patients with chronic hepatitis B and assess relationships with disease phases, age, and gender.

Methods: This case-control study included 198 participants (127 chronic HBV patients, 71 healthy controls) from Khartoum State, Sudan. Platelet indices were measured using automated hematology analyzers. HBV DNA quantification was performed by real-time PCR. Patients were stratified by viral load into immune control (<2,000 IU/mL), immune clearance/escape (2,000-20,000 IU/mL), and immune tolerance (>20,000 IU/mL) phases.

Results: Chronic HBV patients showed significantly elevated platelet counts (290.13±99.74 vs 235.48±50.50 $\times 10^3$/μL, $p<0.001$), mean platelet volume (9.25±1.30 vs 7.66±0.76 fL, $p<0.001$), platelet distribution width (15.87±0.66 vs 15.55±0.64%, $p=0.001$), and plateletcrit (0.27±0.097 vs 0.18±0.033%, $p<0.001$) compared to controls. No significant differences existed across disease phases or between demographic groups.

Conclusions: Sudanese chronic HBV patients demonstrate paradoxically elevated platelet indices, challenging conventional associations with thrombocytopenia. These parameters showed limited correlation with disease phases, suggesting reduced utility as activity markers in this population.

Key words. Chronic hepatitis B, platelet indices, mean platelet volume, Sudan, viral load, disease phases.

Introduction.

Hepatitis represents a major global health challenge, characterized by liver tissue inflammation [1]. While multiple etiological factors can trigger hepatitis—including excessive alcohol consumption, autoimmune disorders, medications, and environmental toxins—viral infections remain the predominant cause worldwide [2]. Among viral hepatitides, types A, B, and C are most prevalent, with types D and E occurring less frequently [3].

Clinical classification of hepatitis depends on inflammation duration [4]. Acute hepatitis, defined as inflammation lasting less than six months, often resolves spontaneously but may progress to fulminant liver failure in severe cases [5]. Chronic hepatitis, persisting beyond six months, poses greater clinical concern due to potential progression to irreversible liver damage, including fibrosis, cirrhosis, and hepatocellular carcinoma [6].

Hepatitis B virus (HBV) infection represents a particularly significant public health concern affecting all age groups. While some patients experience brief, self-limiting acute infections requiring minimal intervention, others develop chronic disease with potentially life-threatening complications [7]. Chronic HBV infection can lead to progressive liver scarring, hepatic failure, and malignant transformation, substantially increasing morbidity and mortality rates [8].

The HBV burden is particularly pronounced in Sudan, where the virus represents the primary cause of chronic liver disease and hepatocellular carcinoma, and the second leading cause of acute liver failure [9]. Epidemiological data reveal striking regional variations in HBV prevalence across Sudan, with hepatitis B surface antigen (HBsAg) positivity ranging from 6.8% in central regions to 26% in southern areas. Population exposure rates, indicated by serological markers, range from 47% to 78%. These regional differences extend to transmission patterns, with southern Sudan showing predominantly early childhood transmission, while northern regions demonstrate increasing infection rates with advancing age [10].

Understanding Conventional Thrombocytopenia in Chronic Liver Disease.

In advanced chronic liver disease, thrombocytopenia typically develops through well-established mechanisms. Portal hypertension, resulting from increased hepatic resistance and portal blood flow, leads to splenomegaly and subsequent splenic sequestration of platelets. Approximately 90% of the platelet pool can become sequestered in an enlarged spleen, dramatically reducing circulating platelet counts. Additionally, chronic liver disease impairs hepatic synthesis of thrombopoietin, the primary regulator of megakaryopoiesis and platelet production. Reduced thrombopoietin levels result in decreased bone marrow platelet production, further contributing to thrombocytopenia. These mechanisms create the characteristic low platelet counts observed in patients with cirrhosis and portal hypertension.

Beyond direct viral effects, HBV infection significantly impacts hematological parameters, particularly platelet dynamics. Platelets are anucleate, discoid cellular fragments measuring approximately 3.0×0.5 micrometers in diameter, with mean platelet volume of 7-11 femtoliters. These cellular elements originate from cytoplasmic fragmentation of bone marrow megakaryocytes, with each megakaryocyte producing 5,000-10,000 platelets during its lifespan [11]. Thrombopoietin, synthesized primarily in the liver and kidneys, regulates this process through negative feedback mechanisms responsive to circulating platelet levels [12].

Under physiological conditions, platelets circulate for 5-10 days before removal by splenic macrophages and hepatic

Kupffer cells. Notably, approximately 40% of the total platelet pool remains sequestered within the spleen, available for rapid mobilization during hemostatic demands through sympathetically-mediated splenic contraction.

While traditionally recognized for hemostatic functions, platelets have emerged as crucial mediators in both acute and chronic inflammatory processes. In HBV infection, platelets play dual roles in disease pathogenesis. They facilitate hepatic accumulation of virus-specific CD8+ T lymphocytes and non-specific inflammatory cells, thereby contributing to both viral clearance and liver parenchymal damage. This immunomodulatory function of platelets in HBV-related liver disease underscores their significance beyond traditional hemostasis and highlights their potential as therapeutic targets in managing chronic viral hepatitis [13].

Materials and Methods.

Study Design and Setting:

A case-control study was conducted to investigate platelet indices in Sudanese patients with chronic hepatitis B virus (HBV) infection. The study was performed across multiple healthcare facilities in Khartoum State, Sudan, from November 12, 2022, to February 15, 2023.

Participants.

Sample Size and Study Population:

The study population consisted of 198 participants recruited through convenience sampling. The case group comprised 127 patients with confirmed chronic HBV infection, while the control group included 71 healthy individuals recruited from analogous geographic regions. Both male and female participants were enrolled to ensure representative sampling.

Selection Criteria.

Inclusion criteria for cases: Participants were eligible if they met the following criteria: (1) Sudanese nationality; (2) laboratory-confirmed chronic HBV infection evidenced by persistent hepatitis B surface antigen (HBsAg) positivity for ≥6 months; and (3) age ≥18 years.

Exclusion criteria: Participants were excluded if they presented with: (1) non-Sudanese nationality; (2) active malignancy; (3) pregnancy; (4) autoimmune liver disease; (5) co-infection with hepatitis A, C, D, or E viruses; or (6) history of blood transfusion within the preceding 3 months.

Control group selection: Healthy controls were recruited from individuals attending routine health check-ups and were required to have negative HBsAg status and absence of liver-related symptoms or disease.

Data Collection

Clinical and Demographic Assessment:

Standardized demographic and clinical data were collected through structured face-to-face interviews using a pre-validated questionnaire. Variables assessed included age, gender, current clinical manifestations, medical history, and medication use. Supplementary clinical information was extracted from electronic medical records following approval from attending physicians.

Laboratory Procedures.

Specimen Collection and Processing:

Venous blood samples (3 mL) were collected from each participant using standard phlebotomy techniques and immediately transferred into sterile ethylenediaminetetraacetic acid (EDTA) anticoagulant tubes. All samples were processed within 2 hours of collection to minimize pre-analytical variables and ensure measurement accuracy.

Hematological Analysis:

Complete blood count including platelet indices was performed using automated hematology analyzers (Sysmex KX-21N™ and Mindray BC-5800). The following platelet parameters were measured: platelet count ($\times 10^3/\mu L$), mean platelet volume (MPV, fL), platelet distribution width (PDW, %), and plateletcrit (PCT, %). Quality control procedures were implemented daily according to manufacturer specifications.

HBV DNA Quantification:

Viral DNA extraction was performed from 400 µL EDTA-anticoagulated plasma using the ExiPrep™ Dx viral DNA extraction kit on the ExiPrep 16 Dx automated extraction platform (Bioneer Corporation, Daejeon, Republic of Korea) following the manufacturer's protocol.

Quantitative real-time polymerase chain reaction (qRT-PCR) was conducted using the Exicycler 96 Real-Time Quantitative Thermal Block system (Bioneer Corporation, Daejeon, Republic of Korea). The thermal cycling protocol consisted of initial denaturation at 95°C for 5 minutes, followed by 45 cycles of denaturation at 95°C for 5 seconds and combined annealing/extension at 55°C for 5 seconds.

HBV DNA concentrations were determined by interpolation of cycle threshold (Ct) values against standard curves generated using known concentrations of HBV DNA standards. Results were expressed as international units per milliliter (IU/mL) with a lower limit of detection of 20 IU/mL.

Study Classifications.

HBV Infection Phase Stratification:

Participants in the case group were classified into three distinct phases of chronic HBV infection based on viral load measurements:

1. **Immune control phase:** HBV DNA <2,000 IU/mL
2. **Immune clearance/escape phase:** HBV DNA 2,000-20,000 IU/mL
3. **Immune tolerance phase:** HBV DNA >20,000 IU/mL

This classification system was based on established clinical guidelines for chronic HBV management. It should be noted that comprehensive clinical guidelines typically incorporate alanine aminotransferase (ALT) levels alongside viral load to more accurately differentiate disease phases, particularly distinguishing the immune tolerance phase (high viral load with normal ALT) from the immune clearance phase (high viral load with elevated ALT). The absence of liver function tests in our study represents a limitation in the precision of phase classification.

Age Stratification:

For age-related comparative analyses, all participants were categorized into four discrete groups using 20-year intervals to ensure adequate sample sizes for statistical comparisons.

Statistical Analysis:

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corporation, Armonk, NY, USA). Data distribution normality was assessed using the Shapiro-Wilk test. Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data or median with interquartile range for non-normally distributed data. Categorical variables were presented as frequencies and percentages.

Between-group comparisons of platelet indices were conducted using independent samples t-tests for normally distributed continuous variables or Mann-Whitney U tests for non-parametric data. One-way analysis of variance (ANOVA) followed by post-hoc Tukey's honestly significant difference (HSD) test was employed to evaluate differences among the three HBV infection phases and between age groups. Point-biserial correlation analysis was utilized to assess associations between gender and platelet parameters.

Statistical significance was defined as a two-tailed p-value <0.05. All confidence intervals were calculated at the 95% level.

Ethical Considerations:

The study protocol received scientific ethical approval from the University of Khartoum. Written informed consent was obtained from all participants prior to enrollment after detailed explanation of study objectives, procedures, potential risks, and benefits. All study procedures were conducted in strict accordance with the principles outlined in the Declaration of Helsinki and local regulatory guidelines. Participant confidentiality and data privacy were maintained throughout the study period.

Results.

Demographic Characteristics:

A total of 198 participants were enrolled in this study, comprising 127 patients with chronic hepatitis B (case group) and 71 healthy controls. The gender distribution revealed male predominance in the case group (90 males, 70.9%; 37 females, 29.1%) compared to a more balanced distribution in the control group (39 males, 54.9%; 32 females, 45.1%).

Age distribution analysis showed that the majority of patients in the case group were aged 21-40 years (66.9%), followed by 41-60 years (21.1%), 1-20 years (11.0%), and 61-80 years (4.7%). The control group demonstrated a different age distribution pattern, with 47.9% aged 21-40 years, 25.4% aged 41-60 years, 17.3% aged 1-20 years, and 5.6% aged 61-80 years.

Comparison of Platelet Indices Between Case and Control Groups:

Independent samples t-tests were performed to evaluate differences in platelet indices between chronic hepatitis B patients and healthy controls. All platelet parameters showed statistically significant elevations in the case group compared to controls (Table 1).

Platelet count was significantly higher in chronic hepatitis B patients (290.13±99.74 $\times 10^3/\mu L$) compared to controls (235.48±50.50 $\times 10^3/\mu L$; $t(196)=5.112$, $p<0.001$). Similarly, mean platelet volume (MPV) was elevated in the case group (9.25±1.30 fL) versus controls (7.66±0.76 fL; $t(196)=10.830$, $p<0.001$).

Platelet distribution width (PDW) demonstrated a significant increase in patients (15.87±0.66%) compared to controls (15.55±0.64%; $t(196)=3.246$, $p=0.001$). Plateletcrit (PCT) was also significantly higher in the case group (0.27±0.097%) than in controls (0.18±0.033%; $t(196)=9.599$, $p<0.001$).

Platelet Indices Across Different Disease Phases:

Patients were stratified into three phases based on HBV DNA levels: immune control phase (n=93, 73.2%), immune clearance/escape phase (n=21, 16.5%), and immune tolerance phase (n=13, 10.2%).

One-way ANOVA analysis revealed no statistically significant differences in platelet indices across the three disease phases. Platelet count ($F(2,124)=1.344$, $p=0.265$), MPV ($F(2,124)=0.572$, $p=0.566$), PDW ($F(2,124)=0.745$, $p=0.477$), and PCT ($F(2,124)=1.570$, $p=0.212$) all showed comparable values across disease phases (Table 2).

Gender-Related Differences in Platelet Indices:

Point-biserial correlation analysis was conducted to assess the relationship between gender and platelet indices in chronic hepatitis B patients. No significant associations were observed between gender and any platelet parameter: platelet count ($r=0.125$, $p=0.162$), MPV ($r=0.033$, $p=0.709$), PDW ($r=-0.108$, $p=0.227$), and PCT ($r=0.143$, $p=0.109$) (Table 3).

Age-Related Variations in Platelet Indices:

One-way ANOVA was performed to evaluate age-related differences in platelet indices across four age groups. No statistically significant differences were detected among age groups for any platelet parameter: platelet count ($F(3,123)=0.550$, $p=0.649$), MPV ($F(3,123)=0.286$, $p=0.835$), PDW ($F(3,123)=0.581$, $p=0.628$), and PCT ($F(3,123)=0.953$, $p=0.417$). Mean values and standard deviations for each age group are presented in Table 4.

Discussion.

This study evaluated platelet indices in Sudanese patients with chronic hepatitis B, revealing unexpected findings that challenge conventional understanding of HBV-related hematological changes. Contrary to established literature consistently reporting thrombocytopenia in chronic HBV patients, our cohort demonstrated significantly elevated platelet counts and indices compared to healthy controls.

Contradictory Findings and Mechanistic Explanations:

The paradoxical elevation in platelet parameters observed in our study contrasts sharply with previous reports linking chronic HBV infection to thrombocytopenia. This discrepancy requires careful mechanistic analysis and consideration of population-specific factors.

Compensatory Thrombopoiesis Hypothesis:

The elevated platelet indices in our Sudanese HBV patients likely represent an early compensatory response to subclinical

Table 1. *Comparison of platelet indices between chronic hepatitis B patients and healthy controls.*

Platelet Parameter	Control Group (n=71)	Case Group (n=127)	Mean Difference	95% CI	p-value
Platelet count (×10³/μL)	235.48±50.50	290.13±99.74	54.65	33.57-75.73	<0.001*
MPV (fL)	7.66±0.76	9.25±1.30	1.59	1.30-1.88	<0.001*
PDW (%)	15.55±0.64	15.87±0.66	0.31	0.12-0.50	0.001*
PCT (%)	0.18±0.033	0.27±0.097	0.09	0.07-0.11	<0.001*

*Data are presented as mean±SD. MPV, mean platelet volume; PDW, platelet distribution width; PCT, plateletcrit; CI, confidence interval. *Statistically significant (p<0.05).*

Table 2. *Platelet indices according to chronic hepatitis B disease phases.*

Disease Phase	n (%)	Platelet count (×10³/μL)	MPV (fL)	PDW (%)	PCT (%)
Immune control	93 (73.2)	290.78±99.23	9.20±1.29	15.85±0.68	0.27±0.09
Immune clearance/escape	21 (16.5)	266.38±94.56	9.25±1.13	15.83±0.59	0.25±0.10
Immune tolerance	13 (10.2)	323.77±108.89	9.62±1.64	16.08±0.56	0.31±0.11
p-value	-	0.265	0.566	0.477	0.212

Data are presented as mean±SD or n (%). p-values from one-way ANOVA.

Table 3. *Correlation between gender and platelet indices in chronic hepatitis B patients.*

Platelet Parameter	Correlation Coefficient (r)	p-value
Platelet count	0.125	0.162
MPV	0.033	0.709
PDW	-0.108	0.227
PCT	0.143	0.109

Point-biserial correlation analysis. No significant correlations observed (p>0.05).

Table 4. *Age-related distribution of platelet indices in chronic hepatitis B patients.*

Age Group (years)	n	Platelet count (×10³/μL)	MPV (fL)	PDW (%)	PCT (%)
1-20	14	307.36±101.73	9.19±1.26	15.94±0.37	0.28±0.09
21-40	85	282.87±94.09	9.22±1.31	15.83±0.68	0.26±0.09
41-60	27	308.86±113.67	9.46±1.30	15.90±0.70	0.30±0.12
61-80	6	284.00±132.26	9.00±1.52	16.17±0.80	0.25±0.10
p-value	-	0.649	0.835	0.628	0.417

Data are presented as mean±SD. p-values from one-way ANOVA.

platelet consumption and sequestration, occurring before the development of significant liver fibrosis and portal hypertension. Evaluating fibrosis is crucial to validate this hypothesis. The simultaneous elevation of all platelet parameters—count, MPV, PDW, and PCT—suggests an integrated response involving enhanced megakaryopoiesis, premature platelet release, and increased total platelet mass production.

The significantly elevated MPV (9.25±1.30 vs 7.66±0.76 fL) provides strong evidence for this hypothesis, indicating the release of younger, larger platelets from bone marrow. This finding suggests active thrombopoietic stimulation rather than passive platelet accumulation. Similarly, the increased PDW (15.87±0.66 vs 15.55±0.64%) reflects a heterogeneous platelet population containing both mature and immature forms, consistent with enhanced bone marrow production.

Inflammatory Cytokine Pathways:

Chronic HBV infection triggers persistent hepatic inflammation, leading to sustained elevation of inflammatory cytokines, particularly interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). IL-6 directly stimulates thrombopoietin gene expression in the liver, resulting in enhanced megakaryopoiesis independent of platelet count feedback mechanisms. This cytokine-mediated pathway could explain the sustained elevation in platelet production despite normal or elevated circulating platelet counts.

TNF-α contributes to this process by promoting premature platelet release from megakaryocytes and stimulating bone marrow platelet production. The inflammatory milieu associated with chronic HBV infection may create a state of compensatory hyperproduction that precedes the eventual development of consumptive thrombocytopenia seen in advanced liver disease.

Population-Specific Genetic Factors:

The unique findings in our Sudanese population may reflect genetic variations affecting thrombopoiesis regulation. Potential polymorphisms in genes controlling thrombopoietin production (THPO), thrombopoietin receptor sensitivity (MPL), or megakaryocyte differentiation (GATA1/FOG1) could result in enhanced platelet production responses to inflammatory stimuli.

Additionally, unique HLA haplotypes prevalent in the Sudanese population may influence HBV immune response patterns, cytokine production profiles, and subsequent thrombopoietic responses. Environmental factors, including nutritional status and endemic co-infections, may also modulate hematopoietic responses in ways not observed in other populations.

Disease Phase Considerations:

Despite our hypothesis that different disease phases would demonstrate varying platelet responses, we observed no significant differences across immune control, clearance/escape, and tolerance phases. This unexpected finding may reflect several factors:

1. The predominance of patients in the immune control phase (73.2%) may have limited statistical power to detect meaningful differences.
2. HBV DNA levels alone may inadequately reflect the degree of hepatic inflammation or immune activation.
3. The compensatory mechanisms may be similarly activated across all phases of chronic infection.
4. Cross-sectional sampling may not capture the dynamic nature of disease progression.

Clinical Implications:

These findings have several important clinical implications for managing Sudanese patients with chronic hepatitis B:

Early Disease Monitoring:

The elevated platelet indices may serve as early biomarkers of hepatic inflammation in HBV infection, potentially identifying patients at risk for disease progression before conventional liver function abnormalities develop. The elevated MPV particularly warrants attention as it may indicate ongoing inflammatory thrombopoiesis that could transition to consumptive thrombocytopenia with disease progression.

Risk Stratification:

Patients with extremely elevated platelet counts and MPV may represent a subgroup with robust compensatory mechanisms, potentially indicating better short-term prognosis but requiring closer monitoring for eventual decompensation. Conversely, patients with relatively lower (though still elevated) platelet parameters within the HBV group might be at higher risk for progression to thrombocytopenia.

Therapeutic Considerations:

The hypercoagulable state suggested by elevated platelet counts and activation markers may influence antiviral treatment decisions and monitoring strategies. Clinicians should be aware that conventional thrombocytopenia-based risk assessments may not apply to this population.

Treatment Response Monitoring:

Serial platelet index measurements could potentially serve as accessible markers for monitoring treatment response, with declining values potentially indicating disease progression or treatment failure, while stable elevations might suggest maintained compensatory capacity.

Study Limitations.

Several significant limitations must be acknowledged:

Sample Size and Power:

While our overall sample size was adequate, the distribution across disease phases was uneven, with relatively small numbers in the immune clearance/escape (n=21) and immune tolerance (n=13) phases. This limitation may have reduced our ability to detect meaningful differences between phases.

Laboratory Limitations:

The most significant limitation of this study is the absence of liver function tests (ALT, AST, albumin, bilirubin), inflammatory markers, and hepatic fibrosis assessment data. To substantiate our core hypothesis of "compensatory thrombopoiesis in early stages preceding cirrhosis," it would be essential to demonstrate that our patient cohort did not possess advanced liver fibrosis. The incorporation of non-invasive fibrosis markers that could be calculated from available blood data (such as FIB-4 index or APRI score) would substantially strengthen the manuscript's conclusions. Additionally, we did not measure thrombopoietin levels, which would have provided direct evidence for our mechanistic hypotheses.

Future Research Directions.

Based on our findings and limitations, several research directions should be prioritized:

Comprehensive Liver Assessment Studies:

Future investigations should incorporate comprehensive liver evaluation including:

· Non-invasive fibrosis assessment using transient elastography (FibroScan) or magnetic resonance elastography.
· Validated serological markers such as FIB-4 index, APRI score, and Enhanced Liver Fibrosis (ELF) panel.
· Complete liver function tests including albumin, bilirubin, and prothrombin time.
· Inflammatory markers (ALT, AST, GGT) to assess hepatic inflammation.

Longitudinal Cohort Studies:

Prospective studies following patients over time would provide crucial insights into:

· Natural history of platelet parameter changes with disease progression.
· Correlation between platelet trends and development of complications.
· Predictive value of early platelet elevations for long-term outcomes.
· Response patterns to antiviral therapy.

Mechanistic Validation Studies:

Laboratory investigations should include:

· Cytokine profiling (IL-6, TNF-á, thrombopoietin levels).
· Platelet function assessment (aggregation, activation markers).
· Genetic analysis of relevant polymorphisms affecting thrombopoiesis.
· Bone marrow evaluation in selected patients.

Comparative Population Studies:

Studies comparing platelet responses across different populations would help determine whether our findings are specific to Sudanese patients or represent a broader pattern in African populations with different genetic backgrounds or environmental exposures.

Conclusion.

This study demonstrates that Sudanese patients with chronic hepatitis B exhibit significantly elevated platelet indices compared to healthy controls, challenging conventional associations between chronic HBV and thrombocytopenia. The simultaneous elevation of platelet count, MPV, PDW, and PCT suggests an integrated compensatory thrombopoietic response to chronic hepatic inflammation, likely occurring before the development of significant liver fibrosis.

However, these platelet indices do not differ significantly across disease phases defined by viral load, suggesting limited utility as markers of disease activity in this population. The absence of age- and gender-related differences indicates that observed changes are primarily disease-related rather than influenced by demographic factors.

The paradoxical findings in our cohort may reflect population-specific genetic factors, unique inflammatory responses, or early-stage compensatory mechanisms not previously described. These results highlight the importance of population-specific research in understanding disease manifestations and the potential limitations of extrapolating findings across different ethnic and geographic populations.

Future research incorporating comprehensive liver assessment, longitudinal follow-up, and mechanistic investigations will be essential to validate these findings and determine their clinical utility for disease monitoring and management in Sudanese patients with chronic hepatitis B.

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