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THE RELATIONSHIP BETWEEN BODY MASS INDEX AND ESTIMATED GLOMERULAR FILTRATION RATE

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Abstract: INTRODUCTION: The increasing prevalence of chronic kidney disease (CKD) is a major health problem. The prevalence of obesity has also been rapidly increasing worldwide. Few studies have examined the relationship between excess body weight and CKD risk. Aim: To evaluate the possible contribution of increased body mass index (BMI) to impaired renal function in the general population sample. **METHODS:** The study involved 500 participants older than 30 years (228 men, 272 women, age 57.58±13.68) who visited their general practitioner in Health Center „Dr Simo Milosevic". Blood samples, blood pressure anthropometric measures were performed on each participant. Estimated glomerular filtration rate was calculated using the abbreviated equation from MDRD study ("The Modification of Diet in Renal Disease Study") and CKD was defined as eGFR less than 60 ml/min/1.73m^2. Statistical analysis was performed using SPSS 19.0 software (IBM, Somers, New York, USA). **RESULTS:** The mean BMI was 25.09±3.54 kg/m2with 0.6% in underweight (BMI<18.5 kg/m2), 17.6% in lower normal (BMI 18.5 to 21.9 kg/m^2), 33.2% in upper normal (BMI 22.0 to 24.9 kg/m^2) and 48.6% in overweight or obese (BMI>25.0 kg/m^2) body mass category. The mean eGFR was 100.33±30.78 ml/min/1.73m^2 with 112±8.62 in underweight, 116.94±3.8 in lower normal, 102.37±2.39 in upper normal and 92.78±1.72 in overweight or obese category. Estimated GFR values decreased significantly with increasing BMI specially in those in upper normal compared to lower normal ($p<0.001$) and overweight and obese compared to lower normal body mass category ($p<0.001$). Compared with participants with lower normal body mass, the non-adjusted odds ratio (OR) for mildly or moderately reduced renal function (eGFR<90 ml/min/1.73m^2) was 2.54 (95% CI 1.41-4.56) for upper normal and 3.26 (95% CI 1.88-5.70) for overweight and obese participants. After adjusting for potential confounding variables (age, sex, diabetes mellitus, hypertension, hypercholesterolemia, hypertriglyceridemia and smoking status) OR for mildly or moderately reduced renal function was 2.23 (95% CI 1.21-4.10) for upper normal 2.65 (95% CI 1.44-4.87) for overweight or obese participants compared to those in lower normal body mass category. **CONCLUSION:** Estimated GFR values decreased significantly with increasing BMI specially in those in upper normal compared to lower normal ($p<0.001$) and overweight and obese compared to lower normal body mass category ($p<0.001$). This study showed that increasing BMI is strongly associated with decreasing eGFR in the general population. The underlying mechanism behind this association remains to be investigated through prospective population- based studies.

Key words: body mass index, estimated glomerular filtration rate, chronic kidney disease, renal function, general population

INTRODUCTION

Chronic kidney disease (CKD) is a global health problem and represents a big economic burden for health systems. Global prevalence of CKD lies between 11 and 13% with the third stadium having the largest share. All CKC stadiums are related to the increased risk for cardiovascular morbidity, early death and/or poorer quality of life [1].

The prevalence of obesity has also been rapidly increasing worldwide so much that obesity acquired the proportions of a global epidemic of chronic noncommunicable disease of the 21st century. The prevalence of obesity (body mass index ≥30 kg/m^2) almost doubled in the period between 1980 and 2008. In 1980 5% of men and 8% of women were obese while in 2008 it was 10% of men and 14% of women which makes more than half a billion people [2]. If this secular trend continues it is estimated that by 2030 38% of adult world population will be overweight while 20% will be obese [3].

Overweight and obesity have adverse metabolic effects on blood pressure, leading to

hypercholesterolaemia, hypertriglyceridaemia and insulin resistance. Coronary disease risk, ischemic stroke and diabetes mellitus type 2 increases proportionally with the increase of BMI. Increased BMI also increases the risk of developing breast, colon, prostate, endometrial, kidney and gallbladder cancers [4].

All over the world at least 2.8 million people die each year from overweight and obesity [2].

Obesity is a big risk factor for the development of a renal disease. It increases the risk for the development of ''major'' risk factors for CKD such as diabetes and hypertension and has a direct impact on the development of CKD and terminal renal insufficiency [5].

Purpose of the study is examination of possible contribution of increased body mass index (BMI) to the impaired renal function in the general population sample.The hypothesis that the increased BMI is associated with glomerular filtration rate decrease was tested. According to our knowledge, this is the first study which examined the correlation between body mass index and glomerular filtration rate in these regions in the population sample in primary health care.

MATERIAL AND METHOD

The study was conducted as an observational analytical cross sectional study. The study involved participants older than 30 years who visited their general practitioner in Health Center 'Dr Simo Milošević'. Data collection was completed a month after the sample of 500 participants was formed. Blood samples, blood pressure and anthropometric measures were performed on each participant. Laboratory measurements involved determining of glucose, urea, creatinine, total cholesterol and triglyceride concentrations and were performed on each of the participants. Blood pressure was measured on the left upper arm in a sitting position. Body mass and height were measured in the office and BMI was calculated as the quotient of body mass expressed in kilograms and square height expressed in meters. Based on the BMI values, the participants were classified into the categories shown in Table 1 [6].

Table 1. BMI categorization

Category	BMI (kg/m2)
malnutrition	<18,5
lower normal body mass index	18,5 - 21,9
upper normal body mass index	22,0- 24,9
overweight	25,0 do 29,9
obesity	> 30

Participants stated whether they were non-smokers, former or active smokers. Glomerular filtration rate was determined using the shortened formula from "The Modification of Diet in Renal Disease Study" [7].

$$\mathrm{eGFR} = 32788 \times \mathrm{Serum\ Creatinine}^{-1.154} \times \mathrm{Age}^{-0.203} \times [1.210\ if\ Black] \times [0.742\ if\ Female]$$

Stadiums of renal insufficiency were given in the table 2 [8].

Table 2. Classification of chronic kidney disease

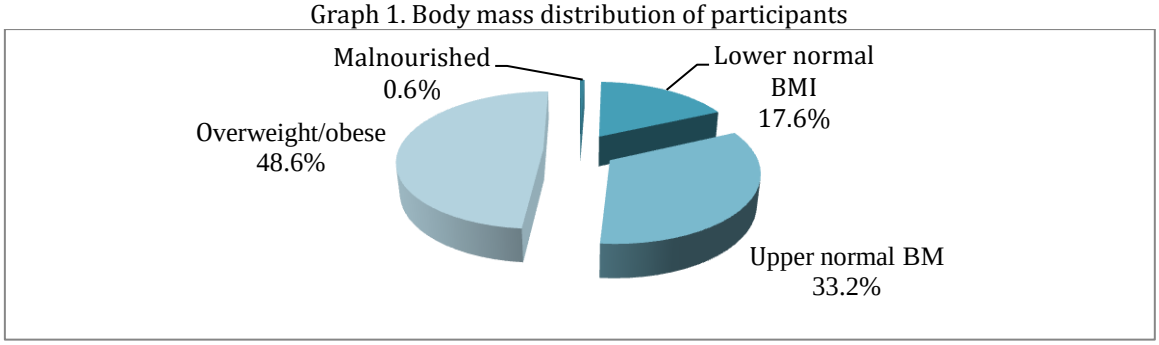
Stadium	GFR	Description
1	>90	Normal renal function but pathological urine findings or structural abnormalities or genetic traits indicate kidney disease
2	60-89	Slightly reduced renal function and other findings (as for stadium 1) indicate renal disease
3A **3B**	45-59 30-44	Moderately reduced renal function
4	15-29	Seriously reduced renal function
5	<15 ordialysis	Very severe renal impairment or end-stage renal insufficiency

CKD is defined as GFR less than 60 ml/min/1.73m^2. SPSS 19.0 software (IBM, Somers, New York, USA) was used to create the database and analyze it. For testing of correlation between body mass index and glomerular filtration ratewith adjusting in relation to the associated variable logistical regression was used. The level of significance was 0.05.

RESULTS

The study involved 500 participants, 228 (45.6%) men and 272 (54.4%) women. BMI mean value was 25.09±3,54 kg/m^2 with 0.6% participants in the category of malnourished (ITM<18.5 kg/m^2), 17.6% in the group of body mass in the range of lower normal (BMI 18.5 up to 21.9 kg/m^2), 33.2% in the group with upper normal body mass (BMI from 22.0 to 24.9 kg/m^2) and 48.6% in the group of overweight or obese (ITM>25.0 kg/m^2) .

Graph 1. Body mass distribution of participants



GFR mean value was 100.33 ± 30.78 ml/min/1.73m^2. GFR mean values in categories according to BMI are presented in table 3.

Table 3. eGFR in BMI categories

BMI categories	GFR (ml/min/1.73m^2)
Malnourished	112±8.62
Lower normal	116.94±3.8
Upper normal	102.37±2.39
Overweight and obese	92.78±1.72

GFR considerably decreased with the increase of the BMI values particularly in the category of overweight and obese participants compared to the participants with lower normal body, (p<0.001) as well as in the group with upper normal body mass compared to the group of lower normal body mass (p<0.001). In comparison to the participants in the group with lower normal body mass, the non-adjusted odds ratio (OR) for mild or moderately reduced renal function (GFR<90 ml/min/1.73m^2) was 2.54 (95% CI 1.41-4.56) for participants with upper normal body mass and 3.26 (95% CI 1.88-5.70) for participants in the group of overweight and obese.

After adjustment in relation to potential contributing factors (age, gender, diabetes mellitus, hypertension, hypercholesterolaemia, hypertriglyceridemia and smoking status) OR for mild or moderately reduced renal function was 2.23 (95% CI 1.21-4.10) in the group with upper normal body weight while it was 2.65 (95% CI 1.44-4.87) in the category of overweight and obese participants compared to those in the category with lower normal body mass.

DISCUSSION

Several previous studies pointed to the significance of the increased body mass index in the development of chronic renal disease. A cross-sectional study conducted in general population in Japan showed that the increased BMI is associated with the decrease of GFR only in men [9]. In the study conducted by Fox et al. ORfor the development of new CKD was 23% (OR, 1.23; 95% CI, 1.08–1.41) for the BMI increase by one SD [10]. Gelber et al. showed that the initial increased BMI as well as its increase during the follow-up period of 14 years is associated with increased risk from CKD [11].

Other studies that examined the relationship between obesity and CKD are presented in table 4.

Table 4. Studies that examined the association between obesity and chronic kidney disease

Study	Participants	Risk factors	Outcome	Results	Comment
PREVEND study [12]	7676 Danish people without diabetes	Increased BMI (overweight orobesity) and central distribution of fat (waist / hip circumference ratio)	Albuminuria 30-300 mg/24h increased or decreased GFR	Obesity + central distribution:higher risk for albuminuria Obesity +/-central distribution: higher risk for increased GFR Central distribution +/- obesity associated with decreased GFR	Cross-sectional study
CARDIA [13]	2 354 people from general population with normal renal function aged 28-40	Obesity (ITM>30 kg/m^2) Risk factors associated with nutrition and the way of life	Incidental microalbuminuria	Obesity (OR 1.9)and unhealthy diet (OR 2.0) are associated with albuminuria	Low-frequency
National population study in Sweden [14]	926 Swedish people with mild/advanced CKD compared to 988 control	BMI ≥ 25 against<25 kg/m^2	CKD against absence of CKD	Higher BMI associated with 3x higher risk from CKD	- The greatest risk lies with diabetic participants but it is also significantly increased in the nondiabetic participants - Cross-sectional study
National population study in Israel [15]	1 194 704 male and female adolescents,candidates for joining the Army	Increased BMI (overweight and obesity) compared to normal BMI	Incidence of terminal CKD	Overweight and obesity associated with higher risk for terminal CKD	Strongest correlation for diabetic CKDbut also significantly higher for nondiabetic CKD
Nord-Trøndelag Health Study (HUNT-1)[16]	74 986 of adult Norwegian people	BMI categories	Incidence of terminal renal insufficiency or renal death	BMI > 30 kg/m^2 associated with more unfavorable outcome	Correlation not present in participants with TA (?)<120/80 mmHg
National cohort of American veterans [17]	453 946 veterans with the initial GFR< 60 ml/min/1,73 m^2	BMI categories from < 20 to>50 kg/m^2	Incidence of tCKD Doubling of serum creatinine Decrease of GFR	Mild and severe overweight are associated with major kidney impairment	Correlation present but weaker in participants with advanced CKD
Kaiser Permanente Northern California study [18]	320 252 adults with/without CKD	Overweight, categories I, II and extreme obesity compared to normal BMI	Incidence of terminal renal disease	Linearly higher risk in higher BMI categories	Correlation still exists after adjustment for the presence of diabetes, hypertension, and initial CKD

Most studies showed existence of a higher risk for CKD in participants with the BMI which is equal to or greater than 25 kg/m^2 while results of our study show increased risk for mild and moderately impaired renal function in the group of participants with upper normal body mass (BMI 22.0 to 24.9 kg/m^2) as well as in the category of overweight and obese (BMI≥25 kg/m^2) compared to the participants from the category of lower normal body mass.

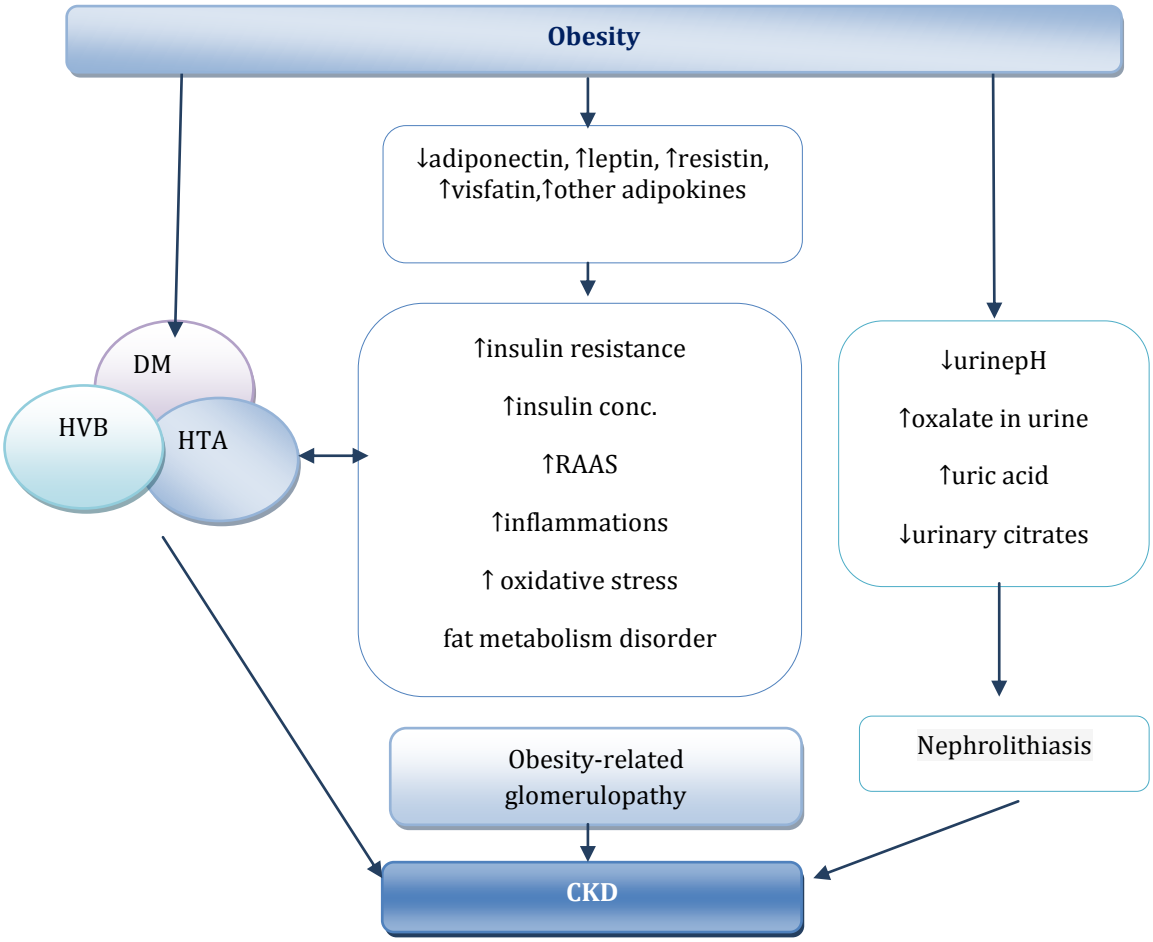
The exact mechanism of contribution of obesity to the development or worsening of CKD

is still insufficiently known. In support of the claim that obesity itself is not responsible for the development of CKD is the fact that most obese people never develop CKD and as many as 25% of obese people do not have metabolic disorders [19]. However, the frequency of so-called glomerulopathy associated with obesity (obesity-related glomerulopathy) which in the observational studies was proven to affect the development of CKD increased by 10 times in the period from 1986 to the year 2000 [20]. Adipose tissue has its endocrine function through the production of adiponectin [21], leptin [22], resistin [23] and numerous other mediators which leads to oxidative stress [24], inflammation [25], insulin resistance [26], RAAS activation [27] and impaired fat metabolism [28]. The effect of the above on the kidneys is reflected through ectopic fat accumulation and increased fat deposition in the renal sinuses [29], development of glomerular hypertension as well as hyperfiltration with consequent damage to the glomerular basement membrane and increased permeability resulting in glomerulomegaly and focal segmental glomerulosclerosis [20].

Obesity is also associated with increased risk for nephrolithiasis. Higher body weight is associated with lower urine pH [30] and increased oxalate excretion [31], uric acid, sodium and phosphate [32]. A diet with a lot of proteins and salt decreases urine pHand citrate concentration, which contributes to the formation of stone. Also, through effects on tubular Na-H transporter and ammoniogenesis, insulin residence may contribute to urinary acidity favouring nephrolithiasis [33].

Apart from obesity having a direct impact to kidneys in pathophysiology of CKD, traditional risk factors such as diabetes mellitus, arterial hypertension and chronic vascular diseases proven to be more frequent in obese persons play a major role here.

Figure 1. Assumed mechanisms of the role of obesity in the development of chronic kidney disease



CONCLUSION

Estimated GFR values decreased significantly with increasing BMI specially in those in upper normal compared to lower normal ($p<0.001$) and overweight and obese compared to lower normal weight category ($p<0.001$). This study showed that increasing BMI is strongly associated with decreasing eGFR in the general population. The underlying mechanism behind this association remains to be investigated through prospective population - based studies.

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