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Bidirectional Relationship between Obesity, Psychiatric Disorders, and Renal Disease: A Systematic Review

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ABSTRACT

The rapid growth of obesity worldwide has made it a significant health problem. In contrast, the dramatic increase in the prevalence of obesity has had a significant impact on the magnitude of chronic kidney disease (CKD), especially in developing countries. A vast number of researchers have reported a strong relationship between obesity and chronic kidney disease, and obesity can serve as an independent risk factor for kidney disease. The histological changes of kidneys in obesity-induced renal injury include glomerular or tubular hypertrophy, focal segmental glomerulosclerosis, or bulbous sclerosis. Furthermore, inflammation, renal hemodynamic changes, insulin resistance, and lipid metabolism disorders are all involved in developing and progressing obesity-induced nephropathy. However, there is no targeted treatment for obesity-related kidney disease.

Despite the apt acknowledgment of the physical comorbidity burden in obesity, its correlation to both mental health and renal health has received relatively less research attention. However, in the last 20 years, there has been a progressive collection of evidence concerning the correlation between obesity, renal disorders, and different psychiatric disorders, especially in individuals who have sought treatment for the conditions. Regardless of this, there are still significant knowledge gaps linked to the strengths as well as directions of the correlations between obesity, psychiatric disorders, and renal disorders. Moreover, owing to the methodological variances between different studies, it is essential to synthesize the existing evidence in these areas to enable researchers and clinicians to have improved comprehension of the extant correlations between obesity, psychiatric disorders, and renal disorders. This will positively impact the clinical assessment and identification of additional research targets in these areas, including the potential neurobiological correlations between psychiatric disorders and obesity. From the management point of view, it has been indicated that early identification and subsequent management of both widespread psychiatric challenges and renal disorders may optimize the outcomes in obese and overweight patients presenting for treatments. As such, there is a need for practicing politicians to have a better understanding of the bidirectional correlations between obesity, psychiatric disorders, and renal disorders. With this background, the present systematic review and meta-analysis have been performed to review and synthesize the extant data and evidence on the bidirectional correlations between obesity, psychiatric disorders, and renal disorders.

The positive bidirectional relationship between body weight and depression is found. The effect of depression on body weight is significant among both males and females in a randomized population, and females who experience depression are most likely to be obese and less likely to have normal weight compared to females without depression. The risks of overweight and obesity are high among people who are less educated or unable, who have poor health statuses, and who had high blood pressure.

Introduction

At present, within the global context, obesity is considered prevalent, particularly in both developed and developing nations, with an increase in the number of obese individuals[1]. Thus, between 2005 and 2015, the rate of obesity and overweight in the United States was approximately 34%, even as the obesity prevalence rates in the UK stood at 24% during the period[2]. Generally, the obesity prevalence rates in low and middle-income nations remain comparatively lower in comparison to those of high-income nations. This can be attributed to increased accessibility and availability of deeply processed foods, even as developing nations have portrayed an increment in the number of obese individuals: nonetheless, such processed foods have been acknowledged to have higher amounts of calories even as they do not have any nutritional value[3,4] in adults has increased considerably[5]. Currently, obesity is considered a fast-growing and challenging universal public health crisis. For instance, in the last 30 years, the global prevalence of obesity (body mass index [BMI] ≥25 kg/m^2. Thus, in the United States, the age-adjusted obesity prevalence between 2013 and 2014 stood at 35% in men and 40.4% in women[6]. However, the obesity challenge has also affected children, with the prevalence rate in the United States being 17% in obesity cases and a further 5.8% in extreme obesity cases among younger persons aged between 2 and 19 years[7]. Consequently, in China, which is the most affected nation, the obesity prevalence rate among adult persons has nearly tripled from 11.7% in 1991 to 29.2% in 2009[8]. As a global health concern, it is projected that obesity prevalence rates will increase by approximately 40% between 2020 and 2030, even as the low-income nations are presently indicating evidence of transition from normal weights (18.5 to 24.9 kg/m^2) to obesity and overweightness (25.0 to 39.9 kg/m^2), similar to what was witness in the United States and other parts of Europe several decades ago[9,87]. The increase in obesity prevalence rates has implications for both psychiatric disorders and renal diseases, given that a higher BMI is among the sturdiest risk factors for the new onset of mental disorders and renal disorders[10,11].

While this applies to all age groups and demographics, women are at higher risk, compared to their male counterparts, of developing most diseases and conditions, as indicated by several studies[7]. Moreover, it has been observed that a diagnosis of obesity considerably increases the likelihood of a broader array of psychiatric disorders across various age groups. These may include psychosis, depression, nicotine addiction, and anxiety, as well as personality and eating disorders. From the clinical perspective, these observations and study findings necessitate the raising of awareness of both psychiatric and renal disease diagnoses in patients who are obese or overweight and, whenever necessary, consult specialists at the initial stages of diagnosis. Increment in fat mass, especially visceral adiposity, has additionally been acknowledged to promote the development and progression of kidney disease through both direct and indirect mechanisms, which makes pharmacological interventions necessary in preventing potentially adverse outcomes[7].

Consequently, some earlier studies have suggested a significant correlation between obesity and psychiatric disorders, particularly mood disorders[12]. For instance, several population-based studies conducted in Canada and the United States have disclosed correlations between obesity and various depressive symptoms, depression history, and various psychological distress measures[13,14]. Still, several surveys conducted in the United States have disclosed gender divergences in this correlation between obesity and psychiatric disorders, with positive correlations observed in women and either no or negative correlations being observed in men[15, 16]. A study conducted in the United States has disclosed the existence of a sturdier correlation between obesity and depression, particularly in individuals aged

below 65 years[17]. This is also in line with the findings of a community-based study conducted in the 1950s that disclosed a stronger correlation between obesity and depression, particularly among individuals of higher socioeconomic status[18]. Nevertheless, the correlation between obesity and depression reported in mostly caucasian populations in both Canada and the United States might not be extendable to various racial, ethnic, and cultural groups[16,19]. Various longitudinal studies have additionally disclosed that depression is a key predictor of the subsequent obesity onset, that a correlation exists between decrement in depression levels and successful weight loss, as well as that depression is a key predictor of poor weight loss success[20,21].

Regardless of the above findings and observations, currently, there is a limited amount of epidemiological data addressing the extant correlations between obesity and psychiatric disorders like substance use disorders and anxiety. For instance, anxiety symptoms have indicated moderate positive correlations to obesity in both clinical and community samples[22,23]. The abuse of alcohol has been linked to a reduced risk of obesity and overweightness[24]. Moreover, according to Simon et al., an evaluation of the lifestyle patterns of individuals with psychiatric disorders like major depressive disorder, bipolar disorder, schizophrenia, low physical activity, and sedentary behavior has been increasingly noted in such individuals [25]. Nearly 50% of persons with psychiatric disorders fail to adhere to the recommended minimum of 150 minutes of physical exercise every week[15]. Still, individuals suffering from severe psychiatric disorders commonly portray unhealthy dietary habits that include reduced consumption of fruits, vegetables, and high-fiber diets but increased consumption of junk foods[16,26]. Moreover, persons experiencing mental disability are highly prone to be heavy smokers in comparison to the general population[16,27]. The initial study describing the correlation between obesity and psychiatric disorders was conducted in 1946 by Nicholson, who reported the correlation between obesity and psychoneurosis and emotional tension[15]. Since then, several studies regarding the existing correlations between such psychiatric conditions and obesity have been conducted to evaluate their bidirectional correlations[28]. Additionally, persons with psychiatric disorders have been reported to portray a 2 to 3-fold heightened risk of developing obesity[29]. On the contrary, obese individuals have approximately 30 to 70% heightened risk of developing a psychiatric disorder[29]. A study conducted in North America has also disclosed that nearly 80% of 10,000 individuals who were diagnosed with depression, bipolar disorder, or schizophrenia were either obese or affected by overweightness[30]. The rationale for the increased number of patients who are obese and have severe psychiatric disorders has been broadly debated.

Psychiatric disorders that include depression, cognitive impairment, and anxiety disorders, among others, have become increasingly prevalent in obese patients with chronic kidney disease. These conditions and disorders have been acknowledged to worsen the quality of life of the patients as they result in prolonged hospitalizations and increased mortality rates. Though a number of studies have been conducted and hypotheses developed with the objective of clarifying the existing bidirectional correlations between obesity, psychiatric disorders, and renal disease, the most widespread explanation has been founded on the cerebrovascular disease occurrence alongside the accumulation of uremic toxins in persons with renal disease[18-24]. Nevertheless, the dearth of direct correlations between the various vascular risk factors with renal disease and obesity proposes that other mechanisms might play active roles with regard to the bidirectional correlations and pathophysiology shared by obesity, renal, and psychiatric diseases. As such, the objective of the present systematic review is to evaluate the bidirectional correlation between obesity, psychiatric disorders, and renal disease. To attain this objective, the study will look into the correlation between obesity and psychiatric

disorders, as well as how the correlation impacts the development of renal disease.

Materials and Methods

SEARCH STRATEGY AND STUDY SELECTION

This systematic review entailed an in-depth search on electronic databases for pertinent research articles. The in-depth search was conducted on virtual databases that included MEDLINE, PsycINFO, Science Direct, Google Scholar, and PubMed, with the objective of locating studies published in the last 20 years. Further, the objective of the researchers in conducting the literature search was mainly to identify articles that focused on the existing bidirectional correlations between obesity, psychiatric disorders, and renal disorders. A psychiatric disorder was described as any International Classification of Diseases, 10th Edition coded category that falls between F00 and F99. Consequently, obesity was based on the WHO definition of BMI ≥30 kg/m^2.

Additionally, to find the apt articles, the researchers utilized MeSH word combinations that included obesity, psychiatric disorders/mental disorders, renal disorders, renal insufficiency, chronic kidney disease, body mass index, depression, anxiety disorders, eating disorders, kidney diseases, glomerulonephritis, nephritis, and nephrotic syndrome. The first search was conducted on PubMed, followed by a comparable search on other electronic databases to identify pertinent articles. The supplemental search on Google Scholar using the above MeSH words was conducted to comb the existing literature further. The restriction on publication date was set to 20 years.

Still, the titles and abstracts of the identified studies that met the set inclusion criteria were assessed independently by two researchers. In instances of insufficient information within the study abstract, the two authors were required to independently evaluate the full texts of the articles to ensure that they met the inclusion criteria for this systematic review and meta-analysis. The potential disagreements concerning the articles that met the inclusion criteria were mainly sorted out through discussions and consultations with a third independent author. After this, the authors consolidated and drew up the abstract lists after removing duplicates. Additionally, an independent and manual assessment of the reference lists of included studies was conducted to identify potential articles by the authors. It is worth noting that citation indexing and conference proceedings were excluded from this systematic review, with the latter mainly due to concerns regarding the study's quality and insufficient data reporting.

INCLUSION AND EXCLUSION CRITERIA

Using intervention, outcomes, patient, comparison, and research design criteria, every study that evaluated the correlation between obesity, psychiatric disorders, and renal disorders, and vice versa, was included if they satisfied the following inclusion criteria. Firstly, to be included in the present systematic review and meta-analysis, the study had to quantitatively measure the association between obesity as the explanatory variable and specific psychiatric disorders and renal disorders as the outcome variable, or vice versa. Thus, the psychiatric disorder or renal disorder outcomes needed to be necessarily mentioned as "risks" to be included owing to their provision of the quantitative approximate about the strength of the correlation/relationship. Also, studies conducted on populations without prior medical comorbidities, including diabetes, were included. The rationale of doing this entails the observation that chronic medical disorder is a key confounder concerning the existing correlations between obesity, psychiatric illnesses, and renal disorders[31,32]. Further, the inclusion criteria also included studies that did not utilize alternative definitions of obesity, including sarcopenic obesity and abdominal obesity, as well as studies published in the English language and have also been published in peer-reviewed journals.

Consequently, the exclusion criteria took in sponsored clinical trials, editorials and opinions, as well as narrative reviews. Also, systematic reviews

and meta-analyses that did not employ standard tools in the evaluation of the existing correlations between obesity, psychiatric disorders, and renal disease were excluded. Studies were also excluded in instances where the bidirectional correlations was assessed without being associated to the target populations. Studies published in languages other than English, non-peer-reviewed journal articles, dissertations, secondary studies, and non-academics authored articles were excluded. Also excluded were inaccessible articles with inadequately sound materials and methods sections.

DATA EXTRACTION AND QUALITY ASSESSMENT

For the present systematic review, two authors were tasked with concurrently conducting data extraction and quality assessment of the included studies. Thus, the data extracted from the included studies included the author's names, study publication year, place where the study was conducted, study population attributes, study design, size of the sample, primary objectives of the study, significant moderators, and fully adjusted measure of association, including risk (relative risk (RR) or Odds ratio (OR)). The researchers utilized an adapted Newcastle–Ottawa Quality Assessment Scale version to critically appraise the included studies categorized as observational studies. The tool was chosen owing to its better psychometric attributes, including inter-rater reliability and content validity[33]. The tool included sampling procedure representativeness, response rate, validity of assessment measures utilized, and if the study controlled a minimum of three key confounders. Reporting on the various methodological aspects of the study apart from the numerical scores has been proposed to be increasingly appropriate for non-randomized observational studies and included in various systematic reviews, which made the tool most suitable for quality assessment[34]. In light of this, a 60% response rate was regarded as sufficient, based on earlier systematic reviews that focused on observational studies[35]. Therefore, the individual quality assessment tool components were rated (criteria not reported, criteria not met, and criteria met), even as an overall rating was derived for each study (high, moderate, and poor) included in the systematic review. For the effects estimations, the researchers depended on the study authors' reported values, and neither the summary measures were computed nor any additional analysis performed.

Results

The study selection process yielded 1298 articles retrieved after an in-depth search on the different virtual databases. The articles were further screened, which led to removing 836 duplicates, and an additional 191 articles were removed as they were found ineligible through automation. Additionally, 152 articles were excluded for other reasons, including the need for more alignment with the research objectives of this systematic review and animal-based studies. Also, dissertations and studies published in non-peer-reviewed journals were excluded. Studies that were published in languages other than English were excluded. The exclusion also included opinion pieces, scoping reviews, secondary studies, articles not authored by academics, and other studies not classified as primary. As a result, only 119 studies found to be eligible underwent additional screening, leading to the exclusion of 66 more articles. The remaining 53 articles were sought for retrieval, out of which 18 articles were irretrievable. Therefore, only 35 articles underwent evaluation for eligibility, leading to the exclusion of an additional 9 studies after full-text screening for various reasons, including protocol (2 articles), preprint (3 studies), failure to report limitations (3 studies), and failure to evaluate the targeted intervention (1 study). As a result, only 26 studies satisfied the inclusion criteria. They qualified for inclusion in the present systematic review and meta-analysis, as indicated in the PRISMA flow diagram in Figure 1 below.

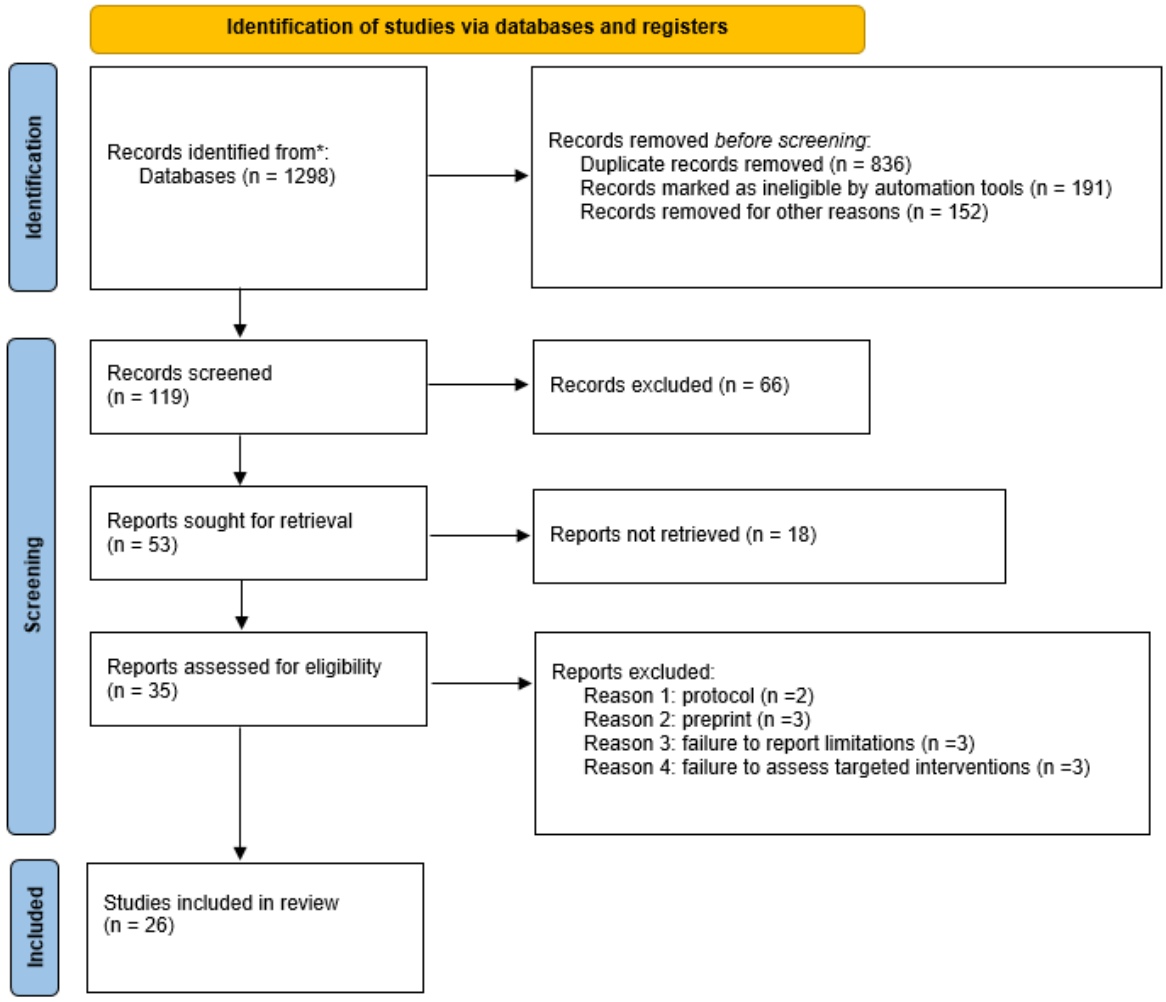

Figure 1: PRISMA flow diagram indicating the studies selection and inclusion process

Discussion

THE BIDIRECTIONAL CORRELATIONS BETWEEN OBESITY AND PSYCHIATRIC DISORDERS.

A review of the previous literature has disclosed that obesity might be considerably linked to psychiatric disorders, including different mood disorders[14,36]. Several community-based studies conducted in the United States and Canada have disclosed the extant correlations between obesity and depressive symptoms, depression history, and psychological distress measures[17,37]. Studies conducted in the United States have reported gender differences in the correlation, with positive correlations between obesity and depression being reported in women and negative or no correlations being reported in men[38]. Additionally, a recent study conducted in the United States has reported a stronger correlation between obesity and depression in individuals aged below 65 years[39].

Despite the considerable amount of extant literature focusing on the association between obesity and psychiatric disorders, the present systematic review and meta-analysis have focused on the strength of the bidirectional correlations between obesity and various psychiatric disorders. In this regard, based on the analysis of the included literature, it can be observed that the existent evidence of the bidirectional correlation is not only voluminous but additionally strongest for depression, even as a larger number of the included studies have reported significant association for the existence of depression in obesity[40-42]. Nevertheless, given that a more substantial proportion of the studies reviewed were cross-sectional, it is difficult to effectively determine the existing cause-and-effect correlations between obesity and depression, owing to the study design limitations. The establishment of the cause-and-effect correlations

may be best determined through longitudinal study designs. Moreover, only a limited number of longitudinal studies were included in this systematic review and provided evidence of the bidirectional correlations between obesity and depression, and this was further replicated in various cross-sectional and observational studies that offered sturdier evidence of the correlation[38,41,43,44]. The observed variability concerning the effect size across several studies might be attributed to the methodological differences, including the cutoffs employed in the BMI measurements, the methodologies utilized in the measurement of psychiatric outcomes, including depression (clinical and rating scales), the different follow-up lengths in the longitudinal study designs, as well as nature of the utilized effect estimate (RR and absolute risk estimate). The subgroup assessment is based on parameters that include gender, age, and divergences in measurement methods, which have been reported in a limited number of studies, and this can be attributable to the observed differences.

Consequently, concerning anxiety disorders, the number of studies reviewed that focused on the correlations between obesity and anxiety disorders were comparatively fewer in comparison to those that focused on other psychiatric disorders. Based on the findings of this systematic review, the extant bidirectional correlation between obesity and anxiety disorder was found to be less pronounced in comparison to the correlation between obesity and other psychiatric disorders, especially depression. Thus, one of the studies has disclosed that obese persons have higher odds about the development of lifetime panic disorders[16]. However, despite a recent study with a pooled odds ratio indicating a significant correlation, a higher inconsistency index was also observed[45]. Except for social anxiety and certain phobias, extant evidence has been mixed, especially in studies that conducted subgroup analysis focusing on the different anxiety subtypes[46,47]. On the contrary, in their study, Simon et al. have disclosed that the positive correlations between obesity and anxiety or mood disorders are largely modest, with odds ratios that range between 1.2 and 1.5. However, even such modest odds ratios have significant public health implications, owing to the higher obesity prevalence rates (nearly 25%) and higher anxiety prevalence rates[25,36](25%). The approximated lifetime prevalence rate of mood disorders in persons with BMIs that are under 30 and in individuals with BMIs that are 30 and above translate to the 24% population attributable risk, indicating that a quarter of obesity cases within the general population can be correlated to mood and anxiety disorders[48]. Though the above calculation indicates the significance of correlation in terms of public health, it has not shown the direction of the causal association. Moreover, it is appropriate to conclude that over a fifth of cases involving mood disorders within the general population can be attributed to the existing correlations with obesity (21% population-attributable risk). Nevertheless, at present, there is no means to distinguish the causal relationship direction between obesity and psychiatric disorders and the probability of various unmeasured causes inducing the correlation between them. The limited number of longitudinal studies that evaluated the existing correlations between obesity and anxiety disorders has precluded apt conclusions about the correlation's direction.

Concerning personality disorders, the extant correlation between obesity and personality disorders has been observed to be increasingly intricate. A limited number of studies have assessed certain personality traits in individuals who are obese, and in these, impulsivity and neuroticism have been constantly replicated[49]. Furthermore, a study that focused on obese persons attending bariatric surgical clinics disclosed that nearly a quarter of the patients had clinical symptoms indicating the existence of borderline personality disorders[50]. It has additionally been indicated that the odds of an obese individual having a personality disorder are high, even as cluster C traits (dependent and avoidant) are normally predominant[51].

Still, according to Camacho-Barcia et al., eating disorders, obesity, and other psychiatric disorders might form a vicious cycle, and several studies have assessed psychiatric disorders within the contexts of obesity and comorbid eating disorders[52]. Nevertheless, the direct correlation between eating disorders and obesity has been infrequently researched. In one of the few studies to focus on the subject, the researchers have reported that, although eating disorders and obesity continue to increase within the general population, the odds of having obesity and comorbid eating disorders have increased by nearly 4.5 times, indirectly indicating the extant underlying correlation between the two disorders[53]. On the other hand, a recent prospective study has indicated increments in the prevalence rates of obesity in adult persons who have a childhood history of ADHD[54]. In evaluating the strengths of the bidirectional correlation between obesity and ADHD, the study has further disclosed that persistent ADHD during childhood was linked to the development of obesity later in life, and this was more pronounced in women compared to men[54].

Additionally, several neuroimaging studies have expressly implicated a highly common neurobiology in eating and substance use, including the reinforcement of reward pathways[52,55]. Therefore, there has been an increasing tendency to regard obesity as an aspect of addiction[55]. Nonetheless, only a few studies have focused on evaluating this correlation. Thus, in the present systematic review and meta-analysis, one of the studies reviewed has focused on the correlations between obesity, substance abuse, and depression and disclosed that the rates of obesity were higher in individuals with substance use disorder, with the correlation being strongest in women than men[56].

ASSOCIATION OF OBESITY WITH CKD AND OTHER RENAL COMPLICATIONS

Some population-based studies have disclosed the existence of a relationship between the measures of obesity and the development and progression of both renal disorders and psychiatric disorders. Thus, concerning renal diseases, a higher BMI has been linked to the existence and development of proteinuria, especially in persons without kidney disease. Moreover, some bigger cohort population-based studies have disclosed that higher BMI appears to be correlated with the development and existence of low approximated glomerular filtration rate (GFR)[57-59] with increased rapid loss of approximated GFR over time, along with the ESRD incidence[60,61]. Higher BMI levels alongside class II obesity and above have been found to correlate with the rapid progression of chronic kidney disease, particularly in individuals with pre-existing chronic kidney disease[62].

In this regard, a limited number of studies evaluating the correlation between abdominal obesity through the use of WC and WHR with chronic kidney disease have reported a relationship between albuminuria and higher girth, decrement of GFR, and ESRD incident independent of the level of BMI[21,63,64]. Consequently, an association between higher albuminuria prevalence and higher visceral adipose tissue measured using computed tomography has been reported in males[65]. Additionally, the reporting of BMI-independent correlation between obesity and poor renal outcomes has been noted in studies focusing on the existing correlations between mortality in individuals with ESRD and kidney transplant and disclosed that visceral adiposity played a direct role in the relationship[66]. Generally, the correlations between obesity and renal disorders have been observed to persist despite the adjustments for potential mediators of obesity's metabolic and cardiovascular effects that include diabetes mellitus and high blood pressure, indicating that obesity might negatively impact kidney function through in part unassociated with such complications (vide infra).

Obesity's deleterious effects concerning the kidneys extend to complications like kidney malignancies and nephrolithiasis. Moreover, higher

BMI has been linked to increased prevalence rates and incidence rates of nephrolithiasis[67,68]. Still, a significant correlation has been found between overtime weight gain, increased baseline WC, and a higher incidence rate of nephrolithiasis[62]. Obesity has also been linked to several kinds of malignancies, especially kidney cancers. For instance, a population-based study conducted in the UK with a sample of 5.24 million concluded that a 5 kg/m^2 BMI was linked to a 25% elevated risk of kidney cancers, even as 10% were attributed to higher BMI[69]. Still, an additional large cohort study that evaluated the global obesity burden on malignancies approximated that between 17% and 26%of kidney cancers in both men and women, concurrently, could be linked to higher BMI[70]. Similarly, it has been observed that, across populations from diverse parts of the globe, the correlation between obesity and renal disorders, including kidney cancers, has been consistent in women and men[71]. Of the different cancers evaluated, kidney cancers were ranked third highest concerning correlation with obesity[71].

Regarding the action mechanisms underlying obesity's effects on renal functioning and renal disorders, it is noteworthy that obesity leads to intricate metabolic abnormalities with wide-ranging effects on conditions that affect the kidneys. However, the precise mechanism through which obesity causes or worsens renal disorders remains unclear. Thus, the observation that most obese and overweight persons do not develop renal disorders and the distinction of approximately 25% of obese and overweight persons as being metabolically healthy indicates that an increase in BMI alone is not adequate to induce a renal disorder[72]. Therefore, some of the damaging renal consequences related to obesity might be mediated through downstream comorbid diseases that include hypertension and diabetes mellitus; however, the various effects of visceral adiposity may adversely and directly affect the kidneys, induced through the adipose tissue's endocrine activities through the production of leptin, resistin, and adiponectin[73]. These entail the development of oxidative stress, inflammations, renin-angiotensin-aldosterone system activation, insulin resistance, increased insulin production, and abnormal lipid metabolism[73,74]. Such effects are prone to bring about pathological changes to the kidneys, which may underlie the increased risk of developing renal disorders reported in the studies reviewed[74]. Moreover, the effects also include the accumulation of ectopic liquid and increment in renal sinus fat deposition, glomerular hypertension development, and increment in glomerular permeability as a result of the hyperfiltration-linked glomerular filtration barrier injury, as well as the development of segmental and focal glomerulosclerosis and glomerulomegaly[75]. Available statistics indicate that between 1986 and 2000, the incidence rate of obesity-related glomerulopathy (ORG) increased 10-fold [73]. It is important to note that, normally, ORG presents together with other pathophysiological processes associated with different conditions and advanced ages, thereby leading to increasingly accentuated kidney damage, particularly in individuals who are elderly and those with high blood pressure[73,74].

Additionally, obesity has been linked to several risk factors that have been acknowledged to contribute to the increased incidence and prevalence rates of nephrolithiasis. For instance, an increment in BMI has been linked to low urine pH and an increment in urinary oxalate, phosphate, sodium, and uric acid excretion[76,77]. Sodium and protein-rich diets might result in increasingly acidic urine, as well as a decrease in the levels of urinary citrate, leading to a higher risk of kidney stone development. Obesity's insulin resistance attribute might additionally predispose an individual to nephrolithiasis regarding its adverse effects on ammonia genesis, the tubular Na-H exchanger, and the acidic environment promotion[78-80]. This is further complicated by the observation that certain weight loss therapies lead to the worsening as opposed to enhancement in the risk of development of kidney stones; for instance, the performance of gastric surgery might result in a significant increment in the absorption rate of

enteral oxalate alongside the increased risk of nephrolithiasis[81].

The various mechanisms underlying the increased risk of renal disorders observed in individuals who are obese and overweight have been insufficiently characterized. Further, insulin resistance alongside the resultant hyperinsulinemia, the increment in the insulin-like growth factor 1 production, and several intricate secondary humoral effects might exert stimulating effects concerning the growth of different kinds of tumor cells[82]. Recently, the adipose tissue's endocrine function, its observed effects on immunity, and the inflammation environment generation with intricate effects on renal cancers have been noted as additional clarifications[83-85].

Conclusion

The study's findings reveal bidirectional correlations between psychiatric disorders and obesity in both genders, highlighting a significant increase in the likelihood of developing psychiatric and renal disorders among overweight or obese individuals. Stronger and reciprocal correlations are observed with depression, modest correlations with anxiety disorders, and limited correlations with other psychiatric disorders. Despite risks for both genders, correlations appear stronger in females, suggesting a potential gender moderation. While obesity correlates with renal disorders, it's likely not an independent causal factor; instead, harmful renal effects are mediated by hypertension and dysglycemia, emphasizing the role of hyperglycemia below the threshold for type 2 diabetes in obesity-related renal disorders.

Conflict of Interest:

All authors declare no conflicts of interest.

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Author contribution

All authors played several overlapping contributory roles such as Conceptualization, design, cross-referencing, and fact-checking; Formal Analysis and interpretation of data; project administration, curation, visualization, writing – original draft, writing – review & editing; supervision, oversight, and leadership, correspondence, data curation, quality control, internal review, communications, data collection and archiving, software, literature search, validation, and approval.

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