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PREVALENCE AND MANAGEMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN INDIA: A META-ANALYSIS

Internal Medicine

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ABSTRACT

Electronic databases were searched for English-language literature published up until April 2021. Included were original data, published in whatever format, that documented the prevalence of NAFLD in the Indian population. Age (adults or children) and risk category—that is, average-risk group (community population, control arm participants, unselected participants, hypothyroidic individuals, athletes, aviation crew, and army personnel) and high-risk group (obesity or overweight, diabetes mellitus, coronary artery disease, etc.)—were the basis for the subgroup analysis of prevalence. The random-effects model was used to pool the prevalence estimates. I2 was used to evaluate heterogeneity. **Results:** There were sixty-two datasets from fifty research (children aged eight and adults aged fifty-four). Estimates of the combined prevalence of NAFLD from 23,581 adult and 2903 children participants were made. The estimated pooled prevalence among adults was 38.6% (95% CI 32–45.5). The estimated prevalence of NAFLD in the high-risk and average-risk subgroups was 52.8% (95% CI 46.5–59.1) and 28.1% (95% CI 20.8–36), respectively. A significant amount of the global liver disease burden is caused by non-alcoholic fatty liver disease (NAFLD). The prevalence of NAFLD in the Indian population has been investigated by a number of groups. Goal: To determine the prevalence of NAFLD in the population, a meta-analysis and systematic review of the published literature were conducted. **Methods:** Electronic databases were searched for English-language literature published up until April 2021. Included were original data, published in whatever format, that documented the prevalence of NAFLD in the Indian population. Age (adults or children) and risk category—that is, average-risk group (community population, control arm participants, unselected participants, hypothyroidic individuals, athletes, aviation crew, and army personnel) and high-risk group (obesity or overweight, diabetes mellitus, coronary artery disease, etc.)—were the basis for the subgroup analysis of prevalence. The random-effects model was used to pool the prevalence estimates. I2 was used to evaluate heterogeneity. Results: There were sixty-two datasets from fifty research (children aged eight and adults aged fifty-four). Estimates of the combined prevalence of NAFLD from 23,581 adult and 2903 children participants were made. The estimated pooled prevalence among adults was 38.6% (95% CI 32–45.5). The estimated prevalence of NAFLD in the high-risk and average-risk subgroups was 52.8% (95% CI 46.5–59.1) and 28.1% (95% CI 20.8–36), respectively.

KEYWORDS

Barrett's Oesophagus, high-grade dysplasia, low grade dysplasia, gastro-oesophageal reflux disease

INTRODUCTION

In the absence of excessive alcohol consumption, non-alcoholic fatty liver disease (NAFLD) is a prevalent disorder marked by an excess of fat in the liver, ranging from simple steatosis to cirrhosis, hepatocellular carcinoma (HCC), and steatohepatitis.[1] NAFLD is predisposed to metabolic syndrome and related disorders such as diabetes, obesity, and dyslipidemia.[2] As the prevalence of obesity and type II diabetes rises, NAFLD is becoming as a significant public health issue.[3] In Western nations, the total prevalence of NAFLD ranges from 15 to 40%, but in Asian nations, it ranges from 9 to 40%.[1] The data from Asian nations came from a variety of published series, and the population and definition of NAFLD were not consistent. In western nations, nonalcoholic fatty liver disease (NAFLD) is a common cause of chronic liver disease requiring liver transplantation.[4] Asian nations like China and Japan have a well-documented rising incidence of NAFLD.[5] Obesity, hyperinsulinemia, and diabetes mellitus (DM) are risk factors for non-alcoholic fatty liver disease. Over the past 20 years, India has seen an increase in the prevalence of diabetes mellitus, obesity, and insulin resistance.[6,7] Therefore, it becomes sense to anticipate that the incidence of NAFLD in India will rise. The prevalence of NAFLD in India is not well documented.[8,9] The majority of the data is derived from research conducted in hospitals with a limited patient population.

METHODS

Design: For the study, we adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

Search Strategy: We looked through electronic databases such as Google Scholar, Embase, Scopus, and Pubmed/Medline. The different phrases for fatty liver disease, state names, and the names of the nation's largest cities were all part of the search approach. To find the extra material, cross-references from the published publications were manually searched.

Inclusion And Exclusion Criteria: Any original data on the prevalence of fatty liver disease in the Indian community, whether in the form of original publications, letters to the editor, brief communications, or short reports, was considered for inclusion in the research. Abstracts, review articles, and literature written in languages other than English were not included. The studies that used ultrasound as the imaging modality to report the prevalence of NAFLD in India were chosen for data extraction and analysis. We included the reported prevalence based on ultrasound in studies that reported the prevalence of NAFLD based on various modalities.

Study Participants: Patients of all ages were included. Studies showing the prevalence of NAFLD in high-risk groups, such as those with obesity, diabetes, and metabolic syndrome, were also included.

Data Extraction: Author name, year of publication, study design, sample size, participant age group (18 years), study setting, number of study centers, study population characteristics, participant risk category, residence, and diagnostic criteria used for NAFLD diagnosis were all taken from the studies. The study population was divided into two categories: high-risk (obesity or overweight, prediabetes, diabetes mellitus, coronary artery disease, metabolic syndrome, obstructive sleep apnea, women with polycystic ovarian syndrome, and people with elevated liver enzymes) and average-risk (community population, control arm participants, unselected participants, hypothyroidic individuals, athletes, aviation crew, and army personnel).

Quality Assessment Of The Studies: A modified checklist for studies providing prevalence data was used to evaluate the quality of the included research. Ten questions covering various methodological quality aspects of a prevalence survey are included in the checklist. Each question's response was classified as either "Low Risk" or "High Risk." Poor, moderate, and high quality were the three categories used to evaluate each study's overall quality.

Statistical Analysis: 95% CIs were used to summarize the proportions of NAFLD prevalence data from individual studies. I 2 statistics were used to evaluate the heterogeneity between trials. The I2 statistic (I2 $ 50%) was used to determine whether significant heterogeneity was present. Due to significant heterogeneity among research, the prevalence estimates from individual studies were combined using a random-effects model. Using funnel plots and Egger's test, publication bias was evaluated. Version 28 of IBM SPSS software was used to analyze the data. Age group, gender, risk category, and urban/rural populations were also subjected to subgroup analysis.

RESULTS

In general 50 papers [9–59] that reported the prevalence of NAFLD in

adults (n = 54) and children (n = 8) were found through the literature search. 2903 children were included in the pediatric data, which were gathered either at a hospital (n = 4) or at school (n = 4). Only eight states and/or Union Territories (UTs) were included in the pediatric investigations. According to Figure 2, the combined estimates of the prevalence of NAFLD were 35.4% (95% CI 18.2–54.7; I[2] 99%). A high prevalence of non-alcoholic fatty liver disease (NAFLD) in children can be explained by the fact that 560 children (560/2903; 19.3%) were included in four data points. The pooled estimate for children who were not obese and those who were obese, according to subgroup analysis, was 12.4 (95% CI 4.4–23.5) and 63.4 (95% CI 59.4–67.3), respectively. The prevalence of NAFLD was 36.8% (95% CI 14.6–62.5%; I2 99.2%) in school-based data and 33.8% (95% CI 8–66.5%; I2 98.4%) in hospital-based data. Estimates of the prevalence of NAFLD by gender were calculated using data from four investigations (n = 2336). The prevalence of NAFLD was 37.1% (95% CI 15.3–62.1; I[2] 98.3%) for females and 36.8% (95% CI 13–64.6; I[2] 98.6%) for boys.

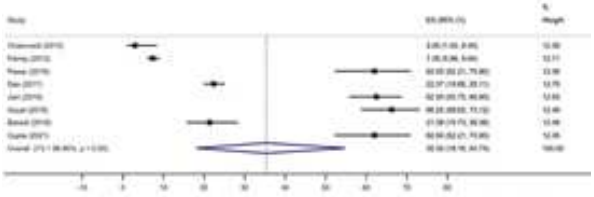

Fig 1: Pooled estimates of NAFLD prevalence by the random effects model in children

NAFLD in Adults: Either the community (n = 9) or the hospital (n = 45) provided the prevalence data for the adult population. The majority of the adult data (n = 47) came from the urban population. A total of 23,581 people participated in the survey. Delhi 12, Tamil Nadu 10, Haryana 6, West Bengal 5, Uttar Pradesh, and Maharashtra each had four studies, Karnataka three, Kerala two, and Andhra Pradesh, Chandigarh, Odisha, Puducherry, Rajasthan, Uttarakhand, and Jammu & Kashmir one each were among the 15 states/UTs where the single-center studies were carried out. Multicentricity was present in one investigation. The adult population's overall pooled estimate of NAFLD prevalence was 38.6% (95% CI 32–45.5; I[2] 99.1%) (Figure 3). Using data on gender distribution from 16 datasets (n = 10,282), the gender-specific prevalence of NAFLD was calculated. For males, the prevalence of NAFLD was 39.4% (95% CI 27.7–51.7%; I[2] 98.5%), while for females, it was 35.4% (95% CI 23.5–48.3%; I[2] 98.5%). According to research conducted in hospitals and communities, the estimated prevalence of NAFLD was 40.8% (95% CI 32.6–49.3%; I[2] 98.9%) and 28.2% (95% CI 16.9–41%; I[2] 99.4%), respectively. The prevalence of NAFLD was 52.8% (95% CI 46.5–59.1; I[2] 93.8%) in the high-risk (Figure 5) and average-risk (Figure 4) subgroups, respectively, and 28.1% (95% CI 20.8–36.0; I[2] 99.2%). The prevalence of NAFLD was 40.0% (95% CI 32.4–48; I[2] 98.3%) in the urban population and 29.2% (95% CI 17.8–42; I[2] 99.1%) in the rural population. The prevalence of NAFLD in ordinary and high-risk groups, according to subgroup analysis of data from urban populations, was 27.8% (95% CI 18.3–38.3; I[2] 99.3%) and 52.8% (95% CI 46.5–59.1; I[2] 93.8%), respectively.

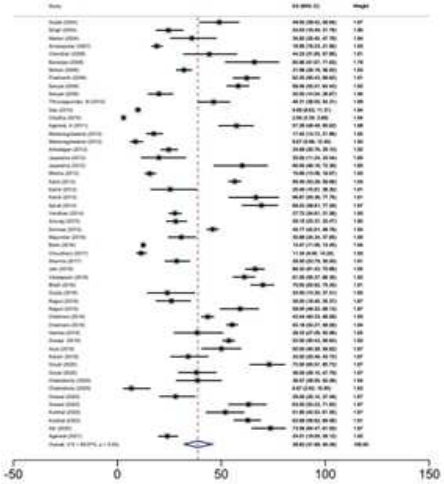

Fig 2: Pooled estimates of NAFLD prevalence by the random-effects model in adults.

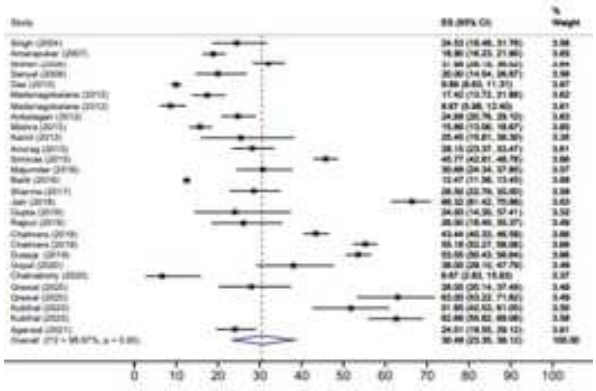

Fig 3: Pooled estimates of NAFLD among average-risk adults.

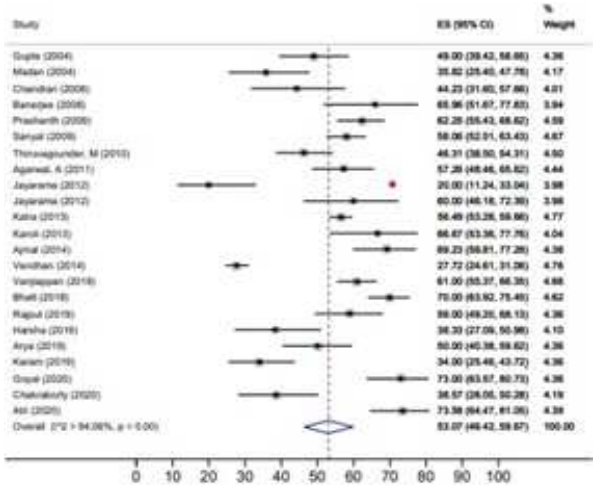

Fig 4: Pooled estimates of NAFLD among high-risk adults

DISCUSSION

In India, the combined prevalence of NAFLD in adults is 38.6%, while in children it is 35.4%. For both males and females, the prevalence is comparable. According to our data, both urban and rural populations in India had a greater incidence of NAFLD than the average predicted global prevalence of 25%.

In India, the overall pooled prevalence of non-alcoholic fatty liver disease (NAFLD) among children under the age of 18 was 35.4% (95% CI: 18.2-54.7%), and the prevalence was same for both boys and girls. Children who were obese had a pooled prevalence of NAFLD of about 60%, which was five times higher than that of children who were not obese. However, a recent worldwide meta-analysis found that the prevalence of NAFLD was greater among Asian obese children, with estimates of 7.6% (95% CI: 5.5-10.3%) among children in the general population and 34.2% (95% CI: 27.8-41.2%) among those being followed up with in obesity clinics.[60] The high prevalence may be explained by the fact that one-fifth of the young people included in our analysis were obese or overweight. Significant heterogeneity among the included studies and sample bias are two other potential explanations for this. There was no discernible difference in the prevalence of NAFLD between studies carried out in hospital settings (33.8%, 95% CI 8-66.5%) and schools (36.8%, 95% CI 14.6-62.5%). India is a young nation; according to the 2011 census, 354 million people, or 29.5% of the 1.2 billion people, were under the age of 15, while another 121 million were between the ages of 15 and 19. The findings of our study indicate that there are almost 168 million children with NAFLD in India alone, if extended to the total population. About 20% of kids and teenagers are overweight or obese, and this number is rising for both high and low socioeconomic categories.[61] Because weight gain throughout school years poses a larger risk of non-alcoholic fatty liver disease (NAFLD) than weight gain in late adulthood, the potential dangers associated with obesity are concerning.[62] The percentage of individuals in India who have NAFLD may continue to climb over the coming decades because the

condition is more common as people age.[63] From the standpoint of public health, these forecasts are crucial.

The estimated pooled prevalence of NAFLD in adults was 38.6%, according to our research. As predicted by the literature, the prevalence of NAFLD rose from average-risk to high-risk subgroups.[64] NAFLD is linked to a number of other conditions that are steadily rising in both rural and urban areas of India, including diabetes, obesity, metabolic syndrome, hypertension, dyslipidemia, coronary artery disease, obstructive sleep apnea, and hypothyroidism.[65–67] There is a correlation between physical exercise and a lower risk of NAFLD.[68]

The prevalence of NAFLD in males (39.4%; 95% CI 51.7%) and females (35.4%; 95% CI 23.5-48.3%) did not differ significantly, according to our data. In contrast, women are more likely to develop advanced fibrosis but had a lower incidence of NAFLD, according to a global meta-analysis.[69] It's interesting to note that NAFLD prevalence was 40.0% in urban areas and 29.2% in rural areas. Forty of the studies that were included of our meta-analysis were hospital-based, four were community-based, and 44/50 (88.0%) were from the urban cohort. On the other hand, 6/50, which comprised 2 hospital-based and 4 community-based, were from the rural cohort. The prevalence of NAFLD in both urban and rural cohorts has been evaluated concurrently in relatively few studies.[43] Studies conducted in hospitals had a greater prevalence of NAFLD than those conducted in communities (40.8%, 95% CI 32.6-49.3% versus 27.2%, 95% CI 40.6%, respectively). This might have caused our research to overestimate the prevalence of NAFLD. A more sedentary lifestyle, less physical exercise, a high-calorie diet, and greater obesity rates are some of the factors contributing to the rising prevalence in the urban population.[62, 70, 71] People in urban settings have a higher prevalence of diabetes than people in rural areas. According to a recent meta-analysis, persons in urban regions were more likely to have metabolic syndrome (32%) than those in tribal areas (28%) and rural areas (22%).[65] The pathophysiology of NAFLD may be influenced by the gut microbiota. India's rural and urban populations have different gut microbiomes, according to a recent study.[72] Future research should examine the potential causes of these variations in India's rural and urban NAFLD prevalence.

India's urban population grew from 286 million in 2001 to 377 million in 2011, according to the country's most recent two population censuses. It is anticipated that these figures will rise, perhaps contributing to the nation's overall health burden.

NAFLD

While liver-related deaths are common in patients with cirrhosis, coronary artery disease is the most common cause of death in patients with non-alcoholic fatty liver disease (NAFLD) without cirrhosis. As a result, it's critical to identify and calculate the burden of these individuals' related comorbidities.

In order to address early diagnosis and management, the Government of India recently incorporated NAFLD into the National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke (NPCDCS). It will take a lot of work to turn this objective become reality.

Limitations

Most of the information came from studies conducted in hospitals. Community-based population-based studies were scarce. The rural population was underrepresented in the data. Data on NASH and lean NASH were scarce. There were just 15 out of 35 states and UTs represented. There was no information on the prevalence of NAFLD across different weight groups, such as overweight, obesity I, obesity II, etc. Ultrasound was the technique we employed to diagnose NAFLD. Subjective evaluation, low diagnostic precision in identifying moderate steatosis, and substantial intra- and inter-observer variability are among ultrasound's drawbacks. There was significant heterogeneity across the included studies. This notable heterogeneity may result from variations in the study population, study site, and study design factors. The included studies used a variety of designs, including cross-sectional, cohort, and case-control. These investigations were carried out in a variety of clinical settings, including the general public, clinics, hospitals, and schools. Major characteristics of the study population, including age, comorbidities, and risk factors for NAFLD, varied as well. The data from heterogeneous studies had to be combined because there were only a few studies available for each subgroup.

Only 23,581 people above the age of 18 and 2903 under the age of 18 were included in the available data for a nation with 1.3 billion people. Only a limited number of patients have been included in the majority of the studies that are currently available, and this may not be representative of the total population. Because these data were available in a limited number of studies, we were unable to evaluate the demographic details of NAFLD, such as the number of males and females affected, age groups, BMI categories (lean versus obese), associated co-morbidities (diabetes, hypertension, metabolic syndrome, or polycystic ovary disease), outcomes, and changing dietary patterns. Additionally, it would be intriguing to evaluate the prevalence of NAFLD with time, something that the current analysis was unable to do because of the limited number of studies. The majority of the studies that were included of the study were of high-risk (86%) or intermediate-risk (14%). The prevalence of NAFLD may not be as high as we think. To estimate the prevalence of NAFLD in India, large-scale prospective studies that include all subgroups are needed.

CONCLUSION:

India has a significant prevalence of NAFLD in both adults and children. To determine the prevalence of NAFLD throughout India and to allocate resources to reduce the disease burden, well-designed community-based research are required.

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