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Association between Non-alcoholic fatty liver diseases and Decline of glomerulus filtration rate : A Meta Analysis

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Abstract

Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is one of the most common forms of chronic liver disease worldwide, increasingly recognized as a potential risk factor for renal function decline. Several observational studies have shown an association between NAFLD and decreased glomerular filtration rate (GFR), but the results are still variable.

Objective: To quantitatively evaluate the association between NAFLD and decreased GFR through a meta-analysis approach of available observational studies.

Methods: A systematic review was conducted using PubMed and ScienceDirect databases up to May 2025. Studies that met the inclusion criteria were independently extracted and analyzed using Review Manager 5.3. Effect sizes were summarized as Standardized Mean Difference (SMD) using a random effects model. Heterogeneity was assessed using the I^2 statistic.

Results: Five retrospective cohort studies involving a total of 4,517 participants (1,450 NAFLD, 3,067 non-NAFLD) met the inclusion criteria and were analyzed. The meta-analysis results showed that individuals with NAFLD had significantly lower GFR than non-NAFLD group (SMD: -0.24; 95% CI: -0.42 to -0.05; $p = 0.01$), with high heterogeneity ($I^2 = 100\%$).

Conclusion: NAFLD was significantly associated with decreased GFR, indicating the potential contribution of NAFLD to renal dysfunction.

Keywords: NAFLD, glomerular filtration rate, GFR, chronic kidney disease, meta-analysis

1. Introduction

Non-Alcoholic Fatty Liver Disease (NAFLD) is the most common chronic liver disease globally, characterized by fat accumulation in hepatocytes without significant alcohol intake. Its prevalence is estimated at 25% worldwide, with the highest rate of up to 30% reported in China (1), and up to 51% in Indonesia (2). NAFLD contributes not only to hepatic complications such as steatohepatitis and fibrosis but also to systemic issues, including increased risks of cardiovascular disease, certain cancers, and chronic kidney disease (CKD) (3,4).

NAFLD is strongly associated with metabolic disorders such as obesity, insulin resistance, and type 2 diabetes mellitus, all of which are key risk factors for kidney dysfunction (5). Recent studies have increasingly reported a relationship between NAFLD and decreased glomerular filtration rate (GFR), the primary marker of CKD and a critical parameter in monitoring kidney damage progression (6–11).

Potential mechanisms include systemic inflammation, oxidative stress, endothelial dysfunction, and subclinical atherosclerosis, which may impair renal perfusion and accelerate nephron injury (3,12). Moreover, adipokines and pro-inflammatory cytokines from visceral fat and fatty liver may contribute to renal dysfunction in NAFLD patients (13,14). Given the variability in findings due to differing study populations and methods, a systematic review and meta-analysis are needed to better synthesize the evidence on NAFLD's association with reduced GFR.

2. Methode

Search strategy and data resources

We systematically searched the PubMed and Science Direct databases from database inception to May 22, 2025 to identify studies exploring the association between NAFLD and decreased glomerular filtration rate (GFR) and CKD incidence using keywords and MeSH terms:

("Non-alcoholic Fatty Liver Disease"[MeSH] OR "NAFLD" OR "MAFLD" OR "MASLD" OR "fatty liver" OR "hepatic steatosis")

AND

("Glomerular Filtration Rate"[MeSH] OR "glomerular filtration rate" OR "GFR" OR "kidney function" OR "renal function" OR "eGFR")

AND

("Chronic Kidney Disease"[MeSH] OR "CKD" OR "renal insufficiency" OR "kidney

dysfunction" OR "renal impairment")

In addition, reference lists from previous publications will be thoroughly reviewed to identify articles not captured in the initial search, and the “related articles” feature of PubMed will be used to find other potentially relevant studies.

Study selection Inclusion criteria

Studies that meet all of the following criteria will be considered for inclusion:

- 1) studies published in English and full text available;
- (2) studies (prospective, retrospective, and cross-sectional) examining the association of decreased glomerular filtration rate and CKD risk between NAFLD and non-NAFLD;
- (3) adults aged 18 years and older;
- (4) NAFLD diagnosed using imaging, histology, or noninvasive assessment methods, such as FIB-4 score, fatty liver index, or NAFLD liver fat score, excluding other causes of hepatic steatosis;
- (5) Glomerular Filtration Rate (GFR) is defined as the estimated rate of blood plasma filtration by the renal glomeruli, expressed in milliliters per minute per 1.73 square meters of body surface area (mL/min/1.73 m²) calculated using a validated estimation formula such as CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration).

Exclusion criteria

The exclusion criteria were as follows: (1) congress abstracts, practice guidelines, reviews, theses, editorials, case reports, non-human studies; (2) studies that did not exclude heavy drinkers and other potential risks of liver steatosis; (3) studies that did not report the distribution and normality of data for the outcome of interest; (4) studies conducted in pediatric populations (<18 years); and (5) concomitant chronic liver diseases that could potentially cause steatosis, such as excessive alcohol consumption and hepatitis virus infection, were explicitly excluded.

Outcome measures

The primary outcome indicator was decreased glomerular filtration rate among individuals with NAFLD compared to those without NAFLD

Data extraction and quality assessment

For each study, data were extracted independently. The name of the first author, year of publication, study population area, study type, number of participants, NAFLD diagnostic method, data distribution, and glomerular filtration rate. Furthermore, the risk of bias was assessed independently. The Newcastle Ottawa Scale (NOS) (Stang, 2010) was used to assess

the quality of prospective and retrospective studies. The NOS scale evaluates studies using a star rating system (up to nine stars) in three ways: participant selection, comparison of study groups, and determination of relevant outcomes. Studies receiving seven or more stars were considered to have a low risk of bias, studies receiving six stars were considered to have a moderate risk of bias, and studies receiving less than six stars were considered to have a high risk of bias. The results of eligible studies were pooled, and the overall effect size estimate was obtained using a random effects model, because this approach considers differences between studies, even in the absence of statistically significant heterogeneity. Sensitivity analysis was performed using a random effects model to combine results from subgroups.

Data Synthesis and analysis

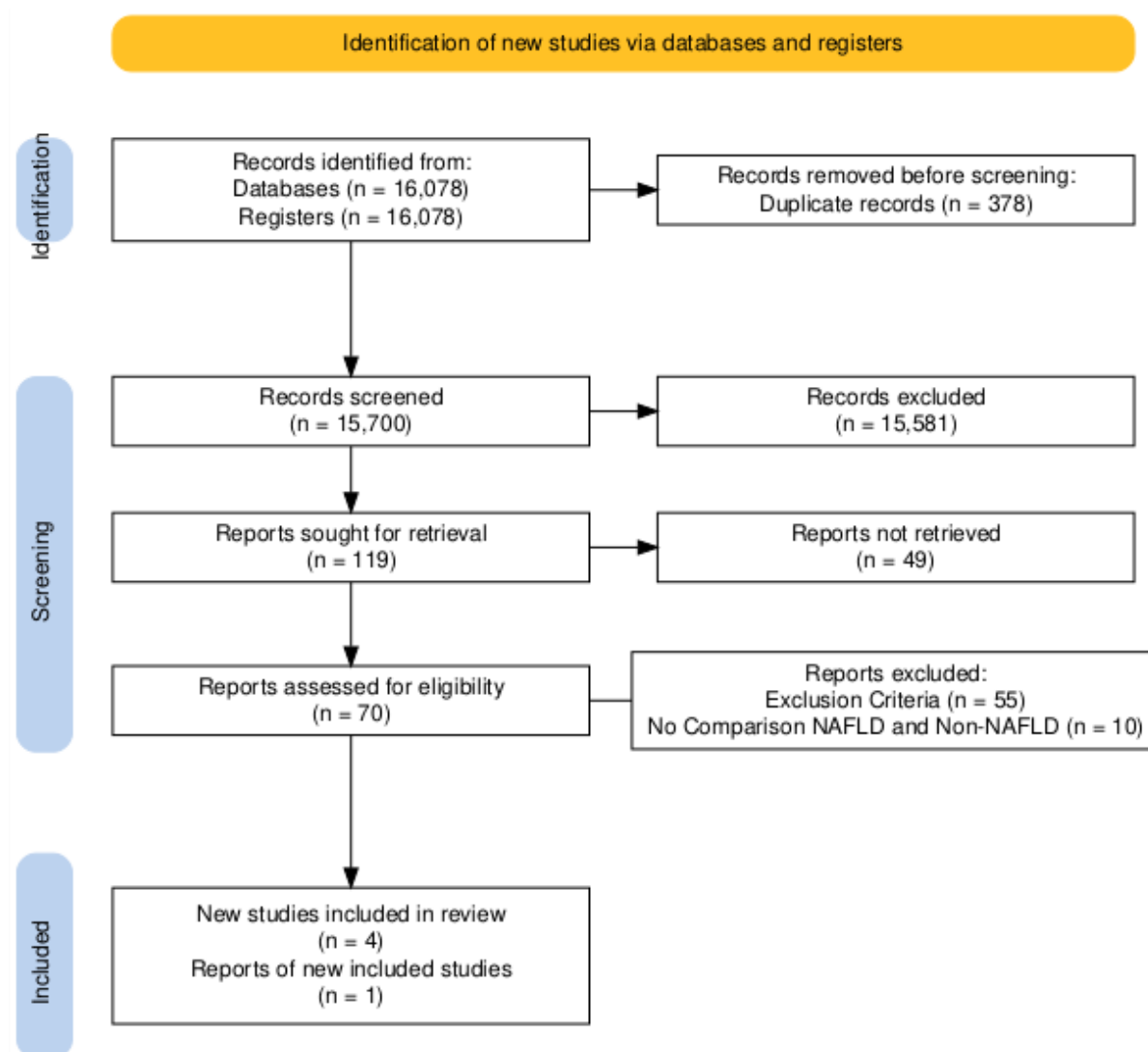
For continuous variables, the mean \pm standard deviation (SD) was extracted using Revman 5.3.

Statistic Analysis

Statistical analysis was performed using Review Manager (RevMan) software version 5.3. Quantitative data in the form of mean and standard deviation of glomerular filtration rate (GFR) from each study were extracted and integrated using a random effects model, which takes into account the variation between studies (heterogeneity). Effect sizes were summarized as Standardized Mean Difference (SMD) with 95% Confidence Interval (CI). The degree of heterogeneity between studies was assessed using the I^2 statistic and the Chi-square (χ^2) test, with I^2 values $>75\%$ indicating high heterogeneity. The Z test was used to determine the statistical significance of the combined effect. In addition, a sensitivity analysis was performed to evaluate the stability of the results by observing the impact of excluding certain studies on the overall effect estimate. The results are presented in the form of a forest plot to visualize the distribution of effects and confidence intervals from each study and the overall combined effect.

3. Result

Initially, 16,078 articles were retrieved from the database. After removing 378 duplicate articles, 15,700 publications were left for the abstract selection process. A total of 15,581 studies were excluded for reasons described in the flowchart (Figure 1). Through bibliography searches of relevant articles, one additional study was found.



Picture 1 Prisma Flow Chart

Finally, a total of 5 studies were included in the meta-analysis (Hashimoto et al, 2022; Heo et al, 2024; Kwon et al, 2023; Sinn et al, 2017; Wei et al, 2023).

As summarized in Table 1, the included studies consisted of five retrospective cohort-based studies (Hashimoto et al, 2022; Heo et al, 2024; Kwon et al, 2023; Sinn et al, 2017; Wei et al, 2023). NAFLD was diagnosed using ultrasonography (Hashimoto et al, 2022; Heo et al, 2024; Kwon et al, 2023; Sinn et al, 2017; Wei et al, 2023).

No	Author & Year	Country / Population	Study design	Sample size (NAFLD vs Non-NAFLD)	Definition NAFLD/MAFLD	Definition Decrease GFR and CKD	Outcome (MD and SD eGFR)	Summary
1	Hashimoto, 2022	Japan, adult population undergoing medical check-up (NAGALA cohort) at Asahi University Hospital	Cross-sectional study and cohort retrospective (two section).	5.688/13.335 ▮ Total participant cross-sectional: 27.371 ▮ Group : Non-FLD without MD: 13.335 (48.7%) Non-FLD with MD: 7.724 (28.2%) FLD tanpa MD: 624 (2.3%) MAFLD (FLD + MD): 5.688 (20.8%) ▮ for Cohort	▮ FLD: Diagnose with ultrasonography abdomen. ▮ MAFLD: FLD + ≥ 1 criteria of metabolic dysfunction (obesity, type 2 DM, or ≥ 2 metabolic factors such as prediabetes, high TG, low HDL, hypertension, large waist circumference)	CKD: eGFR < 60 mL/min/1.73 m ² and / or proteinuria ($\geq 1+$ on dipstick).	Mean eGFR rata-rata (SD) Group: Non-FLD without MD: 77.5 (13.9) MAFLD: 70.9 (13.0) Statistically significant difference (p < 0.001)	MAFLD is associated with an increased risk of CKD (both incidence and prevalence), whereas FLD without metabolic dysfunction does not increase the risk of CKD

				(follow- up): 16.938 participant (after exclusion for CKD baseline and not complete follow-up)				
2	Ji Hye Heo, 2024	South Korea ,	Cohort retrospective longitudinal.	48.175/151.759	Γ NAFLD: Steatosis from USG + exklusion alcohol >30 g/day	Γ CKD: eGFR <60	Mean initial eGFR :	MASLD and NAFLD both are correlated with

		<p>healthy adult population (n=214,145) who undergo routine health checks (Kangbuk Samsung Health Study).</p>		<p>▢ Total subject: 214.145 ▢ NAFLD: 48.175 ▢ MASLD: 57.785 ▢ Kombinasi NAFLD + MASLD: 44.254 ▢ NAFLD-only: 3.921 ▢ MASLD-only: 13.531 ▢ No SLD : 151.759</p>	<p>(man) or >20 g/day (woman) + no viral hepatitis. ▢ MASLD: Steatosis + one or more: obesity (BMI ≥ 23 kg/m²), DM tipe 2, or ≥ 2 risk factor metabolic (HTN, high TG, low HDL rendah, prediabetic, HOMA- IR, high hs-CRP, large waist circumference.</p>	<p>mL/min/1.73 m² ▢ Albuminuria abnormal: ACR ≥ 30 mg/g</p>	<p>No SLD: 103.54 ±13.56 NAFLD-only: 101.74 ±12.70 MASLD-only: 98.18 ±12.86 NAFLD + MASLD: 98.47 ±13.24</p>	<p>dengan increased risk of CKD, with MASLD showing a slightly stronger association.</p> <p>Only the NAFLD + MASLD group had a significant association with CKD.</p> <p>NAFLD-only did not independently increase the risk of CKD, highlighting the important role of metabolic dysfunction</p>
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3	Kwon, 2023	<p>▮ Country: South Korea</p> <p>▮ Population: 21.713 adult (≥ 20 tahun) who already undergo two times medical check up at samsung medical center (≥ 20 tahun)</p>	<p>Cohort study retrospective longitudinal with follow-up median 5,3 years (rentang 2,8–8,3 years)</p>	<p>482/9.414</p> <p>▮ Total participant: 21.713</p> <p>▮ NAFLD-only: 482 (2.2%)</p> <p>▮ MAFLD-only: 1.776 (8.2%)</p>	<p>▮ NAFLD: Fatty liver based on USG, NO alcohol consumption (>20 g/Day man, >10 g/day woman) and NO viral hepatitis</p> <p>▮ MAFLD: Fatty liver based on USG</p>	<p>CKD: eGFR <60 mL/min/1.73 m² dan/atau uACR ≥ 30 mg/g, based on CKD- EPI criteria</p>	<p>▮ mean total eGFR : 94,06 \pm 13,89 mL/min/1.73m²</p> <p>▮ eGFR highest : Non-FLD tanpa MD (97,42 \pm 13,96)</p> <p>▮ eGFR lowest :</p>	<p>▮ MAFLD either alone or in combination with NAFLD, is associated with an increased risk of CKD, whereas NAFLD alone does not show an increased risk.</p>
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				<p>┐ Both-FLD (NAFLD + MAFLD): 4.844 (22.3%)</p> <p>┐ Non-FLD without metabolic dysregulation (MD): 9.414</p> <p>┐ Non-FLD with MD: 5.111</p>	<p>USG, WITH ≥ 1 of: Overweight/obesity (BMI ≥ 23 kg/m²) Diabetes ≥ 2 metabolic dysfunction factors such as high waist circumference, high blood pressure, high triglycerides, low HDL, prediabetes, high HOMA-IR, high hs-CRP</p>		<p>Both-FLD (90,88 \pm 13,39)</p>	<p>┐ MAFLD is better at identifying individuals at risk for CKD, including those with excessive alcohol consumption and viral hepatitis.</p> <p>┐ These results support the use of the MAFLD definition over NAFLD in assessing the risk of metabolic complications such as CKD.</p>
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4	Sinn, 2017	<p>▭ Country: South Korea</p> <p>▭ Population: 41.430 adult subject (≥18 years old) who underwent routine health check-ups at Samsung Medical Center (2003–2013), without CKD at baseline</p>	Cohort retrospective longitudinal	<p>14.223/27.207</p> <p>▭ Total: 41.430</p> <p>▭ NAFLD: 14.223 (34.3%)</p> <p>▭ Non-NAFLD: 27.207 (65.7%)</p>	<p>▭ NAFLD: Diagnosis is based on ultrasonography, after exclusion of secondary causes such as excessive alcohol consumption (≥30 g/day for men or ≥20 g/day for women), hepatitis B/C, cirrhosis, and cancer.</p> <p>▭ NAFLD severity: Measured with</p>	<p>▭ CKD: eGFR < 60 ml/min/1.73 m², calculate with CKD-EPI equation</p> <p>▭ Not included proteinuria in end point definition</p>	<p>▭ NAFLD: 89,7 ± 12,7 ml/min/1.73m²</p> <p>▭ Non-NAFLD: 91,4 ± 13,0 ml/min/1.73m²</p> <p>▭ Statistically significant (p < 0.001)</p>	<p>▭ NAFLD associated with an increased risk of incident CKD, even after adjustment for various metabolic risk factors..</p> <p>▭ The risk of CKD increases progressively with the severity of liver fibrosis.</p>
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					NAFLD Fibrosis Score (NFS), APRI, And FIB-4 score			Γ This study supports the independent role of NAFLD in the pathogenesis of CKD and the importance of monitoring kidney function in NAFLD patients.
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5	Wei, 2023	<p>▭ Country: Tiongkok</p> <p>▭ Population: 41,246 adult participants who underwent ≥ 3 health examinations at the People's Hospital of Guangxi Zhuang Autonomous Region (2008–2015)</p>	<p>▭ Cohort retrospective longitudinal</p> <p>▭ Follow-up prospektif until 2022</p>	<p>11.860/29.386</p> <p>▭ Total: 41.246</p> <p>▭ MAFLD: 11.860 (28.8%)</p> <p>▭ Non-MAFLD: 29.386 (71.2%)</p>	<p>MAFLD: Ultrasonographic diagnosis of fatty liver, accompanied by one of: Overweight/obesity (BMI ≥ 23 kg/m²), or T2DM, or Normal weight + ≥ 2 metabolic components (eg high waist circumference, high blood pressure, high TG, low HDL, prediabetes)</p>	<p>CKD: eGFR < 60 ml/min/1.73 m² (CKD-EPI) or ≥ 2 onset of albuminuria during follow-up</p>	<p>▭ MAFLD: eGFR median = 97,0 (IQR 86,1–106,6) ml/min/1.73 m²</p> <p>▭ Non-MAFLD: eGFR median = 104,7 (IQR 92,5–115,5) ml/min/1.73 m²</p> <p>▭ significant difference (p < 0.001)</p>	<p>▭ MAFLD independently and significantly associated with increased risk of new CKD.</p> <p>▭ The risk is higher in women, as well as men <60 years and those with dyslipidemia.</p> <p>▭ this study emphasized the importance of routine renal function monitoring and early intervention in patients with MAFLD.</p> <p>▭ A multidisciplinary approach is recommended to manage patients</p>
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								with MAFLD and risk of CKD.
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Table 1. Research Synthesis

All studies were conducted in the Asian region, it is:

- one in China (Wei et al, 2023),
- three in Korea (Heo et al, 2024; Kwon et al, 2023; Sinn et al, 2017),
- and one in Japan (Hashimoto et al., 2022).

Overall, in the 5 studies, there were **1,450 cases of NAFLD**, while there were **3,067 non-NAFLD**. Regarding the assessment of study quality, all five studies received eight stars (see Table 2).

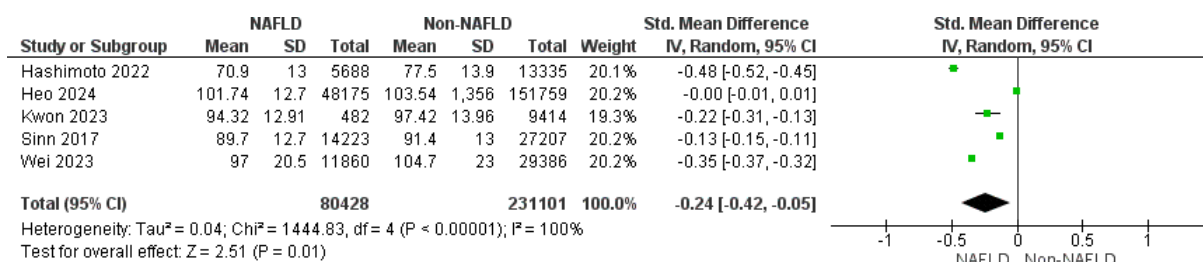
2).

Table 2. Study Quality Assessment

No.	Author & Year	Evaluation tolls and bias assessment	Study Quality Score (NOS)	Brief evidence
1	Hashimoto et al., 2022	not stated explicitly	8/9	Large retrospective cohort study, comprehensive controls, but no explicit mention of tools
2	Heo et al., 2024	not stated explicitly	8/9	Large retrospective cohort design, complete data, but no mention of NOS.
3	Kwon et al., 2023	not stated explicitly	8/9	Large longitudinal study with control of confounder variables, but no specific instrument mentioned
4	Sinn et al., 2017	not stated explicitly	8/9	Large retrospective cohort study, comprehensive control, but no explicit mention of tools.
5	Wei et al., 2023	not stated explicitly	8/9	Large longitudinal cohort study, well-controlled, although not using explicit NOS

The forest plot in this meta-analysis visually confirms that the majority of studies showed a statistically significant decrease in glomerular filtration rate (GFR) in the NAFLD group compared to the non-NAFLD group. Each green box represents the effect estimate from each study, with the size of the box reflecting the relative weight of the study in the analysis. Almost all studies, except Heo's (2024) study, showed a negative difference on the horizontal axis,

indicating a lower GFR in the NAFLD group. The 95% confidence intervals of four of the five studies did not cross the zero line, indicating individual statistical significance. The combined effect is shown as a black diamond at the bottom, which is completely on the left side of the neutral line (SMD = 0), with a range of -0.42 to -0.05, indicating a significant aggregate effect. High heterogeneity ($I^2 = 100\%$) indicates that the variation between studies is quite large, which may be due to differences in population characteristics, NAFLD diagnosis methods, or GFR measurements between studies.



This meta-analysis evaluated the difference in mean glomerular filtration rate (GFR) between individuals with Non-Alcoholic Fatty Liver Disease (NAFLD) and the Non-NAFLD group based on data from five observational studies. Analysis using a random effects model showed that the NAFLD group had a significantly lower GFR than the Non-NAFLD group, with a

Picture 2. Forest Plot Association between NAFLD and Glomerular filtration rate decline Standardized Mean Difference (SMD) of -0.24 (95% CI: -0.42 to -0.05; $p = 0.01$). The Z value of 2.51 indicated statistical significance of the effect, although there was very high heterogeneity between studies ($I^2 = 100\%$, $p < 0.00001$), indicating substantial variation between included studies.

Subgroup studies showed consistency in the direction of effect, with most studies reporting decreased GFR in the NAFLD group. The studies of Hashimoto (2022), Kwon (2023), Sinn (2017), and Wei (2023) reported negative SMDs ranging from -0.13 to -0.48, while the study of Heo (2024) showed neutral results (SMD: -0.00; 95% CI: -0.01 to 0.01). These results provide quantitative evidence that NAFLD may play a role in the decline of kidney function, supporting the hypothesis of a pathophysiological relationship between metabolic hepatic dysfunction and kidney disorders.

4. Discussion

Multiple studies indicate a strong link between Non-Alcoholic Fatty Liver Disease (NAFLD) and reduced glomerular filtration rate (GFR) (3,15–17). NAFLD patients, due to higher metabolic risk, are more likely to develop decreased GFR (15,18). This decline may result from metabolic syndrome–related factors such as insulin resistance, which activates the renin–angiotensin system, a known contributor to kidney damage. Additionally, liver steatosis and inflammation can directly injure the kidneys (19). Steatohepatitis may stimulate inflammatory mediators—cytokines, ROS, and lipopolysaccharides—aggravating insulin resistance, systemic inflammation, and endothelial injury (20–22).

Emerging evidence further supports NAFLD as an independent risk factor for renal impairment, beyond traditional risk factors like diabetes and hypertension (23). In a longitudinal study of 1,525 chronic kidney disease (CKD) patients, Jang et al. (2018) reported that those with NAFLD had a significantly faster annual eGFR decline of -1.06% , particularly among patients with higher fibrosis scores, proteinuria, or baseline eGFR below $45 \text{ ml/min/1.73 m}^2$ (24). Similarly, the Fukuoka Kidney Disease Registry identified a negative correlation between eGFR and liver fibrosis scores such as FIB-4 and NFS, reinforcing the association between advanced liver fibrosis and kidney dysfunction (25). A meta-analysis by Mantovani et al. (2021) involving over 1.2 million individuals found a 43% increased risk of stage ≥ 3 CKD in NAFLD patients (HR 1.43; 95% CI: 1.33–1.54), with greater risk in those with advanced fibrosis (12).

The pathogenic mechanisms linking NAFLD and kidney damage include chronic systemic inflammation and insulin resistance, which activate NF- κ B and JNK pathways and increase oxidative stress, leading to glomerular injury and interstitial fibrosis (24,26,27). These insights highlight the necessity of routine NAFLD screening in patients at risk for CKD and the need for integrated management strategies.

However, this analysis has limitations. All included studies were retrospective cohorts, limiting causal inference. Additionally, the studies were based solely on East Asian populations, restricting generalizability. NAFLD diagnoses were made using ultrasonography, which lacks sensitivity in obese or mildly steatotic patients and cannot distinguish steatohepatitis. Variability in definitions and GFR assessments contributed to high heterogeneity ($I^2 = 100\%$). Moreover, potential selection and publication bias cannot be excluded due to the absence of funnel plot or Egger’s test analyses. These results should be cautiously interpreted and validated through future prospective studies.

5. Conclusion

This meta-analysis found that Non-Alcoholic Fatty Liver Disease (NAFLD) is significantly associated with decreased glomerular filtration rate (GFR), suggesting NAFLD as an independent risk factor for kidney dysfunction. Possible mechanisms include chronic inflammation, oxidative stress, and insulin resistance. Despite study heterogeneity, the consistent findings highlight the need for greater clinical attention to renal health in NAFLD patients and a multidisciplinary approach to managing related metabolic complications.

6. Acknowledgement

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