

# The Association of Sleep Duration, Sleep Quality and Liver Function in Taiwan

Yao-Ching Huang<sup>1,2,3</sup>, Bing-Long Wang<sup>2</sup>, Iau-Jin Lin<sup>2,3</sup>, Shi-Hao Huang<sup>1,2,3\*</sup>,  
Wu-Chien Chien<sup>2,3,4,5</sup>, I-Long Lin<sup>6</sup>, Shu-Min Huang<sup>7</sup>

<sup>1</sup>Department of Chemical Engineering and Biotechnology, National Taipei University of Technology (Taipei Tech), Taiwan

<sup>2</sup>School of Public Health, National Defense Medical Center, Taipei, Taiwan

<sup>3</sup>Department of Medical Research, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

<sup>4</sup>Taiwanese Injury Prevention and Safety Promotion Association, Taipei, Taiwan

<sup>5</sup>Graduate Institute of Life Sciences, National Defense Medical Center, Taipei, Taiwan

<sup>6</sup>Department of Information Management, Master's Program in Digital Technology Innovation Management, Yuan Pei Medical University, Hsinchu, Taiwan

<sup>7</sup>Department of Medical Research, Taipei Medical University Hospital, Taipei, Taiwan

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\*Correspondence:

Shi-Hao Huang  
hklu2361@gmail.com

Received: 07 Jun 2022

Accepted: 01 Jul 2022

Published: 10 Jul 2022

Citation: Haung YC, Wang BL, Lin IJ, et al. The association of sleep duration, sleep quality and liver function in Taiwan. *Int J Clin Invest Case Rep.* 2022; 1(1):14-22.

**Abstract:** Office workers often work overtime, stay up late, lack of sleep, and have poor sleep quality, resulting in a high liver index. Abnormal liver function is the main risk factor for modern social civilization diseases and chronic diseases. The purpose of this study was to explore the relationship between sleep time, sleep quality, and liver function, and analyze the collected data from the Taiwan MJ Health Examination Center from 2001 to 2010. This study mainly found that participants with extremely poor sleep had 1.128 times the chance of developing abnormal liver function compared with participants with good sleep. At the same time, it was found that the average daily sleep time of fewer than 4 hours, compared with people who sleep for 7-8 hours, the probability of abnormal liver function is 1.206 times. Therefore, good sleep quality and proper sleep time will reduce the occurrence of abnormal liver function.

**Keywords:** Sleep Duration • Sleep Quality • Liver Function

**Abbreviations:** NAFLD: Nonalcoholic Fatty Liver Disease; GOT: Glutamic Oxaloacetic Transaminase; GPT: glutamic pyruvic transaminase; ALP: Alkaline Phosphatase; PSQI: Pittsburgh Sleep Quality Index

## INTRODUCTION

Modern office workers often work overtime and lack sleep, which leads to excessive liver load and high liver index. However, many people choose to ignore health warnings. It was not until repeated cases of karoshi (death from too much work) that some people began to pay attention to the health warnings of abnormal liver function [1]. Zheng (2010) further analyzed the liver health examination data of nearly 15,000 young and middle-aged (30-50 years old) corporate employees in 2010, and the top three abnormal liver examinations were fatty liver (45.36%), abnormal GPT (18.74%), Hepatitis B with original (11.53%) [1]. Recent studies have shown that sleep duration and quality related to liver function (including abnormal coagulation factor synthesis, hormone metabolism disorders, and fat metabolism) contribute to fatty liver and cardiovascular disease, but sleep duration is associated with the fatty liver risk to a large extent are inconsistent [2-4]. Usually,



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sleep duration is closely associated with obesity, diabetes, hypertension, cardiovascular disease, Nonalcoholic Fatty Liver Disease (NAFLD), and detrimental serum lipid levels [5]. Recently, Kim et al. (2013) noted a significant association between increased risk of NAFLD and short sleep duration or poor sleep quality in middle-aged Koreans. Kim et al found that women with shorter sleep duration were more likely to develop NAFLD [6]. Although men with alcoholic fatty liver disease were not excluded from the analysis, short sleep duration was strongly associated with fatty liver disease in Japanese men [7].

Poor sleep is not directly related to poor liver function, and there is no need to worry too much about liver function damage if you don't sleep well; however, even if the liver function index is only slightly increased after the blood draw, it should not be ignored. However, there are many reasons for the sudden deterioration of liver function. Lack of sleep is only one of them. The liver must be fully rested during sleep so that its function can return to normal. When the human body is awake, the liver will continue to require metabolism to maintain its function. Once overloaded, it will suddenly dysfunctional. Long-term unimproved will cause harm, the most serious may lead to lesions [1].

Humans fall asleep for up to one-third of their lives, but the function of sleep remains a subject of intense debate [8]. Poor sleep quality and insufficient sleep are common problems in modern society. Good sleep is necessary for good health and quality of life. Sleep is important for maintaining homeostasis in the body, and sleep patterns change as society develops, which can affect the quality of life. The length of sleep is not only an indicator for predicting sleep quality but also an important parameter for predicting quality of life, health status, and longevity. For adults, 7-8 hours of sleep per night is recommended as the optimal amount of sleep [9]. Sleep is a key determinant of metabolic homeostasis, and sleep loss or disruption of sleep-wake patterns are associated with impaired metabolism [10]. Sleep problems are common civilization diseases and health problems in modern society. The importance of sleep to health has always been an important topic. However, research on the association between sleep duration and sleep quality, and liver function is very limited. Using "sleep quality" and "abnormal liver function" as keywords to search the literature in PubMed, most of the studies focused on "sleep apnea" and "non-alcoholic fatty liver disease". Therefore, this study conducted a long-term database analysis to investigate the association between sleep duration and sleep quality, and liver function.

## METHODS

This is a cross-sectional study that analyzed data from MJ Health Examination Center from 2001 to 2010. The subjects were 680,539 in number (339,925 males and 340,614 females), whose ages ranged from 20 to 65 years old. All subjects completed structured questionnaires that included demographic information, age, gender, self-reports, and responses to sleep quality and quantity, marital status, education, smoking, alcohol consumption, and current medical status (hypertension, diabetes, cerebrovascular disease, heart disease). All subjects underwent a series of blood, urine, body measurements, functional tests, physical examination, and medical history. Screening procedures of the same instrument model are used in all check-up centers, and results are centrally managed and stored. All subjects received liver function tests (GOT, GPT, ALP, rGT, bilirubin, Albumin, Prothrombin Time), and the data were coded as "Yes" and "No" to choose one of two to diagnose whether the liver function was abnormal.

Sleep time is divided into five categories: 0-4 hours, 4-6 hours, 6-7 hours, 7-8 hours, and more than 8 hours. Sleep quality was assessed by the Pittsburgh Sleep Quality Index (PSQI). In which sleep quality was self-assessed by questionnaires and divided into the following three categories:

1. Very good sleep (1-3 points)
2. Slightly poor sleep (less than 5 points)
3. Very poor sleep (above 5)

Socio-demographic background variables included gender, marital status, education level, and bad habits including smoking and drinking. Smoking status was never smoking, past smoking, and currently smoking. The drinking status includes never drinking, drinking in the past, and currently drinking, and whether the individual currently has chronic diseases, including hypertension, diabetes, cerebrovascular disease, and heart disease. In this study, SPSS IBM 20.0 was used for descriptive statistics, and multiple logistic regression was used to predict the correlation between variables, and to examine the correlation between sleep time, sleep quality, and liver function.

## RESULT

Table 1 showed that overall males (49.9%) had slightly different percentages than females (50.1%). Men aged 20-39 had the most (49.5%), followed by those aged 40-59 (39.7%) and the least (10.7%) aged over 60 years. Women aged 20-39 had the most (50.3%), followed by those aged

40-59 (38.4%) and the least (11.3%) aged over 60. Marital status includes single or married. The educational level was divided into middle school and below, junior college, university, and above. The lifestyle section includes smoking and drinking. These categories are divided into never smokers, never drinkers, past smokers, past drinkers, current smokers, and current drinkers. The majority of female participants had never smoked or drank alcohol (94.6%, 93.5%), and the majority of male participants

had never smoked or drank alcohol (64.1%, 72.4%). A small number of participants had hypertension, diabetes, cerebrovascular disease, heart disease, and abnormal liver function. Sleep quality is divided into 3 categories: very good sleep, slightly poor sleep, and very poor sleep. Most of the participants slept 7-8 hours (68.4% of men, 65.1% of women), and the sleep quality was between very good and slightly poor sleep quality (49.1% of men, 55.5% of women).

**Table 1:** Demographic variables by gender.

Variables	Male (n =339,925)	Female (n =340,614)
<b>Age</b>	<b>-49.90%</b>	<b>-50.10%</b>
20-39	168410(49.5%)	171392(50.3%)
40-59	135012(39.7%)	130824(38.4%)
≥ 60	36503(10.7%)	38398(11.3%)
<b>Total</b>	<b>339,925</b>	<b>340,614</b>
<b>Marital Status</b>		
Single	79647(23.47%)	98926(29.04%)
Married	246674(72.56%)	224845(66.0%)
Missing	134682(3.96%)	16843(4.96%)
<b>Education</b>		
Highschool	41635(12.3%)	73830(21.6%)
College	141120(41.5%)	150487(44.7%)
University	157170(46.2%)	116297(34.6%)
<b>Smoking</b>		
Never	189989(64.1%)	310746(94.6%)
Past	52526(17.7%)	9871(3.1%)
Current	54002(18.2%)	7697(2.3%)
<b>Drinking</b>		
Never	238382(72.4%)	301312(93.5%)
Past	12397(3.8%)	3690(1.1%)
Current	78601(23.9%)	17305(5.4%)
<b>Hypertension</b>		
Yes	30719(9.0%)	23331(6.8%)
No	309206(91.0%)	317283(93.2%)
<b>DM</b>		
Yes	10178(3.0%)	7967(0.3%)
No	329747(97.0%)	332647(97.7%)
<b>CVA</b>		
Yes	1666(0.5%)	949(0.3%)
No	338259(99.5%)	339665(99.7%)
<b>HeartDisease</b>		
Yes	9639(2.8%)	9743(2.9%)
No	330286(97.2%)	330871(97.1%)

Sleep Duration		
0-4 hours	2388(0.7%)	3628(1.1%)
4-6 hours	67961(20.4%)	72364(21.7%)
6-7 hours	32949(9.9%)	37247(11.2%)
7-8 hours	228101(68.4%)	216638(65.1%)
> 8 hours	2187(0.7%)	3143(0.9%)
Sleep Quality		
Poorly	29583(8.7%)	39364(11.6%)
Fairly well	143291(42.2%)	189012(55.5%)
Well	167051(49.1%)	112238(33.0%)
Liver Function		
Yes	603(0.2%)	240(0.1%)
No	339319(99.8%)	340373(99.9%)

N = Sample Number, (%) = Sample percentage

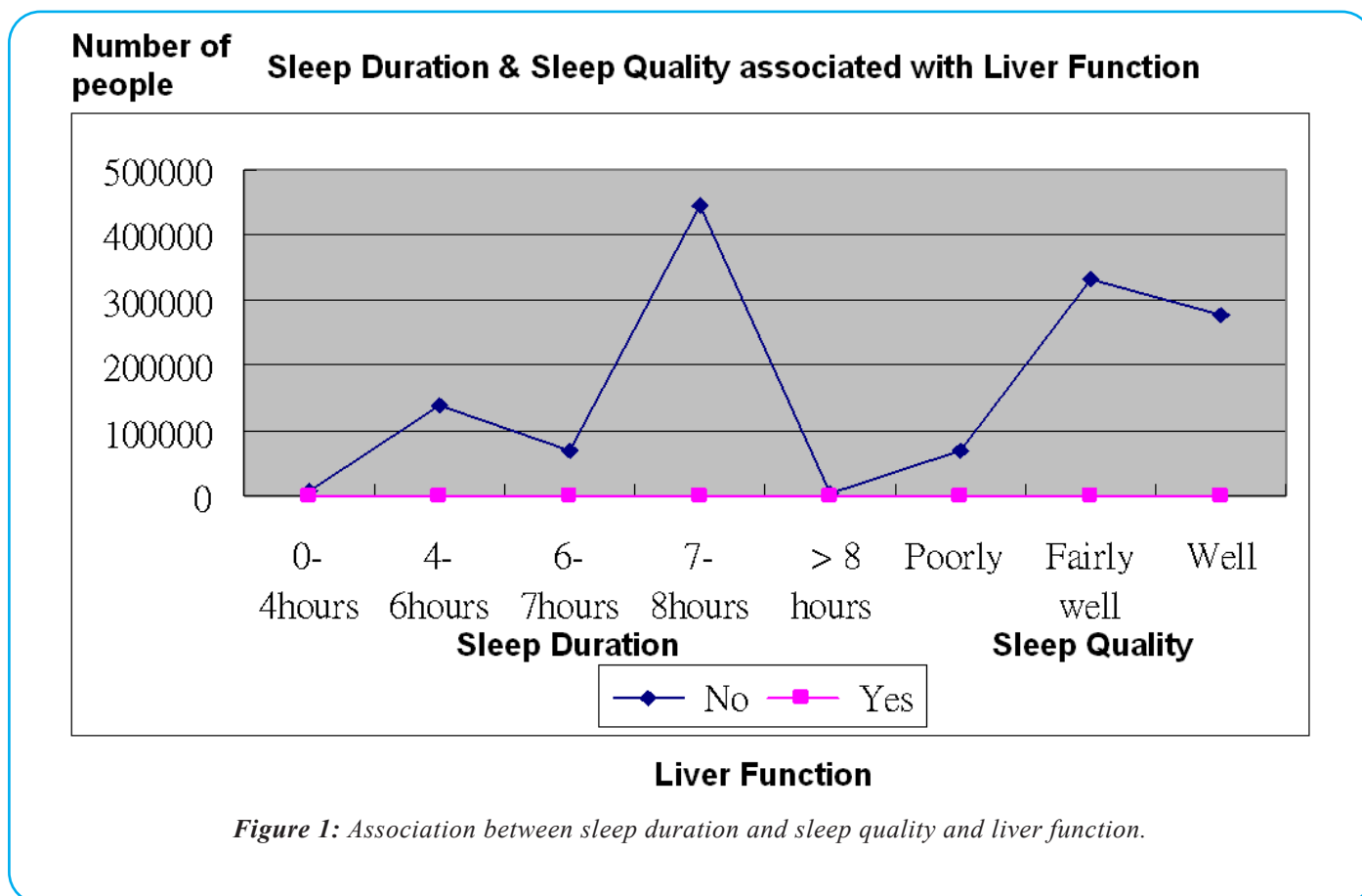


Figure 1: Association between sleep duration and sleep quality and liver function.

Figure 1 illustrates the association between sleep duration and sleep quality and liver function. According to the presence or absence of abnormal liver function, divided by the length of sleep time, most of the participants who did not suffer from abnormal liver function slept for 7-8 hours. Participants with abnormal liver function and sleep duration of 7-8 hours. Divided by sleep quality, the participants who did not suffer from abnormal liver function and had

very good sleep quality. Participants with abnormal liver function and very good sleep quality.

Figure 2 illustrates the correlation between sleep quality and liver function and sleep duration. According to the length of sleep, participants who slept 7-8 hours versus 4-6 hours had very good sleep quality. The majority of participants without abnormal liver function and sleep duration >8 hours versus 4-6 hours and 7-8 hours.

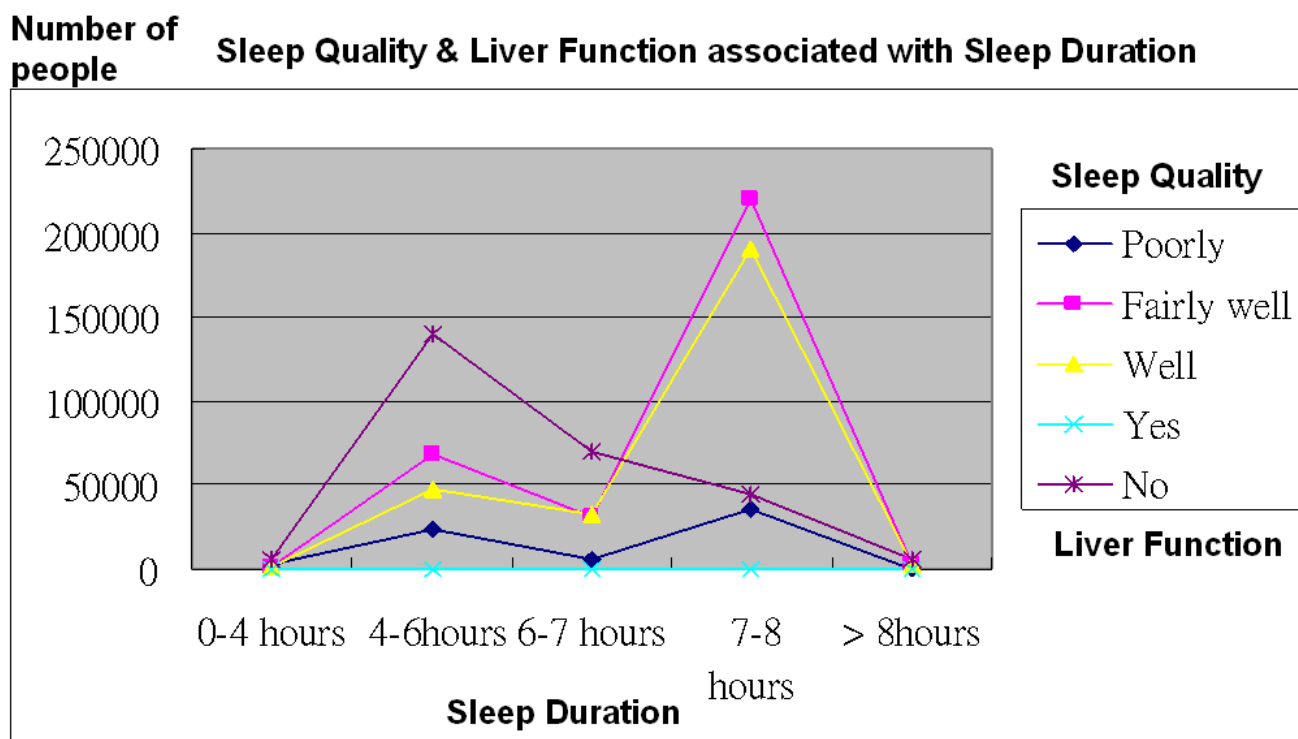


Figure 2: Association between sleep duration and sleep quality and liver function.

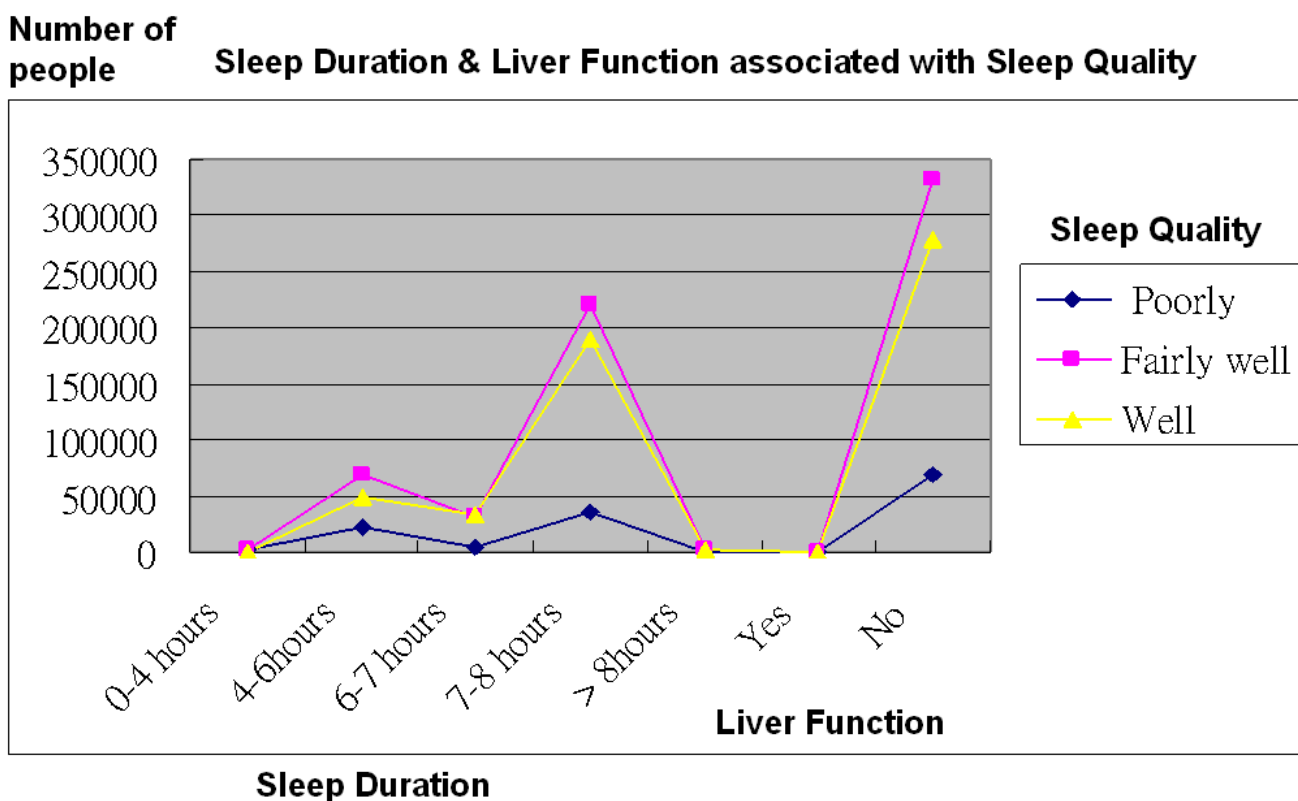


Figure 3: Association between sleep duration and sleep quality and liver function.

Figure 3 illustrates the association between sleep duration and liver function and sleep quality. According to sleep quality, participants who slept >8 hours versus 7-8 hours had good sleep quality and very good sleep quality. Participants with no history of liver disease, very good sleep quality and good sleep quality.

Table 2 shows that in terms of sleep quality, participants

with very poor sleep quality are 1.128 times more likely to suffer from abnormal liver function than those with good sleep quality, and this difference is statistically significant; in terms of sleep time Aspects, participants who slept 0-4 hours were 1.206 times more likely to have abnormal liver function than those who slept 7-8 hours. However, these differences were not statistically significant for sleep durations of 4-6 hours, 6-7 hours, and >8 hours.

**Table 2:** Regression analysis of the relationship between sleep time and sleep quality and liver function.

<b>Liver function</b>	
<b>Variables</b>	<b>OR(95%CI)</b>
<b>Age</b>	
20-39	1
40-59	3.475(2.674-4.516)
≥ 60	5.382(3.972-7.294)
<b>Marriage</b>	1.138(0.895-1.448)
<b>Education</b>	
Highschool	1
College	0.461(0.375-0.567)
University	0.379(0.297-0.483)
<b>Smoking</b>	
Never	1
Past	0.958(0.765-1.201)
Current	0.650(0.483-0.874)
<b>Drinking</b>	
Never	1
Past	4.996(4.005-6.232)
Current	0.570(0.429-0.756)
<b>Hypertension</b>	0.993(0.796-1.238)
<b>DM</b>	1.428(1.076-1.896)
<b>CVA</b>	1.406(0.810-2.438)
<b>Heart Disease</b>	0.629(0.423-0.936)
<b>Sleep Quality</b>	
Fairly well	1
Well	0.787(0.615-1.006)
Poorly	1.128(1.076-1.896)
<b>Sleep Duration</b>	
7-8hours	1
0-4hours	1.206(1.010-1.438)
4-6hours	0.688(0.412-1.148)
6-7hours	0.664(0.262-1.686)
>8hours	0.494(0.305-0.800)
*Adjusted for all variables (including age, marital status, education, smoking, drinking, hypertension, diabetes, cerebrovascular disease and heart disease)	

## DISCUSSION

Past studies have found that people with long-term sleep deprivation have abnormally elevated liver function indexes but did not point out the reason behind it. Dr. Matthew Brady of the University of Chicago convened an experiment with seven young volunteers. First, let everyone sleep 8.5 hours a day in the lab, then come back a month later for four consecutive days, sleep only 4.5 hours a day, and then test the response of their fat cells. It was found that the response of fat cells to sleep loss is very obvious. When fat cells are not sensitive to insulin, fat will run out of cells and enter the blood circulation. When the fat starts to accumulate in other parts of the body, such as in the liver, it will cause fatty liver, which will affect the body's utilization of glucose, and then cause disease. It is concluded that sleep is at least as important in energy metabolism as it is in brain function, and if humans do not get enough sleep, they will store more substances in the body, such as fat cells [8].

Stanford University scholars Kim et al. (2018) published an article in *Clinical Gastroenterology and Hepatology*, the top liver journal in the United States, analyzing the sleep habits of 17,245 American people, and divided them into five groups according to sleep time, respectively, less than or equal to 5 hours per day (15.9%), 6 hours (23.8%), 7 hours (27.1%), 8 hours (26.3%), and  $\geq 9$  hours (7%). It was found that people who sleep less than 5 hours a day are 35% more likely to have an abnormal liver function and 45% more likely to have fatty liver. People who took 6 hours were 24% more likely to have an abnormal liver function and 33% more likely to have fatty liver. People at 7 and 8 hours had no increased risk of abnormal liver function and fatty liver. The conclusion is that people with less sleep have a higher risk of developing abnormal liver function and fatty liver. In addition, past studies have also found that people with less sleep also have a higher proportion of fatty liver, so the author believes that the abnormal liver function caused by less sleep may be caused by chronic liver inflammation caused by the fatty liver [11].

Kim et al. (2018) pointed out that the blood flow of the liver is reduced by 40% when standing compared to lying down, and the blood flow of the liver is reduced by 80% to 85% when exercising than when lying down, and the reduction of blood flow in the liver will directly affect the Liver nutrition and oxygen supply. The liver is most active from 11:00 p.m. to 3:00 a.m., and it is also the best detoxification period for the liver. If you stay up late at this time, the blood flow of the liver will be relatively insufficient, which will increase the burden on the liver. Generally, people who stay up late often eat more dinner

and supper. If they lack exercise, the excess calories will be converted into fat and stored in the liver. Over time, the fat content of the liver will exceed the standard, resulting in the occurrence of fatty liver. Clinical observations have found that most patients with fatty liver have symptoms of insomnia, fatigue, and emotional instability. Therefore, for the treatment of fatty liver, especially severe fatty liver, the importance of adequate sleep should be emphasized [12].

The association between fatty liver and short sleep duration was first reported in Japanese men. In a 2011 article in the *Japanese Journal of Internal Medicine*, Hsieh et al. (2011) pointed out that they analyzed the sleep habits of 8,157 Japanese men and divided them into three groups according to sleep time: less than 5 hours per day (8.5%), 5 to  $<7$  hours (75.5%), and greater than or equal to 7 hours (16%). The results found: People who sleep less than 5 hours a day have a 43% higher chance of developing fatty liver. People with 5 to  $<7$  hours have a 38.5% chance of developing fatty liver. People with a duration of 7 hours or more have a 32.9% chance of developing fatty liver. The conclusion is that people with less sleep have a higher risk of developing abnormal liver function and fatty liver. However, the study did not control for alcohol intake, which affects fatty liver disease and sleep duration [7].

3,968 subjects were evaluated by Imaizumi et al. (2015) in *Obesity Facts*. Fatty liver is detected by ultrasonography. Sleep time was divided into the following categories: less than or equal to 6 hours, 6 hours to less than or equal to 7 hours, more than 7 hours to less than or equal to 8 hours, and more than 8 hours. The proportion of NAFLD tended to decrease with increasing sleep duration in men. Rates of NAFLD were lowest in the group who slept 6 to 7 hours and highest in women who slept more than 6 and more than 8 hours. The distribution is U-shaped. The age-adjusted Odds Ratio (OR) was 1.44 for female NAFLD subjects who slept 6 hours or less compared to the reference value (6 hours to 7 hours or less). It was concluded that sleep deprivation is often associated with nonalcoholic fatty liver disease in women and may be caused by physical obesity [5].

Recently, a large-scale study reported that short sleep duration and poor sleep quality were risk factors for nonalcoholic steatohepatitis in middle-aged Koreans. In the current study, it was confirmed that short sleep duration in women is often associated with nonalcoholic fatty liver disease [6].

Records from 2,429 Japanese subjects were reviewed in Miyake et al. (2015) in the *Journal of Gastroenterology*. The study cohort was divided into two groups: short sleep duration ( $\leq 6$  hours) (n=1,543) and moderate sleep

duration (7-8 hours) (n=886). During the observation period, a total of 296 subjects had NAFLD. Multivariate analysis identified an association between shorter sleep duration and a reduction in NAFLD episodes in men (odds: 0.551, 95% confidence interval 0.365-0.832, p=0.005). There was no association between short sleep duration and NAFLD episodes in women. The incidence of NAFLD in men increased significantly with increasing sleep time as follows: 12.5% (p=0.02) in subjects with 4 hours or less of sleep and 18.4% in subjects with 5-6 hours of sleep, respectively % (p=0.02) and 27.4% (p=0.02) in subjects aged 7-8 hours. Miyake et al. (2015) indicated that sleep loss was associated with a lower risk of nonalcoholic fatty liver disease in men [13]. However, there was no significant association between short sleep duration and fatty liver disease risk in men and observed similar results in men and women, prolonged sleep may prevent fatty liver disease, but this result was not supported by subsequent studies [5,7].

This study has several limitations. First, this study was a cross-sectional survey, which could not identify a causal or temporal relationship between metabolic markers and liver function; and it was difficult to conduct a detailed analysis of sleep quality. Secondly, abnormal liver function diseases involve too many levels, such as fatty liver, abnormal GPT, B liver disease, etc. A complete analysis report is required for each disease. Third, self-reported sleep parameters are not without limitations, overreporting of sleep duration by self-reporting has been described, and self-reporting is only moderately correlated with an objective assessment of sleep

duration. Fourth, the findings found in this study should be considered a limitation of this study based on measures of association effects (indirect effects) rather than causal effect relationships. Finally, future studies should discuss the work in a more in-depth and extensive way [14-22].

## CONCLUSION

The study found that people who slept very poorly were more likely to have abnormal liver function than those who slept well. At the same time, it was found that the average sleep time per day was less than 4 hours, and the probability of abnormal liver function was greater than that of 7-8 hours of sleep. Therefore, good sleep quality and proper sleep time will reduce the occurrence of abnormal liver function. In preventing abnormal liver function, it is important to encourage adequate sleep duration to maintain normal liver function and metabolism.

It is suggested that in daily life, in addition to exercising, going to bed before 11 O'clock every night, avoiding staying up late, and not taking home remedies, herbs, and healthy foods with unknown ingredients are all important factors for maintaining liver health. In terms of diet, it is recommended that people with poor liver health should eat three meals regularly, avoid excessive drinking, quit smoking, and consume foods rich in B group such as dark green vegetables and whole grains; and people with fatty liver should reduce the number of meals Tips for eating desserts, snacks, cutting down on fat intake, having dinner before 8, and avoiding late-night snacks.

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