IOSR Journal of Nursing and Health Science (IOSR-JNHS)
e-ISSN: 2320–1959.p- ISSN: 2320–1940 Volume 8, Issue 6 Ser. II. (Nov - Dec .2019), PP 15-24
www.iosrjournals.org

Association between Obesity and Chronic Kidney Disease

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Abstract: *Over the past two decades increased attention on epidemiological studies of health and diseases are seen common in communities. The first concern is a sever uprising in the emergence of chronic non communicable diseases cause a huge number of mortality and morbidity issues. Obesity is having a greater impact on kidney function, many complications occur with obesity in combination with CKD like cardiovascular diseases, pre mortality, poor quality of life etc.. The prevalence of CKD is increasing in people with increased body mass index, as well as CKD with its related complications and this rate is expected to increase hugely in the future.*

Key Words: *Obesity, CKD, Nephrosclerosis, Kidney damage*

Date of Submission: 26-10-2019 Date of Acceptance: 11-11-2019

I. Introduction

More people worldwide are dying of obesity related cases than ever before. Majority of the world's adult population will be obese by 2030. Obesity in young people increases in Asian countries such as China and India, without effective intervention strategies to reduce obesity, more people will develop CKD and type 2 diabetes at younger ages. In this context explained about the incidence and prevalence, causes and risk factors of obesity and CKD, also highlighted the pathological events occur in obesity, how obesity progresses to CKD and other complications.

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1. Obesity -assessment and prevalence:
1.1 Obesity –assessment

Obesity is defined by classical clinical parameters such as Body Mass Index (BMI), Waist Circumference (WC), and Waist Hip Ratio (WHR). Anthropometric measurements include height, weight, Waist Circumference WC, Hip Circumference (HC), Mid Upper Arm Circumference (MUAC), skin fold

thickness, body surface area and WHR. However, the accuracy depends on the skills and training of the person taking measurements and can vary from observer to observer [1,2].

1.2 Prevalence of Obesity

Over 1.5 billion people worldwide are overweight and by 2030 more than 50 percent of the world population will be obese. It is estimated that 18 percent of men and 21 percent of women worldwide will be obese by 2025, and more than 6 percent of men and 9 percent of women will be severely obese (35 kg/m² or greater) "Nearly 70 percent are related to high BMI due to cardiovascular disease, and more than sixty percent of those deaths occurring among obese people" [**3].** According to WHO, over half of the 177 million cases of DM worldwide are attributed to overweight and obesity [4].

National data indicate that approximately 14 percent of the children and 12 percent of the adolescents are overweight at the 95th percentile of BMI [5]. In India the problem of obesity has been scantily explored even among the effluent groups and the criteria for defining obesity in the Indian context are not well spelled out. Prevalence of abdominal obesity (AO) as well as of General Obesity (GO) was high in India [6].

Table1: Percentage of obesity in various states as recorded in NFHS-4 and NFHS-3

State	Men (15-49 years)who are overweight or obese-NFHS-4	Men who are overweight or obese-NFHS-3	Women who Are overweight or obese-NFHS-4	Women who are overweight or obese-NFHS-3
Andhra Pradesh	33.5		33.2	
Andaman and Nicobar	38.2		31.8	
Bihar	12.6	6.3	11.7	4.6
Goa	32.6	15.5	33.5	20.2
Haryana	20.0	10.8	21.0	17.4
Karnataka	22.1	10.9	23.3	15.3
Madhya Pradesh	10.9	4.3	13.6	7.6
Meghalaya	10.1	5.9	12.2	5.3
Puducherry	37.1		36.7	
Sikkim	34.8	11.9	26.7	15.4
Tamil Nadu	28.2	14.5	30.9	20.9
Telangana	24.2		28.1	
Tripura	15.9	4.8	16.0	7.1
Uttarakhand	17.7	7.9	20.4	12.8
West Bengal	14.2	5.5	19.9	11.4

Table2: Percentage of obesity in rural and urban areas in various states

State	Urban		Rural	
	Men	Women	Men	Women
Andhra Pradesh	44.4	45.6	28.0	27.6
Andaman and Nicobar	38	38.3	38.3	26.6
Bihar	20.1	23.5	10.9	9.7
Goa	35.3	36.3	28.2	28.5
Haryana	21.0	24.3	19.3	18.8
Karnataka	28.6	31.8	17.1	16.6
Madhya Pradesh	17.6	23.8	7.8	9.1
Meghalaya	17.1	18.4	8.1	10.2
Puducherry	40.5	38.1	30.8	33.6
Sikkim	41.5	34.1	29.7	23.1
Tamil Nadu	30.6	36.2	25.6	25.4
Telangana	31.9	39.5	17.9	18.5
Tripura	18.2	23.5	14.9	12.8
Uttarakhand	23.0	28.4	14.1	16.0
West Bengal	20.7	30.6	11.2	15.0

1.3 Risk factors and causes of Obesity:

The increase in obesity prevalence is due to two major factors, plentiful supplies of inexpensive foods and sedentary jobs. Central obesity (CO) is frequently accompanied not only by hypertension but also hyper glyceridemia, low HDL cholesterol, inflammation and pro thrombotic state [8]. The theory of nutrition suggests that overweight comes first among rich and urban people then to rural people with low economic status [9].

Adult obesity is a highly heritable trait, but environmental influences have a major role in the eventual development of obesity and associated co morbidities [10]. Socio economic factors plays an important role in increasing BMI values, along with other associative factors like employment, physical activity at work, food

prices, the prevalence of restaurants, cigarette smoking and urbanization are important driving forces of obesity [11].

II. CKD - Assessment And Prevalence

2.1 CKD assessment

The onset of albuminuria without renal failure and stages 3-5 of CKD can be predicted by assessment of BMI. Improving risk stratification and recommendations on body weight control in the general population is very essential to prevent the further progression of CKD [12].

Increased WC and WHR were associated with high incidence of CKD [13]. WHR is positively and highly associated with CKD and mortality [14]. Albuminuria is an important risk factor in these patients, and all diabetic patients should have a micro albuminuria assessment yearly [15].

Waist to height Ratio acts as predictor of CKD. [16]. Out of all anthropometric indices WC and weight to hip ratio > 0.6 is particularly associated with CKD in elderly females [17]. A Central body fat distribution independent of BMI is associated with a unfavorable pattern of renal hemodynamic measures that could underlie the increased renal risk reported in observational studies [18].

Glucose tolerance tests, BMI and serum triglycerides are the long term predictors of kidney function in male population. Whereas in, women those metabolic, anthropometric parameters seem to be less predictive of e GFR [19]. An abnormal low GFR escapes from medical notice in early stages and which makes people to enter into ESRD. Early recognition of e GFR is very important and which serves the purpose in preventing progression to ESRD. [20].

Lower e GFR and higher albuminuria were much more strongly associated with ESRD than with mortality. Decreased GFR and albuminuria are primary factors in the development of ESRD and greater risk of death and ESRD [21].

2.2. Prevalence of CKD

The prevalence of CKD is substantially increasing over the past decades in many developed and developing countries, representing a global challenge for public health. Patients with kidney failure not only have a poorer life quality but also a huge economic burden for the demands of dialysis and transplantation treatment.

As per GBD statistics, CKD and ESRD stood at 12^{th} place causing mortality and occupied 17^{th} place in disability. Diabetes mellitus is responsible for 895,000 deaths and 3,412,231 disabilities worldwide. The estimated prevalence of CKD is 11 % of the adult population in the United States. Nearly 13 million people have variable degrees of kidney dysfunction from mild to severe functional impairment.

About 1 in 40 of middle-aged men and one in 60 of the women will develop ESRD during their lifetimes. The risk for ESRD has been calculated as 1.1 in 10.000 patients per year. It was highly desirable to identify risk factors of CKD and ESRD [22]. The prevalence of DKD has been increased by > 50 % over the past few decades, and it is now the single largest cause of ESRD and it accounts for 44 % of patients with incident ESRD [23,24].

Statistics indicate that 1 in 10 people in the general population are estimated to have some form of chronic kidney disorder. About 175,000 new people have kidney failure every year in India and require dialysis or kidney transplantation. It has also been estimated that about 60 – 70 % of CKD cases are offshoots of diabetes and hypertension. The absence of a renal registry in India, the true spreading of CKD/ESRD is unknown. India approximately had 100 renal replacement therapy centers, most of them from the private sector and nearly 3000-4000 RRT 's are done annually. Here are around 7.85 million population out of 1 billion population living with Chronic Renal Failure in India. [25].

2.3. Risk factors and causes of CKD

Hypovitaminosis A and other nutritional issues during pregnancy may cause smaller kidney volume at birth and a lower e GFR. Consanguinity and genetic inbreeding increases the risk of congenital anomalies of the kidney and urinary tract and obstructive or reflex neuropathy. Poverty, poor sanitation, pollutants, water contamination, overcrowding, known and unknown nephron toxins may lead to kidney diseases, added to thesis exposures are the growing burden of HTN and DM [26].

Excess body weight may be associated with various structural and functional lesions of the kidney. The spectrum ranges from glomerulomegaly to diabetic nephropathy, to carcinoma of the kidney and nephrolithiasis [27]. Some important dietary factors were strongly associated with CKD like poor physical exercise, poor food habits etc. these are especially among urban people and became challenge. [28]. Coronary artery calcifications (CAC) and BMI were associated with kidney function decline over 1 year [29]. Lipid

abnormalities may play a role in the pathogenesis of renal impairment in type I Diabetic patients. There is a positive association between dyslipidaemia and CKD [30].

There has been recent recognition of epidemics of CKD involving individuals exposed to recurrence extreme heat. They typically present with asymptomatic increases in creatinine and minimal proteinuria which commonly progresses to ESRD [31, 32].

In addition, these associations were modified by daily alcohol consumption in Japanese population [33]. Soluble urokinase-type plasminogen activator receptor (suPAR) plays a pathogenic role in kidney disease has emerged mainly from studies of focal segmental glomerulosclerosis [34]. Kidney stones have major impact on development of kidney disease [35]. Fast foods with sedentary life styles, diabetes, proteinuria, glycosuria, hypotension and hyperglycemia are all the factors acting as risk elements for developing CKD [36]. Diabetes is a major cause of CKD. According to WHO, china and India will have about 130 million people with diabetes in 2025, and those people will consume about 40 % of total health expenditures in the countries. Despite this, only 8.7 % of the general population was able to identify diabetes as a risk factor for kidney disease and among patients with diabetic kidney disease, very few are aware of their kidney condition [37,38,39,40,41*]*.

CKD is both a cause and a consequence of hypertension. Nearly 1 billion people worldwide have high blood pressure and it is expected to rise to 1.56 billion people by 2025, increasing by 24 % in developed countries and 80 % in developing regions such as Africa and Latin America [14,42,43,44]

III. Renal Pathogenesis in Renal Obesity

Obesity, the epidemic of the 21st century, carries a markedly increased risk for comorbid conditions like type 2 diabetes, hypertension, dyslipidemia, cardio vascular diseases, sleep apnea and cancer [45].

3.1 Obesity is a risk factor for CKD :

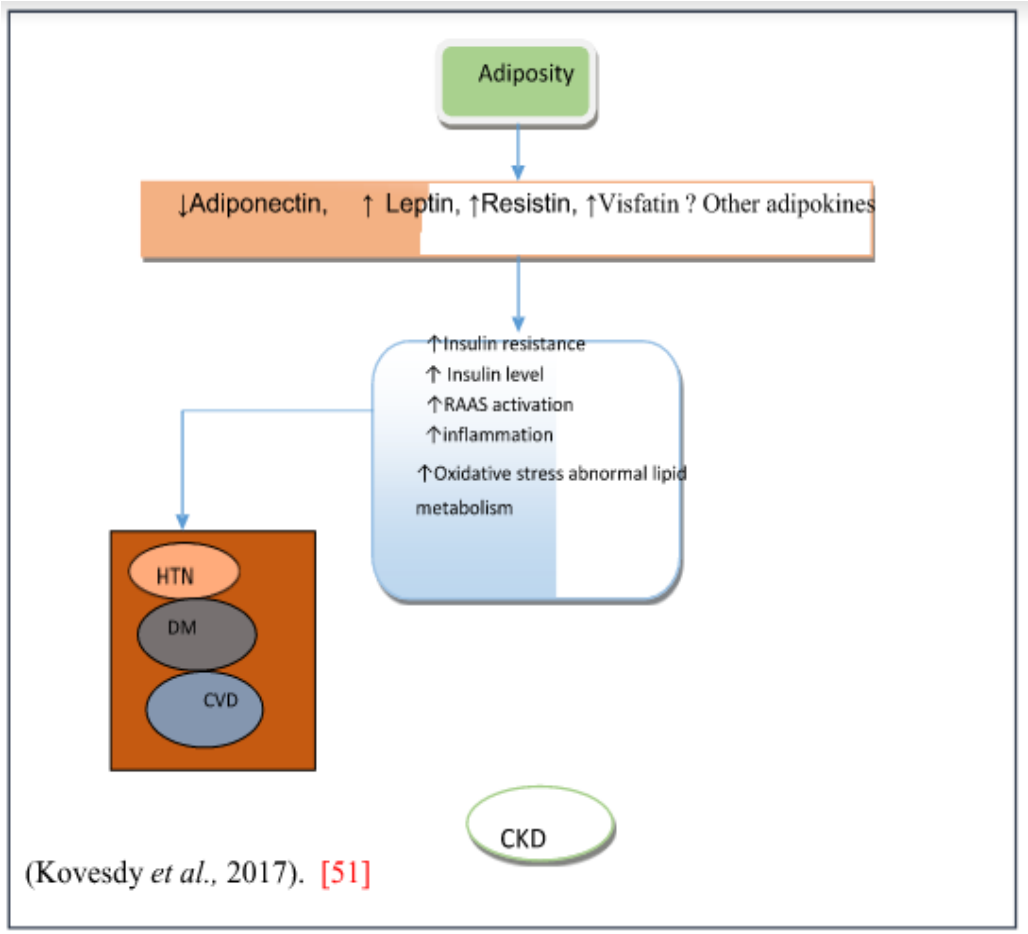
The histopathology of proteinuric obese patients consists of glomeruomegaly with or without FSGS (Focal Segmental Glomerulo Sclerosis). These glomerular changes named as obesity related glomerulopathy. Later it causes altered renal hemodynamics, namely increased renal blood flow, hyper filtration and increased filtration fraction and hypertensive nephron sclerosis. As many studies suggest that excess weight is associated with a hemodynamic, structural and histologic renal changes and also metabolic and biochemical alterations. [46, 47].

Presence of five metabolic syndrome traits like abdominal obesity, impaired fasting glucose, hypertension, hyper triglyceridemia and low cholesterol were associated with a twofold increased odds of CKD compared to presence of zero one trait [48]. In obese people the metabolic needs will be increased, mediates kidney changes. The body size positively related with glomerular size, as nephron number is fixed at birth, weight gain increases the work of single nephron [49].

3.2 CKD pathogenesis

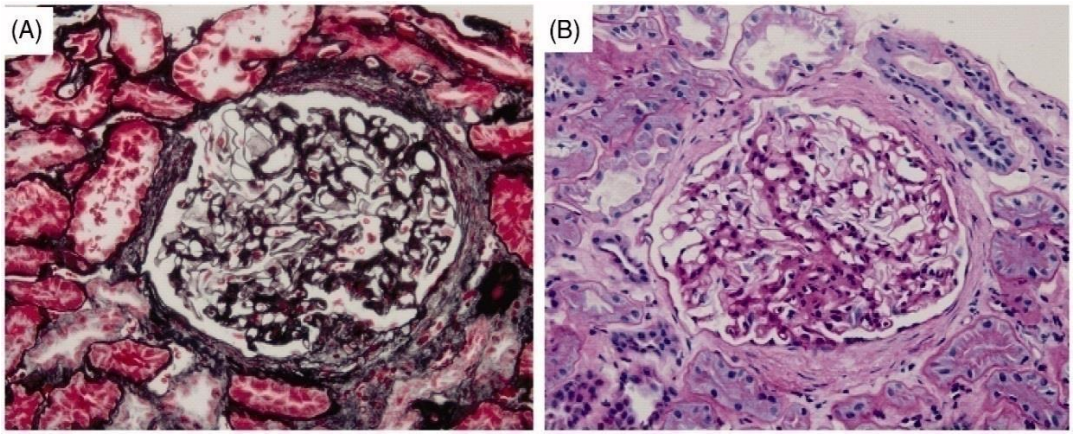
As an individual gains weight, single nephron GFR must increase and this occurs at the expense of increased capillary pressures, in addition increased in arterial blood pressure accompany the increase in renal plasma flow with weight gain, these hemodynamic changes result in increased glomerular capillary pressures (Fig 1). Individuals with reduced nephron mass possess a higher risk for CKD in the setting of overweight and obesity [50].

Fig : 1. CKD Pathogenesis in Obesity



There are 4 categories of FSGS – not otherwise specifies (NOS), tip, hyper cellular and collapsing, based on the location of the scar if it is at vascular pole NOS, adjacent to proximal tubule called tip, increased mesangial cellularity is third stage and collapsing has been shown as resistant to treatment. Dysfunction of the podocyte is a central feature in current working paradigm for the pathogenesis of FSGS. 30 – 60 % of FSGS will progress to ESRD over a 5 – 10 year period. Demographic factors like age, sex, race and ethnicity may have impact on its prognosis [52].

Figure 2: Showing focal segmental glomerular sclerosis
(a) Periodic acid silver methenamine stain, X400 & (b) Periodic acid – Schiff stain, X 400.



In recent years focal segmental sclerosis has become the commonest cause of nephrotic syndrome in adults, FSGS causes development of CKD early as its filtration process is lowered (Fig 2 a & b) [53].

IV. Association of obesity with CKD and other renal complications:

Increased BMI associated with development of proteinuria in individuals even in the absence of CKD. Obesity is associated with increased risk of developing stage 3 CKD [Table – 3]. [54].

Table 3: Effects of overweight and obesity on the kidney

Effects of overweight and obesity on the kidney
Hemodynamic
↑Effective plasma flow
↑Glomerular Filtration rate
↑Glomerular Filtration Fraction
↑Albuminuria
Structural
↑Kidney weight
↑Glomerular Planar Surface
↑Mesangial Expansion
↑Podocyte Injury
Pathologic
Glomerulomegaly
Glomerulosclerosis
Obesityrelatedglomerulopathy
Chronic Kidney disease
↑ Onset of kidney disease
↑ Progression to kidney failure
↑ Proteinuria
End– stage renal disease
↑ Incidence & Prevalence
↑ Graft loss in kidney transplant recipients
Others
↑ Renal cell carcinoma
↑ Nephrolithiasis

Elevated BMI levels (Class II obesity and above) have been associated with more rapid progression of CKD in patients with pre-existing CKD [55]. The deleterious effects of obesity on the kidneys extends to other complications such as nephrolithiasis and kidney malignancies. [56,57].

Overweight and Obesity are associated with various types of cancers. There is evidence that out of 25 percent of the kidney cancers 10 percent of them were associated with overweight [58]. Another large analysis examining the global burden of obesity on malignancies estimated that 17 and 26 % of all kidney cancers in men and women respectively were attributable to weight gain [59]. It is a known fact that obesity is mediated by co morbid conditions such as diabetes mellitus and hypertension effects of adiposity which could impact the kidneys directly, induced by the endocrine activity of the adipose tissue via production of adiponectin, leptin and resistin [60,61].

Higher body weight is associated with lower urine pH and increased urinary oxalate, uric acid, sodium may lead to a more acidic urine and decrease in the urinary citrate, also causes kidney stones [62].

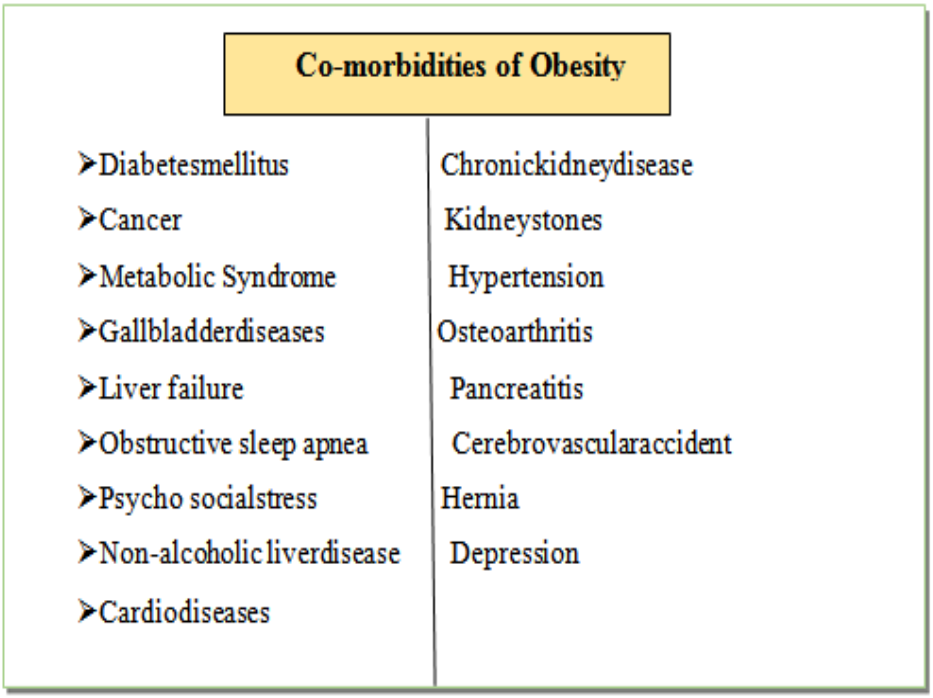
Obesity – associated nephropathy displays a continuum that evolves from glomerulomegaly to glomerulosclerosis and from mild to severe proteinuria in the absence of significant oedema and hypoalbuminemia. There was a positive relationship between BMI and mildly decreased e GFR [63]. Higher BMI plays a major role in the onset and progression of kidney damage and maintaining a normal body weight

will help to prevent complications of CKD [64,65,66]. There is a significant relationship exists between obesity and all-cause mortality [67].

4.1 Co-morbidities associated with Obesity and CKD:

BMI was significantly and independently associated with e GFR, in addition to risk factors like age, triglycerides, low-density lipoprotein cholesterol and fasting blood glucose. [68,69]. Increased renal Plasma Flow (RPF) and GFR occurs with overweight, this develops glomerular hyper filtration and causes irreversible kidney function loss [70].

Figure3: Co-morbidities of Obesity



As the kidney function declines, there is a progressive degeneration in mineral homeostasis, with a disruption of the normal serum and tissue concentrations of phosphorus and calcium, and changes in circulating levels of hormone which includes the parathyroid hormone (PTH), 1,25-dihydroxyvitamin D (1, 25 (OH) 2 D3), and other vitamin D metabolites, FGF-23 and growth hormones [71].

Obesity is a major risk factor for developing high BP, DM and the other co- morbid conditions which contribute to CKD (Fig 3). Obesity causes tubular sodium retention, inflammation, oxidative stress and lipotoxicity at last this leads to CKD and ESRD [72]. Obesity is associated with several co-morbid condition's including Cardio vascular disease, type 2 Diabetes mellitus, Metabolic Syndromes, Dyslipidaemias, Gall bladder disease, fatty liver, osteoarthritis and psycho social problems. Moreover, a recent study showed a causal relationship between obesity and hypovitaminosis D. Obesity is also linked to Alzheimer's disease and greater brain atrophy. An obstructive sleep apnoea is another increasingly recognized major health problem that is associated with both obesity and CKD [45].

Increasing BMI class was positively associated with impaired work productivity and indirect costs. Obesity differentially impacted productivity and costs, depending upon occupation [73]. Neverthless, obesity is associated with increased inflammation, insulin resistance, hypertension and dyslipidaemias [74].

V. Conclusion

The studies reviewed in this section clearly focuses on the fact that obesity causes CKD and several renal complications. Nephrolithiasis, kidney malignancies, increased albuminuria in men. There are number of co-morbidities associated with obesity are metabolic syndromes, gall bladder diseases, liver failure, obstructive sleep apnea, non- alcoholic liver disease, pancreatitis, hernia and depression etc.

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