Association of hepatitis B virus infection and allergy with the risk of gastrointestinal cancer

Xi ZHOU
Kunming Medical College: Kunming Medical University
W.H WANG (wwh2002191@163.com)
Kunming Medical University https://orcid.org/0000-0002-7022-3897
Tianbo Shao
Kunming Medical College: Kunming Medical University
Zhen ZHOU
Kunming Medical College: Kunming Medical University
Dajin Liu
Kunming Medical College: Kunming Medical University
Guoqing Pan
Kunming Medical College: Kunming Medical University
Jingyi Li
Kunming Medical College: Kunming Medical University

Research Article

Keywords: Hepatitis B virus infection, allergy, gastrointestinal cancer(GICA), 1:4 propensity score matching

Posted Date: September 16th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-889104/v1

Abstract

Purpose

To investigate the association of hepatitis B virus infection and allergy with gastrointestinal carcinogenesis, to provide a basis for risk factor identification among gastrointestinal cancer(GICA) risk populations, and for studies concerning the CICA etiology.

Methods

Clinical data of 2,375 GICA patients hospitalized from 2009 to 2020 were retrospectively analyzed, with 48,496 non-oncologic patients in the departments of psychiatry, neurology and cardiology as controls, totaling 50,871 patients. The data were processed using R software and SPSS22.0 for 1:4 propensity score matching.

Results

Overall, HBsAg positivity rate was 3.3% for 50,871 patients. A total of 11,872 patients completed the 1:4 propensity score matching, including 2,375 patients with GICA and 9,497 controls. HBsAg positivity was 4.5% in the GICA group and 3.2% in the control group, showing a significant inter-group difference (P = 0.002, OR = 1.427, 95% CI: 1.138–1.789). The incidence of GICA among patients with a history of allergies was significantly lower at 5.9% (139/2352) than among those without such history at 17.1% (4,592/26,785), also showing a significant inter-group difference (P < 0.001, OR = 3.294, 95% CI: 2.767–3.921). Besides, the incidence of allergies among HBsAb-positive patients was 9.0% (923/10,246), which was high than that among HBsAb-negative patients 7.6% (732/9,591), with a significant inter-group difference between the two groups (P < 0.001).

Conclusion

HBV infection is positively associated with gastrointestinal carcinogenesis. HBsAb positivity is also positively correlated with allergy, while allergy is negatively correlated with gastrointestinal carcinogenesis. The exact mechanism underlying these associations deserves further clarification. In addition, HBsAg positivity rate in Southwest China is approximately 3.3%.

Introduction

Hepatitis B virus (HBV) is a major global health issue, with approximately 250 million people infected with it [1]. In addition to the strong association with hepatocellular carcinoma [1, 2], HBV can also spread through the bloodstream and deposited in extrahepatic tissues such as the pancreas, peripheral blood mononuclear cells, kidney and gastrointestinal tract, which has been linked to glomerulonephritis [3], gallbladder and extrahepatic bile duct cancers, kidney cancer, ovarian cancer [4], pancreatic cancer [5, 6], non-Hodgkin's lymphoma [7, 8], oral cancer, gastric cancer and colorectal cancer [9, 10]. Moreover, the mean age of HBV-infected cancer patients is younger than that of uninfected patients. Moreover, the average age of HBV-infected cancer patients is younger

than that of uninfected patients. Compared to the HBsAg-negative cancer patients, the median ages at diagnosis and death are significantly younger for the HBsAg-seropositive cancer patients [11, 12] .In China, HBV infection is one of the three most common infectious diseases, according to the Ministry of Health. It is an endemic epidemic, with a prevalence ranging between 4.38–8.30%, which shows a certain local variation [13–15]. Moreover, statistical heterogeneity exists in some case-control studies concerning HBV and extrahepatic tumors due to insufficient matching variables, time of diagnosis, age and gender mismatches [7, 16]. In addition, HBsAg plays an important role in both the stimulation and prevention of host-related immune responses [17], and the closely immune-related allergies have a potential correlation with carcinogenesis risk [18, 19]. However, allergy and asthma have not shown an association with the overall cancer risk in research observations by others [20]. Thus, it remains inconclusive as to whether the HBV infection and allergies are correlated with the risk of gastrointestinal cancer(GICA) [9, 21, 22]. In this study, we explore the association of GICA with HBV infection status and allergy in Southwest China arranging a control group according to the propensity score matching principle, with a view to providing a reference for the prevention and prognosis of GICA patients.

Materials And Methods

Data collection

The HBV data of all inpatients and the pathology data of GICA patients (both from January 2009 to May 2015 and from January 2017 to December 2020) were retrieved from the workstations of the Department of Laboratory and Pathology of the First Affiliated Hospital of Kunming Medical University (The Inpatient Department of Oral and Maxillofacial Surgery of the Affiliated Stomatology Hospital of Kunming Medical University was established within the aforementioned hospital), respectively, and saved as Excel files. The Hepatitis B surface antigen (HBsAg), surface antibody (HBsAb), e antigen (HBeAg), e antibody (HBeAb) and core antibody (HBcAb) were routine examinations for all inpatients in our hospital. Fasting venous blood was collected early in the morning, which was centrifuged and tested by enzyme-linked immunosorbent assay (ELISA) or gelatin particle agglutination assay. The data were collated according to the corresponding reference values of five different HBV tests. In accordance with the diagnostic code in the International Classification of Diseases (Tenth Revision of the International Classification of Diseases, ICD—10) [23], all patient data from September 2016 to December 2020 were retrieved from the Department of Medical Record Library for patients having gastroenterology and gastrointestinal surgery, oral and maxillofacial surgery or otorhinolaryngologic problems, as well as non-oncologic patients with psychiatric, neurological and cardiological diseases, which were also saved as Excel files. The present study was approved by the Clinical Research Committee for access to the medical records of the Affiliated Stomatology Hospital of Kunming Medical University (approval No: KYKQ2021MEC034).

Statistical analysis

The above three Excel files were collated and merged using the "rbind" and "merge" packages in the R 4.32 software. Then, the data were checked via the SPSS 22.0 software, where the first recorded data was retained, and the duplicate, incomplete or incorrect data was deleted. The GICA patients and controls were matched 1:4 using the "PS Matching" plug-in program in SPSS 22.0 to balance the differential prognostic feature between them. The admission date was matched on a proximity basis, while the age, gender and test method were

matched exactly. Differences in the five HBV positivity rates between the matched GICA patients and controls, as well as gender differences, were analyzed using multinomial logistic regression and crosstabes for non-parametric statistical analysis. The mean ages in the two groups were expressed as mean and standard deviation. A P value of less than 0.05 indicated a significant difference. Figure 1 illustrates the data collation and analysis processes.

Results

HBV and GICA

A total of 50,871 patients had HBV data from 2009 to 2020, the 2,375 GICA patients contracted gastric, colon, rectal or duodenal cancers, while the 48,496 non-oncologic controls were from the departments of psychiatry, neurology and cardiology. These patients suffered from congenital heart disease, coronary heart disease, schizophrenia, bipolar disorder, etc. 50,871 patients were aged 1–98 years, with a mean of 54.00±18.60 years, and the overall HBsAg positivity was 3.3%. Among patients with GICA, males (1,418, 59.7%) significantly outnumbered females (957, 40.3%) (P=0.014). A total of 1,1872 patients completed the 1:4 propensity score matching including 2,375 GICA patients and 9,497 controls. The L1 values before and after the matching were 0.170 and 0.003, respectively, suggesting a good match. There was no "Summary of unbalanced covariates" +|d|>0.25, indicating that all the matched variables reached equilibrium. There were 7,087 males and 4,785 females, respectively, showing no inter-group difference in gender (P=0.991). For the GICA and the control groups, the mean ages were 59.45±12.61 and 59.46±12.62 years, respectively (P=0.968). Among the 11,872 patients, the positivity rates of HBsAg, HBsAb, HBeAg, HBeAb and HBcAb were 3.4%, 58.9%, 0.2%, 12.3% and 27.0%, respectively. HBsAg positivity was 4.5% for the GICA group and 3.2% for the control group, showing a significant inter-group difference (P=0.002). It was found that the HBsAg positivity was significantly associated with an increased risk of gastrointestinal cancer (OR=1.427, 95% CI: 1.138–1.789). HBsAb positivity rates for the GICA and control groups were 56.2% and 59.6%, respectively, while the HBeAb positivity rates were 13.7% and 11.9%, both exhibiting significant inter-group differences. The HBsAb positivity prominently reduced the risk phase of GICA (P=0.002, OR=0.869, 95% CI: 0.793–0.951), while the HBeAb positivity prominently increased the GICA risk (P=0.021, OR=1.169, 95% CI: 1.024–1.335). No significant differences were noted in HBeAg (P=0.776) or HBcAb (P=0.153) between the two groups (Table 1). The mean ages of HBsAg-negative and HBsAg-positive patients in the GICA group were 59.5±12.7 and 58.2±11.6 years, respectively (P=0.089).

Allergy and GICA

From the Department of Medical Record Library, 2,9137 inpatients at the Department of Gastroenterology and Gastrointestinal Surgery between 2016 and 2020 were retrieved, of whom 2,352 had a history of allergies and the remaining 26,785 patients did not, with mean ages of 56.38±15.61 and 54.09±15.60 years, respectively (P=0.626). The incidence of allergy history among female patients was significantly higher at 1,281 (54.5%) than among male patients 1,071 (45.5%, P<0.001). The incidence of GICA among patients with an allergy history was significantly lower at 5.9% (139/2,352) than among patients without such history at 17.1% (4,592/26,785), showing a significant inter-group difference (P<0.001, OR=3.294, 95%CI: 2.767–3.921) (Table 2).

HBV and allergy

A total of 19,837 patients from 2017 to 2020 were matched between Department of Laboratory Medicine and Department of Medical Record Library, of whom 1,655 had a history of allergies and the remaining 18,182 patients did not, with means age of 52.97±19.73 and 50.00±19.36 years, respectively (P=0.388). The incidence of HBsAg-negative patients with a history of allergies was 8.4% (1,615/19,255), which was higher than 6.9% (40/582) among HBsAg-positive patients, although no significant inter-group difference was found (P=0.193). However, the incidence of allergies among HBsAb-positive patients was higher at 9.0% (923/10,246) than among HBsAb-negative patients at 7.6% (732/9,591), showing a significant inter-group difference (P<0.001, OR=0.835, 95% CI:0.754–0.924) (Table 3).

Discussion

Clinically, failure to routinely check the five HBV serological indicators will lead to biased data. In this study, these five HBV indicators are routine examinations of all inpatients in our hospital. We use 48,496 non-oncologic patients from psychiatric, neurological and cardiological departments as the control group. The number of patients is sufficient to fully satisfy matching by gender, age, test method and admission time on a 1:4 propensity score system, thus avoiding occasional biases. In addition, Yunnan Province is located on the Yunnan–Guizhou Plateau in Southwest China, which is far from the eastern and northern regions and has better medical conditions. Therefore, patients in this region choose hospitals in Kunming, the administrative center, as far as possible. The HBsAg positivity of 50,871 patients in this study is 3.3%, a value lower than other reports, which can represent the general situation of HBV infections in Southwest China [14, 15].

As is well known inflammation caused by a bacterial or viral infection can increase the risk of cancer, such as the strong correlation of HBV infection with non-hepatocellular carcinoma [24, 25], Helicobacter pylori (H. pylori) infection is associated with the progression of gastric precancerous lesions [26, 27]. In H. pylori-infected patients with a family history of gastric cancer in first-degree relatives, eradication of the bacteria can reduce the gastric cancer risk [27]. Both H. pylori and HBV infections are common in China, and there is a strong positive correlation between them, especially during HBV progression [26]. Our results show that the HBsAg positivity in the GICA group (4.5%) is significantly higher than that in the control group (3.2%)($P < 0.05$), which supports the association between the HBsAg seropositivity and the risk of GICA. In addition, our results show that the rate of allergy history among HBsAg-negative patients is higher than that among HBsAg-positive patients, albeit an insignificant difference ($P > 0.05$). Nevertheless,

the incidence of allergies in HBsAb-negative patients (7.6%) is significantly lower than that in HBsAb-positive patients (9.0%) ($P < 0.001$), and the incidence of GICA among patients with a history of allergies is significantly lower than that among patients without such history ($P < 0.001$). Besides, female patients exhibit a significantly higher incidence of allergies than that the male patients($P < 0.001$). However, males significantly outnumber females among GICA patients ($P < 0.001$). Our study demonstrates that HBV infection is positively associated with the risk of GICA, and HBsAb positivity is positively associated with allergy, while allergy is negatively associated with the risk of GICA, suggesting that HBV infection may influence the GICA carcinogenesis through an immune response. Previous studies have shown a negative association of oral pharyngeal, colorectal, pancreatic and cervical with allergies [28]. Dusséaux et al. [17]found that the plasma levels of inflammatory and immunosuppressive cytokine CXCL10 increased after the mice, which were stably engrafted with human hepatocytes with or without an immune system, were given an intraperitoneal injection of HBV. HBsAg acts as

an immunosuppressant by inhibiting the activity of Toll-like receptors(TLRs), which are an innate sensor that recognizes viral nucleic acids, and plays an important role in stimulating the host-associated immunity and blocking the host-associated immune responses. Clinical research has revealed a significant increase in CXCL10 levels in advanced colorectal cancer tissues [29]. Furthermore, CXCL10 plays a crucial role in the pathophysiology of allergic reactions [30]. Huoman et al. [31]treated children with allergic rhinoconjunctivitis by sublingual immunotherapy with Timothy grass pollen and found significantly higher plasma levels of CXCL10 and CXCL11 than the untreated children after 3 years. Taken collectively, the above literature and our study suggest a possible correlation of HBV infection and allergy with the development of GICA.

Admittedly, we cannot exclude potential confounding factors such as smoking, alcohol consumption, family history of cancer, and environmental exposure to chemicals. In addition, the non-oncological patients in the control group from the psychiatric, neurological and cardiological departments may have a lower incidence of HBV infection. In conclusion, our study provides an important supplement to the knowledge about the risk factors for GICA, and the specific mechanisms deserve further clarification through a substantial number of population-based prospective cohort studies concerning the association of HBV infection and allergy with gastrointestinal carcinogenesis.

Declarations

Funding Information This work was supported by the Yunnan health training project of high-level talents (No. L-2018010) and Yunnan Provincial Innovation Team Project Team (No. 202105AE160004).

Authors contributions Zhou completed the manuscript, Wang conceived and designed the study, as well as analyzed the data and revised the manuscript. Shao, Zhou, Liu, Pan and Li retrieved the original data or clinical data collection. All authors were directly involved in the planning, execution or analysis of the study, and read and approved the final manuscript.

Compliance with Ethical Standards

Conflict of Interests The author declares that he/she has no conflict of interest.

Ethical Issues There are no ethical problems for this manuscript.

References

1. Nguyen MH, Wong G, Gane E, Kao JH,Dusheiko G. Hepatitis B Virus: Advances in Prevention, Diagnosis, and Therapy. Clin Microbiol Rev. 2020;33(2):1–38.
2. Khemlina G, Ikeda S, Kurzrock R. The biology of Hepatocellular carcinoma: implications for genomic and immune therapies. Mol Cancer. 2017;16(1):149.
3. Zuo T, Chen P, Jing S, Zhang T,ChangL, Xu Fet al. Quantitative Proteomics Reveals the Development of HBV-Associated Glomerulonephritis Triggered by the Downregulation of SLC7A7. J Proteome Res. 2020;19(4):1556–64.
4. Kamiza AB, Su FH,Wang WC,Sung FC,Chang SN, Yeh CC. Chronic hepatitis infection is associated with extrahepatic cancer development: a nationwide population-based study in Taiwan. BMC Cancer.

2016;16(1):861.

5. Majumder S. Bockorny B,Baker WL,Dasanu CA. *Association between HBsAg positivity and pancreatic cancer: a meta-analysis*. J Gastrointest Cancer. 2014;45(3):347–52.
6. Liu X, Zhang ZH, Jiang F. *Hepatitis B virus infection increases the risk of pancreatic cancer: a meta-analysis*. Scand J Gastroenterol. 2021:1–7.
7. Zhou X, Pan H, Yang P, Ye P,CaoH, Zhou H. Both chronic HBV infection and naturally acquired HBV immunity confer increased risks of B-cell non-Hodgkin lymphoma. BMC Cancer. 2019;19(1):477.
8. Li M, Gan Y,Fan C,Yuan H, Zhang X, Shen Yet al. Hepatitis B virus and risk of non-Hodgkin lymphoma: An updated meta-analysis of 58 studies. J Viral Hepat. 2018;25(8):894–903.
9. Tian T, Song C,JiangL, Dai J, Lin Y, Xu Xet al. Hepatitis B virus infection and the risk of cancer among the Chinese population. Int J Cancer. 2020;147(11):3075–84.
10. Song C, Lv J, Liu Y, Chen JG,Ge Z, Zhu J,*et al.*. Associations Between Hepatitis B Virus Infection and Risk of All Cancer Types. JAMA Netw Open. 2019;2(6):e195718.
11. Lu T, Yang Q,Li MZhang J,ZouJ, Huang L,*et al.*. HBV infection and extra-hepatic cancers in adolescents and 20s: A retrospective study in China. Cancer Epidemiol. 2018;55:149–55.
12. Wei XL, Luo HY,Li CF, Jin Y, Zeng ZL, Ju HQ,*et al.*. Hepatitis B virus infection is associated with younger median age at diagnosis and death in cancers. Int J Cancer. 2017;141(1):152–59.
13. Ott JJ, Horn J. Changing hepatitis B virus epidemiology in rural China. Lancet Infect Dis. 2016;16(2):150.
14. Hou J, Wang G, Wang FCheng J,RenH, Zhuang H,*et al.*. Guideline of Prevention and Treatment for Chronic Hepatitis B (2015 Update). J Clin Transl Hepatol. 2017;5(4):297–318.
15. Yan LB, Liao J, Han N, Zhou LY,Wang XE, Wang YJ,*et al.*. Association between Hepatitis B Virus Infection and Metabolic Syndrome in Southwest China: A Cross-sectional Study. Sci Rep. 2020;10(1):6738.
16. Wei XL, Qiu MZ,Jin Y, Huang YX,Wang RY, Chen WW,et al. Hepatitis B virus infection is associated with gastric cancer in China: an endemic area of both diseases. Br J Cancer. 2015;112(7):1283–90.
17. Dusséaux M, Masse-Ranson G, Darche S, Ahodantin J, Li Y, Fiquet O,*et al.*. Viral Load Affects the Immune Response to HBV in Mice With Humanized Immune System and Liver. Gastroenterology. 2017;153(6):1647–61.
18. Turner MC. Epidemiology: allergy history, IgE, and cancer. Cancer Immunol Immunother. 2012;61(9):1493–510.
19. Jiang X, Dimou NL,Zhu ZH,Bonilla C, Lewis SJ, Lindstrom S,*et al.*. Allergy, asthma, and the risk of breast and prostate cancer: a Mendelian randomization study. Cancer Causes Control. 2020;31(3):273–82.
20. Kantor ED, Hsu M, Du M, Signorello LB. Allergies and Asthma in Relation to Cancer Risk. Cancer Epidemiol Biomarkers Prev. 2019;28(8):1395–403.
21. Chen XZ, Wang R, Hu JK. Hepatitis B virus infection and gastric cancer risk: pitfalls in the potential association. Br J Cancer. 2015;112(11):1844.
22. Song C, Lv J, Liu Y, Chen J, Ge Z, Zhu J,*et al.*. Associations Between Hepatitis B Virus Infection and Risk of All Cancer Types. JAMA network open. 2019;2(6):e195718.
23. Ford MM, Ivanina E, Desai P,HighfieldL, Qiao BZ, Schymura MJ,*et al.*. Geographic epidemiology of hepatocellular carcinoma, viral hepatitis, and socioeconomic position in New York City. Cancer Causes

Control. 2017;28(7):779–89.
24. Mahale P, Engels E,Koshiol J. Hepatitis B virus infection and the risk of cancer in the elderly US population. International journal of cancer. 2019;144(3):431–39.
25. Wei X,QiuM, Jin YHuang Y, Wang R, Chen Wet al. Hepatitis B virus infection is associated with gastric cancer in China: an endemic area of both diseases. British journal of cancer. 2015;112(7):1283–90.
26. Wang J, Chen RC,Zheng YX,Zhao SS, Li N, Zhou RR,*et al.*. Helicobacter pylori infection may increase the risk of progression of chronic hepatitis B disease among the Chinese population: a meta-analysis. Int J Infect Dis. 2016;50:30–7.
27. Choi IJ, Kim CG, Lee JY, Kim YI,KookMC, Park B,*et al.*. Family History of Gastric Cancer and Helicobacter pylori Treatment. N Engl J Med. 2020;382(5):427–36.
28. Sherman PW. Holland E,Sherman JS. *Allergies: their role in cancer prevention*. Q Rev Biol. 2008;83(4):339–62.
29. Wang D, Yu W, Lian J, Wu Q,LiuS, Yang L,*et al.*. Th17 cells inhibit CD8(+) T cell migration by systematically downregulating CXCR3 expression via IL-17A/STAT3 in advanced-stage colorectal cancer patients. J Hematol Oncol. 2020;13(1):68.
30. Smith JS, Rajagopal S, Atwater AR. Chemokine Signaling in Allergic Contact Dermatitis: Toward Targeted Therapies. Dermatitis. 2018;29(4):179–86.
31. Huoman J, Papapavlou G, Pap A,Alm J, Nilsson LJ, Jenmalm MC. Sublingual immunotherapy alters salivary IgA and systemic immune mediators in timothy allergic children. Pediatr Allergy Immunol. 2019;30(5):522–30.

Tables

Table 1. Hepatitis B virus infection with the risk of gastrointestinal cancer: univariable and multivariable logistic regression analyses.

Variable	*GICA (n=2375)*		*Control (n=9497)*		*Univariable*			*Multivariable*		
	No	**(%)**	**No**	**(%)**	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
HBsAg										
Positive	106	4.5	301	3.2	1.43	1.14-1.79	0.002	1.24	0.95-1.63	0.119
Negative	2269	95.5	9196	96.8		2 (reference)		.	. 2 (reference)	.
HBsAb										
Positive	1334	56.2	5660	59.6	0.87	0.79-0.95	0.002	0.87	0.79-0.96	0.006
Negative	1041	43.8	3837	40.4		2 (reference)		.	. 2 (reference)	.
HBeAg										
Positive	5	0.2	23	0.2	0.87	0.33-2.29	0.776	0.65	0.24-1.76	0.394
Negative	2370	99.8	9474	99.8		2 (reference)		.	. 2 (reference)	.
HBeAb										
Positive	325	13.7	1134	11.9	1.17	1.02-1.34	0.021	1.08	0.90-1.30	0.392
Negative	2050	86.3	8363	88.1		2 (reference)		.	. 2 (reference)	.
HBcAb										
Positive	668	28.1	2533	26.7	1.08	0.97-1.19	0.153	1.04	0.91-1.19	0.569
Negative	1707	71.9	6964	73.3		2 (reference)		.	. 2 (reference)	.

OR, odds ratio; 95% CI, 95% confidence interval; HBsAg, hepatitis B surface antigen; HBsAb, hepatitis B surface antibody; HBeAg, hepatitis B e antigen; HBeAb, hepatitis B e antibody; HBcAb, hepatitis B core antibody. The reference category is control.

Table 2. Characteristics of 29137 inpatients from the Department of Gastroenterology and Gastrointestinal Surgery

Variable	No allergy(n=26785)	Allergy (n=2352)	*P*
Age			
Mean ± SD(ys)	54.09±15.60	56.38±15.61	0.626
Sex			
Male	15966(59.6%)	1071(45.5%)	
Female	10819(40.4%)	1281(54.5%)	0.000
Clinic diagnosis			
GIGA	4592(17.1%)	139(5.9%)	
Control	22193(82.9%)	2213(94.1%)	0.000

Table 3. Hepatitis B virus infection with allergy: univariable and multivariable logistic regression analyses.

Variable	Allergy (n=1655)		No allergy (n=18182)		Univariable			Multivariable		
	No	(%)	No(%)		OR	95% CI	*P*	OR	95% CI	*P*
HBsAg										
Positive	40	6.9	542	93.1	1.24	0.90-1.72	0.193	0.97	0.65-1.44	0.880
Negative	1615	8.4	17640	91.6		2 (reference)		.	. 2 (reference)	.
HBsAb										
Positive	923	9.0	9323	91.0	0.84	0.75-0.92	0.000	0.82	0.74-0.91	0.000
Negative	732	7.6	8859	92.4		2 (reference)		.	. 2 (reference)	.
HBeAg										
Positive	1	2.4	40	97.6	3.65	0.50-26.54	0.171	2.70	0.36-20.51	0.336
Negative	1654	8.4	18142	91.6		2 (reference)		.	. 2 (reference)	.
HBeAb										
Positive	117	8.1	1328	91.9	1.04	0.85-1.26	0.725	0.86	0.65-1.13	0.272
Negative	1538	8.4	16854	91.6		2 (reference)		.	. 2 (reference)	.
HBcAb										
Positive	185	7.4	2299	92.6	1.15	0.98-1.35	0.084	1.28	1.03-1.60	0.029
Negative	1470	8.5	15883	91.5		2 (reference)		.	. 2 (reference)	.

OR, odds ratio; 95% CI, 95% confidence interval; HBsAg, hepatitis B surface antigen; HBsAb, hepatitis B surface antibody; HBeAg, hepatitis B e antigen; HBeAb, hepatitis B e antibody; HBcAb, hepatitis B core antibody. The reference category is control.

Figures

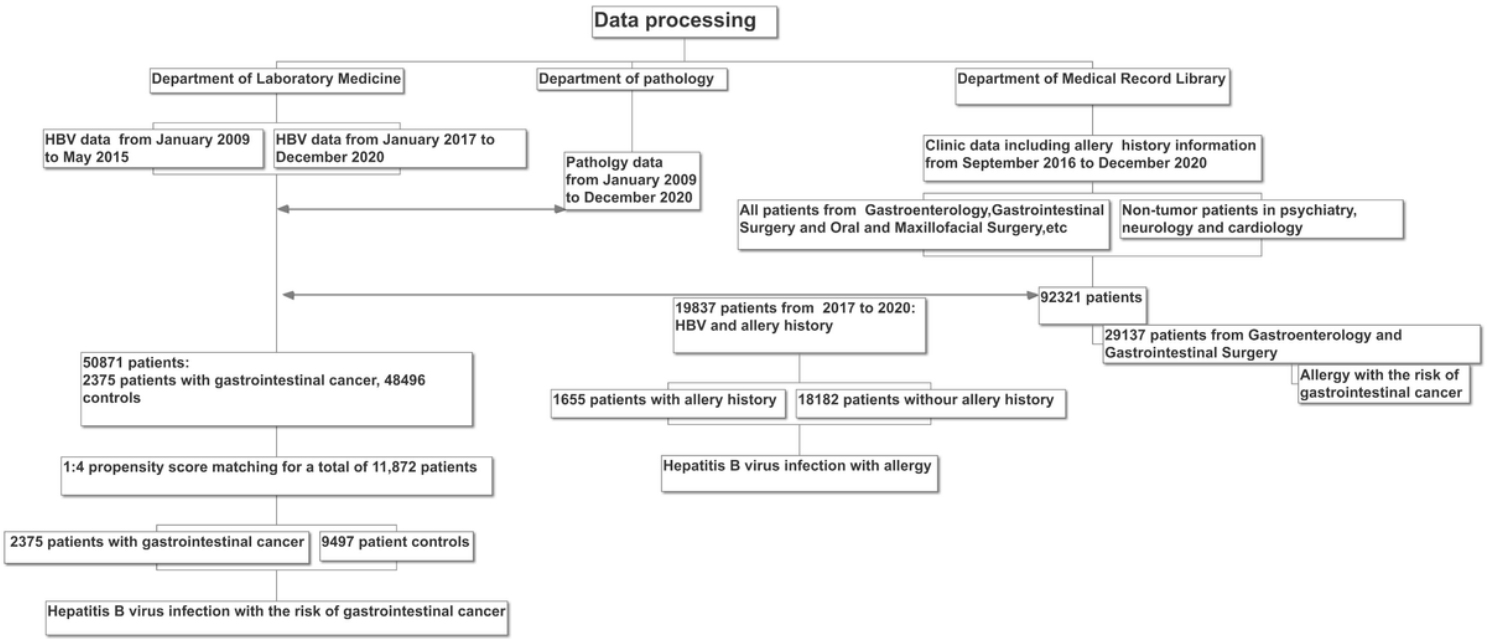

Figure 1

The data collation and analysis processes.