

International Journal of **ATHEROGENIC DIABETIC DYSLIPIDEMIA**

THIS ISSUE

1. Review Article

Editor-in-Chief

Dr. Prof. Subhankar Chowdhury

**VOLUME 4
ISSUE 2**



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***International Journal of ATHEROGENIC DIABETIC
DYSLIPIDEMIA***

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About the Journal

Atherogenic dyslipidemia, characterized by elevated triglycerides (TGs), raised small dense LDL (low-density lipoprotein) levels and decreased HDL (high-density lipoprotein) cholesterol levels, is the most common pattern of dyslipidemia in type 2 diabetic patients. It is characteristically seen in patients with obesity, metabolic syndrome, insulin resistance, and T2DM and has emerged as an essential marker for the increased CVD risk observed in these populations. In fact, the combined presence of dyslipidemia and diabetes escalates the CV risk by 3–4 times.

Dyslipidemia, diabetes and hypertension are all a part of the cluster that includes nonalcoholic fatty liver disease (NAFLD) too, another major CVD risk factor. As diabetic dyslipidemia is characterized by hypertriglyceridemia, the risk of pancreatitis is also high in these patients.

With the increasing burden of these conditions in the world, clinicians can struggle to keep themselves updated in the advances in research and therapy.

With this journal, we aim to keep doctors updated in the current understanding, trends in therapy and new modalities of care. Our objective is:

- ❑ To be the knowledge partner for healthcare professionals by presenting contemporary research and novel treatment options in the field of atherogenic diabetic dyslipidemia.
- ❑ To raise awareness about the latest clinical practices, for better management of the condition, thus improving on the standards of overall disease management
- ❑ To provide researchers of the field with a medium to elicit like thought processes in their peers working on similar innovations or experiments
- ❑ To provide clinicians with a platform to showcase their case studies

International Journal of Atherogenic Diabetic Dyslipidemia will contain literature encompassing all the scientific and clinical aspects that address the cause and management of atherogenic dyslipidemia. The content of the journal shall include, but not limited to subject areas like atherogenic dyslipidemia, obesity, NAFLD, acute pancreatitis, hypertriglyceridemia, pharmacological management/therapeutic options for atherogenic dyslipidemia in type 2 diabetes and new strategies for management.

We hope to provide a platform to publish interesting and informative articles on topics connected with the management of atherogenic diabetic dyslipidemia as well as encourage correspondence and participation from our readers.

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Prevalence of NAFLD—Global and Indian Population

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease globally, affecting one-fourth of the world's population. NAFLD includes simple steatosis, nonalcoholic steatohepatitis, cirrhosis, and hepatocellular carcinoma. NAFLD is the fastest-growing indication for liver transplantation in the US, UK, and low- and middle-income countries. Despite its prevalence, there is limited research on NAFLD in India. **Materials and Method:** Review and extracting data from articles which have published data related to prevalence of NAFLD in Indian and Global population. **Results and Conclusion:** Various studies reported NAFLD, as the major cause of chronic liver disease and it is predicted to affect 30–33% of adults by 2030, with aging and childhood obesity increasing its prevalence. Preventing it requires opting for a healthy lifestyle.

Keywords: NAFLD, NASH, prevalence, incidence, global, Indian, population, old, children

INTRODUCTION

There have been reports of adult NAFLD prevalence in India ranging from 6.7% to 55.1%. Nearly one-third of patients with an asymptomatic increase of liver enzymes may be attributable to non-alcoholic fatty liver disease. Furthermore, it appears that NAFLD affects two-thirds of patients with 'cryptogenic' cirrhosis, according to explant histology data from liver transplant centres. India's healthy population has a prevalence of pediatric NAFLD ranging from 7.3% to 22.4%. As people age, NAFLD becomes more common.¹

It is the leading cause of chronic liver disease globally. It is the most rapidly expanding indication for liver transplantation in the United States, the United Kingdom, and other low- and middle-income nations. The most common chronic liver disease globally is NAFLD. NAFLD is increasingly recognized as a hepatic component of metabolic syndrome (MS) and has been linked to obesity, insulin resistance, type 2 diabetes, dyslipidemia, hypertension, and cardiovascular disease.²

The Middle East and South America have the highest prevalence of NAFLD among adults over the age of 18, followed by Asia, North America, Europe, and Africa. The estimated global prevalence of NAFLD in those over the age of 18 is 25.2%. A recent meta-analysis found that the prevalence of NAFLD has increased significantly throughout Asia. It found a pooled prevalence of 29.6% across Asia, with considerable regional variation. NAFLD is significant for public health because of its worldwide impact on morbidity, mortality, and medical service use.²

NASH and hepatic fibrosis are associated with an increased risk of mortality from any cause, cardiovascular disease, and liver disease in the general population. Even in populations with low body mass index (BMI), such as India, the higher cardiovascular risk linked with non-alcoholic fatty liver has been observed.²

Aim: This review aimed to gain more understanding on the prevalence of NAFLD in global and Indian population.

Methods: Several articles related to the topic of discussion which is prevalence of NAFLD in the global and Indian population were reviewed and data was extracted from them.

Results: NAFLD is a major cause of chronic liver disease globally, with half of adults expected to suffer from it by 2040 and 30–33% by 2030. Aging increases vulnerability to liver injury and fibrosis, impacting the risk and prognosis of various liver diseases, including NAFLD. Childhood obesity has increased the prevalence of NAFLD in recent years. Preventing NAFLD and its progression to severe conditions requires a healthy lifestyle and positive mindset.

DISCUSSION

Global Prevalence of NAFLD

NAFLD is the major cause of liver disease globally. The global incidence of NAFLD is estimated to be 47 instances per 1,000 people, with men having a greater prevalence than women. The estimated global prevalence of NAFLD among adults is 32%, with males having a higher rate (40%) than females (26%). The global prevalence of NAFLD has risen over time, from 26% in research from 2005 or earlier to 38% in studies from 2016 or later.³

The prevalence of NAFLD varies significantly by area, owing to differences in obesity rates, as well as genetic and socioeconomic variables. NAFLD affects more than 40% of the population in America and Southeast Asia. If present trends continue, the incidence of NAFLD is expected to rise dramatically across many global areas by 2030.³

Riazi et al. conducted a recent meta-analysis and assessed the incidence of NAFLD to be 46.9 cases per 1,000 person-years. NAFLD was more common in men (70.8 cases per 1,000 person-years) than in women (26.9 cases per 1,000 person-years). However, because all the included research was done in Asia, it is uncertain if these findings can be generalised to other areas of the world.³

An earlier meta-analysis published in 2016 assessed the incidence of NAFLD as 52.34 per 1,000 person-years in Asia and 28.01 per 1,000 person-years in Israel. Another meta-analysis focused on NAFLD in Asia revealed an incidence of 50.9 per 1,000 person-years, with mainland China having the highest incidence at 63 per 1,000 person-years and Japan having the lowest at 29 per 1,000 person-years.³ (Fig. 1)

The incidence of NAFLD in South Korea was around 45 cases per 1,000 person-years.³



Fig 1. Estimated incidence of non-alcoholic fatty liver disease in China, Japan, and South Korea.³

Asia

Every region has a significantly different prevalence of NAFLD (Fig. 2). In Asia, the prevalence of NAFLD is about 30% overall. Le et al.'s meta-analysis from 2019 involved a literature search that turned up 182 studies including 2,385,999 people, and it projected that 30.5% of Asians were predicted to have NAFLD. A recent meta-analysis by Riazi et al. indicated that the prevalence of NAFLD was 31.6% in Asia, based on 63 studies including 1,000,681 persons. This is in line with a prior meta-analysis by Li et al. that found that 29.62% of Asians had NAFLD.³

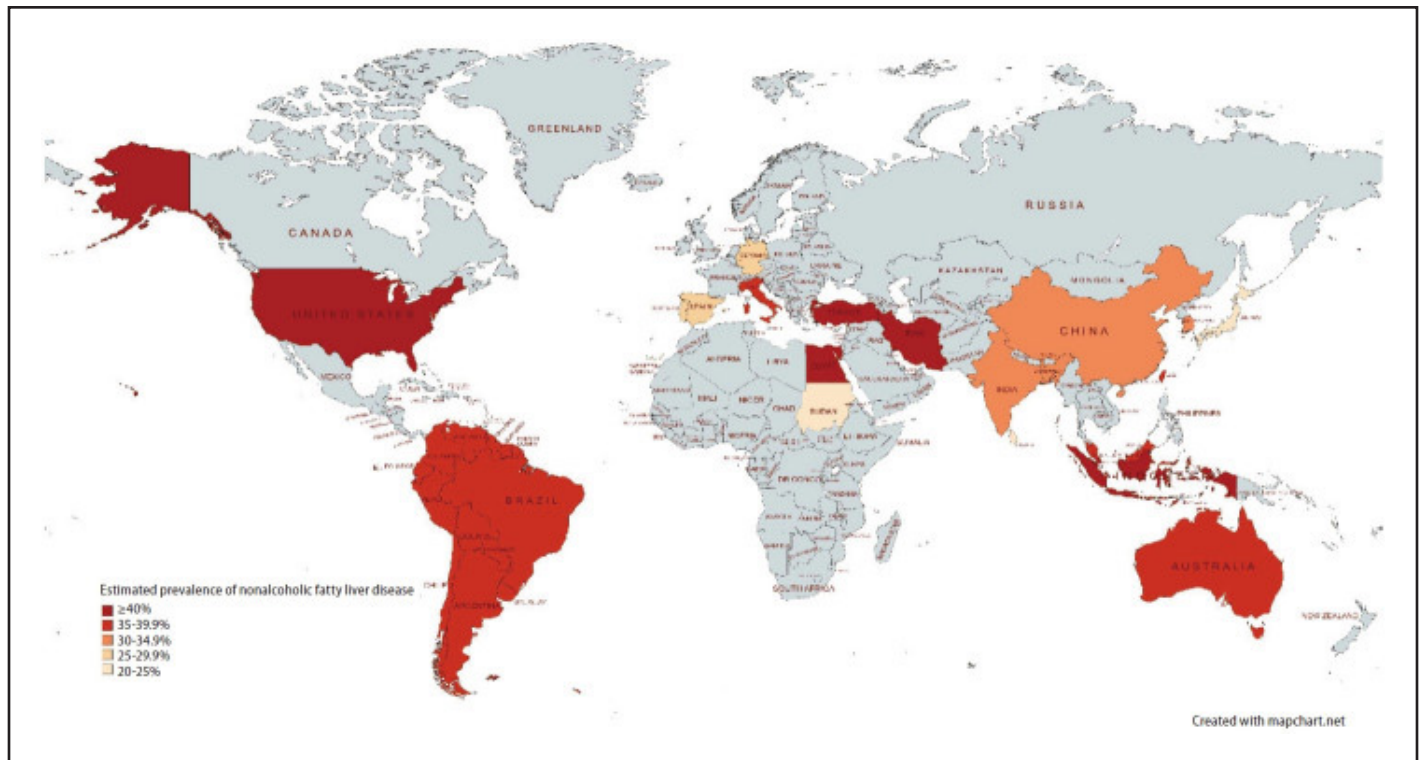


Fig 2. Global Estimated prevalence of non-alcoholic fatty liver disease (NAFLD) [Data for Iran, China, Taiwan, South Korea, Europe (Turkey, Italy, Germany, Portugal, Spain), North America (USA), Egypt, South America, South Asia (India, Bangladesh, Sri Lanka) and Southeast Asia (Indonesia, Malaysia, Singapore), Japan, Sudan and Australia].³

The prevalence of NAFLD in Asia is very varied since it includes nations with a diverse range of ethnicities and socioeconomic characteristics. Southeast Asia has the greatest prevalence of NAFLD (42%). Among Asian nations with more than three studies available, Li et al. found that Iran had the greatest pooled NAFLD prevalence (38.07%), while Japan had the lowest (22.28%).³

Riazi et al. observed similar results, with Iran having the greatest NAFLD prevalence (40.8%), followed by Taiwan (36.1%), South Korea (34.6%), and China (32.5%). On the other side, Japan reported a surprisingly low NAFLD prevalence of 22.3%, which might be attributed to a low obesity prevalence.³

Wu et al. conducted a meta-analysis in China and reported a NAFLD prevalence of 29.88%, whereas Zhou et al. assessed a prevalence of 29.2%. NAFLD prevalence in South Korea is likewise about 30%—a meta-analysis by Im et al. reported a prevalence of 30.3%, while Li et al. found a comparable prevalence of 32.9%.³

A study conducted on young adult males found that NAFLD prevalence increased from 10.66% in 2015 to 16.44% by 2021, with metabolic risk factors like hypertension, hypercholesterolemia, and hyperglycaemia being more prevalent. The

prevalence also increased from 18.6% in 1998–2001 to 21.5% in 2016–2017, while obesity and diabetes rates increased. This suggests a rise in metabolic risk factors may be the cause of the rising prevalence of NAFLD. Japan's lower prevalence of 25.5% is attributed to less common obesity and diabetes, as well as the country's diet reducing red meat and fat consumption.³

Based on data from South Asia, the prevalence of NAFLD was 25.7–32.74% in India, 26.2–33.86% in Bangladesh, and 24.74% in Sri Lanka. According to Li et al., the prevalence of NAFLD in Southeast Asia was 38.5% in Malaysia, 40.43% in Singapore, and 51.04% in Indonesia. Although there is a dearth of data from Central Asia, the Global Burden of Disease Study (GBD) 2019 found that the prevalence of non-alcoholic fatty liver disease (NAFLD) increased from 12.4% in 1990 to 19.7% in 2019. However, these estimates should be interpreted with caution because the GBD relied on intricate modelling and historical trends when data was scarce.³

Europe

Non-alcoholic fatty liver disease (NAFLD) is prevalent in Europe, with estimates of 30.9% and 32.6%, respectively. Cholongitas et al. found a 26.9% prevalence, with Mediterranean nations having a lower prevalence of 23.9%. Turkey has the highest prevalence (48.4%), followed by Italy (38.2%). Germany, Portugal, and Spain have rates ranging from 25 to 27%. A cross-sectional study in France found 18.2% prevalence. In Russia, the prevalence was 40% in the Ural Eye and Medical research (UEMS) and 69.8% in the Ural Very Old Study (UVOS). However, the UVOS participants were older and the diagnosis methodology varied between studies. The prevalence of NAFLD in Europe is not statistically significant.³

North America

NAFLD prevalence in North America is 35.3%, according to Le et al. and Riazi's meta-analysis. Hispanics have the highest frequency of NAFLD, followed by non-Hispanic whites and non-Hispanic blacks. The 2017–2018 National Health and Nutrition Examination Surveys (NHANES) reported 63.7% prevalence among Hispanics, 56.8% in non-Hispanic whites, and 46.2% in non-Hispanic blacks. This may be due to genetic factors like the PNPLA3 mutation, which increases the risk of hepatic steatosis and NASH in Hispanics. Additionally, Hispanics have a higher incidence of central obesity and insulin resistance than non-Hispanic whites. Lower blood triglyceride levels in African-Americans may help reduce NAFLD prevalence.³

South America

A meta-analysis of 19 studies by Rojas et al. estimated the prevalence of NAFLD in South America at up to 59%, but the results may not be fully representative of the general population. Le et al. pooled data from 3 studies and found South America had the highest estimated NAFLD prevalence among the continents at 35.7%. This may be due to genetic susceptibility and a greater prevalence of metabolic risk factors. The high prevalence of PNPLA3 genetic polymorphism, particularly among Native American ancestry, is also prevalent. Obesity is extremely common in the region, with central obesity being the highest. Type 2 diabetes is also increasing in South America, with higher likelihood of diabetes and higher mean cholesterol levels. Physical activity is often inadequate, with Latin America ranking as the top region for physical inactivity.³

Africa

A meta-analysis estimated the prevalence of NAFLD in Africa at 13.5%, with Nigeria at 9% and Sudan at 20%. More recently, the prevalence of NAFLD was found to be 28.2% in the Le meta-analysis and 56.8% in the Riazi meta-analysis. Riazi's meta-analysis included only one study from Egypt.³

NAFLD PREVALENCE IN INDIAN POPULATION

The prevalence of NAFLD in India's general population ranges between 9% and 53%. Most urban studies found a greater frequency than those that served a mostly rural population. One of the first population-based studies from India to demonstrate an 8.7% prevalence rate in primarily nonobese individuals was from rural West Bengal.⁴

A population-based study from coastal south India recently showed an overall NAFLD prevalence rate of 49.8%; after correcting for sex, body mass index (BMI), diabetes, and metabolic syndrome, urban residence was shown to be related with a greater risk of NAFLD (adjusted odds ratio). As part of the continuing community-based Prospective Urban Rural Epidemiology (PURE) cohort research in north India, urban populations had a greater incidence of NAFLD (53.7%) than rural ones.⁴

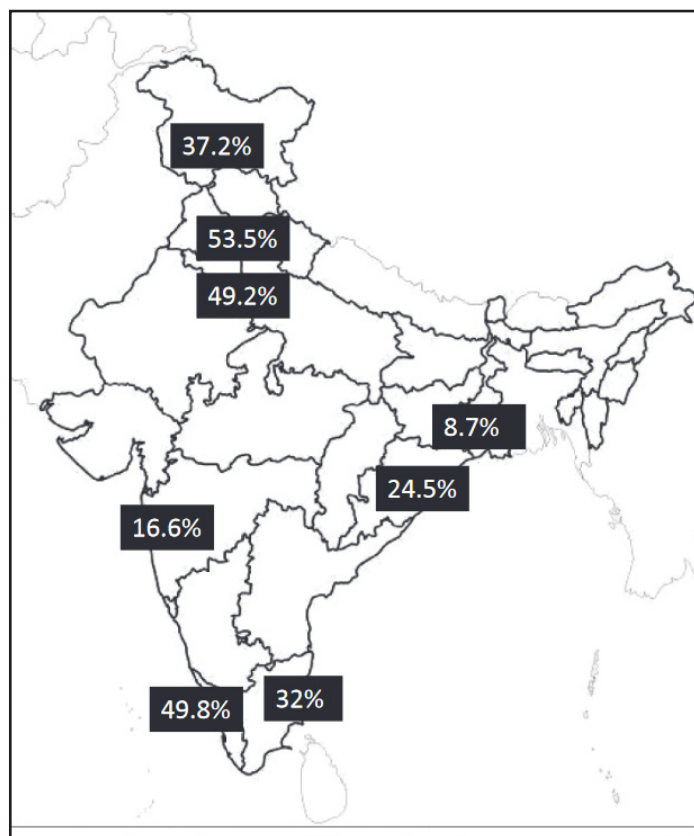


Fig 3. Prevalence of NAFLD in different geographical regions of India.⁴

PREVALENCE OF NAFLD IN CHILDREN

The prevalence of paediatric NAFLD in India ranges from 7.3% to 22.4% in the healthy population. The incidence of NAFLD grows with age.¹

NAFLD is the leading cause of chronic liver disease in young adults in industrialised nations. The prevalence of NAFLD is increasing in tandem with the epidemic of overweight and obesity. The prevalence of fatty liver in India's general adult population ranges between 5% and 28%, with overweight and diabetics having a greater frequency. The global prevalence of paediatric NAFLD ranges between 9 and 37%. Furthermore, the prevalence of NAFLD in normal-weight children and overweight/obese children is reported to be around 3–10% and 8–80%, respectively.⁵

Overweight/obesity, dyslipidaemia, insulin resistance, metabolic syndrome, ethnicity, gender, and family clustering have all been linked to NAFLD in both adults and children.⁵

A study revealed fatty liver on ultrasonography in 22.4% of the children (45.6% in overweight children and 18.9% in normal-weight children). The degree of fatty liver increased with BMI, as did dysregulation in liver enzymes. Low HDL and hypertriglyceridemia were the most prevalent metabolic abnormalities detected.⁵

India's population is young, with 29.5% under 15 years old and 121 million aged 15–19. A study suggests approximately 168 million children in India suffer from NAFLD. The proportion of overweight children and adolescents is around 20%,

increasing in both low-income and high socio-economic groups. The potential risks of obesity are alarming, as weight gain during school years increases the risk of NAFLD. As NAFLD prevalence increases with age, the proportion of adults with NAFLD in India may continue to rise, making these predictions crucial for public health.¹

ELDERLY PREVALENCE OF NAFLD

As individuals live longer, NAFLD has become a rising public health problem throughout the world. NAFLD is a multisystem disease that is strongly linked to metabolic risk factors. The presence of NAFLD raises the risk of liver and cardiovascular disease death. Many studies have revealed that ageing increases the likelihood of advanced fibrosis, which is associated with poor outcomes.⁶

Between 20 and 70, there is a 33% decline in hepatic blood flow, volume, and liver function. This decline affects the pharmacokinetic profiles of drugs that undergo mandatory hepatic oxidation. The octogenarian liver has fewer but larger hepatocytes, increased polyploidy, and a higher binuclear index. It also has fewer mitochondria numbers, potentially impacting oxidative respiration. Additionally, there is a reduction in bile acid synthesis, leading to changes in bile acid secretion and flow. Age-related decline in LDL cholesterol metabolism leads to elevated serum cholesterol levels, which may contribute to increased serum cholesterol levels and increased frequency of gallstone formation.⁷

The aging liver is more susceptible to drug and toxins effects, with diminished regenerative capacity, leading to increased morbidity and mortality in hepatic resections in patients over 60 years old.⁷

Prevalence estimates for NAFLD in older persons range from 32.8% in Rotterdam, Netherlands, to 50.1% in hospital-based research in Taiwan, China. According to a 2016 meta-analysis that employed age stratification, the worldwide prevalence of NAFLD was 28.9% in people aged 60 to 69 and 34.0% in those aged 70 to 79 years.⁶

Studies involving older people of advanced ages found that prevalence increased with age and decreased with age advanced. According to Rotterdam research, the prevalence of NAFLD was 39.6%, 32.1%, and 21.1% in those aged 75–79, 80–84, and >85 years, respectively.⁶

Research from Poland found a 37.2% prevalence of NAFLD in older persons identified using the fatty liver index. The prevalence decreased in those ≥ 80 years (ages ≤ 80 , 68.7% vs. ages ≥ 80 , 36.3%).⁶

Community-based research of an older Taiwanese population (China) aged ≥ 65 years revealed a 41.9% prevalence of NAFLD in those diagnosed ultrasonographically. The study indicated that the prevalence of NAFLD decreased with age, from 45% in 65–70 years to 31.8% in >80 years ($p=0.01$). In addition, the logistic regression study of older persons revealed that age was adversely linked with fatty liver.⁶

LIMITATIONS OF STUDY

This review is limited to the information available in published articles or studies.

CONCLUSION

Notably, NAFLD is a primary cause of chronic liver disease both in India and worldwide. By 2040, it is expected that half of all adults would have NAFLD. Published research indicates that by 2030, it might reach as high as 33%. It has been demonstrated that ageing increases susceptibility to liver fibrosis and damage. It has been linked to a considerable increase in the risk and unfavourable prognosis of several liver diseases, including NAFLD. The rising frequency of pediatric obesity in the past ten years has been linked to a prominent increase in non-alcoholic fatty liver disease (NAFLD) in youngsters.

Maintaining an optimistic mindset and leading a healthy lifestyle can help prevent the onset of non-alcoholic fatty liver disease (NAFLD) and its subsequent progression to a serious health issue.

CONFLICT OF INTEREST

No conflict of interest.

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