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Prevalence of non-alcoholic fatty liver and its related factors in Iran: Systematic review and meta-analysis

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Abstract:

Non-alcoholic fatty liver disease (NAFLD) is a systemic disorder with a complex multifactorial and heterogeneous pathogenesis and has become the most common cause of chronic liver disease in many countries around the world. Numerous studies in Iran have presented different results on the prevalence and risk factors of NAFLD, in this study, which has been done in a systematic review and meta-analysis, provides a good estimate of the prevalence and risk factors of the disease in Iran. Following the peer review of electronic search strategies (PRESS and the preferred reporting items for systematic reviews and meta-analyses [PRISMA] statement, we searched Web of Science, PubMed, Embase, Scopus, and Persian scientific searcher (Elmnet) from inception to September 19, 2022. In the present study, 71 articles were reviewed for qualitative and meta-analysis. The overall mean prevalence of NAFLD in children studies was 22.4% (95% confidence interval [CI]: 10.9% to 33.9%). The prevalence was notably higher in adult studies 40.5% (95% CI: 35.1% to 46%). In 24 studies, the association between NAFLD and sex was reported, 10 of which showed significant relationships. Out of 46 studies observed that NAFLD prevalence increased significantly with body mass index (BMI). Eight out of 14 studies reported significant associations between FBS and NAFLD in children's studies. Though Iran has a high NAFLD prevalence compared to most areas, and due to the unfavorable situation of risk factors contributing to the NAFLD, it is necessary to take the necessary interventions to control these risk factors and prevent NAFLD.

Keywords:

Iran, non-alcoholic fatty liver disease, prevalence, systematic review

Introduction

Non-alcoholic fatty liver disease (NAFLD) is defined as excessive accumulation of fat in the liver[1,2] and growing problems affecting one-third of adults worldwide.[3] NAFLD is a systemic disorder with a complex multifactorial and heterogeneous pathogenesis and has become the most common cause of chronic liver disease in many countries around the world. The chronic liver disease covers a wide range of diseases, from non-progressive to severe forms.[4,5] Compared to the general population, NAFLD increases the risk of mortality from the liver, cardiovascular, and all causes.[6]

The prevalence of NAFLD in the world is estimated at about 25%.[7] Increased urbanization and reduced physical activity and unhealthy nutrition in Asian countries have led to an increase in obesity and thus an increase in the prevalence of the disease by 25%.[8]

NAFLD is affected by several risk factors such as obesity, insulin resistance, type 2 diabetes (T2DM), hypertension, hyperlipidemia, and metabolic syndrome.[9]

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The prevalence of NAFLD in the general population is about 25%, whereas in obese people it increases to 90%.[9] In patients with type 2 diabetes, the prevalence of NAFLD is more than 60%[9,10] and diabetes also accelerates the disease process.[11] The prevalence of NAFLD-related fibrosis increases with age.[11,12] In some studies, the incidence of the disease has been reported more in women[12] and in some studies, it has been higher in men.[13-15]

The prevalence of the disease in the Middle East is estimated at 20–30% and varies between countries.[11,16] Previous studies in Iran showed that the prevalence of mild, moderate, and severe fatty liver disease is 26.7, 7.6, and 0.5%, respectively, estimated NAFLD is also higher in men, obese people, the elderly, patients with systolic hypertension, patients with diastolic hypertension, patients with hypertriglyceridemia, patients with high levels of Homeostatic Model Assessment of Insulin Resistance (HOMA). It was more common in those with metabolic syndrome and those with high serum ALT.[17] NAFLD has also been associated with increased cardiovascular diseases. It is associated with greater overall mortality and predicts the risk of future CVD events.[18,19] Although there are no ideal options available for NAFLD treatment, dietary modification has a major role. Dietary patterns high in fruit and vegetable content were generally found to be associated with a lower prevalence of metabolic syndrome.[20] In these patients, the intake of foods and drinks rich in fructose should be limited.[21]

Numerous studies in Iran have presented different results on the prevalence and risk factors of NAFLD. Such variations in results make them inappropriate for policymaking and they lead to incorrect decisions by medicine to choose the right treatment for patients. Thus, to obtain and reduce the existing discrepancy between the studies, the aim of this study was to provide a good estimate of the prevalence and risk factors of the disease in Iran using a systematic review and meta-analysis.

Materials and Methods

Search strategy and study selection

Following the peer review of electronic search strategies (PRESS)[22] and the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statements[23],we searched Web of Science, PubMed, Embase, Scopus, and Persian scientific searcher (Elmnet) (https://elmnet.ir/) from inception to September 19, 2022.

Search terms were combined using appropriate Boolean operators and included subject heading terms or keywords for three key concepts, tailored to fit each database's requirements. Search concepts were related to NAFLD (e.g., non-alcoholic fatty liver or non-alcoholic steatohepatitis) AND (e. g., epidemiology or frequency or prevalence or incidence) AND Iran (e.g. Iran, Persia). Search strategy in PubMed and web of science databases included the following steps:

a) PubMed

((Non-alcoholic Fatty Liver Disease [Title/Abstract]) AND ((Iran [Title/Abstract]) OR (Persia [Title/Abstract]) OR (Persian [Title/Abstract])) AND ((Epidemiology [Title/Abstract]) OR (Prevalence [Title/Abstract]) OR (Frequency [Title/Abstract])))

b) Web of sciences

(Non-alcoholic Fatty Liver Disease) OR (NAFLD) OR (Nonalcoholic Fatty Liver Disease) OR (Fatty Liver, Nonalcoholic) OR (Fatty Livers, Nonalcoholic) OR (Liver, Nonalcoholic Fatty) OR (Livers, Nonalcoholic Fatty) OR (Nonalcoholic Fatty Liver) OR (Nonalcoholic Fatty Livers) OR (Nonalcoholic Steatohepatitis) OR (Nonalcoholic steatohepatitis) OR (steatohepatitis, Nonalcoholic) OR (Steatohepatitis, Nonalcoholic) OR (Non-alcoholic fatty liver) (Topic) and (Iran) OR (Persia) OR (Persian) (Topic) and (Epidemiology) OR (Prevalence) OR (Frequency).

As scientific databases in Iran do not support subject heading terms or complex Boolean operators, we only searched keywords related to non-alcoholic fatty liver in these databases. IR.MUK.REC.1401.262

Eligibility criteria

Records were included if they (i) were quantitative studies published in a peer-reviewed journal, and (ii) reported a measure of frequency for the prevalence of NAFLD among the Iranian general population.

Data extraction and quality assessment

We extracted data on the author's name, year of publication, location, participants' characteristics (e.g. sex, age), sample size, diagnostic criteria (i.e., ultrasonography or blood tests or liver biopsy or clinical evidence or CT scan) and point prevalence of NAFLD. The risk of bias tool for prevalence studies developed by Hoy was used to assess the methodological quality of the included studies.[24] This checklist contains nine items, and each item is scored 0, 0.5, and 1. A score of 1 is given if the study meets the criterion, a score of 0.5, and a score of 0 is given if the study has insufficient or no description of the criterion, respectively. Selected studies were examined for representativeness, sample size, recruitment, description of the study participants and setting, data coverage of the identified sample, the reliability of the measured condition, and the adequacy of the statistical analysis. The tool was modified to provide a numeric score ranging from 0

to 9 with scores lower than 5 characterized as "low quality," 6–8 as moderate quality, and upper 8 as "high quality."

Statistical analysis

The heterogeneity among prevalence estimates was assessed using the I^2 index and the Q-test for heterogeneity in which a P value <0.1 was considered statistically significant. Based on the degree of heterogeneity among studies, a random-effects (DerSimonian and Laird) method was used to estimate the pooled prevalence of NAFLD among adults and children in Iran. Metaprop, a statistical procedure in the Stata package, was applied to combine the prevalence estimates and related 95% confidence intervals (CIs). After observing substantial heterogeneity across the studies, meta-regression was used to assess whether the following study-level characteristics were associated with NAFLD prevalence in either adults and children studies: diagnostic method (one method, more than one), publication year (before 2010, 2011 to 2015, and after 2015), geographical area of study (categorized as Central (Central included Tehran and Isfahan, Kashan and Yazd), West and Northwest, North and Northeast and South and Southeast) and sample size (categorized as above or below the median sample size: n = 485 for adult studies and n = 887 for children studies). In each subgroup, estimates of the prevalence with 95% CIs were calculated from meta-regression coefficients. Differences between subgroups are reported by P value. Stata 13 (Stata Corp, College Station, TX, USA) was used to analyze the data.

Results

In total, 661 articles were obtained from the search of electronic databases. After removing duplicate articles and checking the inclusion criteria, 71 articles were reviewed for qualitative and meta-analysis [Figure 1] and their information was extracted based on a pre-designed checklist [Table 1].

The majority of studies were conducted in Tehran (17 studies) followed by Fars province (9 studies), Isfahan (10 studies), Amol city (7 studies), and Tabriz (7 studies). More than half of the studies (54 articles) were conducted between 2016 and 2022. The duration of the studies varied from 1 to 8 years. Sample sizes ranged from 70 to 11,245; median n = 485. The age range of the adult and children participants was 18–90 years and 4 to 18 years, respectively. The most retrieved studies were cross-sectional (n = 41, 58%) followed by case–control (n = 23, 32%) and cohort (n = 7, 10%). Overall, 67 (94%) studies were conducted in adults (upper 18 years) and 4 (7%) studies in children/adolescents (lower 18 years).

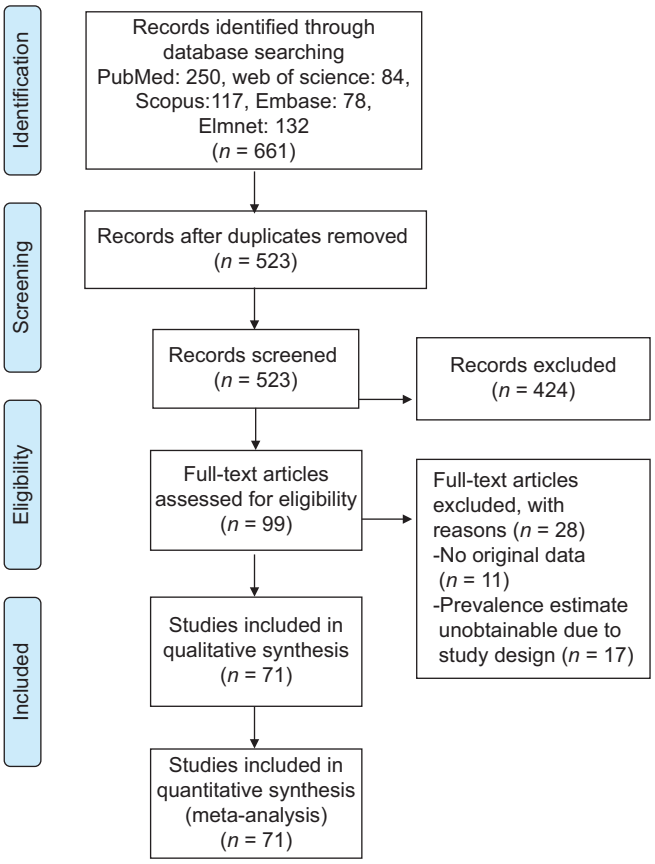

Figure 1: Flow diagram of search strategy for meta-analysis of the prevalence of non-alcoholic fatty liver disease among the Iranian population

The most commonly used diagnostic method was ultrasonography (USG) (n = 51, 72% of studies). Other studies used more than one method. For instance, 11 studies used USG and biochemical tests, three studies used clinical evidence, USG and biochemical tests and one study used USG, CT, and Fibro scan for assessing NAFLD. Only one study had biopsy data and no studies used magnetic resonance imaging (MRI) [Table 1].

The results of the quality assessment revealed that the quality of 22 (31%) studies was high, the quality of 36 (51%) studies was moderate, and that of 13 (18%) studies was low quality (Supplementary Table 1).

There was considerable heterogeneity among both children and adult studies (I^2 = 99% in both cases). The overall mean prevalence of NAFLD in children studies were 22.4% (95% CI: 10.9% to 33.9%, N studies = 4, Figure 2).

The prevalence was notably higher in adult studies (40.5%, 95% CI: 35.1% to 46%, N studies = 60, Figure 2).

Meta-regression showed that there was no statistical evidence that NAFLD prevalence differed by diagnostic method in adult (lower 18 years old) studies. However,

Table 1: Baseline characteristics of the included studies in the meta-analysis

ID	First author	Publication year	Time of study	Place of study	Type of study	Age	Sex, *n* (%)
1	Pourshams[25]	2005	2001-2002	Tehran	Cross-sectional	Mean ± SD: 36.96 ± 8.78	Male: 1465 (75), Female: 494(25)
2	Jamali[26]	2008	2006	Gonbad and Kalaleh	Cross-sectional	Age range: 18-79	Male: 698(34.1) Female: 1351 (65.9)
3	Rafeey[27]	2009	2005-2006	Tabriz	Cross-sectional	Age range: six months to 15 years	_
4	Moayed Alavian[28]	2009	2007	Tehran	Cross-sectional	Age range: 7-18	Male: 433(44.8) Female: 533 (55.2)
5	Khoshbaten[29]	2009	2006	Tabriz	Case-control	Mean ±SD: Case: 42/5 ± 10/7, Control: 45/5 ± 13/5	Case Male: 56(54.9), Female: 46(45.1), Control: Male: 43(42.2), Female: 59(57.8)
6	Mohsen Hosseini[30]	2011	_	Isfahan	Cross-sectional	Age range: 6-18	Male: 413 (44.4) Female: 518 (55.6)
7	ShiasiArani[31]	2013	1389-91	Kashan	Cross-sectional	Age range: 4-18 Mean ±SD: 45.4±15.9	Male: 128 (41.8) Female: 178 (458.2)
8	Bagheri Lankarani[32]	2013	2010-2011	Shiraz	Cross-sectional	Mean ± SD: 43.1 ± 14.1, Age range: 18-88	Male: 340 (41.5) female: 479 (58.5)
9	Eshraghian[33]	2013	2011-2012	Shiraz	Cross-sectional	Mean ± SD: 48.2 ± 12.8	Male: 322(38.7) Female: 510 (61.3)
10	Abangah[34]	2013	2012	Ilam	Cross-sectional	Age range: 16-64	Male: 140 (65.7) Female: 73 (34.3)
11	Einollahi[35]	2013	_	Tehran	Cross-sectional	No Information	Male: 5698 (50.7) Female: 5547 (49.3)
12	Amirkalali[36]	2014	2008	Amol	Cross-sectional	Age range: 18-90 Mean ± SD: 45.4±15.9	Male: 2863(56.7) Female: 2160(43.3)
13	Amirkalali[37]	2014	2008	Amol	Cross-sectional	Age range: 18-90	Male: 2848(56.7) Female: 2175 (43.3)
14	Dehghan[38]	2015	1390	Tehran	Cross-sectional	Age range: 20-55	_
15	Kolahi[39]	2015	1390	Tehran	Case-control	Age range: 20-50	_
16	Ostovaneh[40]	2015	2008-2011	Amol-Zahedan	Cross-sectional	Mean ± SD Amol urban: 40.85±0.33 Amol rural: 40.66±0.34 Zahedan: 37.27 ±0.40	Amol urban: Male: 1504 (46.7), Female: 1407 (54.3), Amol rural: Male: 1659 (54.1), Female: 1075 (45.9), Zahedan: Male: 1065 (48.5), Female: 1013 (51.5)
17	Abedini[41]	2015	2013	Tehran	Cross-sectional	_	Male: 132 (53.6) Female: 114 (46.3)
18	Baharvand-Ahmadi[42]	2015	2011-2012	Khorammabad	Cross-sectional	Mean ± SD: 58.1 ± 12.5	Male: 77 (45.3) Female: 93 (54.7)
19	Motamed[43]	2016	_	Amol	Cross-sectional	Age range: 10-90, Mean ± SD Male: 44.8 ± 16.8, Female: 43.78 ± 15.43	Male: 2860 (56.6) Female: 2192 (43.4)
20	Motamed[44]	2016	2008-2010	Amol	Cross-sectional	Age range: 18-74	Male: 2723 (55.9) Female: 2149 (44.1)
21	Fattahi[45]	2016	2006	Kavar	Cohort	over 18 years	Male: 864 (28.9) Female: 2116 (71.1)
22	Kohan[46]	2016	2013-2014	Shiraz	Case-control	Mean ± SD: case: 43±11.9 Control: 45.9 ±14	Male: 147 (52.1) Female: 135 (47.8)
23	Birjandi[47]	2016	2013	Kavar	Cross-sectional	Age range: 16-88	Male: 471 (29.4) Female: 1129 (70.6)
24	Kohnaki[48]	2016	2014-2015	Ilam	Case-control	Mean ± SD: 42/13±12/15	Male: 138 (46) Female: 162 (54)
25	Pasdar[49]	2016	2015	Kermanshah	Case-control	Age range: 30-65	_
26	Pasdar[50]	2016	2015	Kermanshah	Case-control	Age range: 29-51	Male: 69 (32), Female: 147(68)

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Table 1: Contd...

ID	First author	Publication year	Time of study	Place of study	Type of study	Age	Sex, *n* (%)
27	Pakzad[51]	2016	not report	Isfahan	Case-control	Mean ±SD Case: 48/8 ± 10/8, Control: 42/3 ± 13/4	Male: 64 (60.3) Female: 42 (39.7)
28	Mohseni,[52]	2017	_	Tabriz	Case-Control	Mean ± SD Case: 40.65 ± 8.41 Control: 38.87±8.2	_
29	Mehrabian[53]	2017	2013-2014	Isfahan	Cross-sectional	Age range: 18-42	_
30	Heidari[54]	2017	2015-2016	Zahedan	Cross-sectional	Over 30 years	Male: 82 (32) Female: 173 (68)
31	Motamedi[55]	2017	_	_	Cohort	mean age of 40.3	Male: 20 (27) Female: 54 (73)
32	Honarvar[56]	2017	_	Shiraz	Cross-sectional	Median age: 42	Male: 203 (42.5) Female: 275 (57.5)
33	Naderian[57]	2017	2015-2016	Tehran	Cross-sectional	over 18 years	Male: 139 (44.3) Female: 175 (55.7)
34	Salmanroghani[58]	2018	2016-2017	Tehran	Cross-sectional	over 18 years	Male:322 (54.6) Female: 268 (45.4)
35	Jodi[59]	2018	2016	Tabriz	Cross-sectional	Age range: 32-62	Male: 46 (65.7) Female: 24 (34.3)
36	Eshraghian[60]	2018	2014	Tehran	Cross-sectional	over 18 years	_
37	Langroudi[61]	2018	2016	_	Cross-sectional	Mean ± SD: 61.16 ± 11.34, Age range: 31-91	Male: 185(70.1) Female: 79 (29.9)
38	Salehisahlabadi[62]	2018	2016	Isfahan, Yazd and Shahrekord	Cross-sectional	Age range: 18-65	Male: 215 (41.3) Female: 305 (58.7)
39	Fattahi[63]	2018	2013-2014	Sanandaj city	Cross-sectional	Age range: 20-70	Male: 169 (41.11) Female: 241 (58.89)
40	Mahboubi[64]	2019	2017	Rafsanjani	Cross-sectional	Mean ±SD 55.2±16, Age range: 20-91	Male: : 39 (39), Female: : 61 (61)
41	Doost Mohammadi[65]	2019	2016	Rafsanjani	Case-control	Age range :20-40	Male: 116(60.4), Female: 76(39.5)
42	Zarean[66]	2019	_	Shahrekord	Case-control	Age range: 35-70, Mean ± SD: 50.23±8.70	Male: 920 (39.9) Female: 1386 (60.1)
43	Lotfi[67]	2019	_	Isfahan	Case-control	Age range: 20-60	Male: 321 (53.5) Female: 279 (46.5)
44	Gheibi[68]	2019	2016-2017	Urmia	Cross-sectional	Age range: 2-19	Male: 425 (50.4) Female: 418 (49.6)
45	Keshani[69]	2019	2017	Shiraz	Cohort	over 18 years	Male: 229 (42.7) Female: 308 (57.3)
46	Hosseini Ahangar[70]	2019	2013-2016	Tehran	Cross-sectional	Mean ± SD: 43.28 ± 14.03	Male: 430(43.1) Female: 569 (56.9)
47	Eshraghian[71]	2019	2012-2018	Shiraz	Cohort	Mean ± SD: 32.64 ± 7.04	Male: 130 (42) Female: 180 (58)
48	Mansour-Ghanaei[72]	2019	2017	Guilan Province	Cross-sectional	Age range: 35-60	Male: 330 (52.4) Female: 300 (34.3)
49	Shafiezadeh[73]	2020	2018	Isfahan	Case-control	Mean ± SD: 40±15	Male: 120 (63) Female: 70 (37)
50	Eshraghian[74]	2020	2010-2017	Shiraz	Cross-sectional	_	_
51	Asghari[75]	2020	_	Tabriz	Cross-sectional	Age range: 20-60	Male: 133 (58.3) Female: 95(41.7)
52	Golmohammadi[76]	2020	2016-2017	Kermanshah	Case-control	Mean ± SD: 40.71 ± 6.84	_
53	Etminani[77]	2020	2011-2012	Isfahan	Cross-sectional	Age range: 30-60, Mean ± SD: 45.5 ± 8.6	Male: 163(42.7) Female: 250 (60.5)
54	Motamed[78]	2020	2010-2017	Amol	Cohort	Age range: 10-89	_
55	Motamed[79]	2020	2010-2018	Amol	Cohort	Age range: 10-90	_
56	Fatahi[80]	2021	2018-2019	Tehran	Case-control	Age range: 18-55, Mean ± SD: 43.9 ± 5.9	-
57	Hashemian[81]	2021	2011	Gonbad	Cohort	Age range: 40-75	_

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Table 1: Contd...

ID	First author	Publication year	Time of study	Place of study	Type of study	Age	Sex, *n* (%)
58	Mokhtari[82]	2021	_	Isfahan	Case-control	Age range: 20-60	-
59	Sohouli[83]	2021	2018-2019	Tehran	Case-control	Mean ± SD: 44.04 ± 13.17	Male: 153 (42), female: 213 (58)
60	Tutunchi[84]	2021	-	Tabriz	Case-control	Age range: 20-60	
61	Tutunchi [85]	2021	2019	Tabriz	Case-control	Age range: 20-60, Mean SD: 48.8 ±5.9	Male: 97(46) Female: 113 (54)
62	Farhadnejad[86]	2022	2021	Isfahan	Case-control	Age range: 20-60،	-
63	Eslami [87]	2022	2014-2016	Tehran	Cross-sectional	Mean ± SD 30.946.01	-
64	Gholoobi[88]	2022	2013	Mashhad	Cross-sectional	Mean ± SD: 54.10 9.33	Male: 122 (41.2) Female: 174 (58.8)
65	Moradi[89]	2022	2020	Isfahan	Case-control	Mean ± SD: 38.04 ± 6.7	Male: 71 (58.7) Female: 50 (41.3)
66	Rahimi-Sakak[90]	2022	2021	Tehran	Case-control	Mean ± SD: 42.3 11.9	Male: 395(41.5) Female: 604 (60.4)
67	Salehi-Sahlabad[91]	2022	2020	Isfahan	Case-control	Mean ± SD: 38.1 ± 8.8	-
68	Tandoroost[92]	2022	2015	Kermanshah	Case-control	Age range: 20-65	-
69	Sohouli[93]	2022	2020-2021	Tehran	Case-control	Mean ± SD: 38.15 8.43	Male: 154 (30) Female: 358 (70)
70	Doustmohammadian[94]	2022	2016-2017	Amol	Cross-sectional	Mean ± SD: 46.96 ± 14.67	Male: 1,782 (55.3) Female: 1438 (44.7)
71	Ebrahimi Mousavi[95]	2022	2018-2019	Ahvaz	Case-control	Age range: 19-70	Male: 114 (47) Female: 129 (53)

ID	Study population	Prevalence of NAFLD (%)		Total % (case/ sample)	Diagnostic criteria
		Male % (case/sample)	Female % (case/ sample)		
1	Adults	3 (44/ 1465)	0.4 (2/494)	2.4 (46/1959)	Ultrasonography
2	Adults	_	_	2.04 (42 / 2049)	Ultrasonography
3	Children	_	_	2.3 (34 / 1500)	Ultrasonography
4	Children	_	_	7.1 (69 / 966)	Ultrasonography
5	Adults	_	_	50 (102/204)	Ultrasonography
6	Children	_	_	16.8 (157 / 931)	Ultrasonography
7	Children	_	_	55.3 (163/306)	Ultrasonography
8	Adults	_	_	21.5 (176/ 819)	Ultrasonography
9	Adults	_	_	15.3 (127 /832)	Ultrasonography
10	Adults	_	_	_	Ultrasonography
11	No Information	31.3 (1778 / 5698)	28.2 (1563 / 5547)	30 (3341 / 11245)	Ultrasonography
12	Adults	-	-	43.8 (2210/5023)	Blood tests and Ultrasonography
13	Adults	_	_	43.8 (2200/5023)	Ultrasonography
14	Adults	56 (55/99)	49 (35/71)	53 (90/ 170)	Ultrasonography
15	Adults	56 (55/99)	49 (35/71)	53 (90/ 170)	Ultrasonography
16	Adults	-	-	35.2 (3077 /7723)	Ultrasonography
17	Adults	_	_	49.5 (122 /246)	Ultrasonography
18	Adults	40.2 (31/77)	52.6 (49 / 93)	47.1 (80 /170)	Ultrasonography
19	Adults	40.1 (1147/2860)	44.2 (969/2192)	41.9 (2116/5052)	Ultrasonography
20	Adults	40.4 (1101/2723)	44.1 (947/2149)	42 (2048/ 4872)	Ultrasonography
21	Adults	32.9 (285/864)	27.4 (579 /2116)	28.9 (864/2980)	Ultrasonography
22	Adults	33.3 (49/147)	(45/135)	33.3 (94/282)	Clinical evidence, Blood tests and Ultrasonography
23	Adults	23.4 (110/471)	22 (249/ 1129)	22.4 (359/ 1600)	Ultrasonography
24	Adults	_	_	50 (150/300)	Ultrasonography
25	Adults	-	-	50 (125/250)	Ultrasonography
26	Adults	43.5 (30/69)	48.2 (71/147)	46.5 (101/215)	Ultrasonography
27	Adults	-	-	75.4 (80/106)	Ultrasonography

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Table 1: Contd...

ID	Study population	Prevalence of NAFLD (%)		Total % (case/sample)	Diagnostic criteria
		Male % (case/sample)	Female % (case/sample)		
28	Adults	_	_	_	Ultrasonography
29	Adults	_	28.6 (43/150)	_	Blood tests and Ultrasonography
30	Adults	_	_	86.7 (221/255)	Ultrasonography
31	Adults	_	_	9 (7/74)	Liver biopsy
32	Adults	15.3 (42/275)	26.1 (53/203)	19.8 (478/542)	Ultrasonography
33	Adults	17.3 (24/139)	17.7 (31/175)	17.52 (55/314)	Ultrasonography
34	Adults	53.1 (171/322)	48.6 (130/268)	51 (301/590)	Ultrasonography
35	Adults	74 (34/46)	45.8 (11/24)	64 (45 / 70)	Ultrasonography
36	Adults	_	_	29 (58/200)	Ultrasonography
37	Adults	_	_	72.2 (191/264)	Ultrasonography
38	Adults	53.4(115 /215)	26.8(82/305)	37.8 (197/520)	Ultrasonography
39	Adults	43 (72/169)	30 (73/241)	35 (145 /410)	Blood tests and Ultrasonography
40	Adults	-	-	76 (76 /100)	Ultrasonography and CT scan
41	Adults	-	-	50 (96/192)	Ultrasonography
42	Adults	-	-	16.5 (392/2306)	-
43	Adults	_	_	33.3 (200 /600)	Blood tests and Ultrasonography
44	Children	_	_	14 (117/843)	Ultrasonography
45	Adults	_	_	47.6 (256 / 537)	Ultrasonography
46	Adults	_	_	19.6 (196 / 999)	Blood tests and Ultrasonography
47	Adults	26.1 (34 / 130)	23.3 (42 / 180)	24.5 (76/310)	Biopsy
48	Adults	44.5 (147 / 330)	42.7 (128 / 300)	43.7 (275 / 630)	Ultrasonography
49	Adults	57.5 (69/ 120)	41.5 (29/ 70)	51.6 (98/ 190)	Ultrasonography
50	Adults	_	_	31.2 (129 / 413)	Ultrasonography
51	Adults	_	_	53.5 (122 / 226)	Ultrasonography
52	Adults	_	_	62 (279 / 450)	Clinical evidence, Liver enzymes, and Ultrasonography
53	Adults	42.3 (69 /163)	30.4 (76 / 250)	35.1 (145 / 413)	Ultrasonography
54	Adults	_	_	_	Ultrasonography
55	Adults	_	_	_	Ultrasonography
56	Patient who refer to Hazrat Rasoul Hospital	_	_	_	Ultrasonography, Biochemical tests
57	Participant were enrolled in a pragmatic trial for liver disease	_	_	37%(505/1464)	Ultrasonography, Biochemical tests
58	Adults	-	-	33%(225/675)	Ultrasonography
59	Patient who refer to Hazrat Rasoul Hospital	-	-	45%(166/366)	Ultrasonography, Biochemical tests
60	Adults	_	_	_	Ultrasonography
61	Adults	_	_	45.2%(95/210)	Ultrasonography
62	Adults	-	-	-	Ultrasonography
63	Women with polycystic ovary syndrome who were referred to Hospital	-	-	53.5% (38/71)	Ultrasonography, Biochemical tests
64	Patients referred to the catheterization laboratory of Imam Reza Hospital	54.9% (67/122)	53.4%(93/174)-	54.1% (160/296)	Ultrasonography
65	Adults		-	50.4% (121/240)	Ultrasonography

Contd...

Table 1: Contd...

ID	Study population	Prevalence of NAFLD (%)		Total % (case/sample)	Diagnostic criteria
		Male % (case/sample)	Female % (case/sample)		
66	Adults	-	-	19.6% (196/999)	Ultrasonography, Fibro scan
67	Adults	-	-	34% (225/675)	Ultrasonography
68	Adults referred to radiology clinics	-	-	46.6% (103/221)	Ultrasonography, Biochemical tests
69	Patient who refer to Hazrat Rasoul Hospital	-	-	40.2% (206/512)	Ultrasonography and LFT
70	Adults	-	-	44.6% (1437/3220)	Ultrasonography
71	Adults	-	-	49.7% (121/243)	Ultrasonography, Biochemical tests

in children (lower than 18 years old) studies, there was a statistical significance that prevalence differed by diagnostic method [Table 2]. Using only USG had a higher prevalence estimate than studies using the composition of methods (such as clinical evidence, liver enzymes, and USG) [Table 2].

In adult studies, there was strong significant evidence that prevalence differed by publication year. The highest pooled prevalence of NAFLD was 43.8% (95% CI: 29.2–43.5, *N* studies = 45) for adult studies by publication year [Table 2].

In both adult and children studies, there was no evidence from the meta-regression that prevalence differed by geographical area [Table 2].

In both adult and children studies, the meta-regression showed that prevalence was higher in studies with smaller sample sizes. Moreover, there was significant evidence that the study sample size was associated with NAFLD prevalence in both adult and children studies [Table 2].

In 24 studies, the association between NAFLD and sex was reported, 10 of which showed significant relationships. The association between fatty liver and age was investigated among 32 studies, and 12 studies reported a positive correlation with age (Supplementary Table 2).

Forty-eight studies observed that NAFLD prevalence increased significantly with body mass index (BMI). In 10 out of 23, systolic blood pressure had significantly associated with NAFLD. Moreover, diastolic blood pressure had significantly associated with NAFLD in eight studies Supplementary Table 2).

According to the results, 10 out of 21 studies reported a significant association between NAFLD and serum AST level (Supplementary Table 2). Moreover, there was a significantly correlated between NAFLD with ALT and alkaline phosphatase, respectively.

The association between NAFLD and serum triglyceride was investigated in 31 studies, and 25 of them reported significant findings. LDL, HDL, and total cholesterol (TC) had a significant association with NAFLD in 10 out of 23, 13 out of 25, and 13 out of 25, respectively. Fourteen studies investigated the association between FBS and NAFLD, eight studies reported significant associations. According to the results, 9 out of 14 studies reported significant associations between fasting serum glucose (FSG) and NAFLD (Supplementary Table 2).

Eight studies investigated the association between HOMA and NAFLD, six studies reported significant associations. Moreover, there was a significant association between metabolic syndrome and NAFLD in 10 studies (Supplementary Table Table 2).

Smoking and not having sufficient physical activity had a significant association with NAFLD in 7 out of 16 studies and 11 out of 15 studies, respectively (Supplementary Table 2).

Discussion

The aim of this study was to estimate the prevalence of NAFLD in adults, children, and the risk factors affecting it in Iran.

We found that the overall prevalence of NAFLD in children and adults was 39% (CI: 0.34–0.44). The prevalence of NAFLD in the general Japanese population was 25.5%,[96] in Chile about 23%, and 26.6% in the male in Colombia[97], and 25% in Asia,[8] 15% for adults, 2.1% for children.[98] The prevalence is relatively high in the Middle East, with 16.6% in Saudi Arabia,[11] 48.3% in Turkey,[99] and 33.9% in Iran.[100] In other studies, the prevalence of NAFLD in the general population is estimated at about 25%.[10,11,101]

Pooled prevalence in children and adults was 22.4% (10.9–33.9%) and 40.5% (35.1%–46%), respectively. One study in adults showed that the prevalence varied in the years of publication and the highest prevalence

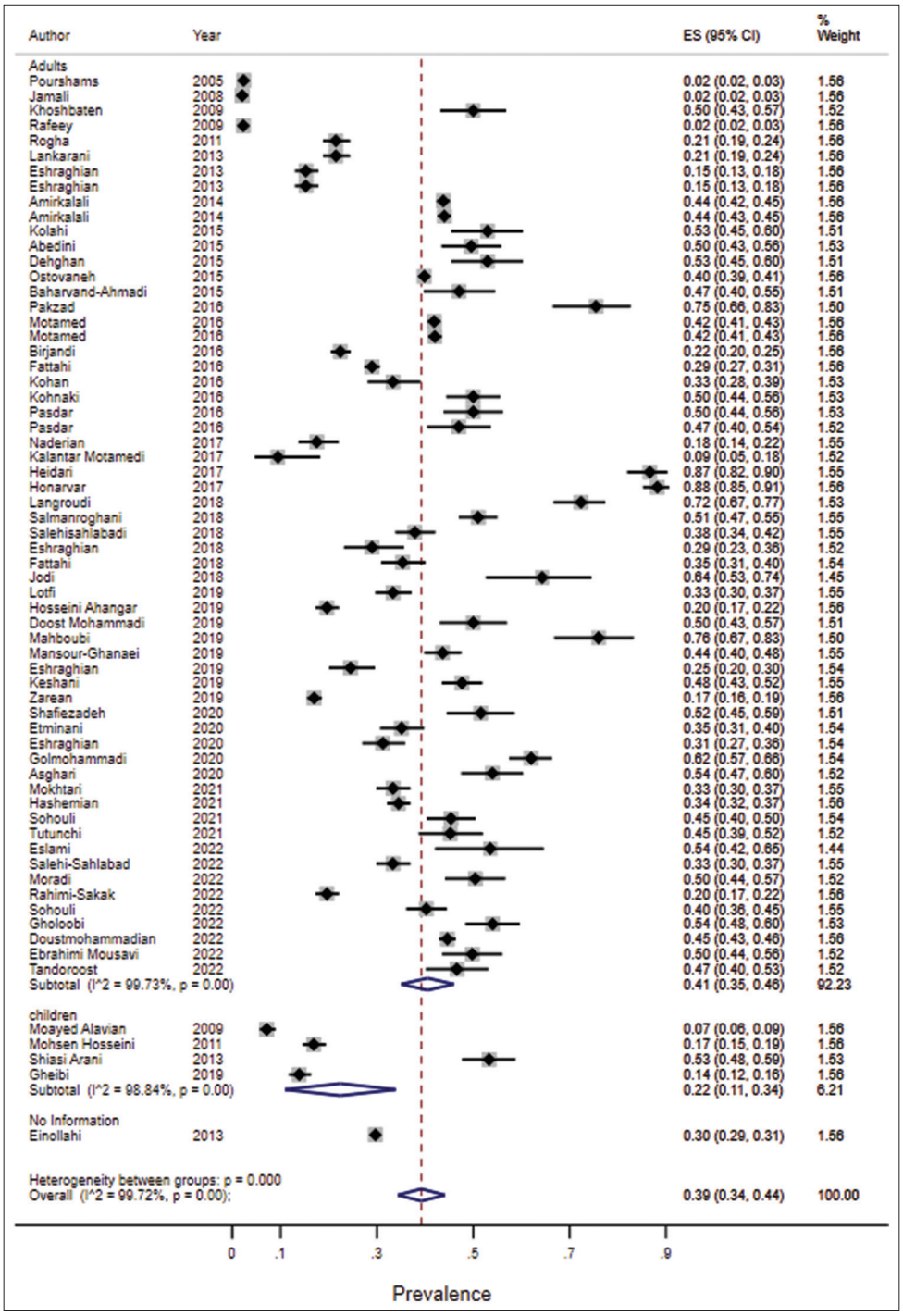

Figure 2: Estimates of the prevalence of NAFLD in Iranian's children and adults

was about 44.5%. Outbreaks appear to be exacerbated in Asia in the United States over the past 5 years, from 15% in 2005 to 25%.[102] Meta-analysis in Asia and Israel shows the incidence of the disease at 52 (95% CI: 28–97) and 28 (95% CI: 19–41) per 1,000 persons per year, respectively.[101] However, there was a significant difference in children.

The present review showed that age was associated with NFALD. The high prevalence of the disease in older people can be explained by the high prevalence of metabolic disorders in older people.[103]

In more studies, there was a significant relationship between NFALD and gender.[17,26,30,54,70,73,104,105] A study conducted in Turkey reported NAFLD related to the male gender more than females (64.0% for men vs. 29.6%).[99] In the Japanese population, the prevalence of NFALD is higher in men than in women (34.11% vs. 15.64%).[96]

Table 2: Met analysis of the prevalence of NAFLD in Iranian's adults and children

Variables	Adult				Children			
	n studies	Prevalence (95% CI)	*P* for difference	Residual I^2	*n* studies	Prevalence (95% CI)	*P* for difference	Residual I^2
Diagnostic method, total: 59						Total: 4		
One (only ultrasonography)	45	41.3 (35–47.7)	0.16	99.8%	2	22.5 (20.3–24.8)	0.001	98.8%
More than one	14	37.5 (30.9–44.2)			2	9.3 (8–10.7)		
Publication year, total: 60						Total: 4		
Lower 2010	4	8.7 (5.3–12.2)	0.001	%99.7	1	7.1 (5.7–8.9)	0.001	98.8%
2011-2015	11	36.3 (33.1–45.1)			2	22.5 (20.3–24.8)		
Over 2016	45	43.8 (29.2–43.5)			1	13.9 (11.7–16.4)		
Geographical area, total: 60						Total: 4		
Central*	23	39 (29.8–48.3)	0.35	99.9%	3	25.5 (8–42.9)	0.19	98.8%
West and Northwest	14	44.2 (32–56.4)			1	14 (11.7–16)		
North and Northeast	8	39.5 (22.3–56.7)			-	-		
South and Southeast	15	40 (29.8–50.3)			-	-		
Study sample size**, total: 60						Total: 4		
<Median	32	48.4 (42–54.8)	0.001	97.8%	1	53.3 (47.7–58.8)	0.001	98%
>Median	28	31.7 (24.1–39.2)			3	12.6 (6.5–18.7)		

*Central included Tehran and Isfahan, Kashan and Yazd, **Median study sample size in adult studies was *n*=485 and in children studies was *n*=887

Our study showed that more than two-thirds of studies used USG as a diagnostic method although the gold standard diagnostic test of liver biopsy[10]; only one study in this meta-analysis used biopsy; however, hepatic USG, computed tomography (CT), and MRI are accepted modalities for detecting hepatic fatty infiltration.[10] The use of ultrasound alone showed a higher prevalence than the combination of other methods. The prevalence using ultrasound in South America is estimated at 30.45%.[101]

In half of the published articles, there was a statistically significant relationship between NAFLD and fasting blood sugar NAFLD has been linked to obesity, insulin resistance, diabetes, hypertension, hepatitis, and metabolic syndrome.[9] A meta-analysis study showed that the incidence of diabetes in the non-obese NAFLD population was 12.6 per 1,000 years. Diabetes increases the burden of liver disease.[106] The prevalence of NAFLD in patients with diabetes is over 60%,[8,101,107,108] and another study showed more than three-quarters of diabetic patients have NAFLD.[109] The steps study showed that 10.85% of people have diabetes and only 56.87% of them take anti-hyperglycemic treatment.[110] The presence of type 2 diabetes appears to accelerate the course of NAFLD and predict advanced fibrosis and mortality.

In most studies, a significant relationship was seen with body mass index. NAFLD prevalence of Chinese obese children was 68.2%.[98] In one meta-analysis, the prevalence of the disease was associated with BMI. Also, 8.6% of people were overweight compared to 4.9% of people with normal BMI.[106] The global prevalence is estimated to be more than 40% in obese people and about 20% in non-obese people. The highest prevalence in non-obese people was in Europe (about 50%) and East Asia at about 38%[106] Previous studies have suggested an association between obesity and NAFLD.[11,108,111] In one meta-analysis, the prevalence in lean individuals is estimated at 10,[112] and in another meta-analysis at 10.[106]

Regarding the relationship between fat disorders and the prevalence of disease, more studies were significantly associated with an increase in triglycerides. Some studies related to HDL mentioned that 10 of the 18 studies were associated with TC. One study found that non-obese maples consumed more cholesterol and less unsaturated fatty acids than obese people.[113] Important issues raised in one meta-analysis study include the possibility of insulin resistance in non-obese individuals with NAFLD.[106] Almost 80% of adults in Iran have at least one lipid disorder in people with high cholesterol, 74.2% are aware of their lipid disorder, and only 22% and 36.5% have the desired levels of HDL and LDL.[114]

No significant relationship was found in most studies that examined the AST level. ALT was correlated in most studies. The mean serum ALT levels were higher in NAFLD patients in a Turkey study,[99] which is consistent with other meta-analysis studies in Iran.[17]

Seven out of sixteen studies in this meta-analysis showed a statistically significant relationship between NAFLD and smoking. The nationwide study of metabolic syndrome prevalence in Iran (steps study) showed that the standardized prevalence of current smoking among adult men and women was 24.4% and 3.8%, respectively.[110,115]

Our study is a comprehensive systematic review and meta-analysis of NAFLD for Iran including data from 71 studies. We also employed a meta-regression method to identify factors associated with NAFLD.

We recognize several limitations. Our study included 71 studies and the distribution of these studies is not uniform in the country, thus further studies from other areas are needed. In all studies, variables and risk factors have not been fully investigated.

Conclusion

Iran has a high NAFLD prevalence compared to most areas, and due to the unfavorable situation of risk factors contributing to NAFLD, such as cholesterol, high-level triglycerides in the blood, metabolic syndrome, obesity, particularly when fat is concentrated, and type 2 diabetes, it is necessary to take the necessary interventions to control these risk factors and prevent the NAFLD.

Ethics approval

This study was supported by Kurdistan University of Medical Sciences, and confirmed by the ethics committee of this university (Ethics code: IR.MUK.REC.1401.262).

Readers can access to supplementary files 1 and 2 through contact with the correspond author.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Quality assessment of studies included in meta-analysis of Prevalence of non-alcoholic fatty liver in Iran

Id	First author	Publication year	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Total	Overall appraisal
1	Pourshams 25	2005	1	1	1	1	1	1	1	1	1	9	High
2	Jamali 26	2008	1	1	1	1	1	1	1	1	1	9	High
3	Moayed Alavian 28	2009	1	1	1	1	1	1	1	1	1	9	High
4	Khoshbaten 29	2009	1	1	1	1	1	1	1	1	1	9	High
5	Rafeey 27	2009	1	1	1	1	1	1	1	0.5	1	8.5	High
6	Mohsen Hosseini 30	2011	1	1	1	1	1	0.5	1	1	1	8.5	High
7	Bagheri Lankarani 32	2013	1	1	1	1	1	0.5	1	0.5	1	8	High
8	Shiasi Arani 31	2013	1	1	1	1	1	1	1	0.5	1	8.5	High
9	Rogha 58	2013	0	0.5	1	1	1	1	0.5	0.5	0	5.5	Moderate
10	Eshraghian 60	2013	1	1	1	1	0	1	1	0.5	0	6.5	Moderate
11	Abangah 34	2013	0.5	1	1	1	1	1	1	1	1	8.5	High
12	Einollahi 35	2013	1	1	1	1	1	1	1	0.5	1	8.5	High
13	Amirkalali 36	2014	1	1	1	1	1	1	1	1	1	9	High
14	Amirkalali 37	2014	1	1	1	1	1	1	1	1	1	9	High
15	Kolahi 39	2015	0.5	0.5	1	1	1	0	0	0.5	0	4.5	Low
16	Dehghan 38	2015	1	0	0.5	1	0.5	0.5	1	1	1	6.5	Moderate
17	Ostovaneh 40	2015	1	1	1	1	1	1	1	1	0.5	8.5	High
18	Abedini 41	2015	0	0	0	1	0.5	1	1	1	0.5	5	Low
19	Baharvand-Ahmadi 42	2015	0.5	0.5	0.5	1	1	1	1	1	1	7.5	Moderate
20	Motamed 43	2016	1	1	1	1	1	1	1	1	1	9	High
21	Motamed 44	2016	1	0.5	1	1	1	0.5	1	1	0.5	7.5	Moderate
22	Pakzad 51	2016	0.5	0.5	0	1	0	0.5	0.5	0.5	0	3.5	Low
23	Pasdar 49	2016	1	1	1	1	1	0	0	1	0.5	6.5	Moderate
24	Pasdar 50	2016	1	1	1	1	1	0	0	1	0.5	6.5	Moderate
25	Kohnaki 48	2016	1	0.5	1	1	1	0	0	0.5	0.5	5.5	Moderate
26	Birjandi 47	2016	1	1	1	1	1	1	1	1	1	9	High
27	Kohan 46	2016	1	1	1	1	1	0.5	0.5	1	0.5	7.5	Moderate
28	Fattahi 45	2016	1	0.5	1	1	1	1	1	0.5	0.5	7.5	Moderate
29	Mohseni 52	2017	1	1	1	1	0.5	1	1	0.5	0.5	7.5	Moderate
30	Motamedi 55	2017	0.5	0	0	1	0.5	1	1	1	0	5	Low
31	Mehrabian 53	2017	0.5	0.5	0.5	1	1	1	1	1	0.5	7	Moderate
32	Heidari 54	2017	0.5	0.5	1	1	1	1	1	1	1	8	High
33	Honarvar 56	2017	0	0	0.5	1	1	0.5	0.5	0.5	0	4	Low

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Supplementary Table 1: Contd...

Id	First author	Publication year	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Total	Overall appraisal
34	Naderian 57	2017	1	1	1	1	1	1	1	0.5	1	8.5	High
35	Fattahi 45	2018	1	1	1	1	1	1	1	1	0.5	8.5	High
36	Langroudi 61	2018	0.5	0	0.5	0.5	1	1	1	0.5	0.5	5.5	Moderate
37	Eshraghian 60	2018	0.5	0.5	0.5	1	1	1	1	1	0.5	7	Moderate
38	Jodi 59	2018	0	0.5	0.5	1	1	1	0.5	1	1	6.5	Moderate
39	Salehisahlabadi 62	2018	0.5	0.5	0.5	1	1	1	1	1	1	7.5	Moderate
40	Mahboubi 64	2019	1	0.5	1	0.5	0.5	0.5	0	0.5	0.5	5	Low
41	Doost Mohammadi 65	2019	1	1	1	1	1	1	1	1	0	8	High
42	Zarean 66	2019	1	1	1	1	0.5	0.5	0.5	0.5	0	6	Moderate
43	Lotfi 67	2019	1	1	1	1	1	0.5	0.5	1	0.5	7.5	Moderate
44	Gheibi 68	2019	0	0	0.5	1	1	1	1	0.5	0.5	5.5	Moderate
45	Keshani 69	2019	1	1	1	1	1	1	1	1	1	9	High
46	Hosseini Ahangar 70	2019	0	0	0.5	0.5	0.5	1	1	0.5	1	5	Low
47	Mansour-Ghanaei 72	2019	0	0	1	1	1	1	1	1	1	7	Moderate
48	Shafiezadeh 73	2020	1	1	1	1	1	0	1	0.5	1	7.5	Moderate
49	Eshraghian 71	2020	0.5	0.5	0.5	0.5	0.5	0.5	1	1	1	6	Moderate
50	Eshraghian 74	2020	0.5	0	0	1	1	0.5	1	0.5	0.5	5	Low
51	Asghari 75	2020	1	1	1	1	0.5	1	1	1	0.5	8	Moderate
52	Golmohammadi 76	2020	0.5	1	1	1	0.5	0	0	0.5	0.5	5	Low
53	Etminani 77	2020	0.5	0.5	0.5	1	1	1	1	1	0	6.5	Moderate
54	Motamed 78	2020	1	1	1	1	0.5	1	1	1	0.5	8	High
55	Motamed 79	2020	1	0.5	1	1	0.5	1	1	1	0.5	7.5	Moderate
56	Fatahi 80	2021	0	0	0	1	1	1	1	1	0.5	5.5	Moderate
57	Hashemian 81	2021	1	1	0	1	1	1	1	1	0.5	7.5	Moderate
58	Mokhtari 82	2021	0	0	0	1	1	1	1	1	0.5	5.5	Moderate
59	Sohouli 83	2021	0	1	0	0	1	1	1	1	0.5	5.5	Moderate
60	Tutunchi 84	2021	0.5	0.5	0	0	1	1	1	1	0.5	5.5	Moderate
61	Tutunchi 85	2021	0	0	0	0	1	1	1	1	0.5	4.5	Low
62	Eslami 87	2022	0	0	0	1	1	1	1	1	0.5	5.5	Moderate
63	Farhadnejad 86	2022	0	0	0	1	1	1	1	1	0.5	5.5	Moderate
64	Gholoobi 88	2022	0	0	0	0	1	1	1	1	0.5	4.5	Low
65	Moradi 89	2022	0.5	0	0	0	1	1	1	1	0.5	5	Low
66	Rahimi-Sakak 90	2022	0	0	0	0	0	1	1	1	1	4	Low

Contd...

Supplementary Table 1: Contd...

Id	First author	Publication year	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Total	Overall appraisal
67	Salehi-Sahlabadi 91	2022	0.5	1	0	1	1	1	1	1	0.5	7	Moderate
68	Tandoroost 92	2022	0.5	0	0.5	1	1	1	1	1	1	7	Moderate
69	Sohouli 93	2022	0	0	1	1	1	1	1	1	0.5	6.00	Moderate
70	Doustmohammadian 94	2022	1	1	1	1	1	1	1	1	1	9.00	High
71	Ebrahimi Mousavi 95	2022	0	0	0	1	1	1	1	1	0.5	6	Moderate

Supplementary Table 2: Risk factors related with NAFLD prevalence in Iran

ID	First name	Publication	BMI	BPD	BPS	AST	ALT	ALP	TG	FSG***	HOMA	LDL
1	Pourshams 25	2005	<0.001	_	_	_	_	_	_	_	_	_
2	Jamali 26	2008	0.001	_	_	_	_	_	_	_	_	_
3	Rafeey 27	2009	_	_	_	_	_	_	_	_	_	_
4	Khoshbaten 29	2009	0.004	_	0.0005	_	_	_	0.0005	NS	_	NS
5	Moayed Alavian 28	2009	<0.001	_	NS	_	<0.001	_	<0.001	NS	_	<0.001
6	Mohsen Hosseini 30	2011	0.000005	_	_	_	_	_	0.01	_	_	_
7	Eshraghian 33	2013	<0.001	NS	NS	_	0.001	_	_	_	_	_
8	Einollahi 35	2013	_	_	_	_	_	_	_	_	_	_
9	Abangah 34	2013	_	_	_	NS	NS	_	0.01	_	_	_
10	Bagheri Lankarani 32	2013	<0.001	<0.001	<0.001	_	_	_	<0.001	0.001	_	NS
11	Shiasi Arani 31	2013	<0.001	<0.001	<0.001	_	_	_	<0.001	_	0.001	NS
12	Amirkalali 36	2014	<0.001	NS	NS	<0.001	<0.001	_	NS	<0.001	<0.001	_
13	Amirkalali 37	2014	NS	-	-	-	<0.001		<0.001	<0.001	<0.001	-
14	Dehghan 38	2015	<0/001	_	_	_	_	_	_	_	_	_
15	Kolahi 39	2015	<0.001	_	_	_	_	_	_	_	_	_
16	Ostovaneh 40	2015	<0.001	<0.001	<0.001	<0.001	<0.001	_	<0.001	<0.001	<0.001	<0.001
17	Abedini 41	2015	<0.001	<0.01	<0.01	_	_	_	<0.001	_	_	<0.001
18	Baharvand-Ahmadi 42	2015	0.005	NS	NS	_	_	_	_	_	_	NS
19	Motamed 43	2016	_	_	_	_	_	_	_	_	NS	_
20	Motamed 44	2016	<0.0001	_	_	_	_	_	_	_	_	_
21	Fattahi 45	2016	_	_	_	_	_	_	_	_	_	_
22	Kohan 46	2016	0.01	_	_	_	_	_	_	_	_	_
23	Pakzad 51	2016	<0/001	_	_	0.001	<0/001	_	0.004	<0/001	_	0.015
24	Pasdar 49	2016	<0.05	_	_	_	_	_	_	<0.05	_	_
25	Birjandi 47	2016	<0.001	<0.001	<0.001	<0.001	<0.001	_	<0.001	<0.001	_	_
26	Kohnaki 48	2016	NS	NS	NS	NS	0.002	NS	0.04	_	-	NS
27	Pasdar 50	2016	<0.001	NS	NS	_	_	_	<0.001	_	_	_
28	Mohseni 52	2017	NS	_	_	<.001	<0.001	_	0.04	NS	-	NS
29	Naderian 57	2017	0.022	_	0.04	_	_	_	<.010	_	_	_
30	Honarvar 56	2017	<0.001	_	_	_	_	_	_	_	_	_
31	Motamedi 55	2017	_	_	_	<0.05		_	_	_	_	_
32	Heidari 54	2017	NS	NS	NS	NS	NS	_	<0.001	NS	_	<0.001
33	Mehrabian 53	2017	NS	NS	NS	NS	0.005	NS	NS	0.03	_	_
34	Salmanroghani 58	2018	_	_	_	_	_	_	_	_	_	_
35	Jodi 59	2018	0.002	_	_	0.002	NS	_	_	_	_	_
36	Salehisahlabadi 62	2018	<0.001	_	_	_	_	_	_	_	_	_
37	Eshraghian 60	2018	0.005	NS	_	_	<0.001	_	_	_	_	_
38	Langroudi 61	2018	NS	NS	NS	_	_	_	_	_	_	_
39	Fattahi 63	2018	<0.05	<0.05	<0.05	_	_	_	_	_	_	_
40	Doost Mohammadi 65	2019	_	_	_	_	_	_	_	_	_	_
41	Gheibi 68	2019	NS	_	_	<0.0001	<0.0001	<0.0001	<0.0001	_	0.02	NS
42	Hosseini Ahangar 70	2019	<0.001	_	_	_	_	_	_	_	_	_
43	Keshani 69	2019	0.03	_	NS	_	_	_	NS	_	_	NS
44	Lotfi 67	2019	<0.001	_	_	_	_	_	_	_	_	_
45	Mahboubi 64	2019	<0/001	_	_	_	_	_	_	_	_	_
46	Mansour-Ghanaei 72	2019	_	_	_	_	_	_	_	_	_	_
47	Zarean 66	2019	<0.001	<0.001	<0.001	NS	<0.001	_	<0.001	NS	_	_
48	Motamed 78	2020	<0.001	_	_	_	_	_	_	_	_	_
49	Asghari 75	2020	_	_	_	<0.0001	<0.0001	<0.0001	_	_	_	NS
50	Eshraghian 71	2020	0.009	_	_	_	_	_	_	_	_	_
51	Eshraghian 74	2020	0.011	_	_	_	NS	NS	NS	_	_	0.04
52	Golmohammadi 67	2020	_	_	_	_	_	_	_	_	_	_
53	Shafiezadeh 73	2020	_	_	_	_	_	_	_	_	_	_
54	Motamed 79	2020	0.001	_	_	_	_	_	NS	_	NS	NS
55	Etminani 77	2020	<0.001	NS	NS	_	<0.01	_	NS	0.01	_	_

Contd...

Supplementary Table 2: Contd...

ID	First name	Publication	BMI	BPD	BPS	AST	ALT	ALP	TG	FSG***	HOMA	LDL
56	Fatahi 80	2021	<0.001	_	_	NS	<0.001		<0.001	_	_	<0.001
57	Hashemian 81	2021	_	_	_	_	_	_	_	_	_	_
58	Mokhtari 82	2021	0.006	_	_	_	_	_	_	_	_	_
59	Sohouli 83	2021	<0.001	_	_	NS	<0.001		0.001	_	_	<0.001
60	Tutunchi 84	2021	<0.001	NS	NS	NS	<0.001	_	<0.001	_	<0.001	NS
61	Tutunchi 85	2021	<0.001	_	_	_	_	_	<0.001	_	_	NS
62	Eslami 87	2022	<0.001	NS	NS	NS	0.005	NS	0.003	_	_	NS
63	Farhadnejad 86	2022	NS	_	_	_	_	_	_	_	_	_
64	Gholoobi 88	2022	0.001	_	_	_	_	_	_	_	_	_
65	Moradi 89	2022	0.001	_	_	_	_	_	-	_	_	-
66	Rahimi-Sakak 90	2022	0.001	_	_	_	_	_	-	_	_	-
67	Salehi-Sahlabadi 91	2022	NS	_	_	_	_	_	-	_	_	-
68	Tandoroost 92	2022	0.001	_	_	_	_	_	-	_	_	-
69	Sohouli 93	2022	0.001	-	-	NS	0.001	-	0.001	0.001	_	0.007
70	Doust mohammadian 94	2022	<0.001	<0.001	<0.001	<0.001	<0.001	_	<0.001	_	_	<0.001
71	Ebrahimi Mousavi 95	2022	NS	NS	NS	_	_	_	_	_	_	_

ID	First name	HDL	TC**	Met*	Fast food use/ High total red meat consumption	Age	Marital status	Physical activity	FBS	Sex	Smoking
1	Pourshams 25	_	_	_	_	_	_	_	_	_	_
2	Jamali 26	_	_	_	_	_	_	_	_	0.001	_
3	Rafeey 27	_	_	_	_	_	_	_	_	_	_
4	Khoshbaten 29	NS	NS	_	_	NS	_	_	_	_	_
5	Moayed Alavian 28	NS	<0.001	_	_	_	_	_	_	_	_
6	Mohsen Hosseini 30	_	_	_	_	0.000001	_	_	_	0.04	_
7	Eshraghian 33	_	_	<0.001	_	NS	_	_	_	_	0.007
8	Einollahi 35	_	_	_	_	_	_	_	_	_	_
9	Abangah 34	_	0.06	_	_	_	_	_	NS	NS	_
10	Bagheri Lankarani 32	NS	0.03	<0.001	_	<0.001	_	_	_	0.004	_
11	Shiasi Arani 31	0.001	NS	_	0.012		_	_	NS	_	_
12	Amirkalali 36	<0.001	<0.001	<0.001	_	NS	_	_	_	_	_
13	Amirkalali 37	<0.001	0.001	_	_	<0.001	_	_	_	NS	_
14	Dehghan 38	_	_	_	_	_	0.04	0.001	_	NS	NS
15	Kolahi 39	_	_	_	0.01	_	0.04	_	_	NS	NS
16	Ostovaneh 40	<0.001	<0.001	<0.001	_	<0.001	_	_	_	_	_
17	Abedini 41	<0.01	<0.01	0.001	_	NS	_	_	<0.001	NS	NS
18	Baharvand-Ahmadi 42	_	_	_	_	NS	_	_	_	NS	NS
19	Motamed 43	NS	_	_	_	<0.001	_	_	_	0.003	_
20	Motamed 44	_	_	_	_	_	_	_	_	_	_
21	Fattahi 45	_	_	_	_	_	_	_	_	_	_
22	Kohan 46	_	_	_	_	_	_	_	_	_	_
23	Pakzad 51	NS	0.001	_	_	0.03	_	NS	<0.001	_	_
24	Pasdar 49	_	_	_	_	NS	_	<0.05	_	NS	_
25	Birjandi 47	<0.001	<0.001	_	_	<0.001	<0.001	_	_	NS	NS
26	Kohnaki 48	NS	NS	_	_	_	NS	NS	NS	_	_
27	Pasdar 50	_	_	<0.001	_	_	_	_	NS	_	_
28	Mohseni 52	NS	NS	_	_	_	_	_	_	_	_
29	Naderian 57	_	_	_	_	_	_	_	_	_	_
30	Honarvar 56	_	_	_	NS	<0.001	0.008	_	_	0.004	_
31	Motamedi 55	_	_	_	_	<0.05	_	_	_	_	_
32	Heidari 54	NS	NS	_	_	NS	_	_	_	<0.001	_
33	Mehrabian 53	_	_	NS	_	_	_	_	_	_	_
34	Salmanroghani 58	_	_	_	_	_	_	_	_	_	_

Contd...

Supplementary Table 2: Contd...

ID	First name	HDL	TC**	Met*	Fast food use/ High total red meat consumption	Age	Marital status	Physical activity	FBS	Sex	Smoking
35	Jodi 59	_	_	_	_	_	_	_	NS	NS	_
36	Salehisahlabadi 58	_	_	_	_	_	_	_	_	<0.001	_
37	Eshraghian 60	_	_	<0.001	_	_	_	_	_	_	NS
38	Langroudi 61	NS	_	_	_	NS	_	_	_	NS	_
39	Fattahi 63	_	_	_	_	S	_	_	_	<0.05	<0.05
40	Doost Mohammadi 65	_	_	_	<0.05	_	_	_	_	_	_
41	Gheibi 68	<0.0001	<0.0001	_	_	NS	_	_	<0.0001	NS	_
42	Hosseini Ahangar 70	_	_	_	_	<0.001	_	_	_	<0.001	_
43	Keshani 69	_	_	_	_	NS	NS	_	NS	_	_
44	Lotfi 67	_	_	_	_	_	_	<0.001	_	_	0.03
45	Mahboubi 64	_	_	_	_	NS	_	_	_	_	_
46	Mansour-Ghanaei 72	_	_	_	_	_	_	0.01	_	_	_
47	Zarean 66	NS	S	<0.001	_	NS	_	<0.001	_	NS	_
48	Motamed 78	_	_	_	_	_	_	_	_	_	_
49	Asghari 75	_	_	_	_	_	_	_	_	_	_
50	Eshraghian 71	_	_	_	_	NS	_	_	_	_	_
51	Eshraghian 74	_	NS	_	_	_	_	_	_	_	_
52	Golmohammadi 76	_	_	_	_	_	_	_	_	_	_
53	Shafiezadeh 73	_	_	_	_	0.001	_	_	_	0.04	_
54	Motamed 79	NS	_	_	_	Men: 0.002, Women: NS	Men: NS, Women: 0.003	_	_	_	_
55	Etminani 77	_	NS	NS	_	_	_	_	_	_	_
56	Fatahi 80	0.01	<0.001	<0.001	_	_	_	0.001	<0.001		
57	Hashemian 81	_	_	_	0.03	_	_	_	_	_	_
58	Mokhtari 82	_	_	_	NS	NS	_	_	_	NS	0.006
59	Sohouli 83	0.01	<0.001		<0.001	NS	_	_	0.001	NS	-
60	Tutunchi 84	0.001	NS	_	_	NS	_	<0.001	0.003	NS	_
61	Tutunchi 85	<0.001	NS	_	_	NS	NS	0.003	_	NS	NS
62	Eslami 87	NS	NS	_	_	_	_	_	0.05		-
63	Farhadnejad 86	_	_	_	_	_	_	_	_		
64	Gholoobi 88	_	_	_	_	_	_	_	_	NS	-
65	Moradi 89	-	-	_	_	_	_	NS	_	NS	NS
66	Rahimi-Sakak 90	-	-	-	0.001	_	_	0.001	_	_	_
67	Salehi-Sahlabadi 91	-	-		0.006	_	_		_	_	_
68	Tandoroost 92	-	-	-	_	_	_	NS	_	_	NS
69	Sohouli 93	0.001	NS	-	_	_	_	0.001	_	0.001	0.007
70	Doustmohammadian 94	<0.001	<0.001	<0.001	_	<0.001	_	_	<0.001	_	0.008
71	Ebrahimi Mousavi 95	_	_	_	0.005	NS	NS	0.04		NS	0.03

*Metabolic syndrome. **Total cholesterol. ***Fasting Serum Glucose (FSG)