

*Short Communication***Is there any Gender Difference in the Association between Obesity, Chronic Kidney Disease and Anemia**Krasimira Atanassova¹, Jelka Masin-Spasovska², Goce Spasovski² and Emil Paskalev³¹St. Anna Hospital, Univesity ²Department of Nephrology, Medical Faculty Skopje, Macedonia, ³Hospital Aleksandrovska, Sofia, Bulgaria**Abstract**

Introduction. Nowadays, obesity has emerged as one of the most independent risk factors for chronic kidney disease (CKD) in both economically developed and undeveloped countries. The number of patients requiring dialysis as a consequence of obesity-related renal diseases, such as diabetes mellitus and hypertension, is increasing worldwide. Moreover, obesity has been shown to favorize the risk of cardiovascular diseases (CVD) with premature death due to CKD and/or end-stage renal disease (ESRD). The aim of the study was to investigate the association between obesity [e.g. body mass index (BMI)], kidney function [e.g. glomerular filtration rate (GFR)] and renal anemia in CKD patients.

Methods. Retrospectively, data from the register of 315 pre-dialysis patients with different stages of CKD not on erythropoiesis stimulation agents (ESAs) during the period between 1 Jan 2013-30 June 2013 were used to assess the association between the degree of CKD impairment with the degree of obesity and anemia. The stage and/or progression of CKD was calculated by GFR, while the degree of obesity by the body mass index (BMI). CKD was defined as a glomerular filtration rate (GFR) <60 mL/min per 1.73 m². Data analysis was performed by means of the simple Microsoft excel program.

Results. Within the study population of 315 CKD patients, 123 were males with mean age of 63.4±1.33 years and 192 females of 57.3±1.2 years. The GFR reduced with the increased BMI in both genders, and majority of patients (n=243) were in CKD stage 3, with a mean GFR of 44.5 ml/min/1.73 m². The BMI values in female patients with first and second degree of obesity negatively correlated with GFR (r=-0.46, p<0.05). Only female patients with second degree of obesity (BMI of 35-39.9 kg/m²) had a positive correlation between the decreased renal function and reduced Hb levels.

Conclusions. Our study provided an unconditional evidence not only for the presence of an association between the degree of obesity (BMI) and the degree of renal function impairment (GFR), but also an association between the higher BMI and the higher degree of kidney anemia seen in women with second degree of obesity.

Further larger scale trials and interventional studies are required to see the effect of body weight reduction on renal function and especially anemia.

Keywords: anemia, body mass index, chronic kidney disease, obesity, renal function

Introduction

Chronic kidney disease (CKD) has recently been recognized not only as a risk factor for end-stage renal disease (ESRD), but also for cardiovascular disease (CVD) which is the leading cause of death in developed countries [1,2]. Besides aging, a number of factors have been associated with CKD such as hypertension, impaired glucose tolerance or diabetes mellitus, dyslipidemia, obesity, and smoking [3,4]. Obesity has also been recognized as a factor related with CKD, but there has been no clear answer to an important question: which is the underlying mechanism of CKD developing in association with increased BMI. It is supposed to be related to the activated renin-angiotensin system, increased sympathetic nerve activity, insulin-resistance or hyperinsulinemia and dyslipidemia [3-5]. A significant association between CKD and BMI was recently found in men but not in women by two epidemiological studies done in Japan and in Singapore [6,7]. Approximate number of overweight persons in 2010 is around 1 billion adults and 475 million of those suffering from obesity [8], similar like worldwide "obesity epidemic". Although the effect of obesity might differ among races, obesity has a significant impact on CKD and ESRD [9]. The increasing number of obesity cases both in the developed and developing countries may be particularly due to the unbalanced diets and sedentary lifestyle [10]. Moreover, obesity is the leading cause of increased mortality worldwide because of the associated inflammatory metabolic disorders such as hypertension, cardiovascular and kidney diseases, dyslipidemia, glucose intolerance, and certain cancer diseases.

In spite of a progressive fall in the incidence of traditional risk factors of cardiovascular morbidity (cigarette smoking, high blood pressure, and hyperlipidemia), there

is an upward trend in the prevalence of obesity and CKD. Furthermore, there is a strong correlation between BMI and the relative risk of progression of CKD. Predominance of oxidative stress in both obesity and azotemia stimulate synthesis of angiotensin II, which in turn increases TGF- β and plasminogen activator inhibitor-1, thereby propagating glomerular fibrosis. Furthermore, local synthesis of angiotensinogen by adipocytes, leptin activation of sympathetic nervous system, and hyperinsulinemia contribute to the development of hypertension in obesity and CKD. In addition, increased renal tubular expression of Na-K-ATPase and a blunted response to natriuretic hormones in obesity promote salt and water retention. Glomerular hyperfiltration from systemic volume load and hypertension results in mesangial cellular proliferation and progressive renal fibrosis [11]. Additionally, obesity-related kidney damage has been posited to be due to hyperlipidemia, increased oxidative stress, increased salt intake, and activation of the sympathetic nervous system [12].

We used the outpatient data in order to assess the degree of obesity in the cohort of registered patients with CKD, and to examine the possible impact of obesity on the degree of renal function impairment and renal anemia and possible gender difference.

Material and methods

Data of 315 patients with CKD from the outpatient nephrology register centre within the Hospital St. Anna Sofia

in the period between 1 Jan. 2013-30 June 2013 were analyzed. All patients included into the study were with various CKD stage, none of them was receiving erythropoiesis stimulation agents (ESAs) or any specific immunosuppressive agents. Various demographic, clinical and biochemical parameters (gender, age, height, weight serum creatinine and hemoglobin levels) were retrospectively collected from patients' database. The body mass index (BMI) and glomerular filtration rate (GFR) were calculated according to the standard estimations and the overweight, first, second and third degree of obesity were defined as having BMI <25-29.9 kg/m², 30-34.9 kg/m², 35-39.9 kg/m² and >40 kg/m², respectively. An estimate of GFR was obtained by the four-variable Modification of Diet in Renal Disease (MDRD) equation. Data processing was performed by means of Microsoft excel data analysis for descriptive statistics. Various stratified groups were compared with t-test or Mann Whitney U test, and association between various parameters was assessed with correlation analysis as appropriate. P value <0.05 was considered significant.

Results

Within the study population of 315 CKD patients, 123 were males with mean age of 63.4±1.33 years and 192 females of 57.3±1.2 years. The results for hemoglobin and GFR in various groups of patients stratified according to the degree of obesity, gender and BMI are presented in Table 1.

Table 1. Degree of obesity (BMI) in men and women with values of average Hb levels and GFR (MDRD)

Degree of obesity	BMI	Gender	Number	Hb level (g/l)	GFR (MDRD) ml/min
below physiological values	< 18.5	female	37	127	78
		male	0	-	-
Physiological values	18.5 - 24.9	female	105	128	58
		male	29	131	59
Overweight	25 - 29.9	female	33	129	61
		male	67	130	51
First-degree obesity	30 - 34.9	female	13	129	50
		male	23	130	44
Second-degree obesity	35 - 39.9	female	3	115	33
		male	3	134	35
Third-degree obesity	> 40	female	1	134	80
		male	1	132	61

There were 37 women with a BMI below the physiological values (malnourished), while there was not a single man with BMI in this category. The majority of patients were within the group with physiological values of BMI, 29 males and 105 females. In addition, another group of 100 patients (67 males) were slightly overweight, the first degree of obesity was found in 36 patients (23 males) and only 6 patients (3 males) had the second degree obesity. Only one male and one female patient had the third degree obesity and were not included in the analysis.

Majority of patients (n=243) were in CKD stage 3, with a mean GFR of 44.5 ml/min/1.73 m². The BMI values in female patients with first and second degree of obesity negatively correlated with GFR (r=-0.46, p<0.05). Unexpectedly, only female patients with second degree of obesity had a positive correlation between the decreased renal function and reduced Hb levels (Figure 1 and 2). The already known correlation between obesity and renal function was also found among males. Namely, the increased BMI was associated with a reduced GFR but not with Hb levels (Figure 3 and 4).

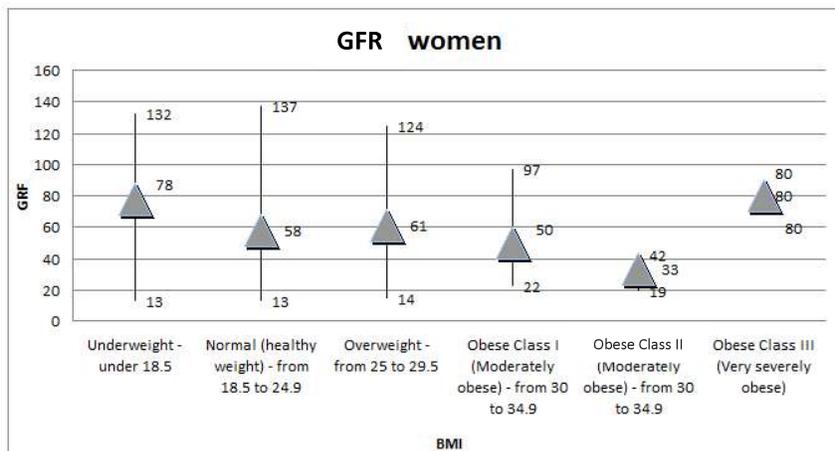


Fig. 1. Glomerular filtration rate (MDRD) and body mass index (BMI) in women

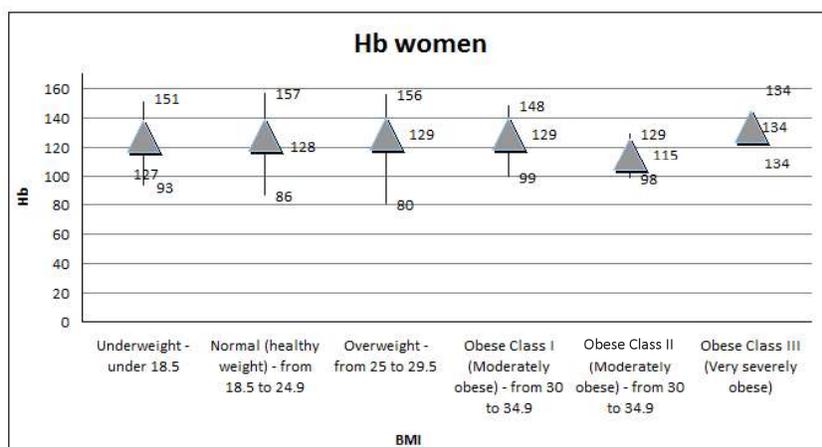


Fig. 2. Average hemoglobin level (g/l) and body mass index (BMI) in women

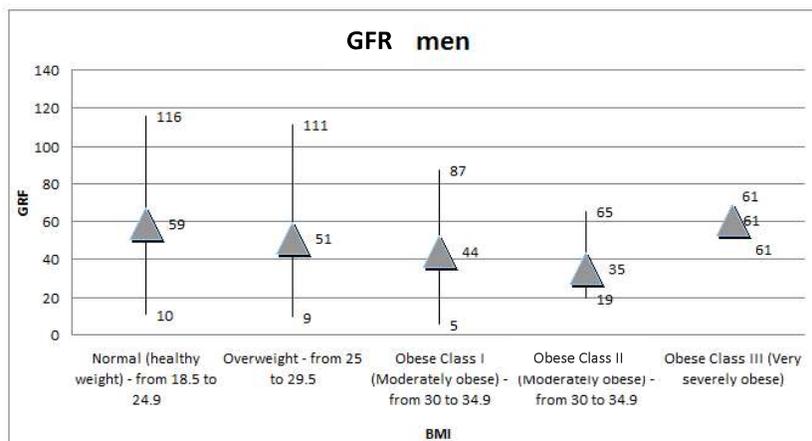


Fig. 3. Glomerular filtration rate (MDRD) and body mass index (BMI) in men

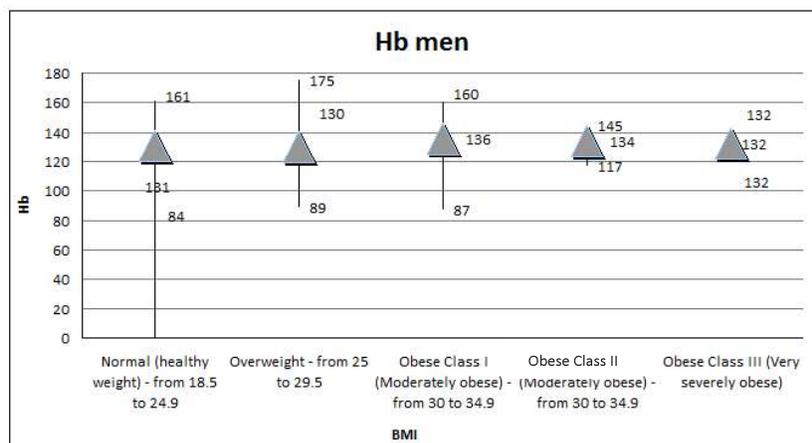


Fig.4. Average hemoglobin level (g/l) and body mass index (BMI) in men

Discussion

This study showed an association between obesity and anemia in female patients with CKD as well as between the degree of obesity and renal function in both, male and female patients. To the best of our knowledge, there are only a few data on the association between overweight and renal function, but data on the association between the obesity and anemia in CKD patients lack in the literature.

Anemia is common in patients with CKD, but not in the earlier stages of CKD. Patients with CKD stage III have a prevalence of concurrent anemia of 5.2%, whereas those with stage IV disease of 44.1% [13], which is in line with the results obtained only for the female patients in our study. Anemia is also with greater prevalence in CKD patients older than 60 years, as compared to the younger patients, most probably secondary to the greater rate of CKD in older individuals and their lower estimated GFR associated with aging [14]. However, our female cohort was younger than 60 years of age, thus the impact of BMI may be even more prominent. In only one study of Karlee JP *et al.* a positive correlation was found between the increased BMI and increased ferritin levels and decreased serum iron and transferrin saturation. Here, despite the involvement of the chronic inflammation in the iron studies, obesity was not found to be associated with anemia [15].

It should be acknowledged that the age of female subjects may be an important factor influencing results of this type of epidemiological studies, because estrogen levels which decline after menopause may exert a protective action on the kidneys. However, BMI in our study was most probably with a greater impact on the impairment of the renal function compared to age, which did not show a significant difference between the various obesity groups. Finally, in the present study, to avoid including CKD secondary to diabetic nephropathy, we excluded subjects with diabetes mellitus or with a fasting blood glucose level of 126 mg/dl or higher. The shortcoming of our stu-

dy is that the analysis was performed with a relatively low or even statistically insufficient number of subjects. Nevertheless, for the first time in patients not treated with ESAs there was a correlation between obesity and decreased renal function with renal anemia in females with second degree of obesity. The already known correlation between the obesity and renal function in both female and male patients was confirmed.

Conclusions

The GFR reduced along with the increase of the BMI in both genders providing unconditional evidence for the association between the degree of obesity and renal function impairment in CKD patients. In addition, an association between BMI and the average hemoglobin level was found only in females with second degree of obesity. It is necessary to carry out such monitoring on larger scale trials, looking for various hygieno-dietetic regimes, races and cultural beliefs differences. After our pilot observational study examining the cross-sectional relationship between BMI, CKD and renal anemia, further follow-up and interventional studies are required to see the effect of body weight reduction on renal function and anemia.

Conflict of interest statement. None declared.

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