Prevalence of Non-alcoholic Fatty Liver Disease in Iran: A Systematic Review and Meta-analysis

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Background: **Non-alcoholic fatty liver disease (NAFLD) has a benign course in several patients; however, a serious form of this disease can turn into liver failure, liver cirrhosis, and hepatocellular carcinoma.** ***Aim:*** **This study aims to estimate the prevalence of NAFLD in Iran.** ***Method:*** **We searched the following databases from January 2000 to December 2022: Scopus, Pubmed/Medline, Embase, Web of Sciences, the Cochrane Library, and Google Scholar also a number of Iranian databases, namely MagIran, SID, and Elmnet. Additionally, the quality of the included studies was evaluated through the Newcastle-Ottawa Scale. We estimated heterogeneity between studies using the I^2 statistic. Furthermore, we performed a synthesis of prevalence estimates through the random-effects DerSimonian and Laird model across the included studies with a 95% confidence interval. To assess the publication bias, we also used Egger's test.** ***Results:*** **Thirty-one studies were eligible for inclusion. The overall number of participants in the present study was 41,971. The overall prevalence of NAFLD in Iran was 33% [CI: 27–37%], with I2 = 99.7% (P < 0.01). The prevalence was 35% [CI: 27–43%] and 37% [CI: 27–47%] in males and females, respectively. We used Egger's test, and no significant publication bias was identified in the overall prevalence (P = 0.45).** ***Conclusion:*** **According to the results of this study, the prevalence of NAFLD in Iran is not only high but alsoa growing trend. Effective strategies for changing lifestyles, changing eating habits, and encouraging physical activities among Iranians are recommended. Also, providing screening tests, especially among high-risk groups, has a significant effect on early diagnosis and NAFLD control. (J Clin Exp Hepatol 2024;14:101209)**

Non-alcoholic fatty liver disease (NAFLD) is a significant challenge for health systems worldwide and accounts for an important part of liver problems.[1] NAFLD has a benign course in several patients; however, a serious form of this disease can turn into liver failure, liver cirrhosis, and hepatocellular carcinoma (HCC).[2] Also, NAFLD is linked with extrahepatic conditions, namely type 2 diabetes mellitus, metabolic syndrome, dyslipidemia, chronic kidney diseases, cardiovascular diseases, and obesity.[3,4] Recent data has revealed that NAFLD has been increasing worldwide over the past few years, which has subsequently led to increased economic costs for health systems.[5] In this regard, research has demonstrated that poor lifestyle, inactivity, high carbohydrate and high fat intake, and poor diet are positively related to the prevalence of NAFLD.[6]

Despite the high rate of NAFLD worldwide, its prevalence seems to be heterogeneous from one country to another.[7] The rate of NAFLD soared from about 391 million cases in 1990 to about 882 million cases in 2017, and its prevalence increased from 8.2 to 10.9, with North Africa and the Middle East having the highest prevalence.[8] In the same vein, NAFLD has been a health challenge in Iran; in this regard, various studies have investigated the causes and prevalence of NAFLD in Iran. Having updated knowledge regarding the trend and epidemiological information of the disease might help Iranian health policy-makers and stakeholders understand the disease burden better and predict its process; this way, they would implement

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Abbreviations: CI: confidence interval; HCC: hepato cellular carcinoma; NAFLD: Non-alcoholic fatty liver disease; NOS: Newcastle-Ottawa Scale; PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analyses
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programs and policies needed to prevent and control NAFLD. Given the numerous challenges imposed by NAFLD on the Iranian health system, we conducted the present study to examine the prevalence of NAFLD in Iran. The purpose of this study is to investigate the prevalence based on the published studies conducted on the prevalence of NAFLD in Iran.

MAIN TEXT

Methods

In the present systematic review, we followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement (Appendix).[9] Also, we registered the protocol of this review in PROSPERO (CRD42022 363598)[10]; the protocol was also approved by the Review Ethics Board of Iran University of Medical Sciences (IR.IUMS.REC.1401.383).

Search Strategy

Two authors of the present paper independently searched the following databases: Scopus, Pubmed/Medline, Embase, Web of Sciences, the Cochrane Library, and Google Scholar, as well as Iranian databases MagIran, SID, and Elmnet, from January 2000 to December 2022. Also, we used Boolean operators with the following related keywords: (Prevalence OR Epidemiology OR Frequency OR Incidence) AND (Non-alcoholic fatty liver OR Non-alcoholic fatty liver disease OR non-alcoholic fatty OR nonalcoholic fatty liver OR nonalcoholic fatty liver disease OR nonalcoholic steatohepatitis OR non-alcoholic steatohepatitis OR MAFLD OR NAFLD OR non-alcoholic) AND (Iran). In addition, two researchers (MaB and SS) from the present study independently reviewed the reference lists of articles to find more related studies. We resolved any discrepancy between the two researchers by consulting a third researcher (SPT) on our team.

Inclusion Criteria

The inclusion criteria in the present study are as follows:

1. Observational studies that reported the prevalence of NAFLD in different populations.
2. Studies published in Farsi and English.
3. Studies that investigated patients who resided in Iran.
4. Studies with sufficient data to calculate prevalence.
5. Studies published in peer-reviewed journals.
6. Studies that focused on patients who were diagnosed with serum-based indicators, imaging, liver biopsy, and ultrasound.
7. Studies that had no gender or age restrictions.

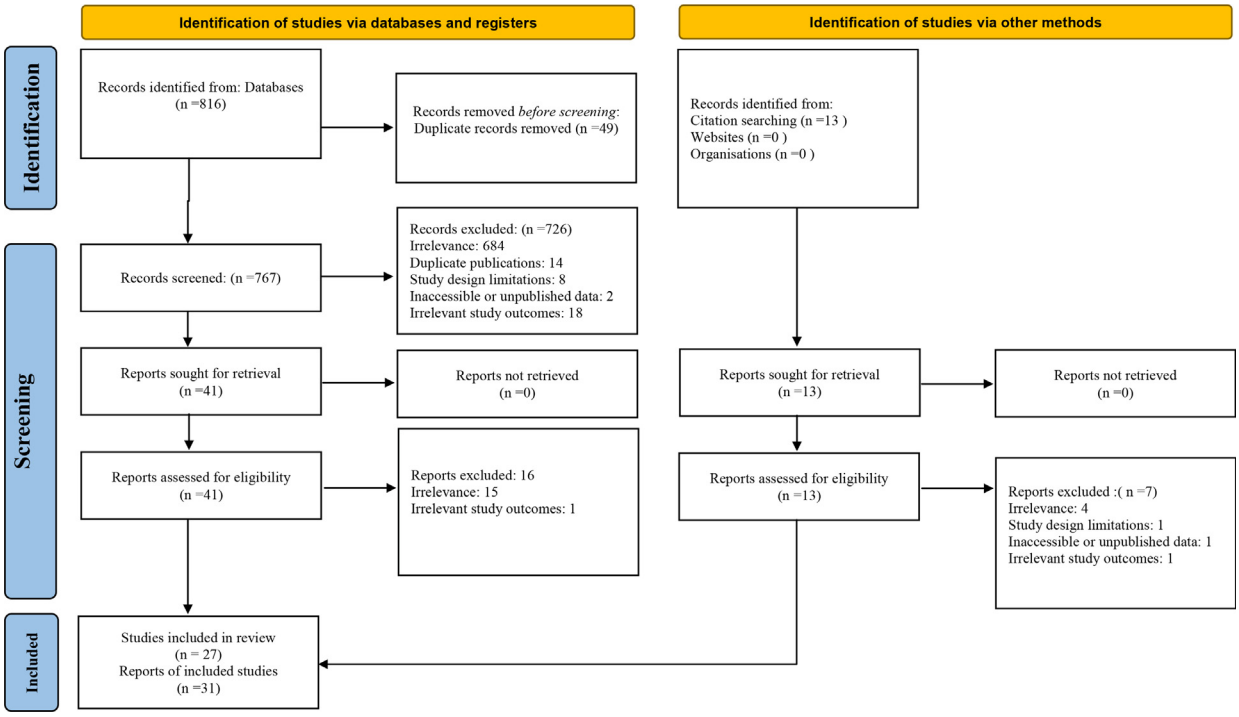

Figure 1 PRISMA flow diagram.

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Table 1 The Main Characteristics of the Included Studies.

First author	Year	City	Mean or range age	Sample size	Diagnostic test	Prevalence (%)	Conditions of participants	Setting
Savadkoohi F	2003	Zahedan	43.6 ± 8.9	247	Ultrasound	32.8	Population based	OPD visitors
Hosseinpanah F	2007	Tehran	60 ± 9	76	Ultrasound	82.9	Type 2 diabetes	Hospital based
Alavian SM	2008	Tehran	41.61 ± 12.04	1120	Fatty liver index or hepatic steatosis index	9.5	School-aged children and adolescents	Public health centers
Jamali R	2008	Golestan	40.59 ± 14.69	2049	Ultrasound	2.04	Population based	OPD visitors
Merat S	2009	Tehran	56.56 ± 10.5	172	Ultrasound	55.8	Type 2 diabetes	Hospital based
Adibi A	2009	Isfahan	12.59 ± 3.25	949	Ultrasound	16.9	Overweight and obese children	Hospital based
Alavian SM	2009	Tehran	15 ± 2.3	966	Ultrasound	7.1	Hepatitis B patients	Blood transfusion Center
Rafeey M	2009	Tabriz	6.53 ± 3.07	1500	Ultrasound	2.3	Children	OPD visitors
Tazhibi M	2010	Isfahan	6–18	1107	Ultrasound	16.9	Children and adolescence	Public health centers
Sohrabpour AA	2010	Tehran-Hormozgan-Golestan	36.1 ± 13.1	5589	Fatty liver index or hepatic steatosis index	2.9	Population based	OPD visitors
Shahbazian HB	2011	Ahvvaz	51 ± 10	272	Ultrasound	70	Type 2 diabetes	Hospital based
Hosseini SM	2011	Isfahan	12.57 ± 3.3	962	Ultrasound	16.8	Children and adolescence	OPD visitors
Razavizade M	2012	Kashan	41.63 ± 11.46	245	Ultrasound	78.4	Population based	OPD visitors
Lahsaee S	2012	Kerman	31.76 ± 11.31	1993	Fatty liver index or hepatic steatosis index	16	Population based	Blood transfusion Center
Shiasi Arani K	2013	Kashan	9.55 ± 2.3	306	Ultrasound	55.3	Children and adolescence	Public health centers
Bagheri Lankarani K	2013	Shiraz	43.1 ± 14.1	819	Ultrasound	21.5	Population based	Hospital based
Eshraghian A	2013	Shiraz	48.20 ± 12.32	832	Ultrasound	15.3	Population based	Public health centers
Montazerifar F	2014	Zahedan	16 ± 2	34	Ultrasound	44.11	Obese adolescant	Public health centers
Saki F	2014	Shiraz	10.57 ± 3.04	102	Ultrasound	54.9	Obese Children	OPD visitors
Jafarian A	2014	Tehran	33	116	Fatty liver index or hepatic steatosis index	12	Cadaveric Organ Donor Population	Hospital based
Amirkalali B	2014	Amol	45.35 ± 15.87	5023	Ultrasound	43.8	Population based	Public health centers
Karimi-Sari H	2015	Tehran	33.96 ± 9.92	114	Fatty liver index or hepatic steatosis index	16.7	Sleeve Bariatric Surgery	Hospital based
Taghavi Ardakani A	2015	Kashan	9.07 ± 1.88	200	Ultrasound	59	Obese Children	OPD visitors
Ostovaneh MR	2015	Amol-Zahedan	37.27 ± 0.40	7723	Ultrasound	35.2	Population based	Public health centers
Adibi A	2017	Isfahan	45.53 ± 8.92	483	Ultrasound	39.3	Population based	Public health centers

(*Continued on next page*)

Table 1 (*Continued*)

First author	Year	City	Mean or range age	Sample size	Diagnostic test	Prevalence (%)	Conditions of participants	Setting
Rabiee B	2017	Amol	48.15 ± 13.41	5052	Ultrasound	21.4	Population based	Public health centers
Heidari Z	2017	Zahedan	50.79 ± 10.49	255	Ultrasound	86.6	Type 2 diabetes	Public health centers
Namakin K	2018	Birjand	12 to 18	200	Ultrasound	54	Overweight and obese children	OPD visitors
Hosseini Ahangar B	2019	Tehran	43.28 ± 14.03	999	Ultrasound	19.6	Population based	Hospital based
Etminani R	2020	Isfahan	45.5 ± 8.6	413	Ultrasound	39.3	Middle-Aged	Public health centers
Amirkalali B	2021	Amol	16 to 65	2308	Ultrasound	46·7	Lean and non-lean populations	Hospital based

OPD, outpatient department.

Exclusion Criteria

Also, we followed the exclusion criteria below.

1. Studies whose designs were controlled trials, case series, and case reports, as well as books, posters, oral presentations, letters to the editor, and opinion articles.
2. Studies with alcoholic patients.
3. Studies with patients who resided outside of Iran.
4. Studies that had insufficient data.
5. Studies whose data were replicated.
6. Studies whose full texts were not available.

Data Extraction

We developed a data extraction form including the following information: the first author's name, publication year, mean or range age of participants, place where the study was conducted, study design, test used for diagnosing NAFLD, number of patients, reported prevalence, and the number of NAFLD patients according to their gender. In the next step, two researchers (SA and NLB) from the present study independently extracted the data from the selected studies and entered it into the data extraction form. We resolved discrepancies between the two reviewers by consensus or by consulting a third researcher (MM) from this study.

Quality Assessment of the Included Studies

The quality of included studies was evaluated through the Newcastle-Ottawa Scale (NOS),[11] which has three domains: selection, comparability, and outcome. Based on the NOS scores, we classified the selected studies into three groups as follows: scores ranging from 7 to 9 were considered low risk of bias (high quality), scores of 4–6 were moderate risk of bias (fair quality), and scores of 1–3 were considered high risk of bias (low quality). Two authors (MeB and AR) of this study independently reviewed each study to assess the risk of bias. Any disputes among the reviewers are resolved by consensus or via consulting with a third author (SJE).

Statistical Analysis

We analyzed the data using Stata Software (version 12), with the statistical significance set at $P < 0.05$. Also, we estimated heterogeneity between studies using the I^2 statistic. Meanwhile, we performed a synthesis of prevalence estimates using the random-effects DerSimonian and Laird model across the included studies with a 95% confidence interval (95% CI). Furthermore, we used Egger's test to assess for publication bias. We also performed a sensitivity analysis to ensure the stability of the results. In order to evaluate the causes of the heterogeneity of the included studies, we included the participants' gender, type of participants, sample size, year of publication, diagnostic test, setting, obese and non-obese populations, risk of bias,

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and geographic region of the subgroup. Also, we performed the meta-regression test according to the year of publication, sample size, and mean age.

RESULTS

Study Selection

A total of 829 records were identified in the comprehensive search. After the exclusion of duplicates and non-relevant records, thirty-one studies were included in the review.[12–42] Figure 1 gives more details regarding the selection process for the included studies.

Characteristics of the Included Studies

The overall number of participants in the included studies was 41,971, with a sample size ranging from 34 to 7723 participants. Also, all the studies had a cross-sectional design. In addition, an ultrasound test was used to diagnose the NAFLD patients. Table 1 presents the characteristics of the included studies.

Overall Prevalence of NAFLD

According to the random model, the overall prevalence of NAFLD in Iran was 33% [CI: 27–39%], with I2 = 99.7% (P < 0.01). The prevalence was 35% [CI: 27–43%] and 37% [CI: 27–47%] in males and females, respectively. Figure 2 shows the overall prevalence of NAFLD in Iran.

Risk of Bias

Table 2 shows the NOS quality assessment scores of the included studies, with a mean score of 6.65. According to the results, 20 studies were considered high quality (low risk) and 11 were moderate (fair risk). The prevalence was 32% [CI: 24–40%] and 34% [CI: 24–44%] in high-quality (low risk) and moderate (fair risk) studies, respectively.

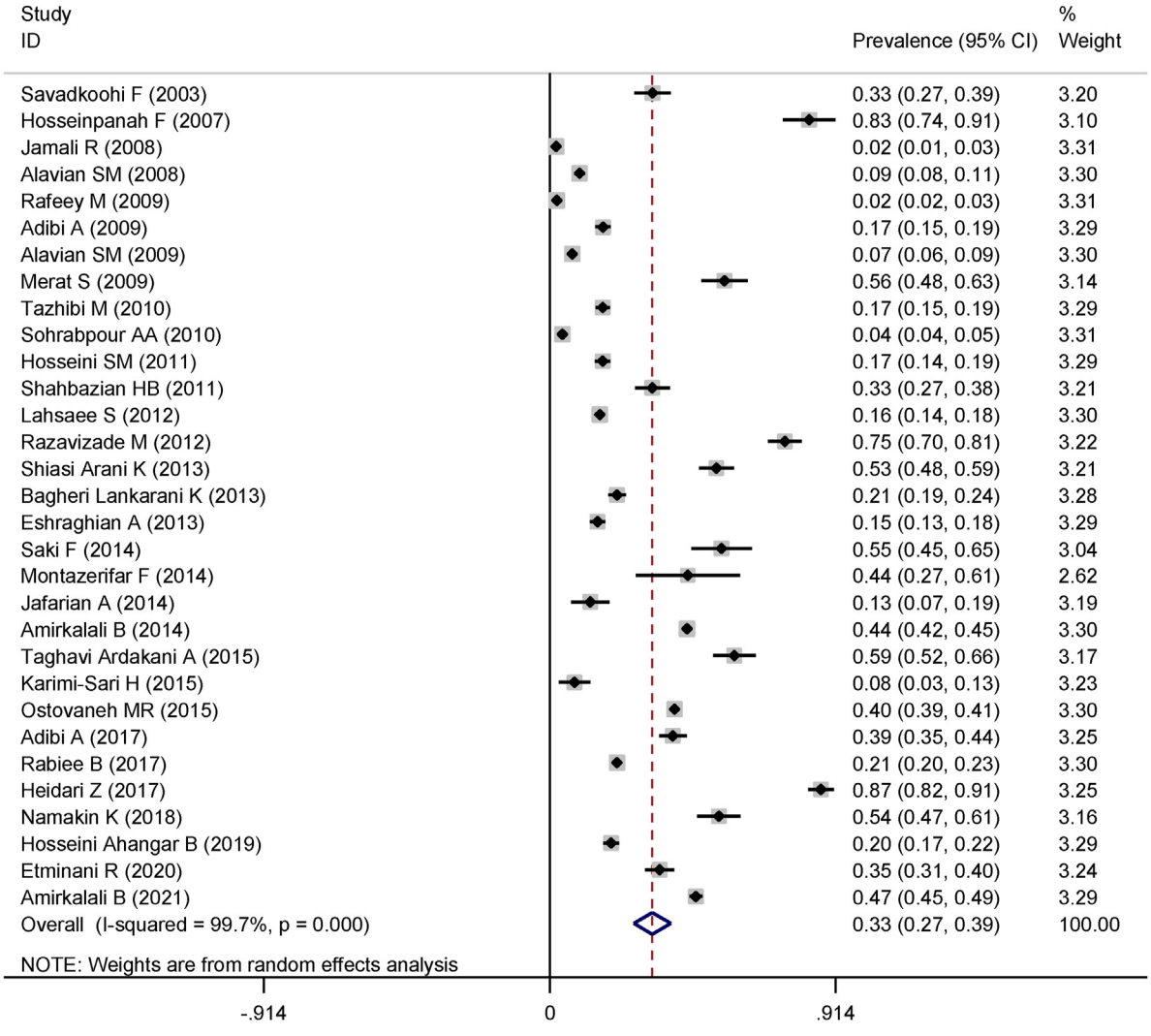

Figure 2 NAFLD prevalence in Iran.

Table 2 Newcastle–Ottawa Quality Assessment.

First author	Year	Representativeness (0,1,2)	Sample size (0,1)	Diagnostic tool (0,1,2)	Comparability of study population (0,2)	Outcome assessment (0,1)	Statistical test (0,1)	Total score (0–9)
Savadkoohi	2003	1	1	0	0	1	1	5
Hosseinpanah	2007	0	1	2	2	1	1	8
Alavian	2008	0	1	2	1	1	1	6
Jamali	2008	1	1	2	0	1	1	6
Merat	2009	1	1	2	2	1	1	8
Adibi	2009	1	1	2	2	1	1	8
Alavian	2009	1	1	2	2	1	1	8
Rafeey	2009	2	1	2	2	1	1	9
Tazhibi	2010	2	1	1	0	1	1	6
Sohrabpour	2010	2	1	2	0	1	1	7
Shahbazian	2011	1	1	2	0	1	1	6
Hosseini	2011	1	1	2	2	1	1	8
Razavizade	2012	1	1	2	2	1	1	9
Lahsaee	2012	1	1	2	0	1	1	6
Shiasi Arani	2013	2	1	2	2	1	1	9
Bagheri Lankarani	2013	1	1	1	1	1	1	6
Eshraghian	2013	1	1	2	2	1	1	8
Montazerifar	2014	1	1	2	0	1	1	6
Saki	2014	1	1	2	2	1	1	8
Jafarian	2014	1	1	2	2	1	1	8
Amirkalali	2014	2	1	1	0	1	1	6
Karimi-Sari	2015	2	1	2	2	1	1	9
Taghavi Ardakani	2015	2	1	2	2	1	1	9
Ostovaneh	2015	1	1	2	2	1	1	8
Adibi	2017	1	1	2	2	1	1	8
Rabiee	2017	1	1	2	2	1	1	8
Heidari	2017	1	1	2	0	1	1	6
Namakin	2018	2	1	2	2	1	1	9
Hosseini Ahangar	2019	2	1	2	2	1	1	9
Etminani	2020	2	1	2	2	1	1	9
Amirkalali	2021	2	1	2	2	1	1	9

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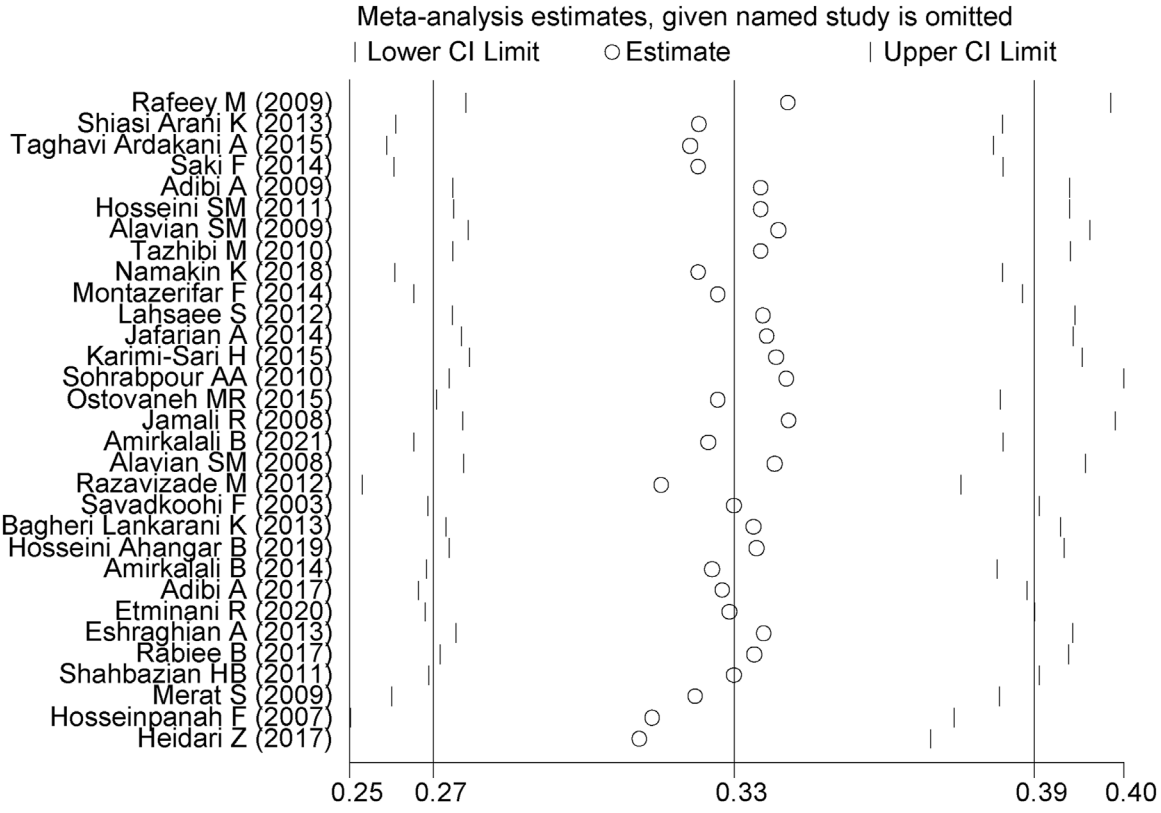

Figure 3 Sensitivity analysis.

Also, Figure 3 shows the results of the sensitivity analysis, confirming that the findings were stable. In addition, we conducted a subgroup analysis. Table 3 shows the prevalence by obesity status, publication year, geographic region, setting, type of participants, diagnostic test, sex, and sample size in the included studies.

The prevalence of NAFLD was found in both obese or overweight patients (33%), and non-obese individuals (32%). However, the prevalence varied based on the year of publication, with studies published between 2000 and 2005 reporting a prevalence of 33%, studies published between 2011 and 2015 reporting a prevalence of 18%, and studies published between 2016 and 2020 reporting a higher prevalence of 43%. When considering geographical regions, we observed that the prevalence of NAFLD in the west, east, north, and south of Iran was 2%, 52%, 26%, and 34%, respectively. Additionally, we found that the prevalence of NAFLD was higher in studies with smaller sample sizes (39% in studies with a sample size of ≤1000) compared to those with larger sample sizes (20% in studies with a sample size >1000). Furthermore, the prevalence of NAFLD varied based on the data collection method. Studies based on outpatient department (OPD) visitors reported a prevalence of 57%, while studies based on hospital-based data reported a prevalence of 61%. Studies based on public health centers reported the highest prevalence of NAFLD at 71%.

According to the publication year (P = 0.19) and age of participants (P = 0.25), meta-regression increased; however, it decreased based on the sample size (P = 0.21). But none of them was statistically significant. Also, the results of Egger's test show no significant publication bias in the overall prevalence (P = 0.45) (Figure 4).

In some of the included studies, participants had comorbidities such as type 2 diabetes, hepatitis B, and other diseases. Additionally, some studies included children as participants, which limits the generalizability of the results to the overall population. To address this issue, we performed an analysis using population-based samples only. The overall prevalence was 43% [CI: 31–55%].

DISCUSSION

We investigated the prevalence of NAFLD in Iran in the present study. Results revealed that the overall prevalence of this disease was 33%, with prevalences of 34% and 31% in adults and children, respectively. In this regard, the prevalence of NAFLD in Iran is lower than in Chile (39.4%),[43] India (38.6%),[44] South Korea (51.4%),[45] and Turkey (48.3%).[46] However, Younossi *et al.*[47] reported a lower

Table 3 Results of Subgroup Analysis.

Variables	Prevalence (CI 95%)	I2 (%)	Number of studies
Obesity status (Total)			
Overweight and obese	33 (15–51)	99.9	7
Non-obese	32 (27–38)	99.6	24
Year of publication			
2000–2005	33 (27–39)	0	1
2006–2010	18 (14–22)	99.1	9
2011–2015	35 (27–43)	99.3	14
2016–2022	43 (28–58)	99.5	7
Regional			
West	2 (2–3)	0	13
East	52 (30–73)	99.2	5
North	26 (17–34)	99.8	12
South	34 (27–42)	98.7	1
Participants			
Children	28 (19–36)	99.6	22
Adults	35 (27–43)	99.7	9
Diagnostic test			
Ultrasound	32 (25–38)	99.7	26
Others	39 (18–61)	99.6	5
Sex			
Male	35 (27–43)	99.4	19
Female	37 (27–47)	99.6	19
Sample size			
Sample size ≤1000	39 (30–48)	99.2	21
Sample size >1000	20 (11–30)	99.9	10
Health status			
Without disease	28 (22–34)	99.7	27
Type 2 diabetes mellitus	65 (37–92)	98.8	4
Obesity status (Children)			
Non obese	11 (3–18)	98.9	4
Overweight and obese	48 (26–69)	98.8	5
Obesity status (Adults)			
Non obese	25 (10 61)	99.8	2
Overweight and obese	34 (26–43)	94	20
Level of quality of studies			
Low risk of bias (high quality)	32 (24–40)	99.5	20
Moderate risk of bias (fair quality)	34[24–44]	96.9	11
Setting			
OPD visitors	57 (42–73)	99.7	9
Hospital based	61 (58–84)	99.8	9
Public health center	71 (60–82)	99.7	11
Blood transfusion Center	53 (44–97)	90	2

OPD, outpatient department

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prevalence of NAFLD (25.24%). Also, compared to other studies conducted in Israel (30%)[48] and Italy (20%),[49] the prevalence of NAFLD in Iran was higher. We think that this difference in prevalence across countries might be because of lifestyle, demographic characteristics, and health services related to treatment, as well as the studied populations and methods for diagnosing fatty liver.[50]

Results also showed that ultrasound was used in 84% of studies for diagnosing NAFLD. Also, the prevalence of NAFLD based on the ultrasound test was 32%, and other methods were 39%. In addition, the ultrasound method has been reported to be non-invasive, accurate, detailed, painless, accessible, and safe for all patients.[51] In Iran, the ultrasound diagnostic method is also commonly used because of its high sensitivity and specificity, easy access, and appropriate insurance coverage.[52]

In recent years, the lifestyle in Iran has changed, and people have become less active. Also, the consumption of carbonated drinks and sweets, the use of fatty foods, and fast foods have become common in Iran, leading to a dramatic increase in obesity that might justify the increasing trend of NAFLD in Iran in recent years.[53] In this regard, about 29 million Iranians are suffering from obesity and overweight, and 85% of the population was sedentary at the time of writing this manuscript.[54]

Our findings showed that the prevalence of NAFLD was higher in obese and overweight people, which was consistent with the findings of other studies.[46–48] Also, various studies have shown that there is a positive correlation between obesity and NAFLD;[55,56] therefore, controlling obesity through public education and lifestyle modification could be a sound measure.[57]

The findings of our study revealed that the highest prevalence of NAFLD was observed on the western side of the country, with a rate of 52%. The western provinces of Iran are the most important sources of livestock breeding and red meat production, and their consumption is also very high in these provinces. In this regard, Hashemian *et al.* argued that the prevalence of NAFLD is positively related to the amount of red meat consumption.[58] Alongside, this several studies reported that red meat consumption is associated with an increased risk of NAFLD.[59,60] Red meat can accelerate obesity, and as a result, people will be prone to various diseases, including NAFLD.[61] Therefore, a change in eating habits and reducing the amount of red meat consumption might be effective in decreasing the prevalence of NAFLD.[62,63]

In the present study, the prevalence of NAFLD was higher in women than men which is consistent with the findings of Summart *et al.*[64] The high prevalence of NAFLD in women can be attributed to fat distribution, their physiology, and sex hormones.[65] In this regard, nutritionists argue that the hormonal changes in women after menopause and lack of estrogen and progesterone hormones increase the appetite in women that might lead to obesity.[66,67] In the same vein, most Iranian women's obesity is due to eating habits as well as being inactive.[68] Also, obesity after pregnancy is pervasive in Iran.[42]

Although NAFLD affects people of any age, even in children,[69] the findings of the present study show that the prevalence of NAFLD in adults was higher than that in children, which is in alignment with the findings of precursory studies.[70–72] In this regard, it has been argued that lack of proper physical activity, accumulation of fat in

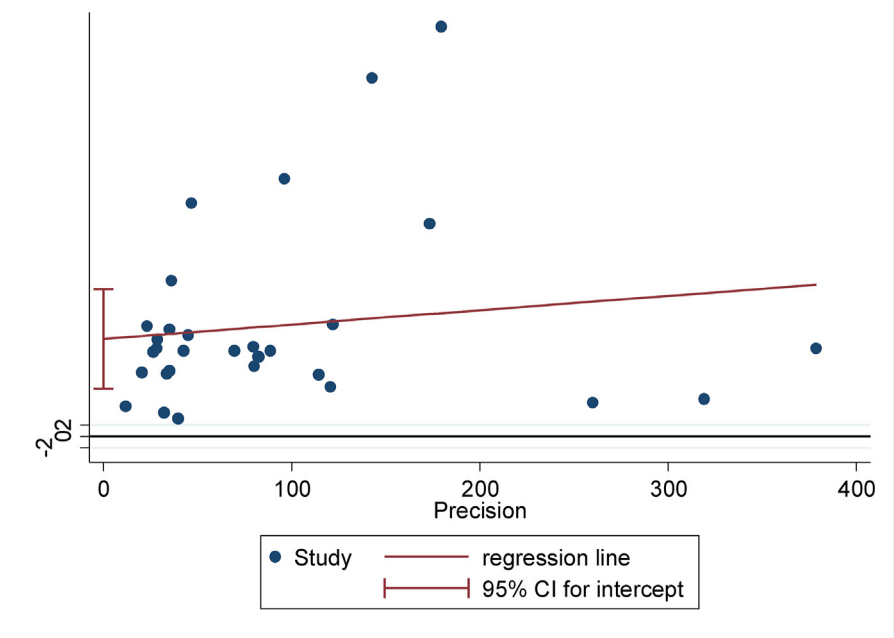

Figure 4 Publication bias.

the body, smoking, and various diseases can increase the potential risk of NAFLD in adults, especially in the adults.[73]

Also, the findings of our study show that the prevalence of NAFLD in type 2 diabetic patients is 2.3 times higher compared to healthy people, which is consistent with the results of studies conducted in other countries.[46,64] Due to the fact that the management of type 2 diabetes is very difficult when it coincides with NAFLD, we thus recommend screening type 2 diabetic patients for NAFLD thoroughly.[74] It is noteworthy to mention that the prevalence of type 2 diabetes in Iran in people over 40 years old is about 24%, which might be a further cause of the prevalence of NAFLD.[75]

To reduce the prevalence of NAFLD in Iran, the following policies and programs have been implemented: raising taxes on fast foods, sugary foods, and soft drinks; food labeling; financial supports for factories that produce healthy food; and the establishment of a public sports federation to encourage people to be more physically active.[76]

LIMITATIONS AND FURTHER RESEARCH

The present study has two limitations. First, the included studies did not have a homogeneous population under investigation. Second, the diversity of diagnostic tests used, different age groups, and risk factors examined can also be the cause of the heterogeneity in the present study. As Iran has a variety of geographical regions and social classes and, in some provinces, no valid study on the prevalence of NAFLD has yet been conducted, we believe that more research is needed in this area.

The results of the present study demonstrated that the prevalence of NAFLD in Iran is not only high but also growing. Also, the cost of NAFLD epidemics might be very damaging to the health system; thus, we argue that a comprehensive NAFLD management program is required. In this regard, effective strategies for changing lifestyles, changing eating habits, and encouraging physical activities among Iranians are recommended. Also, providing screening tests, especially among high-risk groups, can play an important role in early diagnosis and NAFLD control.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

SPT, MaB, MeB, MS, and SA: Conceptualiz and design. MaB, and SA: Data curation. MaB, SA and NLB: Formal analysis. AR, MM, SS, AS, AT and MaB: Investigation. SPT, NLB and MaB: Methodology. SPT, MaB: Project administration. MeB, AR, SA, MM, SS, AS, AT and MaB: Resources. MaB, and NLB: Software. SPT and MaB: Supervision. MeB, AR, SA, MM, SS, AS, AT and MaB: Validation. MeB and SPT: Visualization. MeB and SPT: Roles/Writing - original draft. MaB, AR, SJE and NLB: Writing - review & editing. None: Funding acquisition.

CONFLICTS OF INTEREST

The authors have none to declare.

ACKNOWLEDGMENTS

Not applicable.

FUNDING

Not applicable.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The protocol was also approved by the Review Ethics Board of the Iran University of Medical Sciences (IR.IUMS.-REC.1401.383).

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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SUPPLEMENTARY DATA

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