Significantly Decreased Islet β Cell Function and Increased Fasting Plasma Glucose in Patients With Chronic Hepatitis B: a Cross-sectional Study

Dafeng Liu
the Public and Health clinic Center of Chengdu https://orcid.org/0000-0002-6792-641X
Lingyun Zhou
Sichuan University West China Hospital
Xinyi Zhang
Sichuan University West China Medical Center
Yilan Zeng
the Public and Health Clinic Center of Chengdu
Lang Bai
Sichuan University West China Hospital
Dongbo Wu
Sichuan University West China Hospital
Hong Tang (htang6198@hotmail.com)
Sichuan University West China Hospital https://orcid.org/0000-0002-9790-6225

Research

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Abstract

Background: The contributing factors of abnormal glucose metabolism and the characteristics of the homeostasis model assessment of β cell function (HOMA-β) value in chronic hepatitis B (CHB) patients are unclear and worth studying.

Method: This cross-sectional study recruited 110 CHB patients (CHB group) and 110 patients without hepatitis B virus (non-HBV group); the groups were matched according to sex, age, and body mass index. The contributing factors of abnormal glucose metabolism and the characteristics and differences in glucose metabolism parameters between the two groups were analyzed.

Results: The abnormal glucose metabolism rate was higher in CHB patients with liver cirrhosis (LC) and patients with hepatitis B envelope antigen (HBeAg) (-) status. In addition, under the same glucose metabolism conditions, the fasting plasma glucose (FPG) levels of the CHB group was higher than that of the non-HBV group, especially in those with LC that had higher FPG levels (all p=0.000), while the HOMA-β values was significantly lower in the CHB group than in the non-HBV group, especially under normal glucose tolerance conditions (all p=0.000). Further analyses revealed that the main contributing factors of abnormal glucose metabolism were HBeAg (-) status and hepatitis B envelope antibody levels, but HBV serological and virological indicators had no direct effect on the HOMA-β value.

Conclusion: These findings provide a reference that will allow clinicians to monitor abnormal glucose metabolism in CHB patients, especially those with LC or HBeAg (-) status, focus on the protection of islet β-cell function, and avoid the application of insulin secretagogues in CHB patients with abnormal glucose metabolism.

1. Introduction

Approximately 300 million people worldwide are diagnosed with chronic hepatitis B (CHB),[1]of whom approximately 650,000 die of hepatic failure, liver cirrhosis(LC), and hepatocellular carcinoma (HCC) annually.[2] China is one of the HBV middle- and low-endemic areas worldwide,and approximately 93 million people are infected with HBV; among them, 20 million present with CHB. [1,3]

Although the relationship between hepatitis B virus infection and diabetes mellitus (DM) remains controversial, several studies have shown that the prevalence rate of DM is significantly higher in the HBV-infected population, [4–11]particularly in those with high viral load, with a long duration of CHB, with cirrhosis,[4,6,7–10] or of Asian American race.[8]Our previous study has shown that 59.09% of CHB patients had high homeostasis model assessment of insulin resistance (HOMA-IR) values and 93.64% of individuals had low homeostasis model assessment of β cell function (HOMA-β) values. Moreover, 35.45% of individuals had impaired glucose tolerance (IGT), [12–13]which indicated that the prevalence rates of abnormal glucose metabolism and insulin resistance (IR) were high in patients with CHB.

IR and DM could promote the progression of liver fibrosis and cirrhosis. [14–17]Moreover,IR is independently correlated with the degree of liver fibrosis in patients with abnormal glutamyl transferase levels.[12,14]The

higher the HOMA-IRvalues,the higher the liver stiffness measurement (LSM) levels, an indicator of liver fibrosis. [13, 15] For DM patients with cirrhosis, the leading cause of death is hepatic failure as opposed to complications of DM. Furthermore, DM could also promote HCC and lead to poorer prognosis after liver transplantation[18, 19].Therefore,the coexistence of abnormal glucose metabolism and IR could promotethe progressionand worsen the prognosis of CHB.

Abnormal glucose metabolism and IRare commonly associated with islet β cell dysfunction in the general population, particularly in Asian populations. However, inpatients with CHB, the contributing factors of glucose abnormalities and the characteristics associated with HOMA-β values are unclear and worth further study.

2. Methods

2.1 Subjects

A cross-sectional study with a sample size of 220 patients was conducted in the Public and Health Clinic Centre of Chengdu from January 1, 2012, to June 30, 2013. Among them, 110 patients with CHB were assigned to the CHB group (the source of the cases has been previously explained in the literature).[12–13]One hundred ten patients without hepatitis B virus, hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection who were matched to the CHB group according to sex, age, and body mass index (BMI) were assigned to the non-HBV group. The study was approved by the ethics committee of the Public and Health Clinic Centre of Chengdu (PJ-K2019-019-01). All patients provided written informed consent.

2.2 Inclusion criteria, exclusion criteria and disease diagnosis criteria

The inclusion criteria of the CHB group were as follows:(1)outpatients or inpatients with CHB or post hepatitis B cirrhosis; (2) individuals who agreed to undergo noninvasive ultrasound liver stiffness measurement; and (3) individuals aged18-70 years.

The selection criteria of the non-HBV group were as follows: patients without hepatitis B virus infection, matched to the CHB group according to sex, age and BMI and time.

The following exclusion criteria were used in this study: (1) other hepatitis virus or human immunodeficiency virus infection; (2)hepatocellular carcinoma; (3)ascites; (4)decompensated cirrhosis; (5) BMI > 30 kg/m^2 or < 18.5 kg/m^2.

The diagnostic criteria of the diseases were as follows: CHB diagnostic and typing criteria, impaired glucose regulation (IGR) and DM diagnostic criteria were applied according to the corresponding guidelines. [20, 21]

2.3 Grouping standards

One hundred ten CHB patients were enrolled in the CHB group and 110 patients without hepatitis B virus, hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection who were matched to the CHB

group according to sex, age, and body mass index (BMI) were enrolled in the non-HBV group.

The participants in the CHB group were also divided into LC and non-LC subgroups based on the presence or absence of cirrhosis, respectively, and hepatitis B envelope antigen (HBeAg)(-) and HBeAg(+) subgroups according to HBeAg negative or positive status, respectively.

The participants in the two groups were also divided into three glucose mellitus conditions including noymal glucose tolerance (NGT), IGR and DM.

2.4 Data collection

Demographic information, anthropometric parameters, glucose metabolic parameters were obtained. BMI, HOMA-IR values, and HOMA-β values were calculated.

Databases were established according to the needs of the research. Two researchers simultaneously collected and entered the data into the database. Then, the researchers randomly selected 30% of the data for assessment to ensure data integrity, authenticity, and accuracy.

2.5 Statistical analysis

The Statistical Package for the Social Sciences software version 26.0 (IBM Inc., Armonk, NY, the USA) and Prism Version 8 (GraphPad Inc. US) were used for statistical analysis. Age, BMI, FPG and FINS levels, and HOMA-IR values had a normal distribution, and the statistical analysis was conducted directly. Natural HOMA-β values were logarithmically transformed before the statistical analysis. The measurement data were expressed as x ± SD, ANOVA was used for a multigroup comparison with variance homogeneity and normal distribution data, and the least significant difference (LSD) *t* test was used for further comparison between the two groups. Independent-sample *t*-tests were compared between two groups. The percentage or proportion was expressed for enumeration data, and the chi-square test was used for comparison of these data. Spearman correlation analysis was adopted for two-factor correlation analysis, and multiple stepwise regression was applied for multifactor correlation analysis. Statistical significance was defined as $P < 0.05$.

3. Results

3.1 Baseline conditions

We enrolled a total of 220 patients, among whom 110 were assigned to the CHB group and 110 were assigned to the non-HBV group. No significant differences were observed in terms of age, sex, BMI or glucose metabolism conditions between the two groups (Table 1). For the CHB group,41 (37.27%) patients had LC, and 38 (34.55%) patients were HBeAg(+). In the non-HBV group, there were no cases of LC.

Table 1
Baseline comparison between the two groups (n = 220)

Variables	CHB group(n = 110)	Non-HBV group(n = 110)	t score or χ^2 score	P score
Age (years)	43.86 ± 14.38	42.68 ± 13.34	t = 0.794	0.428
Male (number, %)	90(81.92%)	90(81.92%)	χ^2=0.000	1.000
BMI (kg/m^2)	22.52 ± 2.74	23.14 ± 4.07	t = − 1.245	0.215
Glucose metabolism conditions			χ^2=0.000	1.000
NGT	50(45.46%)	50(45.46%)		
IGR	30(27.27%)	30(27.27%)		
DM	30(27.27%)	30(27.27%)		

Abbreviations: CHB, chronic hepatitis B; non-HBV, without hepatitis B virus infection; BMI, body mass index; NGT, normal glucose tolerance; IGR, impaired glucose regulation; DM, diabetes mellitus.

3.2 Abnormal glucose metabolism rate

The IGR and DM rates in the CHB group were all 27.27% (30/110), of the LC subgroup was significantly higher than that of the non-LC subgroup (Table 2), and of the HBeAg (-) subgroup was also significantly higher than that in the HBeAg (+) subgroup (Table 3).

Table 2
Glucose metabolism conditions comparison between non-LC subgroup and LC subgroup (n = 220) (case, %)

Variables	non-LC subgroup (n = 69)	LC subgroup (n = 41)	χ^2score	P score
Glucose metabolism conditions			-3.588	0.000
NGT	42(60.87)	8(19.51)		
IGR	12(17.39)	18(43.90)		
DM	15(21.74)	15(36.59)		

Abbreviations: LC, liver cirrhosis; NGT, normal glucose tolerance; IGR, impaired glucose regulation; DM, diabetes mellitus.

Table 3
Glucose metabolism conditions comparison between HBeAg (+) subgroup and HBeAg (-) subgroup (n = 110) (case, %)

Variables	HBeAg (+) subgroup (n = 38)	HBeAg (-) subgroup (n = 72)	χ^2score	*P* score
Glucose metabolism conditions			-6.174	0.000
NGT	26(68.42)	24(33.33)		
IGR	7(18.42)	23(31.94)		
DM	5(13.16)	25(34.72)		
Abbreviations: NGT, normal glucose tolerance; IGR, impaired glucose regulation; DM, diabetes mellitus.				

3.3 HOMA-β value and FPG level

Under NGT conditions in the CHB group, the FPG levels (Fig. 1C) was slightly higher and the FINS levels (Fig. 1D), the HOMA-IR values (Fig. 1B), and the HOMA-β values (Fig. 1A) were all significantly lower than those of the non-HBV group (all $P<0.05$).

With the deterioration of glucose metabolism, FPG levels (Fig. 2A), FINS levels (Fig. 2B) and HOMA-IR values (Fig. 2C) continuously increased, while HOMA-β values (Fig. 2D) continuously decreased in the two groups (all $P<0.05$).

Moreover, in the CHB group, the FPG levels was higher and the FINS levels, the HOMA-IR values and the HOMA-β values were all lower than those of the non-HBV group under the same glucose metabolism conditions (all $P<0.05$).

3.4 The change characteristics of glucose metabolism parameters

With the deterioration of glucose metabolism, the FPG levels (Fig. 3A), the HOMA-IR values (Fig. 3C), and the FINS levels (Fig. 3B)were all continuously increased (all $P<0.05$), while the HOMA-β values (Fig. 3D) were all continuously decreased ($P = 0.000$) in both the LC and non-LC subgroups. In the LC subgroup, the HOMA-β values were higher under NGT conditions but significantly lower under IGR and DM conditions, and the FPG levels were higher under NGT and IGR conditions than in the non-LC subgroup.

With the deterioration of glucose metabolism, the FPG levels (Fig. 4A), FINS levels (Fig. 4B) and HOMA-IR values (Fig. 4C) of the two subgroups were all continuously increased, while the HOMA-β values (Fig. 4D) were all continuously decreased in both the HBeAg(+) and HBeAg(-) subgroups, but there was no significant difference between the two subgroups under the same glucose metabolism conditions(all $P > 0.05$).

3.5 The contributing factors of glucose metabolism

According to Spearman correlation analysis, HBeAb levels, ALP levels, GGT levels, and LSM levels were also positively correlated, while HBeAg (+), HBsAg levels, HBeAg levels, and HBVDNA levels were all negatively correlated with FPG levels(Table 4). Based on multiple stepwise regression analysis, HBeAg (-), GGT levels and HBeAb levels were the contributing factors for glucose metabolism, and HBeAb levels was the contributing factor for FPG levels(Table 5).

Table 4
Spearman correlation analysis between glucose metabolism parameters and HBV-related biological and serum parameters (n = 110)

Variable	Glucose metabolism (1 = NGT, 2 = IGR, 3 = DM)		FPG (mmol/L)		FINS (mU/L)		HOMA-IR (mU*mmol/L^2)		HOMA-β (mU/mmol)	
	r	p	r	p	r	p	r	p	r	p
Cirrhosis(1 = without,2 = with)	0.191	0.046			0.322	0.001	0.328	0.000		
HBeAg (1 = negative, 2 = positive)	-0.330	0.000	-0.268	0.005						
HBsAg	-0.350	0.000	-0.334	0.000					0.200	0.036
HBsAb					-0.270	0.004	-0.199	0.037	-0.281	0.003
HBeAg	-0.321	0.001	-0.232	0.015						
HBeAb	0.396	0.000	0.333	0.000			0.240	0.012		
HBcAb	-0.205	0.032								
HBVDNA	-0.202	0.034	-0.190	0.047						
ALP	0.247	0.009	0.286	0.002					-0.361	0.000
GGT	0.354	0.000	0.293	0.002						
LSM	0.260	0.006	0.272	0.004	0.230	0.015	0.306	0.000		

Abbreviations: ALP, alkaline phosphatase. FINS, fasting serum insulin. DM, diabetes mellitus. FPG, fasting plasma glucose. GGT, gamma glutamyl transferase. HbA1c, glycosylated hemoglobin. HBcAb, hepatitis B core antibody. HBeAb, hepatitis B envelope antibody. HBeAg, hepatitis B envelope antigen. HBsAb, hepatitis B surface antibody. HBsAg, hepatitis B surface antigen. HBVDNA, hepatitis Bviral nucleic acid load. HOMA-β, homeostasis model assessment of β cells. HOMA-IR, homeostasis model assessment of insulin resistance. IGR, impaired glucose regulation. LSM, liver stiffness measurement. NGT, normal glucose tolerance.

Table 5
Multiple stepwise regression analysis of influencing factors of HBV-related biological and serum parameters on glucose metabolism parameters (n = 110)

Independent variable		B	Std. Error	Beta	t	p
Glucose metabolism	constant	0.730	0.273	-	2.678	0.009
(1 = NGT, 2 = IGR, 3 = DM)	HBeAg(1 = negative, 2 = positive)	-0.430	0.161	-0.249	-2.663	0.009
	GGT	0.002	0.001	0.298	3.291	0.001
	HBeAb	0.117	0.045	0.242	2.600	0.011
FPG	constant	5.463	0.266	-	20.530	0.000
(mmol/L)	HBeAb	0.494	0.126	0.378	3.933	0.000
FINS	constant	3.069	0.787	-	3.900	0.000
(mU/L)	Cirrhosis (1 = without, 2 = with)	1.123	0.531	0.214	2.117	0.037
HOMA-IR	constant	0.560	0.269	-	2.081	0.040
(mU*mmol/L2)	HBeAb	0.133	0.054	0.225	2.453	0.016
	Cirrhosis (1 = without, 2 = with)	0.426	0.180	0.216	2.358	0.020
HOMA-β	constant	66.452	8.387	-	7.923	0.000
(mU/mmol)	ALP	-0.183	0.074	-0.230	-2.459	0.016

Abbreviations: ALP, alkaline phosphatase. FINS, fasting serum insulin. DM, diabetes mellitus. FPG, fasting plasma glucose. GGT, gamma glutamyl transferase. HBeAb, hepatitis B envelope antibody. HBeAg, hepatitis B envelope antigen. HOMA-β, homeostasis model assessment of β cells. HOMA-IR, homeostasis model assessment of insulin resistance. IGR impaired glucose regulation. NGT, normal glucose tolerance.

Only the HBsAg levels was positively correlated, while the HBsAb levels and ALP levels were negatively correlated with HOMA-β values, but only the ALP levels was a contributing factor for HOMA-β values(Table 5).

4. Discussion

This study revealed that the prevalence rate of both IFG and DM was 27.27% in patients with HBV infection, and the abnormal glucose metabolism rate was higher in CHB patients with LC or HBeAg (-) status.

Some of the findings in this study were similar to those in previous literature, which reported that the prevalence of DM was significantly higher in the HBV-infected population,[4–11]particularly in those with high viral load, with a long duration of CHB, with cirrhosis, [4,6,7–10]or of AsianAmerican race.[8]A meta-analysis

reported that the summary OR of the risk of DM for HBV patients was 1.99 (95% CI, 1.08–3.65) when compared with non-HBV individuals.[4]The prevalence rates of both IFG and DM in this study were higher than the 12.5% for DM and 7.8% for IFG in adults with CHB previously reported in a large HBV-infected multiethnic cohort study. [8]This might be attributed to the differences in the study population: the populations of the two former studies were Chinese, while the population of the latter study was American.

This study also reported a higher abnormal glucose metabolism (including IGR and DM) rate in CHB patients with LC. The prevalence rates of IGR and DM were 43.90% and 36.59% in CHB patients with LC in comparison to 18.42% and 13.16% in CHB patients without LC. This finding is consistent with those from a study that reported[7–10,17]that the odds ratios for DM in chronic hepatitis B cirrhosis patients were1.74, 1.76 and 2.317 (95% confidence interval: 1.43–2.13, 1.44–2.14, 1.528–3.513, respectively) when compared with noncirrhotic chronic hepatitis B patients.[7–10,17]However, the DM prevalence was higher than in other cross-sectional studies reporting a prevalence of 22.2% of DM among CHB patients with liver cirrhosis.[17] The development of cirrhosis may increase the incidence of DM.[7–10, 17]

In addition, it is proposed that this is the first study to indicate that the abnormal glucose metabolism rate was higher in CHB patients who were HBeAg negative, with IGR and DM prevalence rates of 31.94% and 34.72% in patients who were HBeAg negative in comparison to 17.39% and 21.74% in patients who were HBeAg positive. Previous studies suggested that the HBsAg status could influence glucose metabolism, and maternal HBsAg carriers were an independent risk factor for gestational diabetes mellitus (GDM). [22]The incidence of GDM in pregnant women who were HBsAgpositive was 6.48%, which was higher than the 3.41% incidence rate in those who were HBsAg negative.[23]However, there was no significant association between the incidence of DM and viral load, HBeAg carrier status, or other HBV markers in pregnancy, [22–23]and there is no literature reporting glucose metabolism in HBeAg carriers.

Further analyses demonstrated that abnormal glucose metabolism manifested as elevated FPG levels and significantly decreased islet β cell function, as indicated by the HOMA-β values, but it did not manifest as insulin resistance, as indicated by the HOMA-IRvalues. We found that under the same glucose metabolism conditions, the FPG level of the CHB group was continuously higher than that of the non-HBV group;it was more than 6.0 mmol/L under IGR conditions and more than 7.0 mmol/L under DM conditions, while in the non-HBV group, it was lower than 6.0 mmol/L under all three glucose metabolism conditions. Simultaneously, the HOMA-IR value of the CHB group was consistently lower than that of the non-HBV group. However, under NGT conditions, the HOMA-β values of the HBV group was 47.53 mIU/mmol, only half of the reference value (100.00 mIU/mmol), and only one third of the non-HBV group 124.19 mIU/mmol, and these valuescontinuously decreased with the deterioration of glucose metabolism.

A multicenter randomized parallel-group trial showed that the HOMA-β values in patients newly diagnosed with DM was only half the reference value (100 mmol*mIU/L^2); it decreased progressively at a rate of 4.5% annually and deteriorated with the course of the disease.[24] A new staging method for NGT, IGR and DM was proposed according to the function of β cells: normal phase ofβcell function, compensatory phase ofβcell function, decompensatory phase ofβcell function, and failure phase ofβcell function in the general population. The compensatory secretion of βcell function occurs in individuals with NGT and IR and reaches

the peak of compensatory secretion. The decompensatoryphase of βcell function has occurred in individuals with prediabetes or IGR.[25] In recent years, most studies have confirmed that not all individuals with NGT were healthy, and some presented with IR.[26] The risk of developing prediabetes and/or DM significantly increased in individuals with NGT but IR and dysfunction of β cells.[26] Therefore, the HOMA-β values of CHB patients under NGT conditions was even lower than that of those newly diagnosed with DM. The β cell function of the CHB population deteriorates directly to the decompensatory and failure phases, without undergoing normal and compensatory phases, even under NGT conditions, and this change leads to higher FPG levels and a high prevalence of IGR and DM in the CHB population. From this, we could conclude that the evident increase in the FPG levelsinpatients with CHB was associated with worsening β cell function but not insulin resistance.

In this study, it was also demonstrated that most of the HBV serological and virological indicators had negative effects, while LC, HBeAb levels and markers of liver inflammation and fibrosis had positive effects on both glucose metabolism and FPG levels. The main contributing factors for glucose metabolism and FPG levels were HBeAg (-) and HBeAb levels. However, HBV serological and virological indicators had no direct effects on islet β cell function, as indicated by the HOMA-βvalues. Therefore, we speculated that HBV indirectly affected islet β cell function through certain mechanisms.

Fundamental studies have found that hepatitis B virus infection could increase the production of tumor necrosis factor (TNF), especially in HBeAg-negative patients. [27] The overproduction of TNF could decrease the phosphorylation of insulin receptor substrates 1 and 2, inhibit phosphoinositol 3-kinase and protein kinase B, block the phosphorylation of glucose transporter 4, preventthecell uptake of glucose[28] and increase plasma glucose levels. Prostate six-transmembrane protein 2 (STAMP2) can be induced by cytokines, such as TNF alpha, which can inhibit IR in rats.[29] Moreover, hepatitis B virus X protein induces liver fat accumulation and IR by reducing the expression of STAMP2,[30]this leads to the increase in blood glucose levels and high abnormal glucose metabolism incidence.

To our knowledge, this cross-sectional study was the first to compare the differences in HOMA-β values and FPG levels between CHB patients and non-HBV patients, to compare the differences in abnormal glucose metabolism rates between CHB patients with HBeAg(+) and HBeAg(-) status, and to analyze the contributing factors of HBV virological and serological indicators on abnormal glucose metabolism. The results showed that in CHB patients, the FPG levels were higher, while the HOMA-β values were significantly lower. The β cell function of the CHB population deteriorated directly to the decompensatory and failure phases, without undergoing normal and compensatory phases, even under NGT conditions. Furthermore, CHB patients with LC or who were HBeAg negative had a higher abnormal glucose metabolism rate. HBV serological and virological indicators, markers of liver inflammation and fibrosis, and LC could directly affect glucose metabolism. However, the effects on islet β cell function were indirect.

Our study also has some limitations. The sample size was small, and it was a single-center, retrospective study. A further multicenter, prospective study with a large sample size is needed.

The findings of this study provide a reference to allow clinicians to monitor abnormal glucose metabolism in CHB patients, especially those with LC or HBeAg(-),focus on the protection of islet β-cell function, and avoid the application of insulin secretagogues in CHB patients with abnormal glucose metabolism.

5. Conclusions

The increased FPG level of CHB patients was accompanied by significantly decreased islet β cell function, but not insulin resistance. In addition, HBV could directly affect glucose metabolism and could indirectly affect islet β cell function through certain mechanisms. The findings of this study provide a reference to allow clinicians to monitor abnormal glucose metabolism in CHB patients, especially those with LC or HBeAg(-), focus on the protection of islet β-cell function, and avoid the application of insulin secretagogues in CHB patients with abnormal glucose metabolism.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of the Public and Health Clinic Centre of Chengdu (PJ-K2019-019-01). All of patients provided a written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

All data, models, or code generated or used during the study are available from the corresponding author by request: Dafeng Liu, E-mail: liudf312@126.com

Competing interests

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled, “Significantly decreased islet β cell function and increased fasting plasma glucose in patients with chronic hepatitis B: a cross-sectional study”

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Authorship contributions

Concept and design: Dafeng LIU, Lingyun ZHOU, Xinyi ZHANG , Lang BAI, Dongbo WU; Data acquisition: Dafeng LIU, Lingyun ZHOU, Xinyi ZHANG , Lang BAI, Dongbo WU; data analysis and interpretation: Dafeng LIU, Lingyun ZHOU, Xinyi ZHANG , Lang BAI, Dongbo WU; Drafting the manuscript: Dafeng LIU, Lingyun ZHOU, Xinyi ZHANG; administrative, technical, or material support: Dafeng LIU, Lingyun ZHOU, Xinyi ZHANG , Lang BAI, Dongbo WU; study supervision: Yilan ZENG and Hong TANG. All authors read and approved the final manuscript.

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Figures

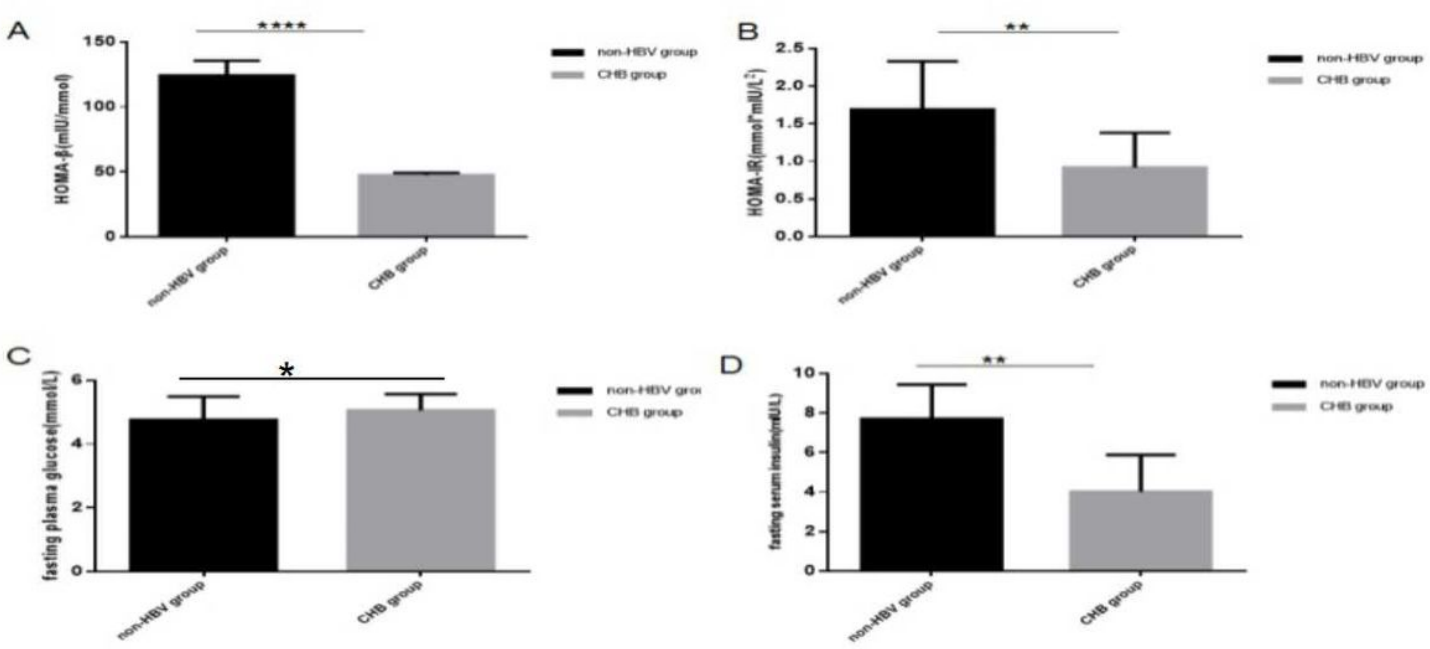

Figure 1

Comparison of metabolic parameters between two groups under NGT condition(n=100,of them CHB group 50 cases, non-HBV group 50 cases). A showed comparison of HOMA-β under NGT condition between two groups. B showed comparison of HOMA-IR under NGT condition between two group. C showed comparison of FPG under NGT condition between two group. D showed comparison of FINS under NGT condition between two group. Abbreviations: FPG, fasting plasma glucose. FINS, fasting serum insulin. HOMA-IR, hemeostasis model assement of insulin resistance. HOMA-β, Hemeostasis model assement of β cells. NGT, normal glucose tolerance. CHB, chrosis hepatitis B. non-HBV, without hepatitis B virus infection. Matched t-test was used for two groups inter-group comparison.*P<0.05,**P<0.01,****P<0.0001.

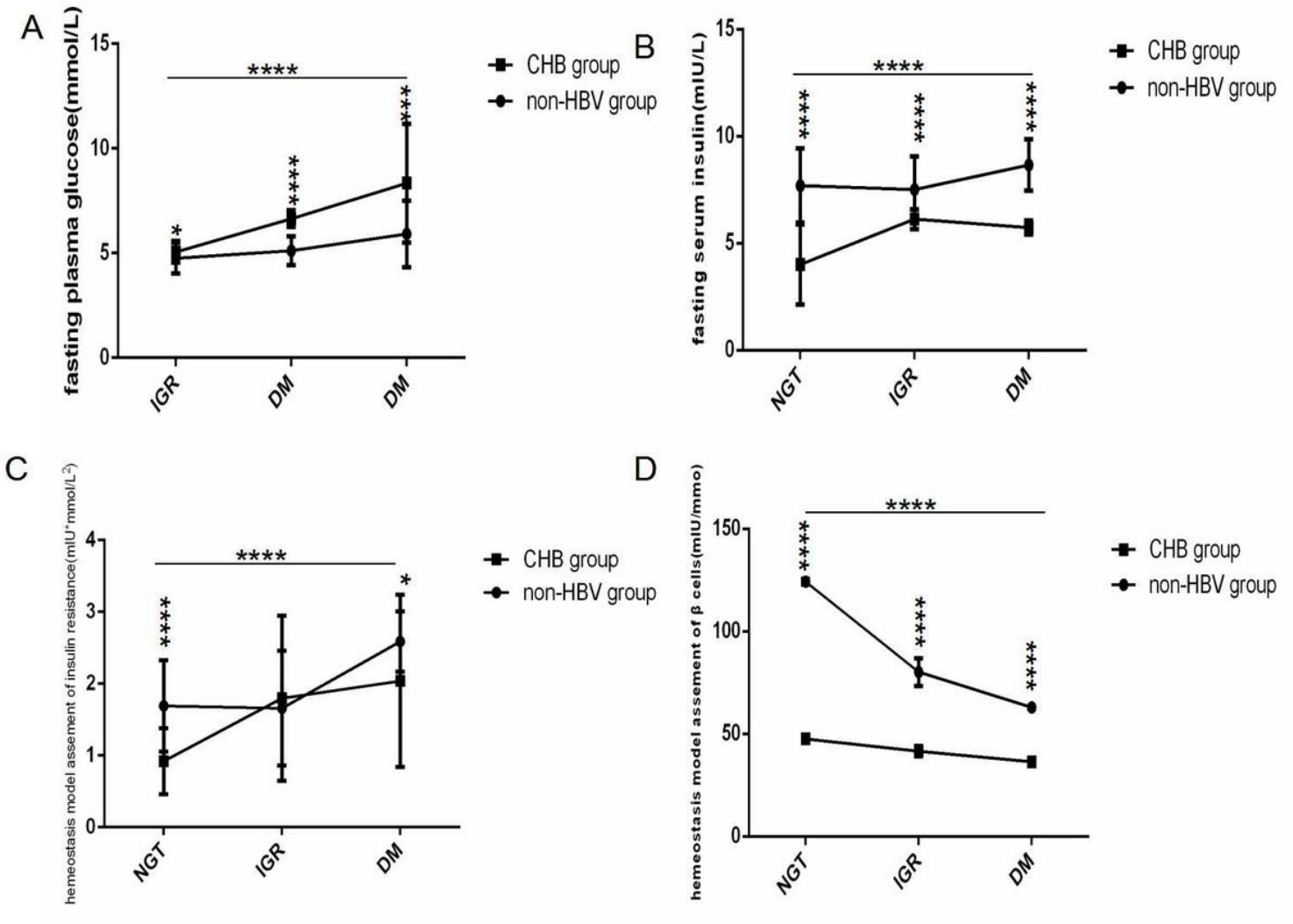

Figure 2

Comparison of the glucose metabolism parameters between the two groups under NGT, IGR and DM conditions (n=220; NGT, IGR, and DM in the two groups, n=50, 30 and 30, respectively). A. FPG levels; B. FINS levels; C. HOMA-IR values; D. HOMA-β values. Abbreviations: FPG, fasting plasma glucose. FINS, fasting serum insulin; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-β, homeostasis model assessment of β cell function; NGT, normal glucose tolerance; IGR, impaired glucose regulation; DM, diabetes mellitus. Two-way ANOVA was used for the interaction comparison (A, B, D, all P<0.0001; C, P<0.01). One-way ANOVA was used for intragroup comparisons (A, B, C, D, all P<0.0001). Unmatched t-tests were used for the intergroup comparisons. * P<0.05, ***P<0.001, ***P<0.001.

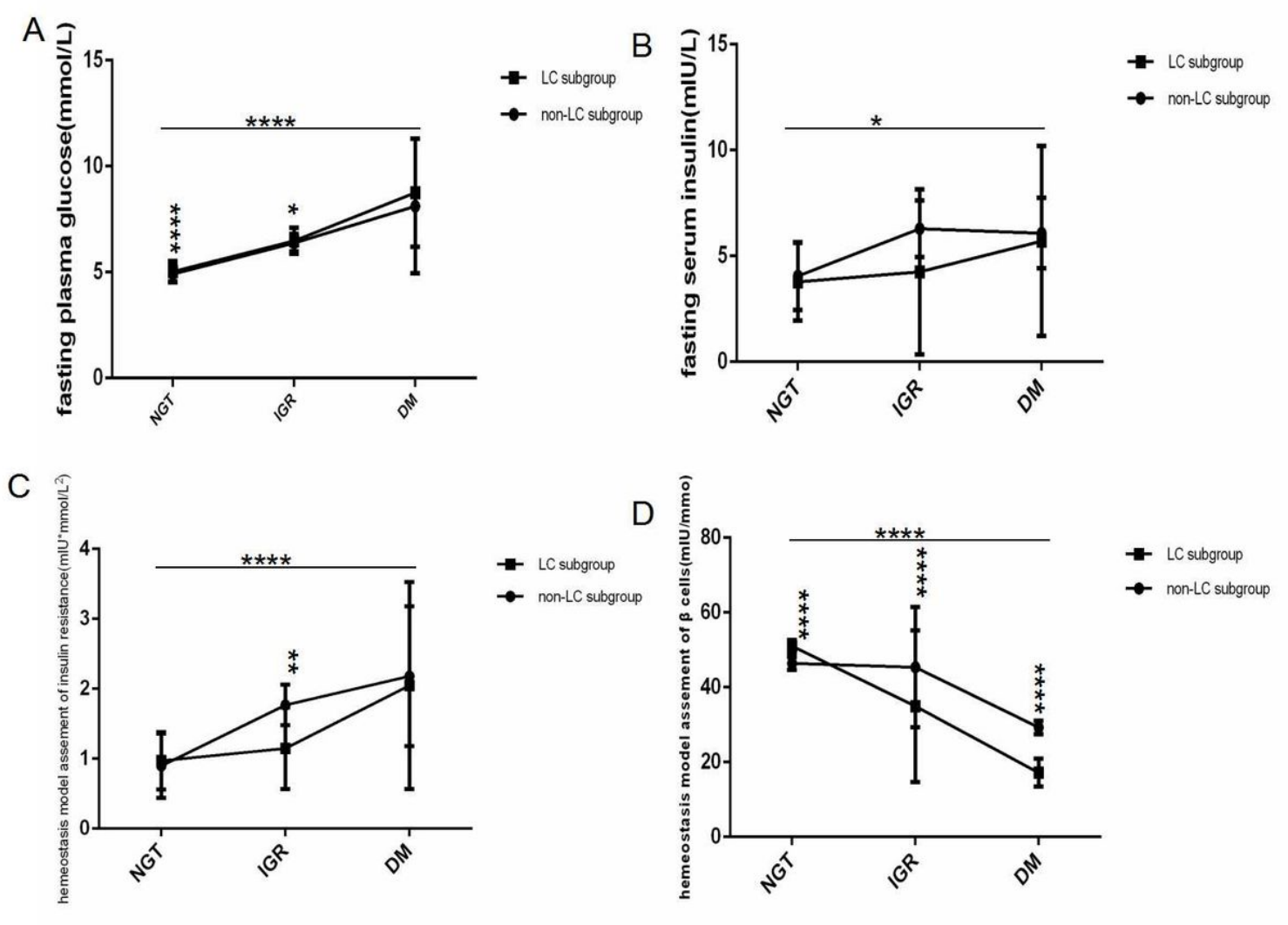

Figure 3

Comparison of glucose metabolism parameters between the non-LC and LC CHB subgroups under NGT, IGR and DM conditions (n=110; NGT, IGR and DM in non-LC subgroup, n=42, 12 and 15, respectively; in LC subgroups, n=8, 18 and 15, respectively). A. FPG levels; B. FINS levels; C. HOMA-IR values; D. HOMA-β values. Abbreviations: FPG, fasting plasma glucose; FINS, fasting serum insulin; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-β, homeostasis model assessment of β cell function; NGT, normal glucose tolerance; IGR, impaired glucose regulation; DM, diabetes mellitus; CHB, chronic hepatitis B; LC, liver cirrhosis. Two-way ANOVA was used for the interaction comparison (A, $P<0.05$; D, $P<0.0001$). One-way ANOVA was used for intragroup comparisons (A, C, D, all $P<0.0001$; B, $P<0.05$). Unmatched t-tests were used for the intergroup comparisons. * $P<0.05$, **$P<0.01$, ***$P<0.001$.

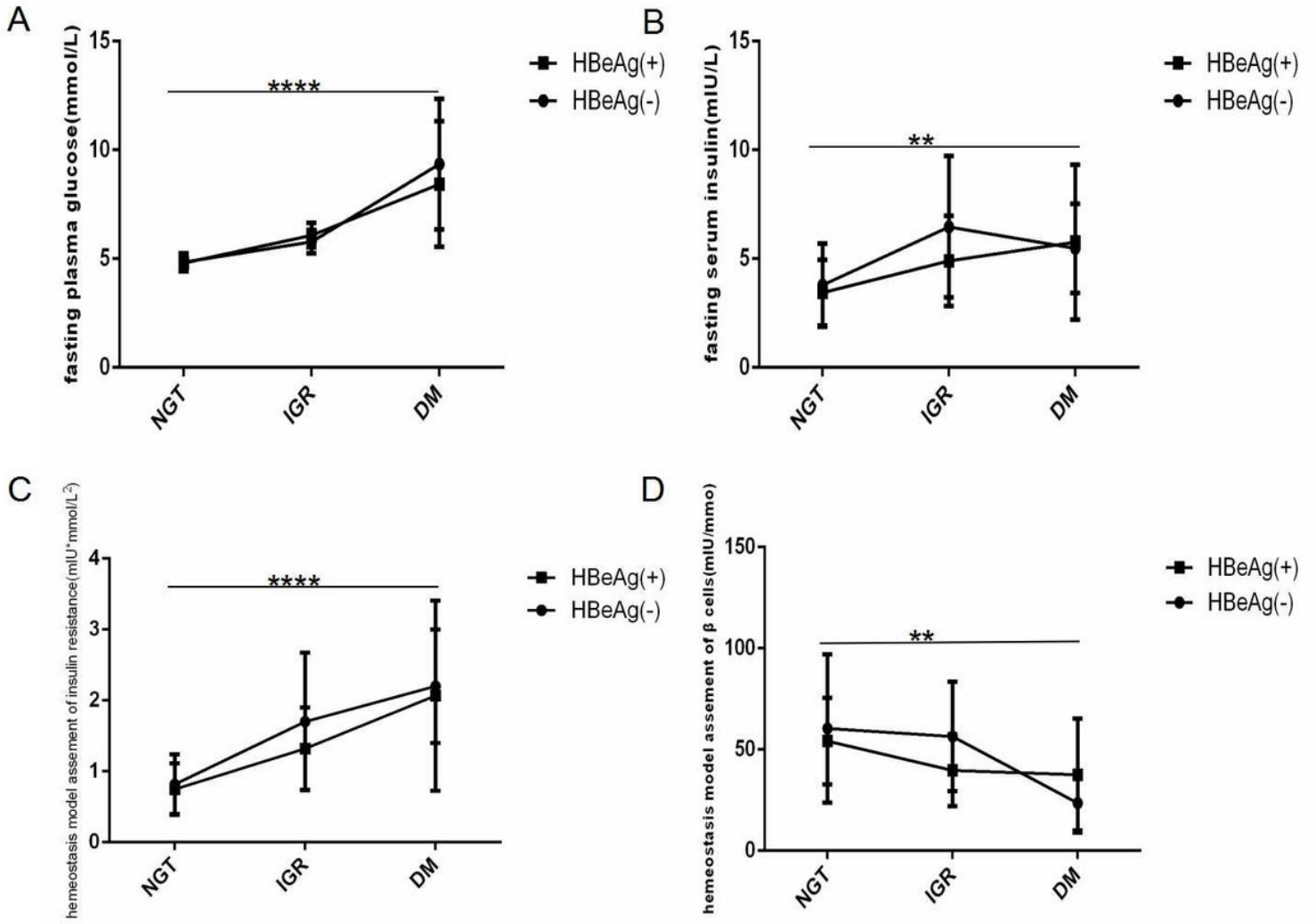

Figure 4

Comparison of glucose metabolism parameters between the HBeAg (+) and HBeAg (-) subgroups under NGT, IGR and DM conditions (n=110; NGT, IGR and DM in HBeAg (-) subgroup, n=24, 23 and 25, respectively; in HBeAg (+) subgroup, n=26, 7 and 5, respectively). A. FPG levels; B. FINS levels; C. HOMA-IR values; D. HOMA-β values. Abbreviations: FPG, fasting plasma glucose; FINS, fasting serum insulin; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-β, homeostasis model assessment of β cell function; NGT, normal glucose tolerance; IGR, impaired glucose regulation; DM, diabetes mellitus; HBeAg (-), hepatitis B envelope antigen negative; HBeAg (+), hepatitis B envelope antigen positive. Two-way ANOVA was used for interaction comparisons (A, B, C, D, all $P>0.05$). One-way ANOVA was used for intragroup comparisons (A, C, all $P<0.0001$; B, D, all $P<0.01$). Unmatched t-tests were used for the intergroup comparisons (A, B, C, D, all $P>0.05$).