Correlation between Body Mass Index (BMI) and Waist Circumference (W.C) With Urine Albumin Excretion in Non-Diabetic Obese Subjects - A Cross Sectional Study

Sujaya.P[1], Arun Menon.S[2], Sundaram. K.R[3], Leela Menon.N[1], Gopalan.M[4], Jeyaseelan.N[5]

[1] Department of Biochemistry, Amrita School of Medicine, Kochi, Kerala, India.
[2] Department of Endocrinology, Amrita School of Medicine, Kochi, Kerala, India.
[3] Department of Bio Statistics, Amrita School of Medicine, Kochi, Kerala, India.
[4] Department of Medical Illustrations, Clinical Skills Simulations, Digital Health & Telemedicine, Amrita School of Medicine, Kochi, Kerala, India.
[5] Department of Anatomy, Faculty of Medicine, SEGi University, Malaysia.

Abstract: *Recent studies indicate that obesity per se may have a detrimental effect on the kidneys and contribute in the long term to the development and progression of Chronic kidney disease (CKD) as central body fat distribution is directly associated with progressive renal damage. The role of Urine albumin creatinine ratio (UACR) as an early predictor of CKD risk in non-diabetic, obese individuals is poorly understood.*

The present study is undertaken to correlate the body mass index (BMI) and Waist circumference (WC) with urine albumin excretion in non-diabetic obese subjects.

The cross-sectional study included 144 non-diabetic obese patients with a mean age of 31.94 +/- 11 9, BMI of 36.78+/- 5.15 and a mean HbA1c of 5.64+/- 0.4476.They had mean UACR 8.49 mg/gm+/- 9.42 estimated by UACR in mg / g =   Urine   albumin (mg / dl)

Urine   creatinine (g / dl).

Calculated value is obtained from Beckman coulter Olympus AU 2700.

Pearson correlation coefficient analysis revealed significant correlation between UACR and W.C (r=0.302(P < 0.001) and between UACR and BMI r = 0.23 (P =0.006). Multiple regression analysis showed significant predictors of UACR as W.C (p = 0.014) and FPG (p = 0.040). A targeted early monitoring of non-diabetic obese individuals with a simple urine estimation of UACR could potentially identify those at risk of progression to CKD.

Keywords: *Body mass index, chronic kidney disease, non-diabetic obesity, urine albumin excretion, waist circumference.*

I.   Introduction

Urine albumin creatinine ratio (UACR) when it is greater than 30 mg/g is a marker for Chronic Kidney Disease (CKD) [1]. UACR, as a useful measure of renal function in diabetic renal disease is well established. Nevertheless, the usefulness of UACR as a predictor of CKD risk in non-diabetic, obese individuals is poorly understood. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease, recommend that all individuals should be assessed for urine albumin excretion as part of routine health examinations to determine whether they are at increased risk for developing CKD [2]. But in the present clinical scenario screening for microalbuminuria is emphasized and routinely done only in patients with T2DM and hypertension owing to their high risk for CKD. Both Obesity and Chronic renal failure (CRF) are escalating health problems throughout the world with incidence rising rapidly in recent years.

Obesity is a complex process which activates cascade of biologic events leading to vascular end organ damage [3]. Emerging evidence indicates that obesity per *se,* specifically targets the kidney and contributes significantly to the development and progression of CKD [4, 5, 6, 7]. The Framingham Offspring data reported obesity as a major risk factor for the development of kidney disease. After a mean follow up period of 18.5years, 9.4 percent had developed kidney disease with a 23% increase in the odds of development of kidney disease for each standard deviation increase in the BMI [8]. This risk was present even after adjustment for age, sex, T2DM, and hypertension. Another study by Hsu et al [9, 10] showed that there is a greater relative risk of development of End-stage renal disease (ESRD) necessitating dialysis, with each gradient increase in BMI. Higher baseline BMI remained an independent predictor for ESRD after additional adjustments for hypertension and T2DM. Similarly, a large cohort study of 177570 individuals found obesity to be one of the most potent risk factors for the development of End-stage renal disease [ESRD] [11].

Ejerblad et al, found a 2.8-fold increased risk of nephrosclerosis among adults who had a BMI of 35 kg/m^2 or higher compared with a lifetime highest BMI lower than 25 kg/m^2. Studies have reported that weight gain, even within the normal range of body mass index, may increase the risk of CKD [12] Central obesity has received more attention as a potential risk factor for renal Disease [13, 14, 15, 16]. It is reported that central body fat distribution is directly associated with renal hemodynamic alterations even independent of overall weight excess leading to progressive renal damage [17, 18]. Population-based study has confirmed the strong relation of microalbuminuria with central adiposity. Their study interpreted that both central adiposity and hypertension are independently associated with increased odds of microalbuminuria [13] .Prataap K et al also found an independent relation of micro albuminuria with central obesity in non-diabetic South Asians [16] ^{which} may explain the high prevalence of diabetic nephropathy in this group.

Obesity is known to be associated with an unfavorable renal hemodynamic profile leading to increased intraglomerular capillary pressure, glomerular hyper filtration, glomeruloslcerosis and increase in urinary albumin excretion, which, over time, progresses to micro albuminuria, proteinuria and CKD [19,20,21,22] Clinical studies have confirmed that glomerular filtration rate (GFR) is indeed higher in obese adults than in normal weight controls [23,24,25]. A post-hoc analysis of the Add Health Wave III cohort of young adults revealed an association between a body mass index over 35 kg/m2 and proteinuria [7]. Conversely, weight loss has been shown to reduce proteinuria in non-diabetic nephropathies making renal disease in obesity accessible for prevention programs [26, 27, 28]. The aim of this study is to evaluate whether routine micro albuminuria screening is warranted in non diabetic obese subjects to detect individuals with undiagnosed CKD.

II. Materials And Methods

The current cross-sectional study was conducted on non-diabetic obese individuals attending the out-patient wing of the obesity clinic, Endocrinology department, Amrita Institute of Medical Sciences (AIMS), Kochi from February 2014- May 2015 over a period of 15 months. The study was conducted after taking the required ethical clearance from the ethics committee of AIMS and the patients participated had signed the informed consent.It included 144 patients with BMI ≥ 25 kg/m^2. Based on the results from the available literature on two important variables, namely, UACR and BMI with 95% confidence and 80% power, minimum sample size came to be 140. Subjects include the age group 18 to 65, both sexes, BMI ≥ 25.0, no history of T2DM, no proteinuria, RBC or pus cells in urine as per routine dipstick urine screening test, no history of sternous physical exercise during the previous 24 hours before the test, HbA1c <6.5%, Serum creatinine <1.4 mg% and eGFR >60 mL/min/1.73m^2 estimated by MDRD equation.

Subjects with clinical suspicion of urinary tract infection, with known cardiovascular disease [CVD] CKD, chronic liver disease [CLD], hypertension , fever, any other acute or chronic illnesses, subjects on anti diabetic drugs,anti obesity drugs, anti hypertensive drugs , nephrotoxic drugs, corticosteroids and NSAID, pregnancy, women on birth control pills and menstruation phase of the menstrual cycle were excluded.

Anthropometric index of BMI and WC in cm was recorded in relaxed standing position. Weight was measured using Hercules electronic weighing scale and standing height was measured using a single stedeometer. Standard measuring tape was used for WC measurement. WC was measured midway between the uppermost border of the iliac crest and the lower border of the costal margin (rib cage) as per the National Obesity Forum guidelines. Severity of central obesity was determined by taking WC measurements. The absolute WC >100 centimeters in both sexes used as measure of central obesity. Severe obesity was defined as BMI >35. Micro albuminuria was defined as UACR (30-300 mg/g). FPG and fasting insulin levels were used to compute the homeostatic model assessment of insulin resistance (HOMA-IR [29], which was calculated in accordance with the formula IR = serum insulin (μIU/mL) $\times$ plasma glucose (mg/dL) /405. Blood pressure in mm Hg was measured using a standard mercury sphygmomanometer.

Spot urine sample in a sterile container was collected for determination of spot urinary albumin excretion and urinary creatinine. Calculated ratio between both is taken for UACR Determination.UACR was calculated as milligram of albumin/g of creatinine.

The venous blood samples were obtained under aseptic precautions in sitting position. Blood samples for estimating FPG were collected in vaccutainers containing fluoride and were centrifuged at 3000g for 15minutes and the plasma was transferred to labeled vials. Samples for HbA1c were collected in vaccutainers with EDTA as the anticoagulant and whole blood was used. Blood samples for estimating other biochemical parameters were collected in vaccutainers without anticoagulant. Blood samples for estimation of FPG s were collected after 12 hours of overnight fasting.

Fasting plasma glucose (FPG) and serum creatinine analysed in Beckman coulter Olympus AU 2700, [30] glycated hemoglobin (HbA1c) in BIO-RAD D-10.

Urine albumin creatinine ratio (UACR) is the ratio between urine albumin (mg/dl) and the urine creatinine (g/dl) UACR is reported in mg/g

Urine albumin (mg / dl) = UACR in mg / g
 --
 Urine   creatinine (g / dl)

Calculated value is obtained from Beckman coulter Olympus AU 2700.

Urine samples contaminated with blood are unsuitable for UACR since albumin levels will be falsely elevated. The patient should refrain from heavy exercises 24 hours before the test.Vigorous exercise can cause a transient increase in albumin excretion [31].

Urine albumin estimation [32] analysed by immunoturbidimetric assay and, urine creatinine [30] by Jaffe's kinetic method**.**

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 20 Windows (SPSS Inc., Chicago, USA).For all the continuous variables the results are given in mean ± standard deviation. To compare the means of parameters that are not following normal distribution Mann Whitney U test was performed. Pearson's correlation coefficient was computed to find out the correlation between two parameters that were following normal distribution. Multiple regression analysis was done to find the predictors of UACR. Log transformation was done for UACR, due to non-normal distribution and high variation among the observation. This study was done with the power of 80%. *P* values of 0.05 or less were considered statistically significant.

III. Results

Total of 144 obese individuals were studied with a mean age of 31.94+/-11.9 years [Table.1]. 75% were females. 5/144 had micro albuminuria [UACR30-300 mg/g]. 85/144 [59.03%] subjects had severe obesity. 124/144 subjects [86.1%] had W.C >100 cm. Pearson correlation coefficient analysis [Table-2] was done using Log transformed UACR.

Table. 1 Baseline characteristics of the study groups

Characteristics	n	Mean	SD
Age(yrs)	144	31.94	11.9
BMI	144	36.78	5.15
W.C(cm)	144	112.61	10.89
SBP(mmHg)	144	125.35	12.35
DBP(mmHg)	144	78.15	6.64
FPG(mgm/dl)	131	98.80	14.75
Fasting insulin(μIU/mL)	111	22.06	13.12
IR	111	5.28	3.28
HBA1c	144	5.64	0.4476
Total cholesterol (TC) (mgm/dl)	129	195.92	41.6
LDL(mgm/dl)	129	129.68	31.99
HDL(mgm/dl)	128	44.38	14.85
TG (mgm/dl)	128	134.03	62.11
UACR(mgm/gm)	144	8.49	9.42
Serum creatinine (mgm/dl)	143	0.9	0.1187
eGFR (mL/min/1.73m^2)	143	90	20.06

Table. 2 Pearsons correlations

Factors		UACR	
	n	Pearson Correlation	P Value
BMI	144	0.23	0.006
FPG	131	0.157	0.073
W.C	144	0.302	0<.001
HBA1c	144	0.159	0.056

*Log transformation was done for UACR due to non normal distribution and high variation among the observation

Positive correlation was observed between parameter of renal function [UACR] and W.C(r=0.302 [*P* < 0.001] [Fig.1], between UACR and BMI r = 0.23 (*P* value 0.006) [Fig.2]. Multiple regression analysis showed that significant predictors of UACR were W.C [p value 0.014] and FPG [p value 0.040]. Even though not statistically significant, it was noted that as BMI increases an increase in mean UACR was observed [Fig.3, Table 3].

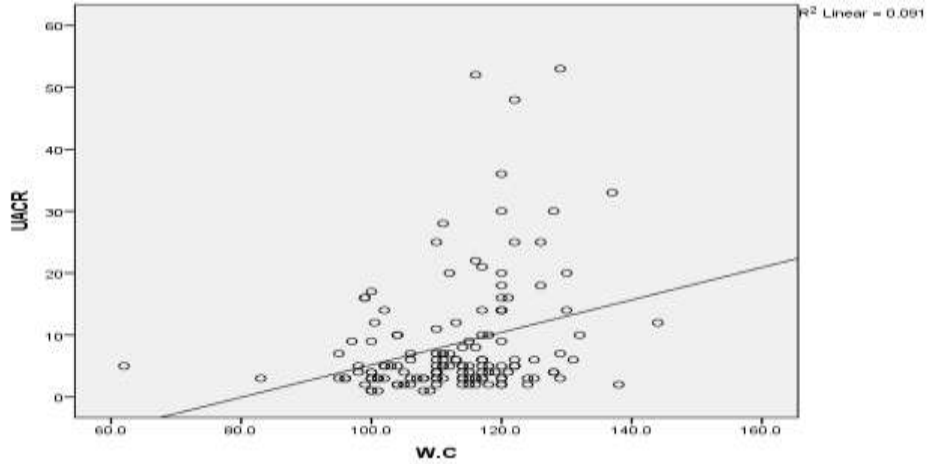**Figure: 1** **S**catter diagram showing the correlation between WC and UACR

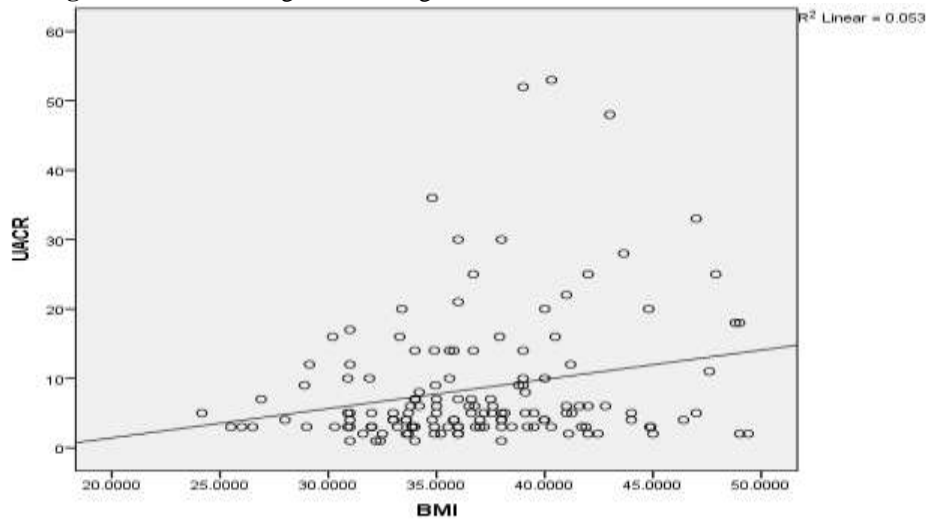**Figure: 2** **S**catter diagram showing the correlation between BMI and UACR

Table. 3 Association of BMI with UACR Anova

BMI	n	UACR Mean	Standard deviation	P value
25-35	59	6.31	5.86	
35-40	51	8.69	9.27	0.057
>40	34	11.97	13.14	

Figure: 3 Association of BMI with UACR
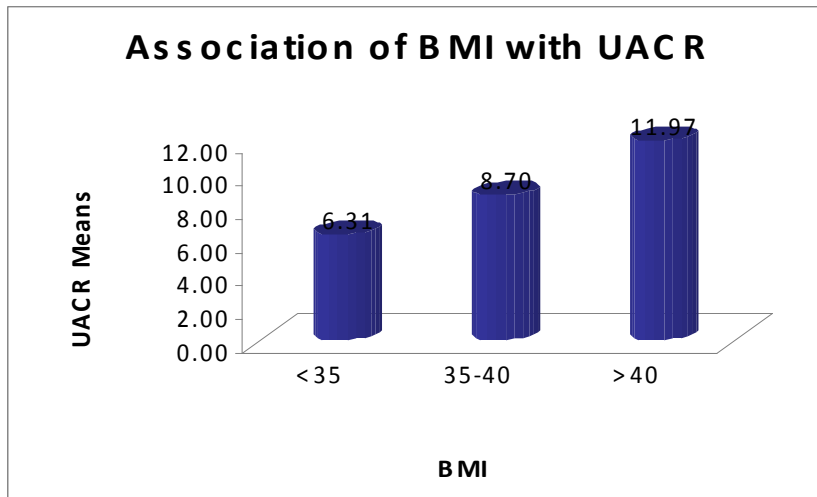
There was an increase in mean UACR also in subjects with W.C >100cm compared with those subjects with <100 cm of W.C, but no statistical significance in difference. Significant increase in mean DBP was observed in subjects with BMI>35 [Table 4].16.2% of our subjects were not insulin resistant [Table 5]

Table. 4 Comparison of Diastolic blood pressure with BMI

Factor	Classification	n	DBP		P Value
			Mean	SD	
BMI	<35	59	76.68	6.018	0.044
	>35	85	79.18	6.896	

#Mann Whitney U Test

Table. 5 Distribution of subjects according to Insulin resistance (IR)

	Normal %	Abnormal %
FPG(n=131) Normal <106 mgm/dl Abnormal>106 mgm/dl	61.8	38.2
Insulin (n=111) Normal <15μU /ml Abnormal > 15μU /ml	72.1	27.9
IR(n=111) Normal <2.5 Abnormal>2.5	16.2	83.8

IV. Discussion

In a study, by Valensi et al [33] on 207 non diabetic, insulin resistant, obese subjects there was 12.1% prevalence of micro albuminuria . In the present study of 144 non diabetic obese individuals the overall prevalence of micro albuminuria was noted to be low at 3.5 %. The lower prevalence of micro albuminuria noted could be due to the fact that only 25% of our study group were prediabetic and 16.2% of our subjects were not insulin resistant.

Our study revealed statistically significant correlation of Waist Circumference, which is a measure of marker for central obesity with UACR (Fig.2) (P Value<.001). WC and FPG were significant predictors of UACR on multiple regression analysis. Central obesity rather than overall BMI has received more attention as a potential risk factor for renal insufficiency in non diabetic subjects in some studies [34, 35]. In a study on German urban adult population micro albuminuria which is a manifestation of general vascular endothelial damage was found to be strongly and independently associated with central adiposity [13]. There are also ample evidences from studies [16, 36] on non-diabetic non-hypertensive human subjects to support that central adiposity is associated with micro albuminuria. Prataap K et al [16] studied whether central obesity is associated with the development of renal injury, independent of risk factors like hypertension and fasting blood glucose and concluded that central obesity is an early and independent risk factor for renal dysfunction in normoglycemic South Asian subjects.

In a study on Korean subjects association between central obesity and micro albuminuria was reported [37]. After a 6 year follow up study, Bonnet et al [14] suggested that the measurement of WC can be used as a screening method for the identification of non-diabetic individuals at risk of developing micro albuminuria. Studies conducted in South India revealed high rate of heritability for abdominal obesity and associated IR in non-diabetic individuals [38,39] Increased susceptibility for central obesity and IR could explain the higher rates of nephropathy in South Indians probably by the mechanism of IR and endothelial dysfunction in the prediabetic state . In a study of 6,500 non diabetic participants, increasing BMI and WC were associated with reduced estimated GFR and increased CKD [36].Scaglione et al in their study concluded that both in non-diabetic normotensive and non-diabetic hypertensive subjects central obesity was more associated with increased urine albumin excretion than with peripheral obesity [40].

It should be noted that 85/144 of our patients had severe obesity BMI >35 [Table-2]. However, study revealed only a nonsignificant correlation between BMI and UACR [Table-3]. There was an increase in mean urine albumin excretion as the BMI increases [Fig.4] in tertiles, but it did not reach statistical significance. Similar observations were made by Cubeddu and Hoffmann [41].They reported that there is no significant relationship between obesity and micro albuminuria and found no difference in albumin excretion in obese glucose tolerant subjects with high BMI.Yesim et al [42] also reported the same in their study on obese and lean women without T2DM.

Adipogenic inflammation, sympathetic activation, RAS activation and central obesity induced hypertension and hyperglycemia, are probably the factors involved.Excess weight gain, especially when accompanied by increased visceral fat, is associated with many features of the metabolic syndrome which increase the risk for

the development of CKD .Ectopic fat accumulation in and around the kidney also may have adverse consequences on renal function. Obesity may increase CKD risk by increasing the metabolic demands on the kidney, which leads to higher glomerular capillary pressure, glomerular hyper filtration and glomerular hyper-trophy .Glomerular hyper filtration is a marker of early kidney damage[43]. Markers of visceral adiposity such as WC are easily obtained in the clinical setting and may provide valuable prognostic information

The measurement of micro albuminuria is a sensitive marker of CKD from very early to more advanced stages of the disease process. A spot urine sample using albumin-to-creatinine ratio is an accepted screening method. Houlihan et al [44] assessed the characteristics of the albumin-to-creatinine ratio as a screening test and found sensitivities 90% for both men and women, with excellent accuracy reflected by area under the receiver operator characteristics curve. Screening studies conducted by several countries have identified the high risk CKD population as mainly hypertensives and diabetics. But predictors of CKD risk other than T2DM and hypertension should also be included in primary CKD screening target [45].

V. Conclusion

Elevated urine albumin excretion is not only a complication or consequence of diabetes or hypertension but also be a risk marker in central obesity. Primary care physicians can use WC as a simple, reliable tool for early screening of obese individuals with CKD risk. Further advances in obesity research may impart insight into inclusion of micro albuminuria screening in the routine management of obesity. Screening can help primary care physicians in early detection and early referral of high risk obese patients to Nephrologists. Since CKD is often asymptomatic until late stage and patient progress to renal failure and dialysis state, it is highly essential to intervene by actively screening the obese population and prevent their progression to renal failure. .

References

[1]. Chapter 1: Definition and classification of CKD KDIGO Kidney Int Suppl. 2013; 3:19.
[2]. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease Kidney Int Suppl. 2013; 3:1.
[3]. Zohreh Soltani & Vaughn Washco &Stephen Morse & Efrain ReisinThe Impacts of Obesity on the Cardiovascular and Renal Systems: Cascade of Events and Therapeutic Approaches Curr Hypertens Rep 2015, 17: 7.
[4]. Karen A. Griffin, Holly Kramer, Anil K. Bidani Adverse renal consequences of Obesity American Journal of Physiology - Renal Physiology Published 1 April 2008, Vol. 294 no. 4,
[5]. Hall JE. The kidney, hypertension and obesity. Hypertension 41: 625–633, 2003.
[6]. Kramer H, Luke A, Bidani A, Cao G, Cooper R, McGee D Obesity and prevalent an incident CKD: the Hypertension Detection and Follow-Up Program. Am J Kidney Dis.2005; 46(4):587.
[7]. Ferris M, Hogan SL, Chin H, Shoham DA, Gipson DS, Gibson K, Yilmaz S, Falk RJ, Jennette JC Obesity, albuminuria, and urinalysis findings in US young adults from the Add Health Wave III study.Clin J Am Soc Nephrol. 2007; 2(6):1207.
[8]. Fox CS, Larson MG, Leip EP, Culleton B, Wilson PWF, Levy D. Predictors of new-onset kidney disease in a community-based population. JAMA. 2004; 291(7):844–50.
[9]. Hsu, C., et al. (2006).Body mass index and risk for end-stage renal disease. Ann Intern Med, Vol. 144, No. 1, (2006 Jan), pp. 21-28.
[10]. Hsu, C., et al. (2009). Risk factors for end-stage renal disease: 25-year follow-up.Arch Intern Med, Vol. 169, No. 4, (2009 Feb), pp. 342-350.
[11]. Veeraish Chauhan, Megha Vaid, Nishtha Chauhan and Akhil Parashar (2012). The Obesity Epidemic and Kidney Disease: A Literature Review, Available from: http:// wwwintechopen.com/books/diseases of renal-parenchyma/theobesity- epidemic-and-kidney-disease-a-literature-review
[12]. Seungho, Ryu, Yoosu Chang, Hee, Yeon Changes in body weight predict CKD inhealthy men. J Am Soc Nephrol 2008 Sep; 19(9):1798-805.
[13]. Liese AD, Hense HW, Doring A, Stieber J, Keil U: Micro albuminuria, central adiposity and hypertension in the non-diabetic urban population of the MONICA Augsburg survey 1994/95. J Hum Hyper tens 15:799–804, 200110.
[14]. Bonnet F, Marre M, Halimi JM, Stengel BLange C, Laville M, Tichet J, Balkau B: Waist circumference and the metabolic syndrome predict the development of elevated albuminuria in non-diabetic subjects: the DESIR study. J Hypertens 24:1157-1163, 2006.
[15]. Ferris M[1], Hogan SL, Chin H, Shoham DA Obesity, Albuminuria, and Urinalysis Findings in US Young Adults from the Add Health Wave III Study. Clin J Am Soc Nephrol 2007 Nov; 2(6):1207-14. 2007.
[16]. Prataap K. Chandie Shaw, MD, Stefan P. Berger, MD, Central Obesity Is an Independent Risk Factor for Albuminuria in Non-diabetic South Asian Subjects Diabetes Care July 2007; vol. 30 no. 7: 1840-1844.
[17]. Arjan J. Kwakernaak, Tsjitske J. Toering and Gerjan Navis Body mass index and body fat distribution as renal risk factors: a focus on the role of renal haemodynamics Nephrol Dial Transplant. 2013 Nov; 28 Suppl 4: iv 42-9.
[18]. Brenner BM. Hemodynamically mediated glomerular injury and the progressive nature of kidney disease. Kidney Int 1983; 23: 647–655
[19]. Bosma RJ1, Krikken JA, Homan van der Heide JJ, de Jong PE, Navis GJ. Contrib.Nepherol 2006; 151:184-202. Obesity and renal hemodynamics.
[20]. Yoshioka T, Rennke HG, Salant DJ, Deen WM, Ichikawa I. Role of abnormally high transmural pres sure in the permselectivitydefect of glomerular capillary wall: a study in early passive Heymann nephritis. Circ Res. 1987; 61(4):531–8.
[21]. Schlaich MP, Socratous F, Hennebry S, Eikelis N, Lambert EA,Straznicky N, Esler MD, Lambert GW. Sympathetic activation in chronic renal failure. J Am Soc Nephrol. 2009; 20:933–939.
[22]. Wolf G, Butzmann U, Wenzel UO. The renin–angiotensin system and progression of renal disease: from hemodynamics to cell biology. Nephron Physiol 2003; 93: 13
[23]. Chagnac A, Herman M, Zingerman B, et al. Obesity-induced glomerular hyperfiltration: its involvement in the pathogenesis of tubular sodium reabsorption. Nephrol Dial Transplant. 2008; 23:3946–3952.

[24]. Bosma RJ, van der Heide JJ, Oosterop EJ, et al. Body mass index is associated with altered renal hemodynamics in non-obese healthy subjects. Kidney Int. 2004; 65:259–265.
[25]. Tomaszewski M, Charchar FJ, Maric C, McClure J, Crawford L, GrzeszczakW, Sattar N, Zukowska-Szczechowska E, Dominiczak AF. Glomerularhyperfiltration: a new marker of metabolic risk. Kidney Int.2007; 71:816–821.
[26]. Hermann J. Kissler, Utz Settmacher Seminars in Nephrology (obesity &renal disease) Jan-2013; Vol.33: No1 *pp75*-89)
[27]. Praga E, Hernandez E, Andres A, Leon M, Ruilope LM, Rodicion JL. Effects of Body-weight loss and captopril treatment on proteinuria associated with obesity. Nephron 70: 35–41, 1995.
[28]. Praga M, Morales E. Obesity, proteinuria and progression of renal failure. Curr Opin Nephrol Hypertens 15: 481–486, 2006.
[29]. Ma F, Qiao L, Yue H, Xie S, Zhou X, Jiang M, Zhang W, Qi J, Wang L, Xu K.Homeostasis model assessment-insulin resistance (HOMA-IR), a key role for assessing the ovulation function in polycysticovary syndrome (PCOS) patients with insulin resistance. Endocr J. 2008 Oct;55(5):943-5.
[30]. SlotC. (1965) Scandj.Clin.LabInvest.17, 381-387.
[31]. Jefferson IG, Greene SA, Smith MA, Urine albumin to creatinine ratio-response to exercise in diabetes Arch Dis Child. 1985 Apr; 60(4):305-10.
[32]. Tietz NW, Ed Clinical guide to Laboratory tests, 3rd Ed Philadelphia WBSaunders Company, 1995:24pp
[33]. Valensi P, Assayag M, Busby M, Paries J, Lormeau B, Attali JR. Microalbuminuria in obese patients with or without hypertension. Int J Obes Relat Metab Disord.1996; 20:574–9. [PubMed]
[34]. Danziger J. Importance of low-grade albuminuria. Mayo Clin Proc. 2008; 83:806–12. [PubMed]
[35]. De Zeeuw D, Parving HH, Henning RH. Microalbuminuria as an early marker for cardiovascular disease. J Am Soc Nephrol. 2006; 17:2100–5. [PubMed]
[36]. Burton JO, Gray LJ, Webb DR, et al. Association of anthropometric obesity measures with chronic kidney disease risk in a non-diabetic patient population.Nephrol Dial Transplant. 2012; 27(5):1860–1866.
[37]. Kim YI, Kim CH, Choi CS, Chung YE, LeeMS, Lee SI, Park JY, Hong SK, Lee KU: Microalbuminuriais associated with the insulin resistance syndrome independent of hypertension and type 2 diabetes in the Korean population. *Diabetes* Res Clin Pract 52:145–152, 2001.
[38]. Davey G, Ramachandran.A Familial aggregation of central obesity in southern Indians International journal of obesity 200024(11):1523-1527(PubMed).
[39]. Snehalathe C, Ramachandran A. Computed axial tomographic scan measurements of abdominal fat distribution& its correlation with anthropometry and insulin secretion.Metabolism,11/1997; 46(10):1220-4.
[40]. Scaglione R *et al*. Central obesity and hypertension: pathophysiologic role of renal haemodynamics and function. Int J Obes Relat Metab Disord 1995; 19:403–409.
[41]. Hoffmann IS, Jimenez E, Cubeddu LX. Urinary albumin excretion in lean, over weight and obese glucose tolerant individuals: its relationship with dyslipidaemia,hyperinsulinaemia and blood pressure. J Hum Hypertens. 2001; 15:407–12.
[42]. Yesim TE, Ugurlu S, Caglar E, Balci H, Ucgul A, Sarkis C. et al. Investigation of microalbuminuria in non-diabetic, normotensive obese women. Intern Med. 2007; 46:1963–5.
[43]. Avry Chagnac, Talia Weinstein, Asher Korzets, Edward Ramadan, Judith Hirsch, Uzi Gafter Glomerular hemodynamics in severe obesity. American Journal of Physiology–Renal physiology, May 2000 Vol. 278 no. 5, F817-F822.
[44]. Houlihan CA, Tsalamandris C, Akdeniz A, Jerums G: Albumin to creatinine ratio:A screening test with limitations. Am J Kidney Dis 39, 2002, 1183– *1189.*
[45]. Vassalotti JA[1], Fox CH, Becker BN Risk factors and screening for chronic kidney disease. Adv Chronic Kidney Dis. 2010 May; 17(3):237-45.