

Distribution of Human Constitutional Types Used In Traditional Mongolian Medicine among Patients with Chronic Hepatitis B

Bayarsaikhan Ochirchuulgan¹, Yong Li², Tsend-Ayush Damba², Badamjav Sevjid¹, Tserendagva Dalkh², and Tsogtsaikhan Sandag^{3*}

¹School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia.

²International School of Mongolian Traditional Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia.

³School of Biomedicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia.

*Correspondence:

Tsogtsaikhan Sandag Professor, MD, Ph.D, Chairman, Department of Microbiology and Immunology, School of Biomedicine, Mongolian National University of Medical Sciences, Mongolia, Tel: +976-91920868, E-mail: tsogtsaikhan.s@mnums.edu.mn.

Received: 25 October 2018; Accepted: 19 November 2018

Citation: Bayarsaikhan Ochirchuulgan, Yong Li, Tsend-Ayush Damba, et al. Distribution of Human Constitutional Types Used In Traditional Mongolian Medicine among Patients with Chronic Hepatitis B. *Gastroint Hepatol Dig Dis.* 2018; 1(3): 1-6.

ABSTRACT

Aim of the study: This study was aimed to clarify possible relationship between human constitutional types used in traditional Mongolian medicine and stages of the disease in patients with chronic hepatitis B (CHB).

Materials and methods: In this cross-sectional study were enrolled 101 patients with established state of CHB. There were selected patients only in 3 certain phases of the disease, namely in immune active, immune inactive and immune reactivation phases. Human constitutional types used for differential approaches of diagnostics, treatment and control of diseases in traditional Mongolian medicine were determined in all participants according with examination tests developed by Sachs R (1995) and modified by Batchimeg et al. (2003).

Results: Most prevalent constitutional types among patients with CHB were single Badgan or Pekan (earth, water) (24.8%) and single Shar or Tripa (fire) (18.9%) types. When patients were classified by dominant humors single Shar dominated subjects presented with 47.5% of patients. Chronic hepatitis B staging classified that 48/47.5% (25 males and 23 females) of patients are in reactivation phase, 35/34.7% (18 males and 17 females) are in inactive phase and 18/17.8% (10 males and 8 females) are in active phase. There was demonstrated significantly increased distribution of inactive phase among single Badgan type patients and reactivation phase among single Shar and dual Shar-Khii type patients ($\chi^2=69.5$; $p=0.001$). Significantly high portion of patients with active phases of CHB was demonstrated Khii dominated humors, while more patients with reactivation phases demonstrated Shar dominated humors and patients with inactive phases – Badgan dominated humors ($\chi^2=55.4$; $p=0.001$). Mean value of serum ALT and AST was significantly low in patients with dominated Badgan humors compared with that of patients with Khii and Shar dominated humors.

Key words

Chronic hepatitis B, Mongolian traditional medicine, Aminotransferases, Hepatitis B e antigen.

Introduction

Numerous studies were focused on the relationship between basic concepts of traditional and modern medicine. In particular, dominant distribution of particular human constitutional types used in traditional oriental medicines among patients with different forms or stages of certain pathology was described for Sasang

typology in Korean medicine [1-3], Yin-Yang typology in Chinese medicine [4] and typology in Indian Ayurveda medicine [5].

Human constitutional typology system in traditional Mongolian medicine was based in constitutional concepts of Tibetan medicine and developed last several centuries with regard to lifestyle of nomadic Mongolian people living in Central Asian continental plateau [6]. In traditional Mongolian medicine the typology system prescribes 3 single, 3 dual and one triple human constitutional types and additional mixed (or combined) types in accordance

with domination of abstraction substances (or humors, or notions, or elements) in human body. Single types are “Khii” (ᠬᠢᠢ, Tibetan-rlung [loong] or wind, or vital energy, or air), “Shar” (ᠰᠢᠷ, Tibetan-mkrispa [kris-pa], or Tripa or mucus, or fire) and “Badgan” (ᠪᠠᠳᠭᠠᠨ, Tibetan-badken or *pekan*, or *phlegm*, or *bile*, or *earth/water*), and dual types are Khii-Shar, Khii-badgan, Shar-Khii, Shar-badgan, Badgan-Shar and Badgan-Khii [7-9]. Our previous study has determined titer of some cytokines in plasma of peripheral blood and lymphocyte overnight culture supernatant of blood donors and has suggested the relationship between types of humors or constitutional types practiced in traditional Mongolian medicine and intensity of specific immune response types in healthy individuals [10].

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV) presenting a major global health problem and it can cause chronic infection and puts people at high risk of death from cirrhosis and liver cancer [11]. Mongolia is the country with high rate of hepatitis B disease burden with 10.6% of positive Hepatitis B surface Antigen (HBsAg) and 78.1 age-standardized incidence rate of liver cancer per 100,000 population [12]. Staging principles in guidelines mostly used for diagnostics, treatment and control of CHB are based on relationship between viral replication and evolution and the host immune response [13]. American Association for the Study of Liver Diseases (AASLD) Guideline for treatment of CHB provides four phases for CHB such as immune-tolerant phase, HBeAg-positive immune active phase, inactive chronic hepatitis B phase and HBeAg-negative immune reactivation phase [13]. Another widely recommended guideline is Clinical Practice Guidelines on the management of hepatitis B virus infection issued by European Association for the Study of the Liver (EASL). Updated in 2017 edition of the Guideline classified CHB into five phases: HBeAg-positive chronic HBV infection, HBeAg-positive chronic hepatitis B, HBeAg-negative chronic HBV infection, HBeAg-negative chronic hepatitis B, and HBsAg-negative phase characterized by serum negative HBsAg and positive antibodies to HBcAg (anti-HBc), with or without detectable antibodies to HBsAg (anti-HBs) [14]. World Health Organization’s (WHO) document named Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection prescribes five non-linear phases: immune tolerant, immune active, inactive chronic hepatitis, immune escape, and reactivation phases [15].

Non-linearity or non sequent development of events is common for above mentioned staging classifications and these phases look more likely as conditions of viral-host interaction. And question is that does development of particular condition of viral-host interaction may be related with personal characteristics of the host? We could not find any reports focused on relationship between stages of chronic hepatitis B and human typology used in Oriental medicine from available sources.

Aim of the study

This study was aimed to clarify possible relationship between human constitutional types used in traditional Mongolian medicine

and stages of the disease in patients with chronic hepatitis B.

Materials and methods

In this cross-sectional study were enrolled 101 (53 males and 48 females) patients aged age 21-81 year with established state of chronic hepatitis B. Patients were diagnosed and attended to the care from February 2015 to August 2017 at three institutions in Ulaanbaatar city, Mongolia: Center for Gastroenterology of First State Hospital, Department of Hepatobiliary Diseases of Third State Hospital, and University Hospital of Mongolian National University of Medical Sciences, and all clinical data was collected before initiation of therapeutic intervention. Staging of chronic HBV infection was performed according to criteria specified in “Guideline for Detection, Diagnosis and Treatment of hepatitis B (HBV) and hepatitis D (HDV) virus infection. 2016” approved by Ministry of Health, Mongolia [16]. The guideline was developed in compliance with WHO Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection [15]. There were selected 101 patients only in certain three phases of chronic HBV: in immune active, immune inactive and immune reactivation phases and without mix (hepatitis A and/or hepatitis C virus) and/or co-infection (hepatitis D virus). Patients in rest two phases described (immune tolerant and immune escape phases) in the guideline were excluded as transient conditions of host immune response to HBV. Following criteria was used to classify patients: 1) for immune active phase – disease characterized by fluctuating aminotransferases (alanine transferase-ALT; and aspartate transferase-AST), high HBV deoxyribonucleotide (DNA) concentrations (> 200 000 IU/mL) and may result in seroconversion from HBeAg (hepatitis B e antigen) to anti-HBe (antibody to hepatitis B e antigen); 2) for immune inactive phase – disease with negative HBeAg, positive anti-HBe, normal ALT and low HBV-DNA concentration (<2000 IU/mL); and for immune reactive or immune clearance phase - disease with positive or negative HBeAg, intermittent or persistent elevation of ALT levels and high HBV-DNA concentration, although not higher than 200 000 IU/mL. Personal and clinical data of patients were collected from the medical records.

Human constitutional types used for differential approaches of diagnostics and treatment of diseases in traditional Mongolian medicine [8,17] determined in all participants according with examination tests developed by Sachs R [18] and modified by Batchimeg et al. [19]. Examination test system includes 100 tests for collection of data using findings from anamnesis, observation and physical examination and all these tests were grouped in four sections such as body characteristics (25 tests), general properties (15 tests), individual’s imagination (41 tests) and special properties (19 tests). Test results expressed with and scores filled in three columns corresponding to Khii, Shar and Badgan humors. Constitution of each subject was determined by calculation of sum of scores using a formula. Dominating humors were defined as follows: Khii dominated humor includes pure Khii, Khii-Badgan and Khii-Shar types; Shar dominated humor includes pure Shar, Shar-Badgan and Shar-Khii types; and Badgan dominated humor includes pure Badgan, Badgan-Shar and Badgan-Khii types.

Pearson's Chi-square coefficient (χ^2) was calculated for distribution of signs, independent-samples T test (t) was used for comparison of mean in different constitutional types. Microsoft Windows Excel and SPSS-17 programs were been used for statistical processing of data.

Results

Age and sex of patients are shown in Table 1.

Age	Sex		Total
	male	female	
20-29	4/3.9	6/5.9	10/9.8
30-39	15/14.9	5/4.9	20/19.8
40-49	20/19.8	14/13.9	34/33.7
≥ 50	14/13.9	23/22.8	37/36.7
Mean	45.5 ± 11.5	48.4 ± 13.9	46.8 ± 12.7
Range	26-73	21-81	21-81
Total	53/52.5	48/47.5	101/100

Table 1: Age and sex of patients with chronic hepatitis B (n/%).

Constitutional characteristics of patients were determined by calculation of body mass index (BMI) formula and has shown obesity in a great portion (66.3%) of patients, in details, 10 (9.9%) of patients has demonstrated underweight range with BMI below 18.5 according with classification of Center for Disease Control and Prevention [20], 2 (1.9%) demonstrated normal range with BMI 18.5-24.9, 36 (35.8%) demonstrated overweight range with BMI 25.0-29.9, 52 (51.6%) demonstrated obesity of class I with BMI 30.0-34.9, 9 (8.9%) demonstrated obesity of class II with BMI 35.0-39.9, and 2 (1.9%) demonstrated obesity of class III with BMI above 40.0.

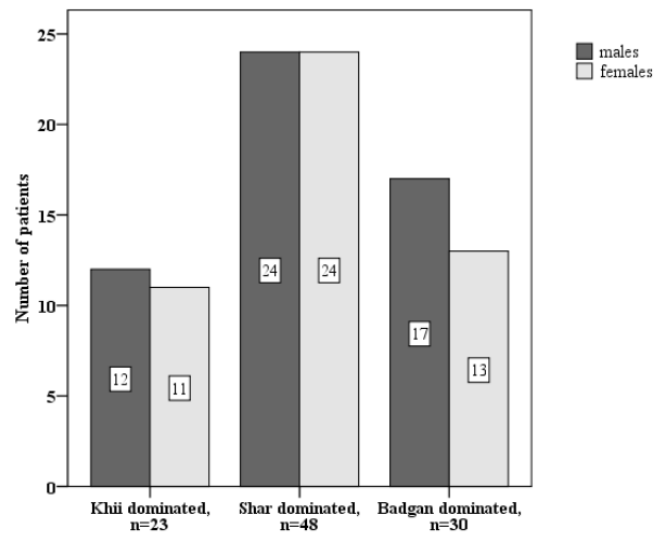
Results of testing for determination of constitutional types presented in Table 2.

Constitutional types	Sex		Total
	male	female	
Badgan	10/9.9	9/8.9	19/18.9
Shar	13/12.9	12/11.9	25/24.8
Khii	8/7.9	6/5.9	14/13.9
Khii-Badgan	1/0.9	3/2.9	4/3.9
Khii-Shar	3/2.9	2/1.9	5/4.9
Shar-Badgan	6/5.9	6/5.9	12/11.9
Badgan-Khii	4/3.9	3/2.9	7/6.9
Shar-Khii	5/4.9	5/4.9	10/9.9
Badgan-Shar	3/2.9	1/0.9	4/3.9
Total	53/52.5	48/47.5	101/100

Table 2: Constitutional types of patients with chronic hepatitis B (n/%).

Most prevalent types among patients with CHB were pure Shar (24.8%) and pure Badgan (18.9%) types. When patients were classified by dominant humors (figure 1) we found that Shar dominated subjects presented with 47.5% of patients. Both constitutional types and dominated humor types did not

demonstrate significant difference in distribution by sex, age and



obesity state of patients ($p>0.05$).

Figure 1: Distribution of constitutional types by dominantly expressed humors among patients with CHB.

Chronic HBV staging classified 48/47.5% (25 males and 23 females) patients with reactivation phase, 35/34.7% (18 males and 17 females) patients with inactive phase and 18/17.8% (10 males and 8 females) patients with active phase. Difference in distribution of patients with different phases of CHB in groups of sex and age was not significant ($p>0.05$), but most patients with reactivation phase (31 of 48) demonstrated overweight range ($\chi^2=16.8$; $p=0.032$).

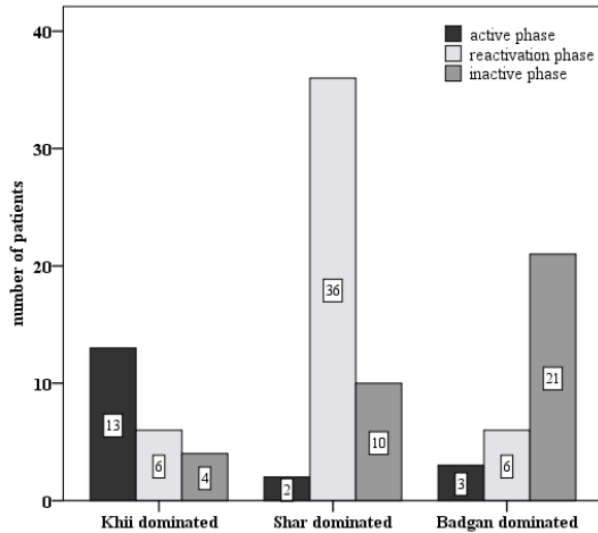
Distribution of constitutional types used in traditional Mongolian medicine among patients with different phases or conditions of chronic HBV infection is shown in Table 3.

Constitutional types	Phases of CHB			Total
	active	reactivation	inactive	
Badgan	1/0.9	5/4.9	13/12.9	19/18.9
Shar	10.9	19/18.8	6/5.9	25/24.8
Khii	7/6.9	5/4.9	2/1.9	14/13.9
Khii-Badgan	4/3.9	-	-	4/3.9
Khii-Shar	2/1.9	1/0.9	2/1.9	5/4.9
Shar-Badgan	1/0.9	7/6.9	4/3.9	12/11.9
Badgan-Khii	1/0.9	-	6/5.9	7/6.9
Shar-Khii	-	10/9.9	-	10/9.9
Badgan-Shar	1/0.9	1/0.9	2/1.9	4/3.9
Total	18/17.8	48/47.5	35/34.7	101/100

Table 3: Distribution of constitutional types in patients with CHB (n/%).

There was demonstrated significantly increased distribution of inactive CHB cases among pure Badgan type patients and reactive HBV infection among pure Shar and Shar-Khii type patients ($\chi^2=69.5$; $p=0.001$). Furthermore, distribution of constitutional

types by dominantly expressed humors among patients with CHB



has revealed with significant difference (Figure 2).

Figure 2: Distribution of constitutional types by dominantly expressed humors in patients with different phases of CHB.

As shown in the Figure 2, significantly high portion of patients with active phases of chronic HBV infection was demonstrated Khii dominated humors, while more patients with reactivation phases demonstrated Shar dominated humors and patients with inactive phases – Badgan dominated humors ($\chi^2=55.4$; $p=0.001$).

Mean value of serum ALT and AST in patients with different constitutional types has not differ ($p>0.05$), but these values demonstrated significantly low mean titer in patients with dominated Badgan humors compared with that of patients with Khii and Shar dominated humors (Table 4).

Transferases	Dominated humor			Total
	Khii (n=23)	Shar (n=48)	Shar (n=48)	
ALT (IU/ μ L)	79.8 \pm 45.3	74.8 \pm 26.8	48.6 \pm 34.4*	68.1 \pm 36.0
AST (IU/ μ L)	63.2 \pm 36.0	55.9 \pm 22.7	38.1 \pm 29.0*	52.3 \pm 29.4

Table 4: Mean values of serum ALT and AST in patients with different dominated humors (M \pm SD).

Note: Statistical significance compared to mean value of patients with Khii and Shar dominated humors ($p<0.01$).

HBeAg positivity analysis in patients with different constitutional types has not shown significant differences ($p>0.05$), but when compared dominantly expressed humor types more patients (16 of 23) with Khii dominated humors demonstrated positive HBeAg, while more patients (21 of 30) with Badgan dominated humors had a seroconversion for HBeAg ($\chi^2=9.4$; $p=0.009$) and Shar dominated patients has a similar portion of HBeAg positive or negative patients (28 and 20 respectively).

Discussion

Tibetan classical manuscript “Gyud-shi” describes physical cause of human typology as follows “...the physical or material causes of the three humors are: the subtle wind element ... becomes the cause of the Wind (Khii) humor and the nervous system; the sperm, which is the cause of the Phlegm (Badgan) humor and of the lymphatic and endocrine systems; the menstrual blood (ovum), which is the cause of the Bile (Shar) humor, the blood and blood circulation and of the metabolic systems. The three humors ... develop the body, and govern the body/mind and its functions. They rule physiology, anatomy and morphology, regulate the functioning of the body, its organs, the brain, nerves, bones, blood circulation, lymphatic systems, digestion etc. Balanced humors give positive health and harmony to the body/mind, and provide a good base for the development of the body/mind, the immune system and protection. On the contrary, the loss of balance among the humors causes energy disharmony and physical and mental disequilibrium which may appear at any time and become the cause of diseases ...” [21]. If we will look trough prism of balanced humors we will summarize key findings of the current study as follows: distribution of human constitutional types used for differential approach of diagnostics and treatment of diseases in traditional Mongolian medicine is significantly different among patients with different phases of chronic hepatitis B. Here we can suggest next statements: 1) immune active phase or condition of CHB may be related with Khii humor; 2) reactivation phase/condition of CHB may be related with Shar humor; and 3) inactive phase/condition – with Badgan humor.

Balmasova IP, et al. [22] reviewed literature reports focused on immunopathogenesis of CHB and described mechanisms of innate and adaptive immunity, which involved in different stages of chronic HBV infection. According to this report active phase of CHB characterized by signs of active liver inflammation in liver histology with elevated infiltration of intrahepatic CD4+ T helper 1 (Th1) and CD8+ cytotoxic (CTLs) lymphocytes, high content of Th17 cells in the liver and in the blood, and decreased in the liver and increased in the blood count of regulatory T cells (Treg). In contrast, inactive phase of CHB characterized by signs of mild inflammation or inactive cirrhosis in liver histology with predominance of inflammatory Th1 cells in liver and low HBV-specific immune response. But patients with reactivation phase of chronic HBV infection have demonstrated signs of normal tissue or cirrhosis and hepatocellular carcinoma in liver histology, predominance of inflammatory Th1 cells and fallen down CD8+ CTL cells. So, findings of our study in accordance with this review let us to suppose that Khii humor domination is correlated with imbalance of immune regulation toward the intensive Th1 mediated cytotoxicity due to CTLs and Th17 mediated inflammation and down regulated Th2 response due to suppressed Treg function in the tissue. In other hand Th1 mediated inflammation is powerful tool against intracellular infection [23,24] and it may frequently affect cells and cause tissue damage, which are typical pathological findings for immune active phase of chronic HBV infection [22]. Shar humor domination is correlated with intensive Th1 mediated inflammation due to activated local macrophages (Kupffer cells) [22]. Zhang JY, et al. [25] found increased number of Th17 cells in

peripheral blood and liver tissue of patients with CHB comparing with healthy liver donors and positively correlated with degree of liver injury with Th17 cell count. If inflammation affecting liver tissue has more intensity in patients with active phase [22,25,26] and the tissue transforming potential is higher in reactivation phase of chronic HBV infection [22,26] we may suggest the Khii humor may be correlated with more aggressive tissue damage and Shar humor may be related with more intensive tissue regeneration.

Our suggestions in previous report [10] prescribes possible matching of Khii humor with Th1 mediated cytotoxic response and have a correspondence with findings of current study. But our previous suggestion pointing matching of Shar humor with Th2 mediated response was built on elevated titer of interleukin -10 (IL-10) in healthy subjects. Report of Das A, et al. [27] have shown a close temporal correlation between IL-10 levels and fluctuations in viral load or liver inflammation and blockade of IL-10 in vitro rescued polyfunctional virus-specific CD8 T cell responses. So we can hypothesize that Shar humor is correlated with higher activity of IL-10 producing regulatory B cells (Breg) [27].

Findings of the study are likely to be not sufficient for development of suggestions which may explain immunological mechanisms of the correlation between Badgan humor and inactive phase of HBV infection. Authors believed that data of subjects with recovered infection or subjects in immune tolerant phase of chronic HBV infection should be analyzed for this purpose.

Conclusion

Distribution of human constitutional types used for differential approach of diagnostics and treatment of diseases in traditional Mongolian medicine is significantly different among patients with different phases of chronic hepatitis B.

Acknowledgement

These results were obtained through research grant No 3687, financed by the Science and Technology Foundation, the Executing Agency of Government of Mongolia. The manuscript is submitted as thesis for Doctor of Philosophy degree candidate Bayarsaikhan Ochirchulgan, PhD student, Department of Gastroenterology and Hepatology, School of Medicine, Mongolian National University of Medical Sciences.

Ethical issues

Design and methods of research works were reviewed in the meeting of Institutional Review Board, Mongolian National University of Medical Sciences (date: 27 February, 2017; protocol no. 2017/D-2017-02) and recognized as corresponding with international and local ethical regulations and approved for initiation of the study.

References

1. Sohn KW, Jeong AS, Yoon MY, et al. Genetic Characteristics of Sasang Typology: A Systematic Review. *JAMS*. 2012; 5: 271-289.
2. Pham DP, Cha SW, Kim JY. Re-interpretation of traditional Asian medicine with constitutional perspective. *Integr Med Res*. 2013; 1: 1-6.

3. Kim HK, Lee HT, So JH, et al. Energy metabolism and whole-exome sequencing based analysis of Sasang constitution: a pilot study. *Integr Med Res*. 2017; 6: 165-178.
4. Wan Q, Ren XJ, Yao SL, et al. Clinical Observation on the Endocrinal and Immune Functions in Subjects with Yin-deficiency Constitution. *Clin J Integr Med*. 2010; 16: 28-32.
5. Shilpa S, Murthy V. Understanding personality from Ayurvedic perspective for psychological assessment: A case. *AYU*. 2011; 32: 12-18.
6. Bold S. Mongolian traditional medicine: Philosophy, theory, learning of healthy body (monography in mongolian language). Ulaanbaatar: Admon; 2012.
7. Kline AW. Tibetan psychiatry. *Yoga journal*. 1988; 47: 86-88.
8. Yoeli-Tlalim R. Tibetan 'wind' and 'wind' illnesses: towards a multicultural approach to health and illness. *Studies in History and Philosophy of Biological and Biomedical Sciences*. 2010; 41: 318-324.
9. Barzul N. Correlation between constitution and types of higher nervous activity and anxiety. [Tesis]. Ulaanbaatar, National Medical University. 1998.
10. Bayarsaikhan O, Chimedtseren S, Badamjav S, et al. Blood Donors with Different Types of Human Constitution Demonstrate Different Level of Cytokines. *CAJMS*. 2018; 4: 126-135.
11. <http://www.who.int/news-room/fact-sheets/detail/hepatitis-b>
12. http://www.wpro.who.int/hepatitis/data/hepatitis_data_statistics/en/
13. Terrault NA, Bzowej NH, Chang KM, et al. AASLD Guidelines for Treatment of Chronic Hepatitis B. *Hepatology*. 2016; 63: 262-283.
14. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *Hepatology*. 2017; 67: 370-398.
15. WHO. Guidelines for the Prevention, Care and Treatment of Persons with Chronic Hepatitis B Infection; 2015.
16. Guideline for Detection, Diagnosis and Treatment of hepatitis B (HBV) and hepatitis D (HDV) virus infection. 2016. (in mongolian language). Ministry of Health. Ulaanbaatar. Mongolia.
17. Burmaa B. Biological age and human constitution used in traditional medicine in patients with coronary pathologies [Dissertation]. Health Sciences University of Mongolia 2010, Ulaanbaatar.
18. Sachs R. Tibetan Ayurveda: Health Secrets from the Roof of the World. Vermont: Healing Arts Press; 2001.
19. Batchimeg O. Logical and methodical aspects of general principles for prevention and diagnosis of diseases in traditional medicine. [Dissertation]. 2003, Ulaanbaatar, Health Sciences University of Mongolia.
20. <https://www.cdc.gov/obesity/adult/defining.html>
21. Arya PY. Physiology of the humours and Constituents. From The essentials of Gyud- Shi. Tibetan Medicine Education Center. 2018.
22. Balmasova IP, Yushchuk ND, Mynbaev OA, et al. Immunopathogenesis of chronic hepatitis B. *World J Gastroenterol*. 2014; 20: 14156-14171.

-
23. Schoenborn JR, Wilson CB. Regulation of interferon-gamma during innate and adaptive immune responses. *Adv Immunol.* 2007; 96: 41-101.
 24. Silva M. Classical Labeling of Bacterial Pathogens According to Their Lifestyle in the Host: Inconsistencies and Alternatives. *Front Microbiol.* 2012; 3.
 25. Zhang JY, Zhang Z, Lin F, et al. Interleukin-17-Producing CD4⁺ T Cells Increase with Severity of Liver Damage in Patients with Chronic Hepatitis B. *Hepatology.* 2010; 51: 81-91.
 26. Desmet VJ. Liver tissue examination. *Journal of Hepatology.* 2003; 39: S43-S49.
 27. Das A, Ellis G, Pallant C, et al. IL-10–Producing Regulatory B Cells in the Pathogenesis of Chronic Hepatitis B Virus Infection. *J Immunol.* 2012; 189: 3925- 3935.