

Influence of Demographic Characteristics and Emotional State of NAFLD in Patients and their Caregivers on Caregiver Burden in China

juan Luo

Guizhou Medical University

Jun Liu

Guizhou Provincial People's Hospital

Huang Lei

Guizhou Provincial People's Hospital

Zhang Yunju

Guizhou University Of Traditional Chinese Medicine

Wang Yun

Guizhou Medical University

Yixia Zhou (✉ zhouyixia2014@126.com)

Guizhou Medicine University

Research

Keywords: Caregiver burden, NAFLD, ZBI, PHQ-9

Posted Date: October 11th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-936641/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Influence of demographic characteristics and emotional state of NAFLD in patients and their caregivers on caregiver burden in China

Juan Luo^{a,b}, Jun Liu^c, Huang Lei^c, Zhang Yunju^b, Wang Yun^a, Yixia Zhou^{a,b,*}

^a School of Nursing, Guizhou Medicine University, Guiyang city, Guizhou province, China.

^b School of Nursing, Guizhou University of Traditional Chinese Medicine, Guiyang city, Guizhou province, China.

^c Department of Hepatobiliary Surgery, Guizhou Provincial People's Hospital, Guiyang city, Guizhou province, China.

Abstract

Objective: This study examines the demographic characteristics of patients and caregivers hospitalized with NAFLD and the impact of patient anxiety and depression on caregiver burden.

Methods: One hundred and forty-five patients with NAFLD and their caregivers were studied. Both patients and family members were required to complete a general information questionnaire, patients were required to complete the Generalized Anxiety Scale (GAD-7), the Patient Health Depression Questionnaire Scale (PHQ-9), and caregivers were required to complete the Zarit Burden Interview (ZBI). Descriptive analysis, univariate analysis, and multiple stepwise regression were used to analyze the effects of each factor on caregiver burden.

Results: The results of the univariate analysis showed that patients' marital status, chronic illness, GAD-7, and PHQ-9 scores, and caregivers' literacy, relationship with patients, full-time caregiving, recreational activities, daily caregiving hours, and monthly economic income were influential factors of caregiver burden ($P < 0.05$). The multiple stepwise regression analysis results showed that the four factors of concluding patient's PHQ-9 score, caregiver-patient relationship, daily caregiving hours, and monthly economic income significantly influenced caregiver burden ($P < 0.05$).

Conclusion: caregiver-patient relationship, length of caregiving per day, and monthly financial income affect caregiver burden. In addition, depression in patients hospitalized with NAFLD is one of the main influencing factors of caregiver burden and should be taken seriously.

Keyword: Caregiver burden, NAFLD, ZBI, PHQ-9

Background

Non-alcoholic fatty liver disease (NAFLD) has now become a serious global public health problem(1). It is estimated that the worldwide prevalence of NAFLD in adults is 25%(2), NAFLD is the most predominant type of liver disease in Western countries, the majority of NAFLD in Europe is 24%, the prevalence of NAFLD in Australia is 20%-30%(2), and the bulk of NAFLD in Asia is also on the rise, with the total prevalence of NAFLD in Japan as high as 29.7%(3). China is not only the country with the fastest-growing prevalence of NAFLD in the world but also the country with the highest prevalence, morbidity, and mortality of NAFLD in Asia(4). NAFLD has replaced chronic hepatitis B as the number one chronic liver disease in China. In the past 20 years, the number of NAFLD cases in China has nearly doubled, with a prevalence of about 15% in adults and 2.1% in children, while the majority of obese children is as high as 68.2%, and the annual rate of new NAFLD cases is about 4%[5, 6]. The latest literature reports that the prevalence of NAFLD in China is as high as 29.2%(7), and China is expected to be the country with the highest number of NAFLD patients and liver-related disease deaths globally(4). The high prevalence of NAFLD is accompanied by several problems, such as an increased incidence of anxiety and depression(8, 9). According to Youssef et al(10), who evaluated 567 NAFLD patients for depression and anxiety symptoms, subclinical and clinical depression detection rates in NAFLD patients were 53% and 14%, respectively. The detection rates of subclinical and clinical anxiety were 45% and 25%, respectively. At the same time, Chinese scholar Tao Yeting(11) reported that anxiety and depression in Chinese NAFLD with mild and above were as high as 51.3% and 62.4%. In the future, as the

number of obese people increases and urbanization accelerates, the prevalence of NAFLD in China will continue to rise in the coming decades. Previous studies have reported and predicted the enormous burden of NAFLD on national finances and medical resources(12, 13), but researchers have overlooked the burden of NAFLD on patients and their caregivers.

Caregiver burden refers to the stress or burden that family members experience when caring for a chronically ill, disabled, or elderly family member[14]. It is divided into an objective burden, which refers to the physical or instrumental assistance provided by the caregiver to the care recipient, and a subjective burden, which refers to the emotional or psychological impact of the former on them(15). Family caregivers are essential caregiving resources for patients with chronic illnesses, providing not only medical support, emotional support, life support, and even financial support. They also save money for the national financial system, and it has been documented that home care workers save the U.S. and Canadian health care systems \$25 billion and \$350 billion(14).

The large amount of support and services that caregivers provide to patients means lower financial income, reduced recreational activities and increased stress in the lives of caregivers. However, there have been few studies related to the burden of caregivers with NAFLD, and the public and health care professionals are poorly informed about the current status of the burden and factors associated with this group. Most studies on caregiver burden have focused on caregiver factors and ignored caregivers. Little is known about the interrelationship between patients' emotional status and demographic characteristics and caregiver burden and how they affect it. Therefore, this study aimed to examine the current status of caregiver burden of patients with NAFLD in China and investigate the impact on the caregiver burden of NAFLD from both patient and caregiver perspectives.

Materials and Methods

Study design

A quantitative cross-sectional design was used for this study.

Study population

Patients with NAFLD hospitalized in Guizhou Provincial People's Hospital from March 2021 to August 2021 were studied. All patients were diagnosed with NAFLD disease at the Guizhou Provincial People's Hospital. Patients were excluded from this study if they had psychiatric disorders, severe infectious diseases, were taking psychotropic medications that prevented them from completing the questionnaire or refused to participate in this study. Caregivers were required to be ≥18 years of age and to participate in the survey voluntarily. Caregivers who were in an employment relationship with the patient were also excluded from the study. This study strictly adheres to the ethical principles of the Declaration of Helsinki. A total of 145 patients with NAFLD and their caregivers were recruited for this study.

Study instruments

Demographic data of NAFLD patients and caregivers were collected in this study. All eligible NAFLD patients were required to complete the Generalized Anxiety Scale (GAD-7), the Patient Health Depression Questionnaire Scale (PHQ-9), and caregivers to meet the Zarit Burden Interview (ZBI). All scales used were translated and localized by Chinese scholars with good reliability and validity.

Demographic data of patients included age, gender, and education level (primary school, secondary school, university), marital status (unmarried, married, divorced, widowed), working or not working (yes, no), mode of payment of medical expenses (medical insurance, NPA, self-payment), disease duration (<3 years, 3-5 years, >3 years), and whether chronic diseases were combined (yes, no); demographic data of caregivers included age, gender, and education level (primary school, secondary school, university), relationship with patients (parents, spouse, children, others), whether they

lived with patients (yes, no), whether they cared for patients alone (yes, no), length of care per day, and other demographic data. Level (elementary school, secondary school, university), relationship with the patient (parent, spouse, child, other), whether they lived with the patient (yes, no), whether they cared for the patient alone (yes, no), length of care per day, length of care, whether they had recreational activities (yes, no), and monthly economic income (<1000 CNY, 1001-3000 CNY, 3001-5000 CNY, > 5000 CNY).

Generalized anxiety scale (GAD-7), developed by foreign scholars Spizer, Chinese scholars He xiaoye(16) conducted the reliability retest. The scale has eight entries with a total score of 0-21: 0-4 is no anxiety tendency, 5-9 is mild anxiety tendency, and ≥ 10 is moderate anxiety tendency.

Patient Health Depression Questionnaire (PHQ-9),a Chinese version translated by Chinese scholars was used(17). The scale has two parts and nine entries, with a total score of 0-27: 0-4 as no depression, 5-9 as a mild depressive tendency, and ≥ 10 as a moderate depressive tendency.

Zarit Burden Interview (ZBI),this scale was developed by Zarit, a foreign scholar, and translated and revised by Chinese scholars in 2006(18). The scale is divided into two dimensions: personal burden and role burden, and includes 22 entries, including 6 entries for personal burden: 2, 3, 6, 11, 12, 13, and 12 entries for role burden: 1, 4, 5, 8, 9, 14, 16, 17, 18, 19, 20, 21. A Likert 5-point scale is used, with a total score of 0-88: 0-19 being no burden or light burden, 20-39 as a mild burden, 40-59 as a moderate burden, and ≥ 60 as a moderate burden.

Quality control

The study subjects were selected in strict accordance with the inclusion and exclusion criteria, and the questionnaires used were translated and retested for reliability by domestic scholars; the investigators were all postgraduate students with a medical background in the subject group, and they were trained uniformly before the

survey, and the questionnaires were summarized and checked at the end of each study. Additional surveys were conducted on time to ensure the completeness of the information. A total of 145 questionnaires were distributed in this study, and 145 valid questionnaires were collected, with a recovery rate of 100.0%.

Data analysis

Data analysis was performed using spss26.0. The basic data of the study subjects were expressed as frequencies and percentages, the measures satisfying positive distribution were expressed as means plus or minus standard deviation ($x \pm S$), and skewed distribution was expressed as median, interquartile spacing, and the independent samples t-test and Mann-Whitney U test were used for one-way analysis. The variables that were significant were subjected to stepwise multiple linear regression analysis. Both univariate and stepwise multiple regression analyses indicated statistically significant differences at $p < 0.05$.

Results

Demographic characteristics of patients and caregivers

The mean age of the 145 patients was 54.06 ± 13.216 years, with a male majority of 109 (75.2%), 116 (80.0%) had an educational level of secondary school or less, 103 (71.0%) were unemployed, 132 (91.0%) had been ill for less than three years, and 48 (33.1%) patients reported the presence of at least one chronic illness. Scores on the GAD-7 and PHQ-9 were 4 (8) and 6 (7.5), respectively, with the lowest score of 0 and the highest score of 21 on the DAD-7, the highest score of 0, and the lowest score of 26 on the PHQ-9, (35) 24.1% and (53) 36.6% on mild anxiety and depression, respectively, and (36) 24.8% and (41) 28.3% (Table 1).

Table 1. Patient characteristics (n=145)

Characteristic		Mean(SD)/	Rnage	Number	%
		Median quartile			
Age	< 35	54.06 ±13.216	20-86	28	19.3
	35-60			67	46.2
	> 60			50	34.5
Sex	Female			36	24.8
	Male			109	75.2
Education	Primary school			56	38.6
	Middle school			60	41.4
	University			29	20.00
Course of disease (years)	< 3			132	91.0
	3-5			7	4.8
	> 5			6	4.2
Job	Yes			42	29.0
	No			103	71.0
marital status	Unmarried			6	4.1
	married			118	81.4
	divorced			11	7.6
	bereft of one's spouse			10	6.9
Medical expenses payment	Own expense			6	4.1
	medical insurance			59	40.7
	NCMS			80	55.2
Chronic	Yes			48	33.1
	No			97	66.9
GAD-7		4(8)	0-21	-	-
PHQ-9		6(7.5)	0-27	-	-

SD, Standard Deviation; GAD-7, The Generalized Anxiety Disorder scale; PHQ-9, The Patient Health Depression Questionnaire; ZBI, Zarit Burden Interview; NCMS: New Cooperative Medical System

More than half of the caregivers were female, 85 (58.6%), and 102 (77.3%) of the caregivers had an educational level of secondary school or less. Most of the caregivers were the spouses and children of the patients, 61 (42.1%) of the spouses and 51 (31.2%) of the children, 91 (64.1%) of the caregivers usually lived with the patients, and 69 (47.6)% cared for the patients alone. In addition, this study showed that 85 (58.6%) of the caregivers were caring for the patients full time with little to no work. Besides caring for patients, only 37 (25.5%) caregivers go out for recreational activities, 107 (74.5%) have no recreational activities other than caring for patients, and most caregivers have low monthly income levels, with 92 (63.4%) caregivers earning less than 3000 CNY.

The mean ZBI score was 26 (18.5), the lowest score was 0, and the highest score was 68, with 91 (68.0%) having a mild or higher caregiving burden (Table 2).

Table 2. Caregiver characteristics (n=145)

Characteristic		Mean(SD)/ Median quartile	Rnage	Number	%
Age	< 35	41.48 (12.572)	18-86	41	28.3
	35-60			71	42.0
	> 60			33	19.5
Sex	Female			85	58.6
	Male			60	41.4
Education	Primary school			41	28.3
	Middle school			61	49.0
	University			43	22.8
Relationship to patients	Parent			16	11.0
	Child			51	35.2
	Spouse			61	42.1
	Other			17	11.7
Living with patient	Yes			93	64.1
	No			52	35.9
Taking care of patient alone	Yes			69	47.6
	No			76	52.4
Taking care of patients full-time	Yes			85	58.6
	No			60	41.4
Take care of time per day		24 (14)	1-24	-	-
Entertainment	Yes			37	25.5
	No			107	74.5
Monthly economic income (CNY)	< 1000			46	31.7
	1000-3000			46	31.7
	3001-5000			28	19.3
	> 5000			25	17.2
ZBI		26 (18.5)	0-79	-	-

SD, Standard Deviation; CNY, Chinese Yuan; ZBI, Zarit Burden Interview.

Regression model

Table 3 demonstrates the results of the univariate analysis of ZBI scores. The results show that four patient factors and 11 caregiver factors significantly affected caregiver burden ($p < 0.05$). The influencing factors from patients were marital status,

chronic illness, and GAD-7 and PHQ-9 scores, and the influencing factors from caregivers were literacy, relationship with the patient, full-time patient care, recreational activities, hours of care per day, and monthly financial income.

Table 3.Univariate analysis of caregiver burden during hospitalization of NAFLD
(n=145)

Subject	Characteristic	t / Z value	P value
Patient	Age	-0.798	0.426
	Sex	-0.198	0.843
	Education	-1.325	0.185
	Course of disease (years)	-0.341	0.733
	Job	-1.301	0.193
	marital status	-2.663	0.008**
	Medical expenses payment	-1.350	0.177
	Chronic	-2.424	0.015*
	GAD-7	-3.586	0.000336**
	PHQ-9	-3.009	0.002**
Caregiver	Age	-0.966	0.336
	Sex	-0.815	0.415
	Education	-3.428	0.001**
	Relationship to patients	-2.805	0.005**
	Living with patient	-1.238	0.216
	Taking care of patient alone	-1.267	0.205
	Taking care of patients full-time	-3.877	0.000106**
	Take care of time per day	-3.007	0.003**
	Entertainment	-4.440	0.000009**
	Monthly economic income (CNY)	-2.895	0.004**

*P < 0.05, **P < 0.01

The ten significant factors in the univariate analysis above were introduced into a stepwise multiple regression analysis with the total ZBI score as the dependent variable. The results showed that four factors, including the patient's PHQ-9 score, caregiver-patient relationship, hours of care per day, and monthly financial income, significantly affected caregiver burden (P < 0.05). The six factors of patient's marital status, chronic illness, GAD-7 score, caregiver's literacy, full-time caregiving for the patient, and recreational activities did not significantly affect the total ZBI score, and the difference was not statistically significant (P > 0.05) (Table 4).

Table 4.Multivariate linear stepwise regression analysis of the factors influencing the caregiver burden (n=145)

	Item	B vaule	SE vaule	β vaule	t vaule	p vaule
Caregiver	Relationship to patients	-2.514	1.254	-0.162	-2.005	0.047*
	Take care of time per day	0.303	0.136	0.184	2.232	0.027*
	Monthly economic income (CNY)	-2.878	0.959	-0.237	-3.002	0.003**
Patient	PHQ-9	0.703	0.186	0.304	3.758	0.000226**

*P < 0.05, **P < 0.01

Discussion

NAFLD disease is initially only simple hepatic steatosis. Patients are unaware or informed but do not pay attention to it and do not take timely lifestyle interventions, seek medical attention, or undergo medication, leading to exacerbation of the disease and the need for hospitalization. Due to traditional culture and social factors, caregivers in China are mainly assumed by family members. Due to the deterioration of the disease, the treatment and daily life of patients during hospitalization impose various burdens on caregivers. Still, current studies have paid less attention to this group and their caregivers. Our study showed that four factors, patient's PHQ-9 score, caregiver-patient relationship, daily caregiving hours, and monthly financial income, were the main factors influencing caregiver burden.

In this study, the only patient factor significantly associated with caregiver burden was depressive tendencies (PHQ-9 score). As the number of people with NAFLD increases, more and more studies have begun to focus on the mental health of people with NAFLD. Many studies have reported that patients with NAFLD face various psychological problems, and depression, in particular, has a high prevalence in this population. Changes in the external environment are one of the factors leading to psychological stress. Hospitalization is a source of anxiety for patients, and undergoing a series of treatments in an unfamiliar hospital environment, coupled with the physical discomfort of patients, leads to depression. Caregivers, mainly the patient's spouse and children, spend a lot of time and money on patient care, hoping to provide the best care

for the patient and promote their physical and mental health. However, when family members perceive the patient's depressed mood, they deny their care and believe they are not doing enough, promoting an increased caregiving burden. Therefore, health care workers should pay attention to the mental health status of patients, receive them warmly, do their best to help them solve their difficulties, explain patiently to them before performing medical operations, and eliminate their fear of the hospital environment and treatment; in addition, they should pay attention to communication with caregivers, fully encourage and affirm their efforts in caring for patients and prevent them from falling into a vicious circle of negative emotions and incompetent care[19].

Zhu Liu's(14) study showed that spouse, partner, or children were the most common caregiver roles; one study noted that the primary caregivers for Alzheimer's disease in China were spouses and children of family members due to various factors such as cultural traditions, level of economic development, and health care system. Similar to the results of the above studies, the primary caregivers of patients hospitalized with NAFLD are also spouses and children. The possible reason for this is that caregivers have multiple conflicting responsibilities while assuming caregiving responsibilities(20). In Chinese families, spouses usually share family responsibilities(21). When a husband or wife is ill, responsibilities that should have been shared by both (parental support, children's education, and financial expenses) are transferred to one person, who is then also faced with the heavy burden of caring for the patient, with a substantial increase in load. Patients' children are primarily young and middle-aged, and at this time, they need to give a lot of time between their career and family. When family members are hospitalized and need to come to the hospital for care, their job, child care, and family need conflict with the caregiving tasks, and when the above roles cannot be balanced with each other, it increases the burden of the caregiver.

This study shows that the number of hours of caregiving per day is one of the main influencing factors of the caregiving burden. Duration of care is one of the most

important predictors of caregiver burden, the longer the caregiving hours provided, the higher the caregiving burden(22, 23), with caregivers providing more than 6 hours of care per day having the highest burden(21). Longer hours of caregiving mean that the patient has to provide more care services, including therapy, meals, and even toileting, and these caregiving activities can be a significant drain on the caregiver's strength and energy, causing fatigue and reducing the caregiver's health. The more time caregivers spend on caregiving, the less or no time they have to participate in social activities, which affects caregivers' social activities and prevents them from resolving negative emotions, exacerbating the caregiving burden. At the same time, hospitals are not only a source of stress for patients but also caregivers. Long-term caregiving in an unfamiliar environment can lead to discomforts such as irritability, decreased appetite, and reduced sleep quality, increasing the caregiving burden(21, 24). Therefore, patients' family members or friends should be encouraged to provide more social support and share the caregiving work to reduce the length of caregiving; caregivers should be advocated to have appropriate weekly gatherings of friends, participate in recreational activities or physical exercise to eliminate negative emotions in a timely manner, enhance physical fitness, and ensure physical and mental health.

The cost of care is one of the critical indicators of the caregiving burden(25). This study reports that the monthly economic income of caregivers is one of the main influencing factors of the caregiving burden. Traditional Chinese culture values "filial piety," so most family members will give up their jobs to participate in caregiving when necessary. This study reported that more than half of the caregivers did not work outside the home since the patient's admission and were full-time caregivers. Thus their economic income dropped sharply, and their economic status was poor. The majority of NAFLD caregivers are middle-aged and young adults. This age group is under financial pressure from children's education and daily living expenses, further increased by family hospitalization.

On the other hand, a decrease in the caregiver's financial income means a further reduction in the cost of care available to the patient, and caregivers may develop a sense of self-blame, attributing to themselves the reason the patient is not receiving optimal care, ultimately increasing their burden. China has the highest prevalence and mortality rate of NAFLD. The healthcare system should pay attention to early screening for NAFLD disease and appropriately increase the medical reimbursement rate for this group of patients to reduce the financial pressure on patients' families. The Chinese people have little awareness of disease prevention and only pay attention to serious health problems, so the proportion of people who purchase disease-related insurance is not high. This phenomenon should attract the attention of relevant departments and increase publicity to promote universal awareness of disease prevention and insurance to reduce financial pressure when diseases occur. In addition, health care professionals should encourage caregivers to recognize their own contributions.

Conclusion

In conclusion, the incidence of caregiver burden was high among patients hospitalized with NAFLD. The main factors affecting caregiver burden were the patient's PHQ-9 score, the caregiver-patient relationship, the number of hours of care per day, and the monthly financial income. Reducing the caregiving burden requires a concerted effort by the patient, the caregiver, the health care provider, and the health care system.

Abbreviations

NAFLD: Non-alcoholic fatty liver disease ; SD:Standard Deviation; GAD-7:The Generalized Anxiety Disorder scale;PHQ-9: The Patient Health Depression Questionnaire; ZBI:Zarit Burden Interview; NCMS: New Cooperative Medical System.

Acknowledgements

We would like to thank all the patients and their caregivers who agreed to participate in this study.

Authors'contributions

Juan Luo: Questionnaire survey; Zhang Yunju and Wang Yun: data analysis,;Jun Liu and Huang Lei: study design;Yixia Zhou: project management. All authors participated in the writing and revision of the paper. The authors declare that all data were generated in-house and that no paper mill was used.

Funding

This study was supported by National Natural Science Foundation of China (Grant Number:81860089),Science and Technology Department of Guizhou Province (3040-04021002),Doctoral Fund of Guizhou University of Traditional Chinese Medicine (2021[02]).

Availability of data and materials

The datasets analyzed in the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

All studies were done in compliance with the regulations and guidelines of Guizhou Medical University institutional care and conducted according to the ethical principles of the Declaration of Helsinki (as revised in 2013).

Consent for publication

We provided detailed explanations and instructions prior to the start of the study, and all research and publication of the paper were done with the consent of the participants.

Competing interests

The authors declared that they have no conflicts of interest to this work.

References

1. Estes C, Anstee QM, Arias-Loste MT, Bantel H, Bellentani S, Caballeria J, et al. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030. *J HEPATOL*. [Journal Article]. 2018 2018-10-01;69(4):896-904.
2. Younossi ZM. Non-alcoholic fatty liver disease - A global public health perspective. *J HEPATOL*. [Journal Article; Review]. 2019 2019-03-01;70(3):531-44.
3. Fan JG. Epidemiology of alcoholic and nonalcoholic fatty liver disease in China. *J Gastroenterol Hepatol*. [Journal Article; Research Support, Non-U.S. Gov't; Review]. 2013 2013-08-01;28 Suppl 1:11-7.
4. Zhou J, Zhou F, Wang W, Zhang XJ, Ji YX, Zhang P, et al. Epidemiological Features of NAFLD From 1999 to 2018 in China. *HEPATOLOGY*. [Journal Article; Research Support, Non-U.S. Gov't; Review]. 2020 2020-05-01;71(5):1851-64.
5. Eguchi Y, Hyogo H, Ono M, Mizuta T, Ono N, Fujimoto K, et al. Prevalence and associated metabolic factors of nonalcoholic fatty liver disease in the general population from 2009 to 2010 in Japan: a multicenter large retrospective study. *J GASTROENTEROL*. [Journal Article; Multicenter Study; Research Support, Non-U.S. Gov't]. 2012 2012-05-01;47(5):586-95.
6. Antonella A, Gaetano-Felice C, Domenico N, Sara B, Pasquale P, Manfredi R, et al. NAFLD and Atherosclerosis Are Prevented by a Natural Dietary Supplement Containing Curcumin, Silymarin, Guggul, Chlorogenic Acid and Inulin in Mice Fed a High-Fat Diet. *NUTRIENTS*. 2017;9(5).
7. Zhou F, Zhou J, Wang W, Zhang XJ, Ji YX, Zhang P, et al. Unexpected Rapid Increase in the Burden of NAFLD in China From 2008 to 2018: A Systematic Review and Meta-Analysis. *HEPATOLOGY*. [Journal Article; Meta-Analysis; Research Support, Non-U.S. Gov't; Systematic Review]. 2019 2019-10-01;70(4):1119-33.
8. Noon SL, D'Annibale DA, Schwimmer MH, Shiels J, Arin J, Durelle J, et al. Incidence of Depression and Anxiety in a Cohort of Adolescents With Nonalcoholic Fatty Liver Disease. *J Pediatr Gastroenterol Nutr*. [Journal Article; Research Support, N.I.H., Extramural]. 2021 2021-04-01;72(4):579-83.
9. Colognesi M, Gabbia D, De Martin S. Depression and Cognitive Impairment-Extrahepatic Manifestations of NAFLD and NASH. *Biomedicines*. [Journal Article; Review]. 2020 2020-07-21;8(7).
10. Youssef NA, Abdelmalek MF, Binks M, Guy CD, Omenetti A, Smith AD, et al. Associations of depression, anxiety and antidepressants with histological severity of nonalcoholic fatty liver disease. *LIVER INT*. [Journal Article]. 2013 2013-08-01;33(7):1062-70.
11. Tao Yeting PQCG. Personality and emotional states in patients with nonalcoholic fatty liver diseases . *Journal of Practical Hepatology*. 2017;20(06):713-9.
12. Younossi ZM, Blissett D, Blissett R, Henry L, Stepanova M, Younossi Y, et al. The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. *HEPATOLOGY*. [Journal Article; Research Support, Non-U.S. Gov't]. 2016 2016-11-01;64(5):1577-86.
13. Allen AM, Van Houten HK, Sangaralingham LR, Talwalkar JA, McCoy RG. Healthcare Cost and Utilization in Nonalcoholic Fatty Liver Disease: Real-World Data From a Large U.S. Claims Database. *HEPATOLOGY*. [Journal Article; Research Support, N.I.H., Extramural; Research Support, Non-U.S.

- Gov't]. 2018 2018-12-01;68(6):2230-8.
14. Liu Z, Heffernan C, Tan J. Caregiver burden: A concept analysis. *Int J Nurs Sci*. [Journal Article]. 2020 2020-10-10;7(4):438-45.
 15. Bastawrous M. Caregiver burden--a critical discussion. *INT J NURS STUD*. [Journal Article]. 2013 2013-03-01;50(3):431-41.
 16. He Xiaoye LCQJ. Reliability and validity of a generalized anxiety disorder scale in general hospital outpatients. *General Psychiatry*. 2010;22(04):200-3.
 17. Xu Yong WHXY. The reliability and validity of patient health questionnaire depression module (PHQ-9) in Chinese elderly. *General Psychiatry*. 2007(05):257-9.
 18. Wang Lie YXHZ. Application and evaluation of chinese version of zarit caregiver burden interview. *Chinese Journal of Public Health*. 2006(08):970-2.
 19. Safarabadi-Farahani A, Maarefvand M, Biglarian A, Khubchandani J. Effectiveness of a Brief Psychosocial Intervention on Quality of Life of Primary Caregivers of Iranian Children With Cancer: A Randomized Controlled Trial. *J PEDIATR NURS*. [Comparative Study; Journal Article; Randomized Controlled Trial]. 2016 2016-07-01;31(4):e262-70.
 20. Alex Gitterman E. *Handbook of Social Work Practice with Vulnerable and Resilient Populations*. New York: Columbia University Press; 2021.
 21. Zuo Y, Luo BR, Peng WT, Liu XR, He YL, Zhang JJ. Informal caregiver burden and influencing factors in gynaecological oncology patients hospitalized for chemotherapy: a cross-sectional study. *J INT MED RES*. [Journal Article]. 2020 2020-11-01;48(11):1220774479.
 22. Park CH, Shin DW, Choi JY, Kang J, Baek YJ, Mo HN, et al. Determinants of the burden and positivity of family caregivers of terminally ill cancer patients in Korea. *Psychooncology*. [Journal Article; Research Support, Non-U.S. Gov't]. 2012 2012-03-01;21(3):282-90.
 23. Lindt N, van Berkel J, Mulder BC. Determinants of overburdening among informal carers: a systematic review. *BMC GERIATR*. [Journal Article; Systematic Review]. 2020 2020-08-26;20(1):304.
 24. Coppel DBBC. Relationships of cognitions associated with coping reactions to depression in spousal caregivers of Alzheimer's disease patients. *COGNITIVE THER RES*. 1985;9(3):253-66.
 25. Fink SV. The influence of family resources and family demands on the strains and well-being of caregiving families. *NURS RES*. [Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.]. 1995 1995-05-01;44(3):139-46.