Survey of non-alcoholic fatty liver disease knowledge, nutrition and physical activity patterns among the general public in Beijing, China

Stephanie Chen BA¹, Samantha Chao BA¹, Monica Konerman MD MSc², Wei Zhang MD PhD^{2,3}, Huiving Rao MD³, Elizabeth Wu MPH², Andy Lin BS², Lai Wei MD PhD³, Anna S. Lok MD²

¹Medical School, University of Michigan, Ann Arbor, MI, United States ²Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI, United States ³Peking University People's Hospital, Peking University Hepatology Institute, Peking University Health Science Center, Beijing, China

Corresponding Author:

Stephanie Chen, University of Michigan Medical School, M4101 Medical Science Building I – C wing, 1301 Catherine Street Ann Arbor, MI 48109, USA Email: sjchen@med.umich.edu

Author Correspondence:

Samantha Chao, University of Michigan Medical School, M4101 Medical Science Building I - C wing, 1301 Catherine Street Ann Arbor, MI 48109, USA Email: skchao@med.umich.edu

Monica Konerman MD, 1500 E Medical Center Drive, 3912 Taubman Center, SPC 5362, Ann Arbor, MI 48109. USA Email: konerman@med.umich.edu

Wei Zhang MD PhD, Peking University People's Hospital, 11 South Xizhimen Street Beijing 100044, China

Email: jisuifanny@163.com

Huiving Rao MD. Peking University People's Hospital, 11 South Xizhimen Street Beijing 100044, China Email: raohuiying@pkuph.edu.cn

Elizabeth Wu, 1500 E Medical Center Drive, 3912 Taubman Center, SPC 5362, Ann Arbor, MI 48109, USA

Email: elizwu@med.umich.edu

Andy Lin, 1500 E Medical Center Drive, 3912 Taubman Center, SPC 5362, Ann Arbor, MI 48109, USA Email: andylin@med.umich.edu

Lai Wei MD PhD, Peking University People's Hospital, 11 South Xizhimen Street Beijing 100044. China Email: weilai@pkuph.edu.cn

Anna S. Lok MD, 1500 E Medical Center Drive, 3912 Taubman Center, SPC 5362, Ann Arbor, MI 48109, USA

Email: aslok@med.umich.edu

Acknowledgements

This study was supported by the University of Michigan Medical School Global REACH Program, University of Michigan - Peking University Health Science Center Joint Institute for Clinical and Translational Research, and Tuktawa Foundation.

Abstract

Background: Despite high prevalence of non-alcoholic fatty liver disease in China, understanding of the disease appears to be low.

Aims: We assessed knowledge of NAFLD among the public in Beijing, China as well as diet and physical activity patterns, which may provide information useful for NAFLD prevention and management.

Methods: We surveyed adult patients and family members in the Peking University Health Science Center (PUHSC) ultrasound clinic and office staff in Beijing, China. Participants provided demographic and medical history data. NAFLD-related knowledge and diet and physical activity were assessed.

Results: 1296 participants at the PUHSC clinic (51% female, median age 35, 61% college-educated) and 494 participants in offices (61% female, median age 43, 74% college-educated) completed the survey. Response rate was 68.4% and 96.7%, respectively. In clinic and offices, 44% vs. 48% were overweight/obese, 5% had a history of diabetes in both groups, and 14% vs. 23% had a personal history of NAFLD. Median knowledge score was 15 out of 25 in clinic vs. 16 in offices. 44.9% reported minimal physical activity. Factors associated with higher NAFLD knowledge scores (>16) on multivariate analysis included college education or higher (OR 1.7, p=0.01), family history of hyperlipidemia (OR 1.96, p<0.001), and number of sugary drinks per week (OR 0.74, p=0.006). No factors were significantly associated with physical activity levels.

Conclusions: Adults in Beijing had low knowledge about NAFLD and most were not physically active. Programs to increase public awareness of NAFLD and promote physical activity are critical to curb this growing epidemic.

Key words: Metabolic syndrome, obesity, health literacy, patient education, lifestyle intervention

Abbreviations: NAFLD – Non-alcoholic fatty liver disease; PUHSC – Peking University Health Science Center; IPAQ – International physical activity questionnaire; AFLD – Alcoholic fatty liver disease; BMI – body mass index; HBV – Hepatitis B virus; HCC – hepatocellular carcinoma

Introduction

Non-alcoholic fatty liver disease (NAFLD) and other obesity-related diseases are increasingly prevalent in China. It is estimated 12-14% of adults in China are obese, 10.9% have type II diabetes, 42.7% have dyslipidemia, and 15% have NAFLD [1-4]. Despite its high prevalence, public awareness and individual knowledge about NAFLD among the general population in China appears limited. Furthermore, there is presently little data regarding diet and physical activity habits among adults in China and whether these lifestyle behaviors are associated with NAFLD awareness and knowledge.

There have been a few studies assessing public understanding of NAFLD in Asian communities. The existing literature demonstrates that the general public in Asia have limited awareness of NAFLD, and those with awareness often have misconceptions. A study done in Hong Kong in 2009 revealed more than 80% of participants had never come across the term "NAFLD," and many incorrectly believed smoking, hepatitis B carrier status, and previous hepatitis A infection were risk factors for NAFLD [5]. A more recent survey of participants attending a forum on lifestyle and digestive diseases in Singapore in 2016 showed higher awareness of NAFLD (71.2%); however, 75% of participants did not believe they were at risk for the disease despite having one or more metabolic risk factors [6].

Given this significant gap between disease prevalence and public awareness in Asian populations, we aimed to assess knowledge of NAFLD in Beijing, which has witnessed rapid economic growth and accompanying changes in diet and lifestyle in the last decade. Furthermore, because development of NAFLD is closely linked to nutrition and activity

levels, an exploration of the diet and activity habits of Beijing residents can provide useful information for prevention and management of NAFLD.

Materials and Methods

Study Design and Population

We conducted the study between July 12 and August 22, 2017. Participants were invited to complete an anonymous, paper-based, self-administered survey. Two medical students from the University of Michigan participating in a global health research program designed, distributed, and collected the survey. The study was supervised by Professor Wei at the People's Hospital Hepatology Institute, Peking University Health Sciences Center (PUHSC) in Beijing, China and Professor Lok at the University of Michigan. The study was approved by the Institutional Review Boards of both universities.

The survey study was conducted on adult patients and their family members in the ultrasound clinic at the Peking University People's Hospital, PUHSC, and on staff from government offices in Beijing. Prior to the study, Professor Wei contacted 20 government institutions located near the hospital for permission to conduct the study; six government research institutes and two manufacturing companies agreed to participate. The survey study was advertised to employees in these offices via their labor unions. Each office that agreed to participate was visited once during the study period. All participation was voluntary and followed verbal consent. No incentive was provided for completion of the survey.

Survey

The survey consisted of four sections: knowledge of NAFLD, diet, physical activity, and demographics/medical history. Content of the survey was modeled after questionnaires

used by prior researchers [7] and by the China National Diabetes and Metabolic Disorders Study [8]. The validated International Physical Activity Questionnaire (IPAQ) was used to assess physical activity [9]. Given the lack of pre-existing validated surveys on this topic, the remaining questions were developed by the research team based on expert consensus and a thorough review of the literature.

Twenty-five questions were used to evaluate knowledge about NAFLD, and one point was given for each correct answer. These questions covered prevalence (n=1), reversibility of NAFLD (n=1), potential health consequences (n=4), common symptoms (n=3), diagnosis (n=3), treatment (n=6), and risk factors (n=7). All questions evaluating knowledge about NAFLD were in true-or-false format except for the question regarding NAFLD prevalence, in which participants were given multiple choice options. The original survey included five questions on common symptoms and seven questions on treatment options, three of these questions were omitted in the analysis based on feedback from participants regarding ambiguity.

The survey was initially developed in English, translated by PUHSC staff, and verified by University of Michigan investigators who are fluent in Chinese for accuracy. Pilot testing was conducted on 20 volunteers in Beijing (men and women aged 30-65 years), and revisions were made based on their feedback. The English version of the survey has been included as supplementary material.

Definitions

Body mass index (BMI) was calculated based on self-reported weight and height. Respondents were categorized as normal weight, overweight, or obese based on BMI categories used in Asian populations, <24, 24-28, or \geq 28 kg/m² [10]. Physical activity levels were categorized as inactive, minimally active, or moderately active based on IPAQ guidelines [11]. Good knowledge of NAFLD was defined as a total knowledge score of >16 out of 25 based on the median knowledge score.

Statistical analyses

Data were analyzed using STATA version 13 (College Station, TX). Continuous variables were expressed as mean ± standard deviation or median (interquartile range, IQR). Comparison between groups was made using the unpaired t-test if variables were normally distributed and nonparametric methods (Mann-Whitney U test) if not. Categorical data were described as proportions and compared using the chi square test. Logistical regression analyses (univariate and multivariate) were performed to identify predictors for NAFLD knowledge and physical activity level. Variables that were significant on univariate analysis plus sex, age, and BMI were included in the multivariate analysis. All p-values represent the results of two-sided tests and values <0.05 were considered statistically significant.

Results

Characteristics of Participants

A total of 1296 participants at the Peking University People's Hospital, PUHSC ultrasound clinic and 494 participants from eight Beijing government offices participated in the survey. The response rate was 68.4% in the clinic and 96.7% in the offices. The demographics, medical history, and self-assessment of NAFLD knowledge of the participants are shown in **Table 1.** Overall, 53.6% of the participants were women and median age was 36. Median BMI was 23.7 overall with 46.6% of participants being overweight or obese. The most common pre-existing metabolic abnormality among

participants was hyperlipidemia (18.7%). The most common metabolic abnormality among family members was hypertension (50.1%). The two cohorts differed slightly in that the office staff were older, more likely to be female, to have a college education or higher, and to have a known diagnosis of NAFLD (though median BMI and proportion with diabetes was similar).

Knowledge of NAFLD

Overall, 30.2% of participants reported having heard of NAFLD prior to the survey with a higher proportion in offices compared to the clinic (32% offices vs. 29.5% clinic). Among participants in the clinic, those with a personal history of NAFLD had higher awareness than those without (41.9% vs. 26.3%). Median knowledge score, out of a total of 25, was 15 in the clinic and 16 in the offices. Median knowledge was slightly higher among participants with a personal history of NAFLD than those without, 16 vs. 15 in the clinic and 17 vs. 16 in the office, respectively.

The percentage of participants that responded correctly to each NAFLD knowledge question is shown in **Figure 1**. More than 90% of both clinic and office participants knew NAFLD is reversible, can cause cirrhosis, is more common in obese persons, and can be managed with changes in diet. Roughly 90% of participants knew NAFLD can be diagnosed by imaging. Approximately half knew NAFLD can be diagnosed by liver biopsy, but only one-third knew NAFLD cannot be diagnosed by blood tests. While more than 95% of participants knew NAFLD can cause cirrhosis, less than 80% recognized NAFLD can lead to liver cancer. Although 94% of participants knew obesity is a risk factor for NAFLD, only 55% recognized diabetes as a risk factor and 25-35% of participants thought excess drinking or smoking were risk factors for NAFLD. The vast

majority (96%) of participants knew treatment options for NAFLD include a reducedcalorie diet, but only 76% recognized increased physical activity is an option and 73% thought liver supplements can be beneficial. Only half of the participants recognized most patients with NAFLD are asymptomatic. The question with the fewest correct responses pertained to prevalence of NAFLD in China, with only 20.5% of participants answering this question correctly (20.3% and 21.0% in clinic and offices, respectively). Most incorrect responses under-estimated the burden of NAFLD in China.

Dietary Habits and Physical Activity

Responses to questions on dietary habits and physical activity are shown in **Table 2**. More than half of the participants (55.4%) perceived their diet to be healthy, 53.8% in clinic and 58.9% in offices. Most participants (88.1%) ate, on average, 3 meals a day with a similar distribution between clinic and office participants (87.9% and 88.6%, respectively). Most participants (58.8%) reported snacking occasionally between meals (60.9% and 53.6% in clinic and offices, respectively). Slightly more than half (59.9%) of the participants reported having no sugary drinks (55% and 69% in clinic and companies, respectively) at all.

The majority (88.9%) of the participants perceived themselves as being physically active, 89.4% in clinic and 87.7% in offices. However, less than a quarter of the participants exercise >3 times a week, 19.6% in clinic and 23.2% in office. Analysis of responses to IPAQ revealed 27.8% of clinic participants were classified as inactive, 44.9% minimally active, and only 27.3% exceeded the minimum physical activity recommendations. The corresponding figures for office participants were 24.5%, 50.1%, and 25.4%, respectively. The median sitting time for both cohorts was 360

minutes/week, and participants in offices spent more time sitting than those in clinic (p<0.001).

Associations with NAFLD Disease Knowledge

Table 3 shows variables associated with high NAFLD knowledge scores. On univariate analysis, a personal history of NAFLD or hyperlipidemia, years of education, moderate physical activity level, and family history of NAFLD, hyperlipidemia, hypertension, or diabetes were significant predictors of higher NAFLD knowledge scores while number of sugary beverages consumed had a negative association. On multivariate analysis, only years of education and family history of hyperlipidemia were significant predictors of higher NAFLD knowledge scores while number of higher NAFLD knowledge score while number of sugary beverages consumed had a negative association.

Discussion

In this survey of nearly 2000 participants living in Beijing, only one-third had baseline awareness of NAFLD. Recent studies suggest as much as 35% of the population in China has NAFLD and that this number will continue to increase [12]. Awareness was higher among participants in government offices than those in the ultrasound clinic, which is likely related to higher education level and a higher prevalence of personal diagnosis of NAFLD in the former.

Awareness of NAFLD among this Beijing cohort was higher than that reported by Leung et al. in a study conducted in Hong Kong (17%) but lower than that reported by Goh et al. in a study conducted in Singapore (70%) [5,6]. It should be noted the study in Hong Kong was conducted in 2009 when NAFLD was less prevalent and less publicized while the study in Singapore was conducted at a public forum on lifestyle and digestive

disease, which might have attracted more health-conscious persons or those more likely to have gastrointestinal or liver diseases related to lifestyle behaviors. The question that was most often incorrectly answered in our study pertained to the prevalence of NAFLD in China with most underestimating its prevalence. Similarly, 42% did not know the prevalence of NAFLD in the Hong Kong study [5] and Goh et al. found only 40% of their participants believed NAFLD was common in Singapore [6]. While awareness of NAFLD in China may be increasing, its significance as a growing epidemic in the country is not fully understood by the public. It is conceivable that the rate at which NAFLD's prevalence in China increases may outpace the general public's knowledge of the disease.

The median knowledge score was 15 (of a total of 25) among participants in the clinic and 16 among those in the offices. As expected, participants with a personal diagnosis of NAFLD had higher knowledge scores, but the difference was small, only one point higher than those without such diagnosis. Furthermore, while personal diagnosis of NAFLD was a predictor of higher knowledge score in univariate analysis, this was not the case in multivariate analysis. The results of our analysis are concerning as they suggest persons who carry a diagnosis of NAFLD are only marginally more knowledgeable about the disease than persons who do not carry the diagnosis. Knowledge about one's disease is associated with positive benefits including improved outcomes [13], and highlight the need to provide better education to patients with NAFLD about the disease.

Most participants (95.6%) recognized NAFLD can lead to cirrhosis but fewer (80.1%) knew it can lead to liver cancer. With the availability of highly effective vaccine and

antiviral therapy for hepatitis B, the prevalence of hepatitis B virus (HBV) infection in China has declined such that China is no longer considered to be a highly endemic country. It is expected the incidence and mortality from HBV-related hepatocellular carcinoma (HCC) will decrease in coming years. The recent approval of direct-acting antiviral drugs that are highly effective in curing hepatitis C in China is also expected to decrease the burden of hepatitis C virus related HCC. On the other hand, the incidence and mortality from NAFLD-related HCC in China is expected to increase due to increasing prevalence of obesity, diabetes, and NAFLD. An increase in liver transplantations and HCC secondary to NAFLD is already evident in Western countries. NAFLD-associated HCC is the second most common indication for liver transplantation in the United States and is predicted to soon become the leading cause [14,15]. One of the most common misconceptions surrounding NAFLD involves understanding of risk factors for the disease. Most participants in this study recognized that obesity is a risk factor for NAFLD, but almost half did not know diabetes is also a risk factor. Understanding the risk associated with diabetes is particularly critical because diabetes also increases the likelihood of developing nonalcoholic steatohepatitis, a more severe form of NAFLD [16]. Additionally, 25-35% of participants thought excess drinking or smoking were risk factors for NAFLD. Previous studies have also demonstrated significant confusion surrounding NAFLD risk factors. Leung et al. found a large proportion of respondents incorrectly identified smoking, hepatitis B carrier status, and previous hepatitis A infection as risk factors (52%, 57%, and 42%, respectively) [5]. In the Singapore study, 75.6% of participants with one or more metabolic risk factors did not believe they were at risk for developing NAFLD [6]. The low awareness of one's

vulnerability may be compounded by the failure to recognize that NAFLD can be asymptomatic. Most patients with NAFLD show no symptoms until cirrhosis develops [17], and barely more than half of the participants surveyed (51.7%) recognized this. Only 22% of the participants surveyed in Hong Kong believed NAFLD could be asymptomatic while 47% in the same study admitted to knowing nothing about the clinical presentation of NAFLD [5]. Along similar lines, a case-control study conducted by Mlynarsky et al. in Israel found a diagnosis of NAFLD in asymptomatic patients had no significant impact on their self-health perception or utilization of health care. Minarsky et al. concluded their findings pointed to a lack of awareness and understanding that NAFLD is a progressive disease and among the general population, NAFLD is not considered a problem until there are signs or symptoms [18]. The vast majority (96.1%) of our participants knew dietary changes can reverse NAFLD; however, fewer (79.1%) knew increased physical activity can have the same benefit. We found that while 88.9% of participants considered themselves to be physically active, their responses to IPAQ indicate that only 27.3% met the minimum weekly physical activity recommendations. Discrepancies between self-perception and the reality of dietary habits and physical activity have also been observed in other studies with patients tending to underestimate their caloric intake and overestimate their physical activity [19,20]. An accurate assessment of one's diet and activity level is critical to motivate changes in lifestyle behavior. More than half of our participants (59.6%) believed liver supplements can reverse NAFLD. To date, there is no approved medication for treatment of NAFLD, and only a few medications have been approved for weight loss [21,22]. Although there are many claims that supplements can reduce

weight, objective evidence in support of such claims is lacking and weight-loss supplements are an increasingly common cause of drug-induced liver injury [23]. Given that NAFLD is of growing concern in both the United States and China, it is interesting to compare the knowledge base of this Beijing cohort to American counterparts. Ghevariya et al. surveyed 5000 residents in Brooklyn, New York to assess awareness of NAFLD and cirrhosis as well as knowledge of predisposing factors for both conditions. They found significant gaps in knowledge regardless of age, gender, or educational status. 98% of the participants had never had a discussion regarding NAFLD with their primary physician. 70% believed NAFLD was hereditary, and only 5% believed NAFLD could affect individuals who did not drink alcohol. An overwhelming majority (96%) was not aware the disease was reversible in its early stages, and a similar proportion (95%) did not feel fatty liver could lead to serious health problems [7]. The results of the Brooklyn study reiterate what appear to be universal misunderstandings surrounding predisposing risk factors for NAFLD and the magnitude of the disease and its sequelae. In comparison, the Beijing residents surveyed in this study seem to be more aware of the potential for NAFLD to cause liver cirrhosis and the steps patients can take to reverse the disease process early on.

Our study is one of the first to survey knowledge about NAFLD as well as diet and physical activity in persons not presenting to a health fair or being evaluated in a clinic for diabetes or liver disease. There are, however, several limitations to our study. By virtue of being a survey study, our results are limited by volunteer bias, self-report bias, and non-response bias. Issues with the survey itself, including misinterpretation of questions and unfinished surveys, also impacted accuracy of our data analysis.

Additionally, we recognize that some of the knowledge-based questions may have been ambiguous in their construction. For example, we considered it incorrect for participants to indicate that blood tests could be used to diagnose NAFLD because there is no blood test specific for diagnosis of NAFLD. However, we acknowledge that blood tests are necessary as they exclude other chronic liver diseases. While we aimed to survey a representative sample of individuals, the participants were more educated than the average Chinese citizen. In addition, the sample size of 1790 participants was not large enough to be representative of the more than 20 million people living in Beijing. Furthermore, because this study came out of a collaboration between teams in Ann Arbor and Beijing, it would have been ideal if comparative data were available in Ann Arbor; however, enrollment of a similar number of participants in Ann Arbor would not be sufficient for generalization of the results to the general population in China vs. the United States.

In conclusion, in this survey of nearly 2000 adults in Beijing, we found a low awareness of NAFLD and a gross under-estimation of its prevalence. There were many misconceptions, particularly surrounding risk factors, the commonly asymptomatic presentation of NAFLD, and the potential to cause HCC. We also found most participants overestimated their activity level, and a substantial proportion did not recognize the importance of physical activity in reversing NAFLD. Patient education directed at these gaps in knowledge and at promotion of physical activity is critical to curb this rapidly growing public health problem in China and worldwide.

Compliance with Ethical Standards

Disclosure of Potential Conflicts of Interest

Anna Lok has received research funding from BMS, Gilead, and TARGET Pharma and serves as an advisor/consultant for Gilead, Reseverlogix, Roche, Spring Bank, and Viravaxx. Lai Wei receives research funding from Abbvie and BMS and serves as an advisor/consultant for Abbvie, Ascletis, BMS, Gilead, and MSD. Stephanie Chen, Samantha Chao, Monica Konerman, Wei Zhang, Huiying Rao, Elizabeth Wu, and Andy Lin declare that they have no conflict of interest.

Ethical Approval

All procedures performed involving human participants were in accordance with the ethical standards of the institutional research committees of University of Michigan and Peking University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

References

- 1. Fan JG. Epidemiology of alcoholic and nonalcoholic fatty liver disease in China. *J Gastroenterol Hepatol* 2013;28:11-17.
- Zhao J, Su C, Wang H, Wang Z, and Zhang B. New Evidence on the Effect of Medical Insurance on the Obesity Risk of Rural Residents: Findings from the China Health and Nutrition Survey. *Int J Environ Res Public Health*. 2018;15: 383.
- IDF Western Pacific members. c2018. Brussels (Belgium): International Diabetes Federation; Available at: <u>https://www.idf.org/our-network/regions-</u> members/western-pacific/members/101-china.html. Accessed July 1, 2018.
- Lu Y, Wang P, Zhou T, et al. Comparison of Prevalence, Awareness, Treatment, and Control of Cardiovascular Risk Factors in China and the United States. *J Am Heart Assoc.* 2018;7:e007462.
- Leung CM, Lai LS, Wong WH, et al. Non-alcoholic fatty liver disease: an expanding problem with low levels of awareness in Hong Kong. *J Gastroenterol Hepatol.* 2009;24:1786-1790.
- 6. Goh GB, Kwan C, Lim SY, et al. Perceptions of non-alcoholic fatty liver disease an Asian community-based study. *Gastroenterology Report.* 2016;4:131-135.
- 7. Ghevariya V, Sandar N, Patel K, et al. Knowing What's Out There: Awareness of Non-Alcoholic Fatty Liver Disease. *Front Med.* 2014;1:4.
- Yang W, Lu J, Weng J, et al. Prevalence of diabetes among men and women in China. *N Engl J Med.* 2010;362:1090-1101.

- The International Physical Activity Questionnaire (IPAQ)—Short Form. Available at: http://www.ipaq.ki.se. Accessed March 22, 2017.
- 10. Criteria of weight for adults. The National Health and Family Planning Commission of the People's Republic of China. April 18, 2013
- 11. Guideline for data processing and analysis of the International Physical Activity Questionnaire (IPAQ). Available at: http://www.ipaq.ki.se/scoring.pdf. Accessed October 22, 2017.
- 12. Lu ZY, Shao Z, Li YL, Wulasihan M, Chen XH. Prevalence of and risk factors for non-alcoholic fatty liver disease in a Chinese population: An 8-year follow-up study. *World J Gastroenterol*. 2016;22:3663–3669.
- 13. Gold DT, McClung B. Approaches to patient education: emphasizing the longterm value of compliance and persistence. *Am J Med*. 2006;119: 32S-37S.
- 14. Pais R, Barritt AS 4th, Calmus Y, et al. NAFLD and liver transplantation: current burden and expected challenges. *J Hepatol*. 2016;65:1245-1257.
- 15. Said A, Ghufran A. Epidemic of non-alcoholic fatty liver disease and hepatocellular carcinoma. *World J Clin Oncol*. 2017;8:429-436.
- 16. Williams KH, Shackel NA, Gorrell MD, McLennan SV, Twigg SM. Diabetes and nonalcoholic fatty liver disease: a pathogenic duo. *Endocr Rev.* 2013;34:84-129.
- 17. Ahmed M. Non-alcoholic fatty liver disease in 2015. *World J Hepatol*. 2015;7:1450-1459.
- Mlynarsky L, Schlesinger D, Lotan R, et al. Nonalcoholic fatty liver disease is not associated with a lower health perception. *World J Gastroenterol*. 2016;22:4362-4372.

- Block JP, Condon SK, Kleinman K, et al. Consumers' estimation of calorie content at fast food restaurants: cross sectional observational study. *Brit Med J*. 2013;346:f2907.
- 20. Harris CL, George VA. Dietary restraint influences accuracies in estimating energy expenditure and energy intake among physically inactive males. *Am J Mens Health*. 2010;4:33–40.
- 21. Oseini A, Sanyal, A. Therapies in non-alcoholic steatohepatitis (NASH). *Liver Int.* 2017;37:97-103.
- 22. Hendricks, E. Off-label drugs for weight management. *Diabetes Metab Syndr* Obes. 2017;10:223-234.
- 23. Walter J, Navarro V, Rossi S. Drug-induced liver injury associated with weight loss supplements. *Current Hepatology Reports*. 2018;17;245-253.