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The effect of body mass index on estimated glomerular filtration rate in patients with IgA nephropathy; a systematic review and meta-analysis of the cohort studies

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ABSTRACT

Introduction: The study is motivated by the growing concern surrounding chronic kidney disease worldwide and the need for early identification and effective management to slow or prevent kidney disease progression. To achieve this goal, we evaluated the correlation between body mass index (BMI) and estimated glomerular filtration rate (eGFR) in patients with IgA nephropathy through a systematic review and meta-analysis.

Materials and Methods: The data were acquired after conducting a comprehensive exploration of the international databases of PubMed, Scopus, Web of Science, Cochrane, and the Google Scholar search engine until June 2024. The study heterogeneity was evaluated utilizing the I2 index. The data were scrutinized employing STATA 14, and a *P* value < 0.05 was considered significant.

Results: Seven studies with a sample size of 1354 normal BMI people and 1020 obese or overweight patients were included in this meta-analysis. Based on the findings of the weighted mean difference (WMD), individuals who are overweight or obese had a lower eGFR (WMD = -7.34 [CI; -9.62, -5.05], *P*<0.001).

Conclusion: The results demonstrated that the eGFR was significantly lower in obese or overweight people compared to individuals with normal BMI; therefore, we conclude that being overweight or obese may hurt kidney function.

Registration: This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (CRD42023417633) and Research Registry (UIN: reviewregistry1665) websites.

Meta-analysis

Implication for health policy/practice/research/medical education:
In a meta-analysis, we found that the eGFR was lower in obese or overweight people compared to individuals with normal BMI. This finding that individuals with IgA nephropathy who are overweight or obese have significantly lower eGFRs compared to those with a normal BMI suggests that excess body weight may have detrimental effects on kidney function in this patient population. This implication is crucial, as it highlights the importance of monitoring BMI in patients with IgA nephropathy and supports the need for targeted interventions aimed at maintaining a healthy BMI, such as weight management strategies.

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Introduction

Among the most common types of glomerulonephritis worldwide, immunoglobulin A (IgA) nephropathy occupies the lead position. In this disease, IgA1 deposition initiates an inflammatory response which leads to podocyte injury and tubulointerstitial damage. IgA nephropathy is accompanied by a decline in kidney function. Kidney function is a major predictor of the disease course and may greatly affect our treatment protocols and drug dosages. Thus, GFR meticulous measurement is necessary in patients with IgA nephropathy (1,2).

Two tests are frequently used in clinical settings to estimated glomerular filtration rate (eGFR): serum creatinine and cystatin C. Serum creatinine is usually the first to assess patients' GFR in clinical practice. Different equations including modification of diet in renal disease (MDRD) and chronic kidney disease-epidemiology collaboration (CKD-EPI) are used to calculate GFR based on patients' serum creatinine. Although these equations are reasonably accurate for kidney function screening in the general population, a more precise GFR estimation is crucial in patients with particular kidney diseases (3,4). Body composition, health state, diet, and medications considerably impact GFR estimation. In a patient with IgA nephropathy low GFR, edematous state, dialysis, and acute-on-chronic kidney injury may also affect serum creatinine and bias GFR estimation. Extremely high/low body mass index (BMI) is a factor that may impact creatinine-based GFR measurements. Alterations in body composition and declines in muscle mass in people with extremely low/high BMI are associated with lower serum creatinine levels. This will lead to GFR overestimation (5-7).

Several studies showed that high BMI accelerates interstitial fibrosis in IgA nephropathy. Obesity is an independent risk factor for mesangial matrix expansion in IgA nephropathy which may increase disease severity (8-10). Hence, accurate GFR estimation is invaluable for such patients, or at least clinicians should be aware that there may be an overestimation of GFR in obese patients with IgA nephropathy. We created a systematic review and meta-analysis to determine the impact of BMI on eGFR accuracy in IgA nephropathy patients. The results will help clinicians to have a bright view of patients' kidney function and consider proper management based on it.

Objectives

The objective of this study is to investigate the correlation between BMI and eGFR in patients with IgA nephropathy through a systematic review and meta-analysis. The study aims to provide a comprehensive understanding of how BMI affects eGFR in this patient population, considering the implications for kidney function and disease progression.

Materials and Methods

Study design

This study is a systematic review and meta-analysis of the cohort study, which aimed to evaluate the effect of BMI on eGFR in patients with IgA nephropathy. All included articles in this review research were cohort. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were conducted to search the literature (11).

Search strategy

To make a complete search, international databases, such as Cochrane Library, Embase, Dimension, EBSCO, DOAJ, CINAHL, Web of Science, Scopus, PubMed, and Google Scholar search engines were searched with standard keywords, and using Medical Subject Headings (MeSH). Keywords in the search strategy included: Body mass index, Quetelet index, glomerular filtration rate, IgA type nephritis, glomerulonephritis, diabetic nephropathy, and Kimmelstiel-Wilson disease. The search strategy was conducted without any language and area limitations. AND and OR were used as combination keywords. The search strategy was conducted without language and location limitations and started from the initial to June 2024. For example, the PubMed search strategy is as follows:

((Body Mass Index OR Quetelet's index) AND (Glomerular Filtration Rate)) AND (IgA Type Nephritis OR "Glomerulonephritis, IgA" OR diabetic nephropathies OR Kimmelstiel-Wilson disease)

PICO (population, intervention, comparison, outcome)

- Population or patients: Patients with IgA nephropathy
- Intervention: Obese or overweight or high BMI,
- Comparison: Normal BMI
- Outcome: The effect of BMI on eGFR in IgA nephropathy patients

Inclusion criteria

Cohort studies that assessed the effect of BMI on eGFR in IgA nephropathy patients.

Exclusion criteria

Exclusion criteria included studies that lacked the required data, duplicate studies, study designs other than cohort studies, studies without available full text, low-quality studies, and qualitative assessment studies. Also, studies that evaluated the effect of BMI on other kidney function parameters in IgA nephropathy patients, or studies that evaluated the effect of BMI on eGFR in patients other than IgA nephropathy, were excluded.

Quality assessment

Two researchers, who were not involved in conducting the search strategy, separately assessed the initial articles

based on the Newcastle Ottawa Scale checklist (12). This checklist uses a star system for quantitative evaluation of the study quality. According to this checklist, the scores assigned to each article range from zero (the lowest quality) to 10 (the highest quality) stars. The cut-off point was set at six. In case of disagreement, the third reviewer reassessed the article, and the discussion was resolved by reaching a consensus on a single option.

Data extraction and risk of bias

To prevent data collection bias risk, two researchers extracted the required data separately by a checklist, including the authors' names, publication year, sample size, cohort duration, mean age, mean BMI, country, and standard mean of eGFR in IgA nephropathy patients with normal BMI and patients with obese or overweight. In cases of inconsistencies, the third researcher reassessed the data.

Statistical analysis

Regarding being quantitative nature of BMI measurement, the effect size effect size was taken into account. The weighted mean difference (WMD) is a classic effect-size parameter that indicates the strength of the association. Extracted studies were pooled based on the sample size, mean, and standard deviation. After the heterogeneity assessment of the studies using the I^2 index, fixed model was used. STATA 14 software utilized to analyze the data. A *P* value less than 0.05 was considered significant.

Results

After conducting thorough searches across multiple databases, a total of 973 articles were retrieved. Through a meticulous examination of their titles, it was determined that 628 of these articles were duplicates and subsequently removed. Moving forward, the abstracts of the remaining 345 articles were meticulously reviewed, resulting in the exclusion of 214 articles due to their inaccessibility in full-text form. Subsequently, the full text of the remaining 131 articles was carefully scrutinized, leading to the exclusion of 81 articles due to inadequate information required for comprehensive data analysis. This left us with a total of 45 articles. However, upon further evaluation, an additional 38 articles were excluded based on other predetermined exclusion criteria. Consequently, after this extensive screening process, a final selection of 7 articles was included in the systematic review and meta-analysis procedure (Figure 1).

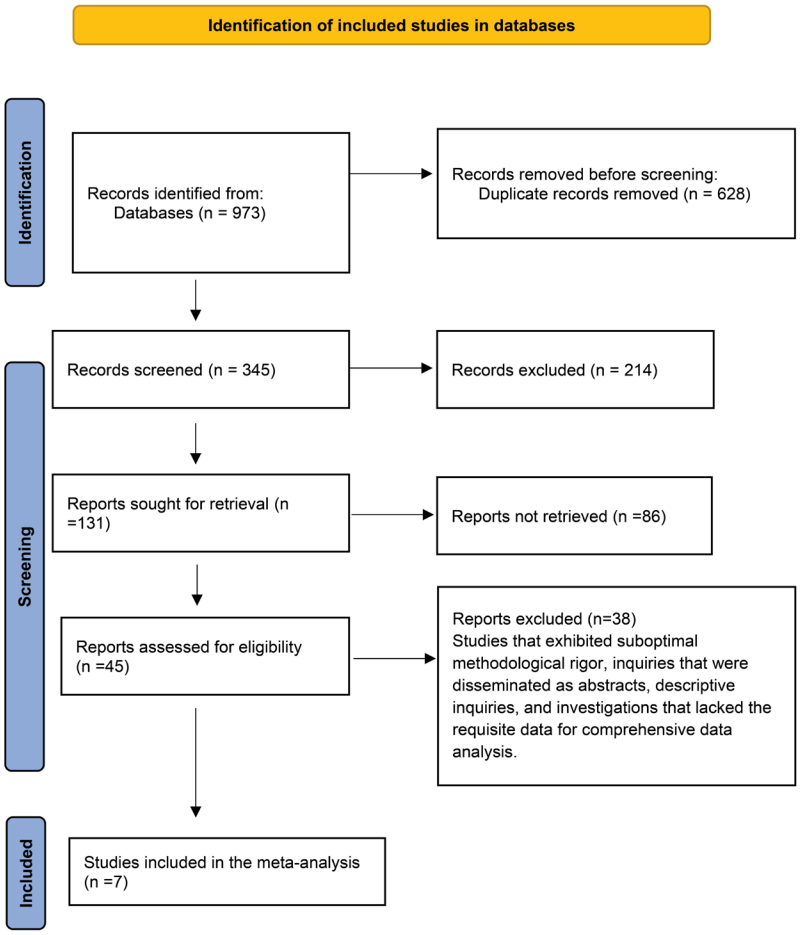

Figure 1. PRISMA Flowchart of the study.

Demographic information of studies

In this review, 7 retrospective cohort studies were included in which the mean difference eGFR biomarker was compared in two groups of normal BMI with obese or overweight. The population of these studies was from Japan, China, France, South Korea, and India countries. The average age of the studies is between 27 and 46.6 years. The sample sizes of the participants were 1354 in the normal BMI group and 1020 in the obese or overweight group (Table 1).

Pooled effect size eGFR

Pooled estimation of eGFR as the study groups was reported in Table 2. According to the results of the WMD, eGFR was lower in the obese or overweight group (WMD = -7.34, [-9.62, -5.05], $P < 0.001$; Figure 2). The results of I^2 (0.0%) test showed that there is no heterogeneity between the studies. The Galbraith plot (Figure 3) showed that all studies are within the (±2) confidence interval.

Publication bias and sensitivity analysis

The publication bias in this review was assessed by Egger's ($P = 0.969$) and Begg's ($P = 0.677$) tests, both of which indicated showed that there is no publication bias in the studies included in the meta-analysis. The funnel plot (Figure 4) also shows the absence of publication bias. The robustness of the meta-analysis results was evaluated with the sensitivity analysis (Figure 5). As the output shows, none of the studies were outside the pooled estimation range, and this shows that the results of the meta-analysis are not influenced by the results of a single study.

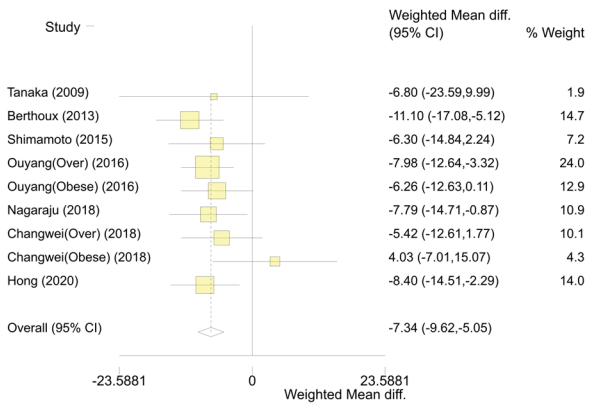

Figure 2. Forest plot of pooled effect size eGFR in studies.

Discussion

Our study is a meta-analysis of seven relevant studies address the BMI effect on GFR estimation in patients diagnosed with IgA nephropathy. The results indicate GFR overestimation in patients who are obese or overweight.

Kidney function assessment has been a crucial subject in clinical nephrology for decades. Serum creatinine, the most commonly used laboratory measure for estimating GFR, is strongly associated with muscle mass. Thus, any variation in muscle mass should be corrected or it may decline GFR estimation accuracy. Most equations do not incorporate muscle mass and BMI into GFR estimation. A systematic review by Sriperumbuduri et al discusses different equations' accuracy in the obese population. The CKD-EPI equation which is widely used to estimate GFR neglects BMI and muscle mass, resulting in overestimation

Table 1. Characteristics of included study in this meta-analysis

First author	Country	Publication year	BMI (kg/m²) cut point	Sample size	Male frequency	Mean age (Normal BMI group)	Mean age (High BMI group)	Cohort duration (year)
Shimamoto (13)	Japan	2015	23	193	95	33.7 ± 11.8	36.3 ± 11.5	5
Nagaraju (14)	India	2018	23	51	31	27/00	29/00	1
Ouyang (Over) (15)	China	2016	23-27.5	855	443	34.78 ± 10.91	40.48 ± 11.8	4/00
Ouyang (Obese) (15)			> 27.5				42.42 ± 12.02	
Hong et al (16)	South Korea	2020	25	505	245	40 ± 15.2	44.1 ± 13.3	NA
Changwei Wu (over) (17)	China	2018	25-28	431	143	36.63 ± 10.54	42.49 ± 11.9	NA
Changwei Wu (Obese) (17)			> 28				37.88 ± 10.19	
Berthoux (18)	France	2013	25	331	233	37 ± 14	46.6 ± 13.6	9.2
Tanaka et (19)	Japan	2009	25	74	35	38.5 ± 15.8	42.3 ± 15.6	1

Table 2. Pooled estimation of eGFR in obese or overweight compared with normal BMI

Variable	Number of studies	WMD (95% CI)	*P* value group	Heterogeneity test		Publication bias	
				I^2	Chi-square	Egger's	Begg's
eGFR	7	-7.34 (-9.62, -5.05)	<0.001	0.0%	0.62	0.969	0.677

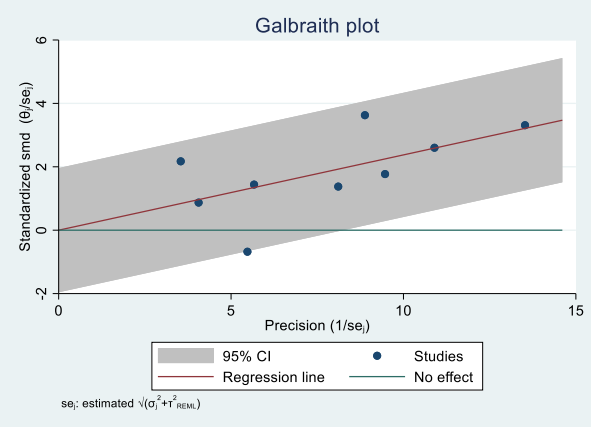

Figure 3. Galbraith plot for evaluation heterogeneity in meta-analysis.

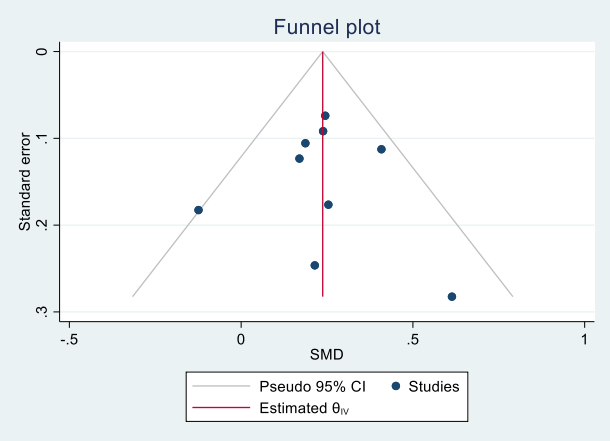

Figure 4. Funnel plot of publication bias in included studies for meta-analysis

of GFR in patients with BMI higher than 30 kg/m² (7).

In a meta-analysis conducted by Chang et al, the effect of body indexes such as BMI, waist circumference (WC), and waist-to-height ratio (WHR) on GFR was observed. Elevated indexes that indicate obesity were associated with a decline in GFR and a mortality rate enhancement. This reveals accurate GFR estimation significance in patients who are overweight (20). Wuerzner et al suggested indexing GFR for lean body mass or height instead of body surface area to obtain a more accurate eGFR when drug dosage adjustment is necessary (21).

Kanbay et al discussed the effect of BMI on IgA nephropathy prognosis. Their findings demonstrated that obesity is associated with accelerated progression of IgA nephropathy and lower GFR levels in affected patients. The study conducted by Kanbay et al suggests GFR measurement to confirm this faster progression in every patient who is overweight. Clinicians should be aware that GFR overestimation in such cases may result in kidney function deterioration (22). In patients with extremely low or high BMI, a good alternative for kidney

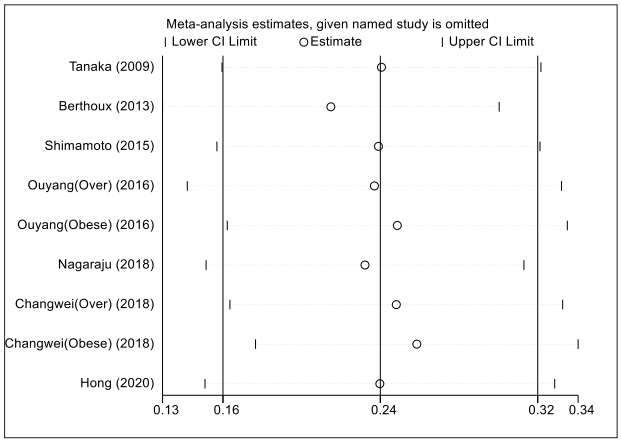

Figure 5. Sensitivity analysis for estimated effect size.

function assessment could be iohexol plasma clearance which is clinically feasible and has higher accuracy (23). Another solution when iohexol clearance is unavailable is using deindexed eGFR equations. It is customary for the equations used to calculate eGFR to be indexed to the surface area of the body. Using deindexed eGFR equations and having consistency in evaluating patients' eGFR with a certain equation and laboratory technique is the key to an accurate GFR estimation in moderate to severely obese patients (24-26).

Conclusion

In conclusion, the study demonstrated that the eGFR was lower in the obese or overweight group compared to the normal BMI individuals. This finding highlights the impact of obesity on kidney function and emphasizes the importance of maintaining a healthy weight to reduce the risk of kidney-related health issues. Additionally, further research is needed to explore the specific mechanisms through which obesity affects kidney function and to develop targeted interventions for individuals at risk. Healthcare professionals must address weight management as part of overall kidney health promotion and disease prevention strategies. By raising awareness of the link between obesity and kidney function, we can work towards improving the health outcomes of individuals and reducing the burden on healthcare systems.

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Authors' contribution

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Resources: All authors.
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Validation: Hediyeh Mesbahi and Sara Ghaseminejad Kermani.
Visualization: Sara Rasta and and Mahin Roozitalab.
Writing–original draft: All authors.
Writing–reviewing and editing: All authors.

Conflicts of interest

There are no competing interests.

Ethical issues

The Hormozgan University of Medical Sciences Ethics Committee (Endocrinology and Metabolism Research Center) approved this study with an ethical code of (IR.HUMS.REC.1402.301). Additionally, this investigation has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (International Prospective Register of Systematic Reviews) website with (ID: CRD42023417633) and Research Registry website with (Unique Identifying Number (UIN) reviewregistry1665)). Besides, the author has observed ethical issues (including plagiarism, data fabrication, and double publication).

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