The prediction model of fatty liver was established by blood biochemical indexes

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Research

Keywords: fatty liver, NHANES, Prediction model, Platelet count, glucose, ALT

Posted Date: November 23rd, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1094067/v1>

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Abstract

Background

The main cause of chronic liver disease is fatty liver, which includes alcoholic fatty liver and non-alcoholic fatty liver disease. This study is aimed to establish the prediction model of fatty liver, and provide help for the prevention and treatment of fatty liver, especially NAFLD in the future.

Methods

Datasets from 2017 to March 2020 NHANES required for the analysis were downloaded from the NHANES web site and R 4.1.1. Software was used for data analysis. A total of 3762 subjects were enrolled in this study, which were divided into model construction group and model validation group in a 2:1 ratio.

Results

The study selected 6 indicators to build the prediction model, which are as follows: ALT, Platelet count, Creatinine, LDH, HS C-Reactive Protein, Glucose. Then the prediction model was constructed. The area under ROC curve of the model was 0.7471. In the validation population, the area under the ROC curve of the model was 0.7816.

Conclusions

F score has a good predictive effect on fatty liver, which can be used as an important means for the prevention and treatment of fatty liver, especially NAFLD in the future.

1. Introduction

The main cause of chronic liver disease is fatty liver, which includes alcoholic fatty liver and non-alcoholic fatty liver disease (NAFLD). It includes complex pathological manifestations, from simple fat accumulation to non-alcoholic steatohepatitis (NASH), which is an important factor in other metabolic disorders, and also an important cause of type 2 diabetes and cardiovascular disease(1). In the United States, NAFLD has affected the lives of a quarter of people and has become the second leading cause of liver transplantation(2). Alcoholic liver disease is a related disease state characterized by early fatty liver (alcoholic steatosis). NAFLD and alcoholic steatohepatitis are both important causes of serious complications such as HCC and liver cirrhosis(3–6).

The pathophysiological feature of fatty liver is the accumulation of large amounts of fat in liver parenchymal cells (liver cells). Under normal circumstances, these cells are particularly adept at storage

and excretion of fat to promote the body's metabolic needs. However, in disease states, they are prone to accumulate fat at a super-pathological level(1). NAFLD is characterized by excessive accumulation of triglycerides in the liver, which is a common complication of obesity and is related to insulin resistance and metabolic syndrome(7). According to MRI evaluation, more than 5% of the fat in the liver is considered to be early liver steatosis(8). It is characterized by lipid apoptosis, inflammation and fibrosis of liver cells(9).

The diagnosis of fatty liver requires imaging and histological examination, while the diagnosis of NAFLD is more complicated(10, 11). The initial challenge was when to suspect fatty liver, because most patients are asymptomatic. Due to the lack of cost-effective, non-invasive tests with high predictive value, and the lack of effective treatments, comprehensive NAFLD screening is not currently recommended(12). Therefore, it is necessary to explore a new effective clinical prediction model for fatty liver, so that the high-risk population can change their lifestyle earlier, better prevent the occurrence of fatty liver and reduce the incidence of various complications. In this study, the clinical prediction model of fatty liver was established by using the database of National Health and Nutrition Examination Surveys (NHANES), and its good predictive effect was verified, which could become an important means for the prevention and treatment of fatty liver in the future.

2. Methods

2.1 Study Sample

Datasets from 2017 to March 2020 NHANES required for the analysis were downloaded from the NHANES web site. After excluding the information deficit group, a total of 3762 subjects were enrolled in this study, which were divided into model construction group and model validation group in a 2:1 ratio. The characteristics of the study population are shown in Table 1.

Table 1
Characterization of the study population

	Model building population	Model validation population
Gender		
male	1216(48.48%)	583(46.49%)
female	1292(51.52%)	671(53.51%)
Age	50.886±17.466	50.426±17.455
Race/Hispanic origin		
Mexican American	313(12.48%)	173(13.8%)
Other Hispanic	258(10.29%)	119(9.48%)
Non-Hispanic White	855(34.09%)	420(33.49%)
Non-Hispanic Black	626(24.96%)	324(25.84%)
Other Race - Including Multi-Racial	456(18.18%)	218(17.38%)
ALT (IU/L)	21.858±16.028	21.494±16.31
Creatinine (umol/L)	79.781±50.448	78.064±39.511
Glucose (mmol/L)	5.855±1.983	5.924±2.042
Platelet count (1000 cells/uL)	242.271±64.939	243.785±64.918
fatty liver		
have	65(2.59%)	24(1.91%)
none	2443(97.41%)	1230(98.09%)
N	2508	1254

2.2 Statistical analysis

Analyses were conducted using R 4.1.1. A total of 59 laboratory tests and physical examination indicators such as body weight were included. After screening risk factors, the prediction model was incorporated to reflect the prediction accuracy by the area under the ROC curve, and the prediction accuracy of the model was verified in the validation population. Bootstrap test was used for the prediction model, and repeated sampling was conducted for 500 times.

3. Results

3.1 Screening of impact factors

The 59 indexes were used for machine learning and predictive analysis. The influence of indexes on fatty liver was shown in Figure 1a. The Alignment Diagram of the influence of various factors on fatty liver can be seen in Figure 1b. We select the first 6 indicators to build the prediction model, which are as follows: Alanine Aminotransferase (ALT, IU/L) (VIF= 1.1), Platelet count (1000 cells/uL) (VIF= 1.1), Creatinine, refrigerated serum (umol/L) (VIF= 1), Lactate Dehydrogenase (LDH) (IU/L) (VIF= 1.1), HS C-Reactive Protein (mg/L) (VIF= 1.1), Glucose, refrigerated serum (mmol/L) (VIF= 1).

3.2 Prediction model Construction

The model was constructed with the included indicators in 2508 subjects.

$$\text{F score} = -3.54200 + 0.27464 \times ((\text{ALT}/10)^1) - 2.36968 \times ((\text{Creatinine}/100)^1) + 0.92544 \times ((\text{Glucose}/10)^1) + 1.39671 \times ((\text{Platelet count}/100)^{-2})$$

ALT: IU/L, Creatinine: umol/L, Glucose: mmol/L, Platelet count: 1000 cells/uL.

The area under ROC curve of the model was 0.7471, as shown in Figure 2. 95% CI was [0.6789, 0.81], the optimal threshold was 0.0198, the specificity was 0.5686, the sensitivity was 0.8125, the accuracy was 0.5749, the positive likelihood ratio was 1.8834, the negative likelihood ratio was 0.3298. The diagnostic odds ratio was 5.7114, positive predictive value was 0.0474, and negative predictive value was 0.9914. (Bootstrap resampling times= 500)

3.3 Validation of prediction effect of prediction model

ROC curves were also used to assess the predictive effect of F score on fatty liver disease in 1254 subjects. The area of F score under ROC curve in the validation population was 0.7816, as shown in Figure 3. 95% CI was [0.68, 0.8852], specificity was 0.848, sensitivity was 0.75, and accuracy was 0.8461, the positive likelihood ratio was 4.9332; the negative likelihood ratio: 0.2948; the diagnosis odds ratio: 16.7326, positive predictive value was 0.0878, and negative predictive value was 0.9943. (Bootstrap resampling times= 500)

It can be seen that F score has a good predictive effect on fatty liver in the validated population.

4. Discussion

Liver function enzymes are important markers of the severity of many liver diseases, especially aspartate aminotransferase (AST) and alanine aminotransferase (ALT)(13). The study by Helene Gellert-Kristensen et al. found that the concentration of ALT has an important correlation with the risk of fatty liver, cirrhosis and HCC(14). And ALT is an independent related factor of metabolic syndrome, obesity, diabetes and other diseases(15, 16). Alcohol intake is an important factor leading to fatty liver and one of the important reasons leading to elevated ALT. Moderate alcohol consumption does not cause a significant increase in ALT, but long-term alcohol intake can cause an increase in ALT and liver changes(17–19).

NAFLD is closely related to ALT activity and is a common cause of unexplained ALT elevation(20, 21). Unexplained elevated ALT should consider the possibility of NAFLD(16). This is also consistent with our experimental results, ALT is one of the most important factors related to fatty liver.

Studies by Muhammad et al. have shown that creatinine is significantly elevated in patients with fatty liver, which is obviously correlated with fatty liver(22). Creatinine is an important indicator of model for end-stage liver disease (MELD) score, which measures liver function and predicts survival in patients with liver disease(23–26).

NAFLD is closely linked with hepatic insulin resistance(27, 28). It is the liver manifestation of metabolic syndrome, and increased glucose is one of the important manifestations(29). Insulin resistance is a key pathogenic factor of metabolic syndrome and the most common risk factor for NAFLD(30–32). In patients with insulin resistance, insulin cannot inhibit liver glucose production, but it continues to stimulate adipogenesis, leading to hyperglycemia, hyperlipidemia, liver steatosis and type 2 diabetes(33, 34). However, in our study, insulin content was not an important correlation factor of fatty liver. This may be because the level of insulin does not directly reflect the liver insulin resistance like glucose(35, 36).

Researches showed that platelet count is related to NALFD and liver cirrhosis(37–39), and can reflect the degree of liver injury(40). Studies have also shown that platelet count is closely related to insulin resistance, and its severity and complications(41, 42). This may have the following reasons: (1) the influence of portal hypertension; (2) splenic sequestration of platelets; (3) liver damage may also cause TPO release defects and reduce platelet production in the bone marrow(43–45).

There are also some shortcomings in this study, for example, the included population is from the NHANES database, and the model still needs prospective research verification. Whether there are other indicators that can improve the accuracy of the model also needs to be explored in the future, but at present, the model can predict the occurrence of fatty liver with satisfactory accuracy by using blood biochemical indicators.

5. Conclusion

F score has a good predictive effect on fatty liver, which can be used as an important means for the prevention and treatment of fatty liver, especially NAFLD in the future.

Abbreviations

1. NAFLD: non-alcoholic fatty liver disease
2. NASH: non-alcoholic steatohepatitis
3. NHANES: National Health and Nutrition Examination Surveys
4. ALT: Alanine Aminotransferase

- 5. LDH: Lactate Dehydrogenase
- 6. AST: aspartate aminotransferase
- 7. MELD: model for end-stage liver disease

Declarations

Ethics approval and consent to participate

The data were obtained from NHANES database and no ethical review was required.

Consent for publication

Not applicable.

Acknowledgement

None.

Availability of data and materials

All data for the study can be obtained from the corresponding author and author

Competing interests

The authors declare that they have no competing interests.

Funding

None.

Authors' contributions

Study concept and design: Yan XU, Rong LIU.

Data extraction: Yan XU;

Data analysis and interpretation: Yan XU.

Drafting of the manuscript: Yan XU;

critical revision of the manuscript for important intellectual content: Rong LIU.

Statistical analysis: Yan XU.

Acknowledgements

None.

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Figures

Figure 1

a: Correlation of various factors and fatty liver. X10: Alanine Aminotransferase (ALT) , X54: Platelet count, X18: Creatinine, X23: Lactate Dehydrogenase (LDH), X66: HS C-Reactive Protein, X20: Glucose, X13: Aspartate Aminotransferase (AST), X38: Monocyte percent, X35: Body Mass Index, X17: Creatine Phosphokinase (CPK), X33: Uric acid, X32: Triglycerides, X21: Gamma Glutamyl Transferase (GGT), X12: Alkaline Phosphatase (ALP), X36: White blood cell count, X69: Total Cholesterol, X30: Cholesterol, X53: Red cell distribution width, X55: Mean platelet volume, X44: Segmented neutrophils num. b: The Alignment Diagram of the influence of various factors on fatty liver. X10: Alanine Aminotransferase (ALT) , X54: Platelet count, X18: Creatinine, X23: Lactate Dehydrogenase (LDH), X66: HS C-Reactive Protein, X20: Glucose, X68: Fatty liver.

Figure 2

The ROC curve of the prediction model in the model building population.

Figure 3

The ROC curve of the prediction model in the validation model population.