

World Journal of *Clinical Cases*

World J Clin Cases 2022 December 26; 10(36): 13148-13469



MINIREVIEWS

- 13148** Liver injury in COVID-19: Holds ferritinophagy-mediated ferroptosis accountable
Jia FJ, Han J
- 13157** Amebic liver abscess by *Entamoeba histolytica*
Usuda D, Tsuge S, Sakurai R, Kawai K, Matsubara S, Tanaka R, Suzuki M, Takano H, Shimozawa S, Hotchi Y, Tokunaga S, Osugi I, Katou R, Ito S, Mishima K, Kondo A, Mizuno K, Takami H, Komatsu T, Oba J, Nomura T, Sugita M
- 13167** Living with liver disease in the era of COVID-19-the impact of the epidemic and the threat to high-risk populations
Barve P, Choday P, Nguyen A, Ly T, Samreen I, Jhooty S, Umeh CA, Chaudhuri S
- 13179** Cortical bone trajectory screws in the treatment of lumbar degenerative disc disease in patients with osteoporosis
Guo S, Zhu K, Yan MJ, Li XH, Tan J
- 13189** Probiotics for preventing gestational diabetes in overweight or obese pregnant women: A review
Deng YF, Wu LP, Liu YP

ORIGINAL ARTICLE

Retrospective Cohort Study

- 13200** Effectiveness of microwave endometrial ablation combined with hysteroscopic transcervical resection in treating submucous uterine myomas
Kakinuma T, Kakinuma K, Shimizu A, Kaneko A, Kagimoto M, Okusa T, Suizu E, Saito K, Matsuda Y, Yanagida K, Takeshima N, Ohwada M
- 13208** Antibody and complement levels in patients with hypersplenism associated with cirrhotic portal hypertension and therapeutic principles
Zhang K, Zeng M, Li YJ, Wu HF, Wu JC, Zhang ZS, Zheng JF, Lv YF

Retrospective Study

- 13216** Case series in Indonesia: B.1.617.2 (delta) variant of SARS-CoV-2 infection after a second dose of vaccine
Karuniawati A, Syam AF, Achmadasyah A, Ibrahim F, Rosa Y, Sudarmono P, Fadilah F, Rasmin M
- 13227** Endobronchial ultrasound-guided transbronchial needle aspiration in intrathoracic lymphadenopathy with extrathoracic malignancy
Li SJ, Wu Q
- 13239** Analysis of the clinical efficacy of two-stage revision surgery in the treatment of periprosthetic joint infection in the knee: A retrospective study
Qiao YJ, Li F, Zhang LD, Yu XY, Zhang HQ, Yang WB, Song XY, Xu RL, Zhou SH

- 13250** Prognostic factors for disease-free survival in postoperative patients with hepatocellular carcinoma and construction of a nomogram model
Luo PQ, Ye ZH, Zhang LX, Song ED, Wei ZJ, Xu AM, Lu Z
- 13264** Oral higher dose prednisolone to prevent stenosis after endoscopic submucosal dissection for early esophageal cancer
Zhan SG, Wu BH, Li DF, Yao J, Xu ZL, Zhang DG, Shi RY, Tian YH, Wang LS
- 13274** Predictive value of the unplanned extubation risk assessment scale in hospitalized patients with tubes
Liu K, Liu Z, Li LQ, Zhang M, Deng XX, Zhu H
- 13284** Classification of rectal cancer according to recurrence types - comparison of Japanese guidelines and Western guidelines
Miyakita H, Kamei Y, Chan LF, Okada K, Kayano H, Yamamoto S
- 13293** Risk of critical limb ischemia in long-term uterine cancer survivors: A population-based study
Chen MC, Chang JJ, Chen MF, Wang TY, Huang CE, Lee KD, Chen CY
- 13304** Serum Spondin-2 expression, tumor invasion, and antitumor immune response in patients with cervical cancer
Zhang LL, Lin S, Zhang Y, Yao DM, Du X
- 13313** Thoracic para-aortic lymph node recurrence in patients with esophageal squamous cell carcinoma: A propensity score-matching analysis
Li XY, Huang LS, Yu SH, Xie D
- 13321** Anastomotic leakage in rectal cancer surgery: Retrospective analysis of risk factors
Brisinda G, Chiarello MM, Pepe G, Cariati M, Fico V, Mirco P, Bianchi V

META-ANALYSIS

- 13337** Successful outcomes of unilateral *vs* bilateral pedicle screw fixation for lumbar interbody fusion: A meta-analysis with evidence grading
Sun L, Tian AX, Ma JX, Ma XL

CASE REPORT

- 13349** Pregnancy-induced leukocytosis: A case report
Wang X, Zhang YY, Xu Y
- 13356** Acute moderate to severe ulcerative colitis treated by traditional Chinese medicine: A case report
Wu B
- 13364** Solitary hyoid plasmacytoma with unicentric Castleman disease: A case report and review of literature
Zhang YH, He YF, Yue H, Zhang YN, Shi L, Jin B, Dong P
- 13373** Recurrence of intratendinous ganglion due to incomplete excision of satellite lesion in the extensor digitorum brevis tendon: A case report
Park JJ, Seok HG, Yan H, Park CH

- 13381** Two methods of lung biopsy for histological confirmation of acute fibrinous and organizing pneumonia: A case report
Liu WJ, Zhou S, Li YX
- 13388** Application of 3D-printed prosthesis in revision surgery with large inflammatory pseudotumour and extensive bone defect: A case report
Wang HP, Wang MY, Lan YP, Tang ZD, Tao QF, Chen CY
- 13396** Undetected traumatic cardiac herniation like playing hide-and-seek-delayed incidental findings during surgical stabilization of flail chest: A case report
Yoon SY, Ye JB, Seok J
- 13402** Laparoscopic treatment of pyogenic liver abscess caused by fishbone puncture through the stomach wall and into the liver: A case report
Kadi A, Tuergan T, Abulaiti Y, Shalayiadang P, Tayier B, Abulizi A, Tuohuti M, Ahan A
- 13408** Hepatic sinusoidal obstruction syndrome induced by tacrolimus following liver transplantation: Three case reports
Jiang JY, Fu Y, Ou YJ, Zhang LD
- 13418** *Staphylococcus aureus* bacteremia and infective endocarditis in a patient with epidermolytic hyperkeratosis: A case report
Chen Y, Chen D, Liu H, Zhang CG, Song LL
- 13426** Compound heterozygous p.L483P and p.S310G mutations in GBA1 cause type 1 adult Gaucher disease: A case report
Wen XL, Wang YZ, Zhang XL, Tu JQ, Zhang ZJ, Liu XX, Lu HY, Hao GP, Wang XH, Yang LH, Zhang RJ
- 13435** Short-term prone positioning for severe acute respiratory distress syndrome after cardiopulmonary bypass: A case report and literature review
Yang JH, Wang S, Gan YX, Feng XY, Niu BL
- 13443** Congenital nephrogenic diabetes insipidus arginine vasopressin receptor 2 gene mutation at new site: A case report
Yang LL, Xu Y, Qiu JL, Zhao QY, Li MM, Shi H
- 13451** Development of dilated cardiomyopathy with a long latent period followed by viral fulminant myocarditis: A case report
Lee SD, Lee HJ, Kim HR, Kang MG, Kim K, Park JR
- 13458** Hoffa's fracture in a five-year-old child diagnosed and treated with the assistance of arthroscopy: A case report
Chen ZH, Wang HF, Wang HY, Li F, Bai XF, Ni JL, Shi ZB

LETTER TO THE EDITOR

- 13467** Precautions before starting tofacitinib in persons with rheumatoid arthritis
Swarnakar R, Yadav SL

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Janardhan Mydam, MD, Assistant Professor, Consultant Physician-Scientist, Statistician, Division of Neonatology, Department of Pediatrics, John H. Stroger, Jr. Hospital of Cook County 1969 W. Ogden, Chicago, IL 60612, United States. mydamj@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The WJCC is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for WJCC as 1.534; IF without journal self cites: 1.491; 5-year IF: 1.599; Journal Citation Indicator: 0.28; Ranking: 135 among 172 journals in medicine, general and internal; and Quartile category: Q4. The WJCC's CiteScore for 2021 is 1.2 and Scopus CiteScore rank 2021: General Medicine is 443/826.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xu Guo*; Editorial Office Director: *Jin-Lei Wang*.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

December 26, 2022

COPYRIGHT

© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Retrospective Cohort Study

Antibody and complement levels in patients with hypersplenism associated with cirrhotic portal hypertension and therapeutic principles

Kun Zhang, Min Zeng, Ye-Juan Li, Hong-Fei Wu, Jin-Cai Wu, Zhen-Sheng Zhang, Jin-Fang Zheng, Yun-Fu Lv

Specialty type: Immunology**Provenance and peer review:**

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind**Peer-review report's scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C

Grade D (Fair): D

Grade E (Poor): 0

P-Reviewer: Abi-Mosleh L, India; Sripongpun P, Thailand**Received:** September 16, 2022**Peer-review started:** September 16, 2022**First decision:** October 19, 2022**Revised:** October 30, 2022**Accepted:** November 30, 2022**Article in press:** November 30, 2022**Published online:** December 26, 2022**Kun Zhang, Min Zeng,** Department of Geriatric Center, Hainan General Hospital, Haikou 570311, Hainan Province, China**Ye-Juan Li,** Reproductive Medicine Center, Maternal and Child Health Care Hospital of Hainan Province, Haikou 570311, Hainan Province, China**Hong-Fei Wu, Jin-Cai Wu, Zhen-Sheng Zhang, Jin-Fang Zheng, Yun-Fu Lv,** Department of General Surgery, Hainan General Hospital, Haikou 570311, Hainan Province, China**Corresponding author:** Yun-Fu Lv, Doctor, MD, PhD, Academic Research, Chief Doctor, Professor, Research Scientist, Surgeon, Department of General Surgery, Hainan General Hospital, No. 19 Xiuhua Road, Xiuyin District, Haikou 570311, Hainan Province, China. yunfu_lv@126.com

Abstract

BACKGROUND

Hypersplenism associated with cirrhotic portal hypertension is a common condition often resulting from hepatitis B-related cirrhosis. However, the levels of immunoglobulin (Ig) and complement in patients with hypersplenism associated with cirrhotic portal hypertension remain unclear. This study was undertaken to determine the levels of Ig and complement in these patients, the relationship between these levels and Child-Pugh class and their clinical significance.

AIM

To investigate the antibody (Ig) and complement levels in patients with hypersplenism associated with cirrhotic portal hypertension and their clinical significance.

METHODS

Clinical data of 119 patients with hypersplenism associated with cirrhotic portal hypertension were statistically analyzed and compared with those of 128 control patients.

RESULTS

IgA and IgG levels in patients with hypersplenism were significantly higher than controls ($P < 0.001$). There was no significant difference in IgM between the two

groups ($P = 0.109$). C3 and C4 levels in patients with hypersplenism were significantly lower than controls ($P < 0.001$). As liver function decreased, IgA and IgG levels increased ($P < 0.001$), and C3 and C4 levels decreased ($P < 0.001$).

CONCLUSION

Patients with hypersplenism associated with cirrhotic portal hypertension have significantly higher antibody (IgA and IgG) levels and significantly lower complement (C3 and C4) levels, which are both related to liver damage. Clinically, the administration of anti-hepatitis virus agents and protection of liver function should be strengthened.

Key Words: Hypersplenism associated with cirrhotic portal hypertension; Complement; Treatment; Hepatitis; B-immunoglobulin

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Patients with cirrhotic portal hypertension and hypersplenism are clinically common. The spleen is an important immune organ, but studies on antibody and complement levels in patients are scarce. This study found that IgA and IgG levels increased and complement levels decreased in our patient population compared to the healthy controls. These findings indicate liver damage, supporting the need for anti-viral treatment in these patients.

Citation: Zhang K, Zeng M, Li YJ, Wu HF, Wu JC, Zhang ZS, Zheng JF, Lv YF. Antibody and complement levels in patients with hypersplenism associated with cirrhotic portal hypertension and therapeutic principles. *World J Clin Cases* 2022; 10(36): 13208-13215

URL: <https://www.wjgnet.com/2307-8960/full/v10/i36/13208.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v10.i36.13208>

INTRODUCTION

Hypersplenism associated with cirrhotic portal hypertension is a common condition often resulting from hepatitis B-related cirrhosis[1]. Hepatitis B is a chronic infectious disease caused by hepatitis B virus (HBV) infection[2]. Under normal circumstances, the immune system protects the body by defending against external invading pathogens, maintaining physiological balance and eliminating diseased cells through cellular and/or humoral immunity. An abnormal immune response, whether hyperactive (*i.e.* allergy) or hypoactive (*i.e.* immunodeficiency), can cause tissue damage and immunopathological reactions[3].

HBV infection is a global public health issue; in particular, China has a high prevalence of HBV[4]. The pathogenesis of HBV infection is not yet fully understood. Numerous studies have shown that the immunopathological response and the interaction between the virus and host cells are the main causes of liver cell damage[5]. The progression and outcome of HBV infection is therefore related to the host's immune response. Immunosuppression or immune system disorder can cause HBV replication, leading to chronic infection, and then develop cirrhosis. Liver cirrhosis caused by any reason may lead to hypersplenism related to portal hypertension[6] and possibly liver cancer.

Antibodies are important effector molecules that mediate humoral immunity by binding to specific antigens. They are immunoglobulins (Ig) produced by plasma cells, which are differentiated from B cells and memory B cells in the immune system under antigen stimulation[7]. They are distributed in the serum, tissue fluid, exocrine fluid and on the surface of some cell membranes. They demonstrate antibody-dependent cell-mediated cytotoxicity and play a role in neutralization, opsonization and complement activation[8,9].

By combining different heavy and light chains, Igs form complete antibody molecules that can be classified into five types: IgG, IgM, IgA, IgD and IgE. IgG is the only antibody that can cross the placental barrier and is the main component of serum Igs[10]. It is the main antibody produced during the immune response and the "main force" to fight against infection; in fact, most antibody activity in the serum is related to IgG. It activates complement through the classical pathway and binds to Fc receptors on the surface of macrophages and natural killer cells to regulate antibody-dependent cell-mediated cytotoxicity[11]. IgM accounts for 5%-10% of the total serum Ig pool. It is the first antibody to be produced during ontogeny[12] and to appear in the primary humoral immune response, serving as the "vanguard" for specific defense against infection. IgA is an exocrine Ig that participates in local mucosal immunity and plays an important role as the "border guard" for local defense against infection. IgE is mainly present in the allergic response[13], and IgD is present only in trace amounts[14,15].

Complement proteins play vital roles in the immune response, affecting both innate and adaptive immunity, regulating the immune response at different stages and influencing the immunological function of antibodies. In particular, the complement protein C3 plays a critical role. The level of serum C3 is proportional to the total amount of complement, and the serum C3 and C4 levels provide a good estimate for the total serum complement level[16,17]. However, the levels of Ig and complement in patients with hypersplenism associated with cirrhotic portal hypertension remain unclear. This study was undertaken to determine the levels of Ig and complement in these patients, the relationship between these levels and Child-Pugh class and their clinical significance.

MATERIALS AND METHODS

Patients and methods

A total of 119 patients with hypersplenism were compared with a control group of 128 patients. All methods were performed in accordance with the relevant guidelines and regulations/Declaration of Helsinki. Informed consent was obtained from all patients.

The hypersplenism group was composed of hypersplenism caused by cirrhosis and portal hypertension. Patients with hypersplenism caused by non-cirrhotic portal hypertension, such as lymphoma, pulmonary tuberculosis, connective tissue and inflammatory diseases, were excluded. The 119 patients included 93 males and 26 females, with a male-to-female ratio of 3.6:1. Their ages ranged from 41 years to 82 years, with a mean of 51 years. Among them, 95 patients (80.0%) had hepatitis B cirrhosis, 13 (10.9%) had hepatitis C cirrhosis, 3 (2.5%) had biliary cirrhosis, and 8 (6.6%) had other types of cirrhosis. Liver cirrhosis and splenomegaly (as assessed by B-Mode ultrasound and computed tomography), mono- or multilineage peripheral cytopenias (as assessed by laboratory tests) and moderate or severe varices in the lower esophagus and gastric fundus (as assessed by computed tomography and endoscopy), were found in all patients.

Furthermore, all patients underwent surgical treatment. Specifically, 45 patients (37.8%) underwent hepatic lobectomy for concomitant liver cancer, 33 (27.7%) underwent devascularization of the lower esophagus and gastric fundus + splenectomy for massive gastrointestinal bleeding (≥ 1000 mL), 12 (10.1%) underwent splenectomy for splenomegaly in which the spleen extends beyond the midline of the abdomen or below the line joining the two anterior superior iliac spines and reduced quality of life, 15 (12.6%) underwent splenectomy + portal-azygos disconnection for moderate or severe hypersplenism, 11 (9.3%) underwent splenectomy alone, and 3 (2.5%) underwent portacaval shunt alone. Liver tissue was collected during the operation and sent for pathological examination, which revealed cirrhosis.

The control group was composed of surgical patients without hypersplenism associated with cirrhotic portal hypertension. These patients had no history of hepatitis virus infection or cirrhosis caused by other reasons. The liver function was normal, and the spleen volume was not enlarged. The 128 control patients included 65 males and 63 females, with a male-to-female ratio of 1:1. Their ages ranged from 20 years to 93 years, with a mean of 49 years. Specifically, 49 patients with cholecystolithiasis and 9 with gallbladder polyps underwent laparoscopic cholecystectomy, 38 with choledocholithiasis underwent choledocholithotomy, 19 with inguinal hernia and femoral hernia underwent laparoscopic hernia repair, and 13 with nodular goiter underwent subtotal thyroidectomy.

Detection method

Ig, C3 and C4 were detected by turbidimetric inhibition immunoassay. Briefly, 2 mL of peripheral venous blood was drawn from the patient, placed in a dry test tube and sent to the hospital laboratory for routine detection.

Statistical analysis

Statistical analysis was performed using SPSS software v25.0 (IBM Corp., Armonk, NY, United States). Measurement data were expressed as (average of $\bar{x} \pm$ standard deviation) and [mean (P_{25} , P_{75})]. The *t*/*z* test and Wilcoxon rank sum test for two independent samples were used for comparison between groups. $P < 0.05$ or $P < 0.001$ were considered statistically significant.

RESULTS

Comparison of sex and age between the two groups

There were significantly more males than females in the hypersplenism group compared to controls ($P < 0.05$). There was no significant difference in age between the two groups ($P > 0.05$).

Comparison of Ig levels before treatment between the two groups

Compared with the control group, IgA and IgG levels were significantly higher in the hypersplenism group ($Z = -6.61$ and -7.16 , respectively; $P < 0.001$). There was no significant difference in IgM levels between the two groups ($Z = -1.60$, $P = 0.109$) (Figure 1).

Comparison of complement levels between the two groups before treatment

Compared with the control group, C3 and C4 levels were significantly lower in the hypersplenism group ($t/z = 4.28$ and -6.65 , respectively; $P < 0.001$) (Figure 2).

The relationship between Child-Pugh class and Ig and complement levels in patients with hypersplenism associated with cirrhotic portal hypertension

For comparison of IgA, there were significant differences between class A and B ($Z = 3.773$, $P < 0.001$) and class A and C ($Z = 2.373$, $P = 0.018$) but not between class B and C ($Z = 0.190$, $P = 0.850$). For comparison of IgG, there were significant differences between class A and C ($t = 3.732$, $P < 0.001$) and class B and C ($t = 2.225$, $P = 0.032$) but not between class A and B ($t = 1.252$, $P = 0.213$). There were no statistically significant differences between the IgM groups. For comparison of C3, there were significant differences between class A and B ($t = 3.149$, $P = 0.002$), and class A and C ($t = 3.857$, $P < 0.001$) but not between class B and C ($t = 0.486$, $P = 0.630$). For comparison of C4, there were significant differences between class A and B ($Z = 3.364$, $P < 0.001$) but not between class A and C ($Z = 1.851$, $P = 0.064$) nor class B and C ($Z = 0.298$, $P = 0.765$) (Figure 3).

DISCUSSION

Based on B-Mode ultrasound and computed tomography findings, endoscopy revealed moderate-to-severe varices in the lower esophagus and gastric fundus. Liver tissue was collected during the operation and sent for pathological examination. These findings supported the diagnosis of cirrhotic portal hypertension. Dameshek[18] proposed four criteria for a diagnosis of hypersplenism: (1) Splenomegaly; (2) One or several types of cytopenia; (3) Bone marrow is normal or in hyperplastic state; and (4) Pathological changes of blood cells disappeared after splenectomy. The clinical manifestations of portal hypertension include splenomegaly, and for patients with hypersplenism, peripheral cytopenia should be present and blood counts should become normal after splenectomy[4]. The diagnosis of hypersplenism in cirrhotic portal hypertension is consistent with all patients[19].

Although there was a significant difference in sex composition between the two groups, there was no significant difference in age. Hence, there should be no age-related effect on the Ig and complement measurements between the hypersplenism patients and controls. IgA and IgG levels were significantly higher than controls, indicating that patients with hypersplenism associated with cirrhotic portal hypertension had elevated serum levels of the two dominant Igs. This phenomenon has gained the attention of clinicians[11] and has been repeatedly confirmed[20,21]. Elevated serum Ig levels are of great significance in clinical diagnosis[20] and are suggestive of liver damage.

In this study, hypersplenism patients with Child-Pugh class C had significantly higher IgA and IgG levels than those with class A or B, indicating that the liver function was inversely correlated with serum levels of the two main Igs. There was no significant difference in IgM among the Child-Pugh classes, which may be related to its low total amount in all groups. There are two reasons for the increased Ig levels in the class C patients. Namely, a large number of antibodies are produced to eliminate the virus, and cirrhosis caused by HBV results in liver cell dysfunction and a reduced ability to remove antibodies[22]. Further research is required to determine whether and to what extent enhanced splenic macrophage function is correlated with increased Ig levels in patients with hypersplenism associated with cirrhotic portal hypertension[23].

The significantly lower serum levels of complements C3 and C4 in patients with hypersplenism associated with cirrhotic portal hypertension are also related to liver function impairment. One possible explanation is the reduced ability of damaged liver cells to synthesize complements. Another possibility is the development of a portal systemic collateral circulation, allowing a large amount of endotoxin to enter the bloodstream, which simultaneously activates the classical and alternative pathways, resulting in a large amount of complements to be consumed[24] and a substantial reduction in C3 and C4 levels[25].

This study shows that increased liver function impairment corresponds to lower levels of C3 and C4. As a type of globulin with antibody activity in human serum or fluid, Igs are antimicrobial and antiviral and enhance phagocytosis. Moreover, they can kill or dissolve pathogenic microorganisms with the assistance of complements, which is an important defense function in anti-infection immunity. Therefore, understanding serum Ig levels and their relationship to liver function in patients with hypersplenism associated with cirrhotic portal hypertension is of great clinical significance for assessing the disease progression and strengthening liver-protective treatment.

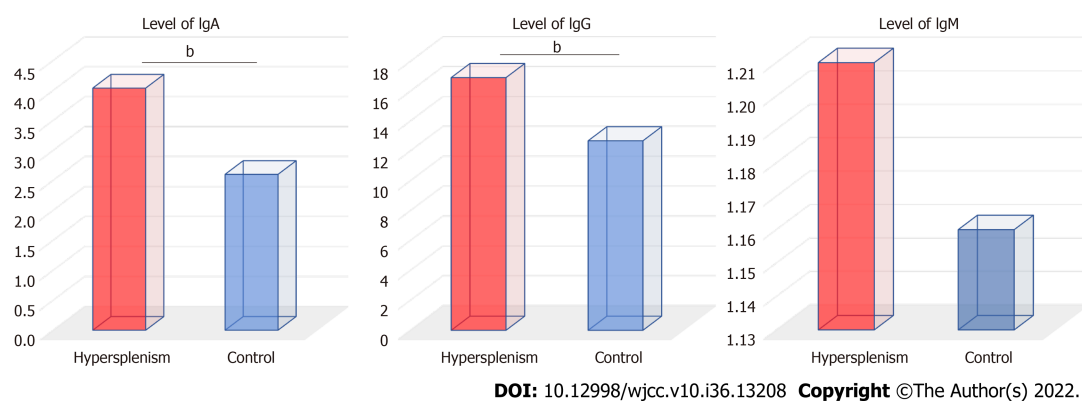


Figure 1 Comparison of immunoglobulin levels (g/L) between the hypersplenism group and the control group. ^b $P < 0.001$. Ig: Immunoglobulin.

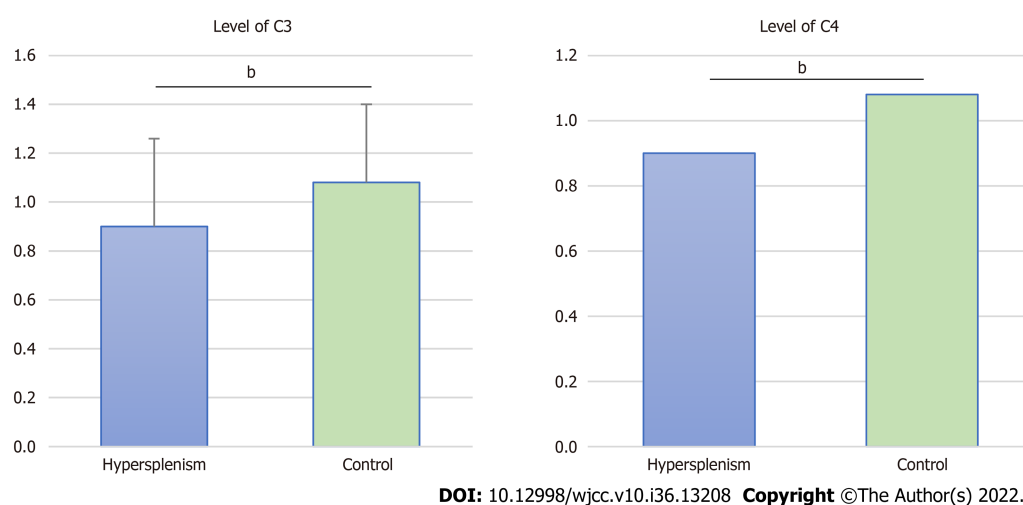


Figure 2 Comparison of complement levels (g/L) between the hypersplenism group and the control group. ^a $P < 0.05$; ^b $P < 0.001$.

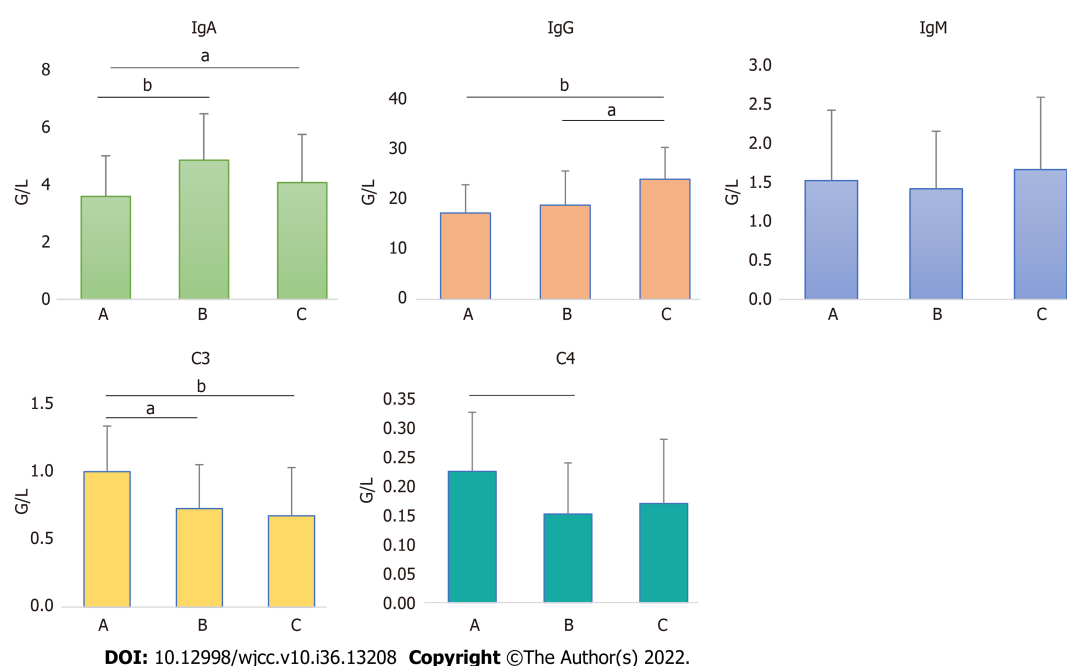


Figure 3 Relationship between Child-Pugh class and immunoglobulin and complement levels. ^a $P < 0.05$; ^b $P < 0.001$. Ig: Immunoglobulin.

CONCLUSION

Patients with hypersplenism associated with cirrhotic portal hypertension have significantly higher antibody (IgA and IgG) levels and significantly lower complement (C3 and C4) levels. The increase of antibodies and the decrease of complement are related to liver function damage. Clinically, the administration of anti-hepatitis virus agents and protection of liver function should be strengthened[26-28].

ARTICLE HIGHLIGHTS

Research background

The antibody and complement levels in patients with cirrhosis and hypersplenism due to portal hypertension are not clear, which affects the diagnosis and treatment to some extent.

Research motivation

There are no studies determining the levels of immunoglobulins (Ig) and complements in patients with hypersplenism due to cirrhosis and portal hypertension, which affects the diagnosis and treatment.

Research objectives

To investigate the antibody (Ig) and complement levels in patients with hypersplenism due to liver cirrhosis and portal hypertension and how to treat them.

Research methods

The levels of IgA, IgG, IgM, C3 and C4 were determined and compared in 119 patients with confirmed hypersplenism and 128 control patients.

Research results

The levels of IgA and IgG in the hypersplenism group were significantly higher than those in the control group ($P < 0.001$). The levels of C3 and C4 in the hypersplenism group were significantly lower than those in the control group ($P < 0.001$). The worse the liver function was, the higher the IgA and IgG levels were ($P < 0.001$) and the lower the C3 and C4 levels were ($P < 0.001$).

Research conclusions

Antibodies in patients with liver cirrhosis and portal hypertension and hypersplenism were significantly increased, while complements (C3 and C4) were significantly decreased. Both the increase of antibody and the decrease of complement are related to the damage of liver function.

Research perspectives

It is important to know the antibody (Ig) and complement levels of patients with hypersplenism due to cirrhosis and portal hypertension. Anti-hepatitis virus and liver function protection should be strengthened in treatment.

FOOTNOTES

Author contributions: Zhang K, Zeng M, Li YJ, Wu JC, Zheng JF and Lv YF contributed equally to this work; Lv YF was responsible for project design and thesis writing; Zhang K and Li YJ were responsible for implementation and statistical information; Wu JC, Zheng JF and Zeng M were responsible for data and statistical information collection; Wu HF and Zhang ZS participated in data collection and registration; all authors have read this article and consent to publication.

Supported by Hainan Provincial Department of Science and Technology, Qiongke[2020]256.

Institutional review board statement: The patient data and research content submitted in this project comply with relevant laws and regulations. The study was approved for implementation by the Ethics Committee of Hainan General Hospital, approval No: Med Eth Re [2020] 086.

Conflict-of-interest statement: All authors report no relevant conflicts of interest for this article.

Data sharing statement: All data generated or analyzed during this study were included in this published article.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license

their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: China

ORCID number: Yun-Fu Lv 0000-0003-0451-399X.

S-Editor: Xing YX

L-Editor: Filipodia

P-Editor: Xing YX

REFERENCES

- 1 Lv Y, Wu H, Lau WY, Zheng J, Wu J, Zeng M. Impact of total splenectomy on peripheral lymphocytes and their subsets in patients with hypersplenism associated with cirrhotic portal hypertension. *Sci Rep* 2021; **11**: 21246 [PMID: 34711891 DOI: 10.1038/s41598-021-00692-x]
- 2 Kennedy M, Alexopoulos SP. Hepatitis B virus infection and liver transplantation. *Curr Opin Organ Transplant* 2010; **15**: 310-315 [PMID: 20445447 DOI: 10.1097/MOT.0b013e32833991f8]
- 3 Rouse BT. Virus-induced immunopathology. *Adv Virus Res* 1996; **47**: 353-376 [PMID: 8895836 DOI: 10.1016/s0065-3527(08)60739-3]
- 4 Lv Y, Yee Lau W, Wu H, Han X, Gong X, Liu N, Yue J, Li Q, Li Y, Deng J. Causes of peripheral cytopenia in hepatic cirrhosis and portal hypertensive splenomegaly. *Exp Biol Med (Maywood)* 2017; **242**: 744-749 [PMID: 28299974 DOI: 10.1177/1535370217693113]
- 5 Duriez M, Mandouri Y, Lekbaby B, Wang H, Schnuriger A, Redelsperger F, Guerrero CI, Lefevre M, Fauveau V, Ahodantin J, Quetier I, Chhuon C, Gourari S, Boissonnas A, Gill U, Kennedy P, Debzi N, Sitterlin D, Maini MK, Kremsdorf D, Soussan P. Alternative splicing of hepatitis B virus: A novel virus/host interaction altering liver immunity. *J Hepatol* 2017; **67**: 687-699 [PMID: 28600137 DOI: 10.1016/j.jhep.2017.05.025]
- 6 Baig S, Alamgir M. The extrahepatic manifestations of hepatitis B virus. *J Coll Physicians Surg Pak* 2008; **18**: 451-457 [PMID: 18760074]
- 7 Zabel F, Mohanan D, Bessa J, Link A, Fettelschoss A, Saudan P, Kündig TM, Bachmann MF. Viral particles drive rapid differentiation of memory B cells into secondary plasma cells producing increased levels of antibodies. *J Immunol* 2014; **192**: 5499-5508 [PMID: 24821969 DOI: 10.4049/jimmunol.1400065]
- 8 Vaerman JP. [Effector mechanisms of IgA]. *Ann Biol Clin (Paris)* 1984; **42**: 61-70 [PMID: 6375472]
- 9 Sawa T, Kinoshita M, Inoue K, Ohara J, Moriyama K. Immunoglobulin for Treating Bacterial Infections: One More Mechanism of Action. *Antibodies (Basel)* 2019; **8** [PMID: 31684203 DOI: 10.3390/antib8040052]
- 10 Hädege D. [Evolution of the immunoglobulins]. *Allerg Immunol (Leipz)* 1985; **31**: 231-243 [PMID: 2936216]
- 11 Feizi T. Immunoglobulins in chronic liver disease[J]. *Sci Rep* 1968; **9**: 193-198 [PMID: 4172757 DOI: 10.1136/gut.9.2.193]
- 12 Zhang Q, Gao Y, Peng Y, Fu M, Liu YQ, Zhou QJ, Yu J, Zheng XQ. Epidemiological survey of human cytomegalovirus antibody levels in children from Southeastern China. *Virol J* 2014; **11**: 123 [PMID: 24996226 DOI: 10.1186/1743-422X-11-123]
- 13 Antunes J, Kochuyt AM, Ceuppens JL. Perioperative allergic reactions: experience in a Flemish referral centre. *Allergol Immunopathol (Madr)* 2014; **42**: 348-354 [PMID: 24269183 DOI: 10.1016/j.aller.2013.08.001]
- 14 Liu A H, Jena P K, Wysocki L J. Tracing the development of single memory-lineage B cells in a highly defined immune response. *J Exp Med* 1996; **183**: 2053-2063 [PMID: 8642316 DOI: 10.1084/jem.183.5.2053]
- 15 Richard K S Loh, Sandra Vale, Andrew McLean-Tooke. Quantitative serum immunoglobulin tests. *Aust Fam Physician* 2013; **42**: 195-198 [PMID: 23550242]
- 16 Yang X, Sun J, Gao Y, Tan A, Zhang H, Hu Y, Feng J, Qin X, Tao S, Chen Z, Kim ST, Peng T, Liao M, Lin X, Zhang Z, Tang M, Li L, Mo L, Liang Z, Shi D, Huang Z, Huang X, Liu M, Liu Q, Zhang S, Trent JM, Zheng SL, Xu J, Mo Z. Genome-wide association study for serum complement C3 and C4 levels in healthy Chinese subjects. *PLoS Genet* 2012; **8**: e1002916 [PMID: 23028341 DOI: 10.1371/journal.pgen.1002916]
- 17 Ritchie RF, Palomaki GE, Neveux LM, Navolotskaia O, Ledue TB, Craig WY. Reference distributions for complement proteins C3 and C4: a practical, simple and clinically relevant approach in a large cohort. *J Clin Lab Anal* 2004; **18**: 1-8 [PMID: 14730550 DOI: 10.1002/jcla.10100]
- 18 Dameshek W. Hypersplenism. *Bull N Y Acad Med* 1955; **31**: 113-136 [PMID: 13230762]
- 19 Lv Y, Gong X, Xie X, Wang B, Yang Y, Li Y. Clinical study on the relationship between hematocytopenia and splenomegaly caused by cirrhotic portal hypertension. *Cell Biochem Biophys* 2014; **70**: 355-360 [PMID: 24696075 DOI: 10.1007/s12013-014-9920-9]
- 20 Lin S, Sun Q, Mao W, Chen Y. Serum Immunoglobulin A (IgA) Level Is a Potential Biomarker Indicating Cirrhosis during Chronic Hepatitis B Infection. *Gastroenterol Res Pract* 2016; **2016**: 2495073 [PMID: 27123003 DOI: 10.1155/2016/2495073]
- 21 Watt K, Uhanova J, Gong Y, Kaita K, Doucette K, Pettigrew N, Minuk GY. Serum immunoglobulins predict the extent of hepatic fibrosis in patients with chronic hepatitis C virus infection. *J Viral Hepat* 2004; **11**: 251-256 [PMID: 15117327 DOI: 10.1111/j.1365-2893.2004.00507.x]
- 22 Ortank Z, Toyran A, Sen S, Mart Kömürçü SZ, Güvener E. [Evaluation of serum IgG, IgA and IgM levels as indicators of hepatic fibrosis in patients with chronic hepatitis C infection]. *Mikrobiyol Bul* 2011; **45**: 296-305 [PMID: 21644073]

- 23 **González-Quintela A**, Alende MR, Gamallo R, González-Gil P, López-Ben S, Tomé S, Otero E, Torre JA. Serum immunoglobulins (IgG, IgA, IgM) in chronic hepatitis C. A comparison with non-cirrhotic alcoholic liver disease. *Hepatogastroenterology* 2003; **50**: 2121-2126 [PMID: [14696478](#)]
- 24 **Zhu C**, Song H, Xu F, Yi W, Liu F, Liu X. Hepatitis B virus inhibits the expression of complement C3 and C4, *in vitro* and *in vivo*. *Oncol Lett* 2018; **15**: 7459-7463 [PMID: [29731897](#) DOI: [10.3892/ol.2018.8223](#)]
- 25 **Chang WY**, Chuang WL. Complements as new diagnostic tools of hepatocellular carcinoma in cirrhotic patients. *Cancer* 1988; **62**: 227-232 [PMID: [2454720](#) DOI: [10.1002/1097-0142\(19880715\)62:2<227::aid-cnrcr2820620202>3.0.co;2-d](#)]
- 26 **Lei Z**, Xia Y, Si A, Wang K, Li J, Yan Z, Yang T, Wu D, Wan X, Zhou W, Liu J, Wang H, Cong W, Wu M, Pawlik TM, Lau WY, Shen F. Antiviral therapy improves survival in patients with HBV infection and intrahepatic cholangiocarcinoma undergoing liver resection. *J Hepatol* 2018; **68**: 655-662 [PMID: [29155069](#) DOI: [10.1016/j.jhep.2017.11.015](#)]
- 27 **Xu XF**, Xing H, Han J, Li ZL, Lau WY, Zhou YH, Gu WM, Wang H, Chen TH, Zeng YY, Li C, Wu MC, Shen F, Yang T. Risk Factors, Patterns, and Outcomes of Late Recurrence After Liver Resection for Hepatocellular Carcinoma: A Multicenter Study From China. *JAMA Surg* 2019; **154**: 209-217 [PMID: [30422241](#) DOI: [10.1001/jamasurg.2018.4334](#)]
- 28 **Huang G**, Li PP, Lau WY, Pan ZY, Zhao LH, Wang ZG, Wang MC, Zhou WP. Antiviral Therapy Reduces Hepatocellular Carcinoma Recurrence in Patients With Low HBV-DNA Levels: A Randomized Controlled Trial. *Ann Surg* 2018; **268**: 943-954 [PMID: [29521740](#) DOI: [10.1097/SLA.0000000000002727](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

