

Investigating Associated Factors with Glomerular Filtration Rate : Structural Equation Modeling

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Abstract

Background: glomerular filtration rate (GFR) is a valid indicator for kidney function. Different factors can affect GFR. The purpose of this study is to assess direct and indirect effects of GFR-related factors using structural equation modeling. **Patients and methods:** We analyzed data from baseline phase of Ravansar Non-Communicable Disease cohort study. Data on socio-behavioral, nutritional, cardiovascular, and metabolic risk factors were entered in a conceptual model in order to test direct and indirect effects of factors related to GFR, separately in male and female, using the structural equation modeling. **Results:** Of 8927 individuals participated in this study, 4212 subjects were male (47.20%) and 4715 subjects were female (52.80%). The obtained mean and standard deviation of GFR was 76.05 (\pm 14.31) per 1.73. GFR for 0.2%, 11.3%, 73.0% and 15.50% of people were <30, , and , respectively. Hypertension and aging in both gender and atherogenic factor in male directly, and in female directly and indirectly had a lower effect on GFR. Blood urea nitrogen and smoking in male and female, directly or indirectly through other variables, were associated with a lower GFR. In female, diabetes had a lower direct and indirect effect on GFR. Obesity in female was directly associated with uper and indirectly associated with lower GFR. **Conclusion:** According to our results, aging, hypertension, diabetes, obesity and high lipid profile, and BUN had a decreasing direct and indirect effects on GFR. Although low GFR might have different reasons and it is not a consistent sign of CKD, our findings, are in line with other reports, provide more detailed informations about important risk factors of low GFR. Public awareness about such factors can improve public practice of positive health behaviours.

Background

Increased prevalence of chronic kidney disease (CKD) is associated with increased number of deaths as well as other complications in the form of other chronic diseases including cardiovascular diseases. Glomerular filtration rate (GFR) is a valid indicator for kidney function[1, 2]. eGFR is the most widely used assessment of kidney function, eGFR is also used to monitor disease progression[3]. In 2013, reduced GFR resulted in 4% (2.2 millions) of deaths worldwide, more than half of which caused by cardiovascular (1.2 million people) and end-stage renal diseases (ESRD) .[4]The results of clinical trials have shown that decreased GFR is an independent risk factor for all causes of deaths and adverse cardiovascular conditions such as myocardial infarction and stroke[5, 6]. There is also strong evidences suggesting that development and progression of CKD has been mainly caused by risk factors of cardiovascular diseases including high blood pressure, diabetes, and dyslipidemia . According to the literature, known risk factors for CKD development and progression include: age, diabetes mellitus (DM), high blood pressure, obesity, dyslipidemia, and smoking[10-16].

Based on the results of previous studies, GFR depends (directly and/or indirectly) on several factors. One of methods for assessing direct and indirect effects of relevant factors on GFR is structural equation model (SEM). SEM is one of the most useful methods for the concurrent testing of complex relationships between variables and assessment of the effect of latent variable[17]. SEM is a powerful multivariate analysis method, which allows for the simultaneous verification of a series of regression equations and the concurrent assessment of the relationships between different variables [18]. This method reduces measurement errors by involvement of several observed variables for each latent variable. The ability to test the model with several dependent variables and the concurrent direct and indirect effects of several independent variables on the dependent variable are amongst the features of SEM. Unlike traditional regression models that treat each covariate in the model as an independent variable with a direct effect on GFR, SEM assesses all pathways of different factors as independent and/or dependent (i.e., mediator) factors toward GFR. Using SEM, this study aimed to determine the most important risk factors associated with GFR in a group of subjects aged 35 - 65 who participated in the cohort study of Ravansar. Given the structural, biological and metabolic changes in different gender groups and the effect of each on the risk factors associated with eGFR, the participants were assessed in two different gender groups in the present study.

Methods

Study Design and Participants

For the purpose of this cross-sectional study, data from baseline phase of Ravansar Non-Communicable Disease (RaNCD) cohort study was used. Ravansar, a city in Kermanshah Province is located in the western part of Iran close to the border with Iraq with a population mainly comprised of Kurdish ethnicity. RaNCD cohort is part of the large PERSIAN (Prospective Epidemiological ReSearch in IrAN) study. The data used in this study pertained to more than 10000 participants aged 35 to 65 who had voluntarily entered the study and signed informed consent forms for participation. The study began in November 2014 and continues to date. The recruitment phase data of the participants has been collected for the cohort and includes general data , nutrition questionnaire and biological samples, More information is available in the cohort protocol [19-21].

Measurements

Anthropometric indices were determined by bioelectric impedance device. The subjects' heights were measured by a stadiometer with an accuracy of 1 cm. Body mass index (BMI) was calculated by dividing weight (kg) to squared height (m) [22]. Participants were classified into 5 groups in terms of percent body fat (PBF): 5-10 (Essential Fat), 11-14 (Athletes), 15-20 (Fitness), 21-24 (Average), and 24> (Obese) for male and 8-15 (Essential Fat), 16-23 (Athletes), 24-30 (Fitness), 31-36 (Average), and 37> (Obese) for female [23].

According to the third report of the National Cholesterol Education Program (NCEP) on diagnosis, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III), waist to hip ratio (WHR) in female and in men were classified as abnormal [24]. According to guidelines of international kidney foundation, CKD is defined as renal abnormalities or $\text{GFR} < 60 \text{ ml/min/1.73 (1.0 ml/s/1.73)}$ present for more than three months. Renal abnormalities can be diagnosed by pathologic disorders or markers of dysfunction, including abnormalities in blood or urine test [25]. In this study, Modification of Diet in Renal Disease (MDRD), and nonstandardized equation (our creatinine values were not standardized for the most part) were used for estimating GFR from age, sex, and creatinine level [26, 27]. Non-use of race variable is due to non-racial differences in this population (almost all participants are from Kurdish ethnicity). $\text{eGFR} = 1.86$ (0.742 if Female)

According to CKD Stage cut-point, eGFR was categorized into 4 groups of >90 , 60-90, 30-59, $<30 \text{ ml/min/1.73}$. To analyze the structural part, eGFR was used as quantitative variable in the model. Blood pressure was measured after 15 minute of rest twice from the right arm and twice from the left using a sphygmomanometer (Riester Duplex 1948, Germany). The mean value of the two measurements was taken as the systolic and diastolic blood pressure. Given the criteria recommended by the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-8), people with systolic blood pressure $\geq 140 \text{ mmHg}$ and/or diastolic blood pressure $\geq 90 \text{ mmHg}$ and/or a history of taking blood pressure-controlling medications were classified as hypertension [28]. Diabetes mellitus (DM) was defined based on the American Diabetes Association's criteria for fasting blood sugar (FBS) $\leq 126 \text{ Mg/dl}$ and/or patients who used insulin and/or glucose-lowering agents [29]. Smoking was introduced as a self-reported variable (1- none smokers, 2- smokers, 3- former smokers). Blood urea nitrogen (BUN) was calculated based on the quantitative values. Plasma atherogenic index was calculated according to the following formula [30].

$$\text{Atherogenic coefficient} = \frac{[\text{Total cholesterol}] - [\text{HDL cholesterol}]}{[\text{HDL cholesterol}]}$$

Physical activity calculated according to individual's activity per day was another variable introduced based on the 22-item questionnaire in RaNCD cohort study. Finally, METs (as an indicator for level and measure of physical activity) were extracted and entered the model. MET is the amount of oxygen consumed at rest (about $3.5 \text{ ml O}_2/\text{kg}/\text{min}$) and equals to resting metabolic rate. MET for each activity was extracted using compendium of physical activities [31].

Nutritional status was determined according to a valid and reliable food frequency questionnaire customized to the local culture [32]. Consumption of red meat (including red meat, processed meat, liver, heart, gizzard) was another variable derived from food frequency questionnaire calculated based on grams of meat intake per day.

Statistical Methods

Spearman's rank correlation was applied, and stepwise linear regression was obtained to assess the associations between the study variables and to implement the conceptual framework. Then, structural equation modeling (SEM) was used with maximum likelihood estimation (MLE). SEM includes causal modeling, analysis of covariance structures, and latent variable models. This model is a generalization of multivariate regression that allows one to estimate the strength and sign of direct and indirect effects for complicated causal schemes with multiple dependent and independent variables [33]. In order to create constructs (or factors), we applied confirmatory factor analysis (CFA). CFA is a multivariate statistical technique which is used to test consistency of measures of a construct with researcher's understanding of the nature of that construct (or factor). The objective of confirmatory factor analysis is to test whether the data fits a hypothesized measurement model. Path standardized coefficients (β) as the effect sizes of this model were calculated. CMIN/DF Normed chi-square (CFI) Comparative fit indices (GFI) Goodness-of-fit indices (RMSEA) Root mean squared error of approximation (NFI) normed fit index (and AGFI) adjusted goodness-of-fit index (were applied for assessing fitness of the model. Statistical analysis was performed using AMOS-SPSS 22 and STATA 14.0 (STATA Corp, College Station, TX). P-value less than 0.05 was considered as statistically significant. As the percentage of missing data was less than 2%, it was excluded from analysis.

Results

Out of 8927 individuals participated in this study, 4212 (47.20%) subjects were males and 4715 (52.80%) subjects were females. The mean of age was 48.2±2.10 (range:35-65). Prevalence of hypertension in females and males was 16.35% and 10.22%, respectively. Prevalence of BMI was 37% in females and 16.61% in males. The mean of atherogenic coefficient was 187.80 in females and 180.12 in males. Table 1 shows distribution and statistical comparison of the studied variables between four groups of eGFR. The mean of eGFR was 76.05±14.31 ml/min/1.73. The corresponding values for males and females were 80.07±13.89 ml/min/1.73 and 72.46±13.76ml/min/1.73, respectively. In fact, lower eGFR was associated with older age, hypertension, diabetes, blood lipids, increase in BUN, and lower physical activity (Table 1).

Structural equation modeling (SEM) with maximum likelihood estimation (MLE) was applied to assess the conceptual model (Fig. 1). Confirmatory Factor Analysis (CFA) was used to confirm a group of variables with an internal consistency with a latent variable. Waist circumference was removed from the model due to low loading factor and poor fitting. For other variables, applied CFA goodness of fit indices were at appropriate levels (CMIN/DF: 1.19, GFI: 0.99, RMSEA: 0.005, CFI: 0.99). These indices indicated acceptable fitting of the model.

Table 1: Comparison of studied variables between four groups of GFR

Variable	Male eGFR (ml/min per 1.73m ²)				pvalue	Female eGFR (ml/min per 1.73m ²)				pvalue
	<29	30-59	60-90	>90		<29	30-59	60-90	>90	
Age(mean ±SD)	50.00 10.21	54.00 8.11	47.20 7.90	47.8 7.80	<0.001	55.90 8.00	52.01 9.01	47.70 8.10	45.70 7.1	<0.001
BUN(mean ±SD)	37.50 15.48	16.49 4.56	14.9 3.83	14.29 3.82	<0.001	37.10 24.80	13.61 4.23	12.18 3.51	11.09 3.39	<0.001
PA (mean± SD)	35.93 6.99	40.65 8.00	42.70 10.25	42.54 11.19	<0.001	38.72 4.88	39.77 5.31	39.33 4.51	38.50 3.66	<0.001
AF (mean± SD)	171.90 31.57	189.16 39.74	181.24 36.71	173.77 34.84	<0.001	164.97 31.88	203.58 44.01	185.66 36.75	177.32 4.84	<0.001
Red meat (mean ±SD)	21.69 17.14	21.32 28.41	23.64 39.86	21.31 29.29	0.37	18.54 19.30	24.20 35.76	24.61 36.22	22.70 28.98	0.37
Organ meat(mean± SD)	2.90 1.62	5.02 10.01	4.46 9.48	4.20 8.10	0.02	1.35 1.37	5.69 15.51	5.02 9.76	4.62 8.57	0.02
Process meat(mean ±SD)	1.23 2.01	2.50 7.71	1.9 6.01	1.89 7.64	0.005	0.32 1.02	3.04 9.84	2.26 6.83	2.51 7.58	0.005
BMI, n (%)										
18.4	0(0.0%)	1(0.48%)	66(2.11%)	20(2.29%)	0.5	0(0.0%)	13(1.61%)	50(1.47%)	3(0.58%)	0.006
18.5-24.9	3(37.50%)	76(36.89%)	1080(34.54%)	315(36.12%)		1(10.00%)	215(26.70%)	700(20.66%)	108(21.09%)	
25.0 - 29.9	4(50.00%)	86(41.74%)	1451(46.41%)	411(47.13%)		4(40.00%)	326(40.49%)	1390(41.02%)	205(40.03%)	
30.0 -34.9	1(12.50%)	37(17.96%)	463(14.81%)	106(12.15)		5(50.00%)	187(23.22%)	937(27.65%)	159(31.05)	
35	0(0.0%)	6(2.91%)	66(2.11%)	20(2.29%)		0(0.0%)	64(7.95%)	311(9.17%)	37(7.22%)	
PBF, n (%)										
5-10	0(0.0%)	1(0.50%)	27(0.90%)	7(0.80%)	0.2	0(0.0%)	1(0.12%)	4(0.11%)	2(0.40%)	0.009
11-14	0(0.0%)	3(1.45%)	116(3.71%)	37(4.24%)		0(0.0%)	26(3.22%)	74(2.18%)	7(1.36%)	
15-20	0(0.0%)	30(14.56%)	462(14.77%)	122(13.99%)		0(0.0%)	80(9.93%)	241(7.11%)	31(6.05%)	
21-24	0(0.0%)	40(19.41%)	444(14.20%)	106(12.15%)		2(20.00%)	187(23.22%)	681(20.10)	97(18.94%)	
>24	8(99%)	132(64.07%)	2077(66.44%)	600(68.80%)		8(80%)	511(63.47%)	2388(70.48%)	375(73.24%)	
WHR , n (%)	3(37.50%)	81(39.32%)	1191(38.09%)	335(38.41%)	0.9	6(60.00%)	601(74.65%)	2591(76.47%)	384(75.00%)	0.4
BP, n (%)	4(50.00%)	63(30.58%)	298(9.53%)	65(7.45%)	<0.001	6(60.00%)	230(28.57%)	495(14.61%)	43(8.39%)	<0.001
Diabetes ,n (%)	0(0.0%)	37(17.96%)	243(7.77%)	58(6.65%)	<0.001	1(10.00%)	93(11.55%)	272(8.02%)	31(6.05%)	<0.001
Smoking, n (%)										
No smoker	5(62.50%)	130(63.10%)	1993(63.75%)	557(63.87%)	<0.001	8(80.00%)	725(90.06%)	3226(95.21%)	500(97.65%)	<0.001
Current smoker	1(12.50%)	31(15.04%)	701(22.41%)	217(24.88%)		0(0.0%)	32(3.97%)	61(1.80%)	4(0.78%)	
Former smoker	2(25.00%)	45(21.84%)	432(13.81%)	98(11.23%)		2(20.00%)	48(5.96%)	101(2.598%)	8(1.56%)	

Table 1. The values outside the parentheses are the number of people, and the values inside the parentheses are the percentages. Data are expressed as mean SD. P values were estimated using two-way analysis of variance or t-test. BUN, Blood Urea nitrogen; PA, physical activity; BP, Blood pressure; AF, atherogenic Factor; WHR, Waist to hip ratio; BMI, Body mass index; PBF, Percent body fat; GFR, glomerular filtration rate.

For females, atherogenic index had a direct () and indirect () lower effects via BUN, high blood pressure, diabetes and obesity as intermediate variables on eGFR. BUN had direct () and indirect () lower effects via high blood pressure on eGFR. High blood pressure was associated with lower eGFR (). Diabetes had direct () and indirect () lower effects on eGFR. Obesity had direct and positive () and indirect and negative () effects on eGFR. Diabetes and BUN were associated with high blood pressure (and respectively). For males, atherogenic index had a lower direct effect () on GFR. BUN had direct () and indirect () lower effects via high blood pressure, as an intermediate variable, on GFR. High blood pressure had () lower direct effect on GFR. Smoking had lower direct () and indirect () effects, via obesity and high blood pressure, as intermediate variables, on GFR. Physical activity had direct () and lower effect on obesity. Meat consumption in females had a direct (-0.01) and indirect (-0.03) effect on GFR (no effect on eGFR in males). (Table 2). All goodness of fit indices indicated that the model has acceptable fit. The results of the model fitness were reported in Figure 2.

Table 2: SEM results in 35-65-year-old- by sex at RaNCDC cohort study

Female			Male			Variable
Indirect effect (95%CI)	Direct effect (95%CI)	Total effect (95%CI)	Indirect effect (95%CI)	Direct effect (95%CI)	Total effect (95%CI)	
-0.01 (-0.020, 0.009)	-0.06 (0.03-, 0.08-)	0.07- (0.05-, 0.10-)	-0.005 (0.001-, 0.01-)	-0.02 (-0.05-, -0.01)	-0.03 (-0.005-, -0.06)	GFR >--- Smoking
-0.01 (-0.02, -0.03)	-0.19 (-0.23, -0.17)	0.20- (-0.23, -0.17)	---	-0.13 (-0.16, -0.10)	-0.13 (0.10-, 0.16-)	AF --->GFR
-0.02 (-0.02, -0.01)	-0.22 (-0.26, -0.18)	-0.24 (-0.28, -0.20)	0.01- (0.006-, 0.01-)	-0.17 (0.13-, 0.22-)	-0.18 (0.14-, 0.23-)	BUN --->GFR
---	-0.12 (-0.15, -0.09)	-0.12 (-0.15, -0.09)	---	-0.12 (0.09-, 0.15-)	-0.12 (0.09-, 0.15-)	HTN--->GFR
-0.03 (-0.06, 0.005)	-0.01 (-0.02, 0.003)	-0.04 (-0.08, -0.001)	---	---	---	Meats--->GFR
0.02 (0.01, 0.03)	0.07 (0.04, 0.10)	0.09 (0.06, 0.12)	0.01 (0.02, 0.007)	0.12 (0.15, 0.08)	0.13 (0.17, 0.10)	Obesity--->HTN
-0.02 (-0.01- 0.02 -)	0.10 (0.007, 0.13)	0.08 (0.07, 0.13)	---	---	---	Obesity---<GFR
-0.02 (-0.02, -0.01)	-0.04 (0.01-, 0.07-)	-0.06 (-0.09, -0.03)	---	---	---	Diabetes--->GFR
---	0.08 (0.06, 0.11)	0.08 (0.06, 0.11)	---	0.11 (0.14, 0.08)	0.11 (0.14, 0.08)	Obesity--->Diabetes
---	0.17 (0.14, 0.21)	0.17 (0.14, 0.21)	---	0.11 (0.15, 0.06)	0.11 (0.15, 0.06)	Diabetes--->HTN
---	-0.16 (-0.20, -0.13)	-0.16 (-0.20, -0.13)	---	-0.20 (0.17-, 0.24-)	-0.20 (0.17-, 0.24-)	PA--->Obesity
---	0.13 (0.10, 0.16)	0.13 (0.10, 0.16)	---	0.19 (0.15, 0.22)	0.19 (0.22, 0.15)	Lipid profile --->Obesity
---	0.15 (0.12, 0.18)	0.15 (0.12, 0.18)	---	0.07 (0.04, 0.11)	0.07 (0.11, 0.04)	BUN --->HTN

Note. BUN, blood urea nitrogen; PA, physical activity; BP, blood pressure; AF, atherogenic factor, WHR; waist to hip ratio; BMI, body mass index; PBF, percent body fat. Interpretation of one result as an example: In female, atherogenic variable had direct () and indirect () decreasing effects via mediating variables (BUN, high blood pressure, diabetes and obesity) on GFR.

Note. BUN, blood urea nitrogen; PA, physical activity; BP, blood pressure; AF, atherogenic factor, WHR; waist to hip ratio ; BMI, body mass index; PBF, percent body fat. Interpretation of one result as an example: For females, atherogenic variable had direct (and indirect (decreasing effects via mediating variables (BUN, high blood pressure, diabetes and obesity) on GFR.

Discussion

In this population-based study, we examined factors associated with glomerular filtration rates (GFR) in both genders. The findings of our study showed that obesity, diabetes, blood urea nitrogen, atherogenic factor, hypertension, meat consumption, and smoking were associated with lower GFR.

Several risk factors (hypertension, diabetes, high blood lipids, smoking) can affect on eGFR which has been reported from studies elsewhere [34]. Multivariate analysis of a retrospective cohort study on patients with renal disease in Japan (2012) showed that smoking, high blood pressure, high triglycerides, and low HDL each had an independent effect on CKD. Other studies also showed similar results regarding the effects of high blood pressure and high TG and LDL levels on CKD [35, 36].

In the current research, obesity in females had direct (positive) and indirect (negative) effects, via hypertension and diabetes, on GFR. Results from studies on effect of obesity on GFR are not similar [37, 38]. Iseki et al. reported an independent relationship between obesity and ESRD [14]. Like obese people, overweight people were highly likely to develop ESRD [39]. Hypotheses suggest that low muscle mass is associated with low levels of serum creatinine resulting in low GFR in normal people with no CKD. Nonetheless, obesity increases the risk for type 2 diabetes, high blood pressure and dyslipidemia [40], which in turn lead to low GFR.

A meta-analysis showed that there is a U-shape relationship between eGFR and death rate; eGFR < 60 ml/min/1.73m² increases death rate incrementally, but eGFR > 105 ml/min/1.73m² results in sharp decrease in death rate [41].

In RaNCD cohort study, low value of eGFR in females was due to inadequate physical activity and high prevalence of metabolic risk factors such as obesity, high blood lipids, and high blood pressure.

eGFR was also related to BUN which had negative direct and indirect relationship with GFR in both males and females. The value for BUN is in fact a sign of proper kidney functioning. The main causes of increased BUN are high-protein diets, low GFR, and congestive heart failure. BUN may increase independent from changes in creatinine and GFR. Such increase is due to reabsorption from proximal tube through the activity of renin-angiotensin-aldosterone sympathetic nervous systems [42]. There is a non-linear relationship between increasing BUN and decreasing GFR. Significant GFR decrease (>75%) is associated with an increase in BUN in the early stage of a renal disease. On the other hand, a relatively minor decrease in GFR is associated with a relatively high increase in urea concentrations and serum creatinine [43]. In our study, BUN had a negative and indirect effect via high blood pressure, as an intermediate variable on GFR. Findings of previous studies suggested that high blood pressure is significantly associated with increased kidney damage in females and males [44, 45]. A meta-analysis study in 2014 showed a significant relationship between high blood pressure and incidence of ESRD [46]. In the current research, high blood pressure was directly related to decrease in GFR. Meat consumption in women has a direct and indirect effect on GFR, which is consistent with similar studies [47, 48].

Dyslipidemia is an important risk factor for cardiovascular disease and CKD. In a study of 12728 subjects with a 2-year follow up, it was found that high triglyceride and low HDL both were risk factors for increased creatinine. These lipid profiles had confusing effects on creatinine after adjustment for other risk factors [46]. The mechanism through which fat causes damage to kidneys is not clear, but glomeruli sclerosis and atherosclerosis seem to have similar effects [49]. The current research findings showed that atherogenic index had direct and indirect relationship with low levels of GFR.

It is worth noting that this study is the first study that uses SEM for assessing the risk factors associated with GFR. The most important strength of the present study was the sample size which was large enough to investigate the association between all the above mentioned variables with GFR. Using SEM and path analysis, we were able to investigate both direct and indirect effects of GFR risk factors. However, our study suffered from the following limitations:

Using a cross-sectional study, we were unable to confirm that the studied exposures had an exact causal relationship with the level of eGFR. The researchers' definition of eGFR was only based on serum creatinine criterion which could lead to biased classification. Other studies have shown that eGFR measurement for subjects with normal kidney functioning was performed with less accuracy than those with CKD. However, it was more accurate than serum creatinine or Cockcroft-Gault equation.

Conclusion

Findings of the present study confirmed the results of previous studies on the risk factors of eGFR including hypertension, diabetes, blood lipids, BUN, obesity and smoking. Although low eGFR might have different reasons and is not a consistent sign of CKD, our findings are in line with reports from elsewhere and provides more detailed information about important risk factors of low GFR. Awareness of such risk factors will lead to positive health behaviours in general public. Future studies are recommended to investigate the effect of other variables including medications and food on eGFR.

Declarations

Ethics approval and consent to participate

From all participants in the cohort study after knowing the objectives of the study, informed written consent was obtained. The cohort study was given ethical approval by the Ethics Committee of Kermanshah University of Medical Sciences (ethics approval number: KUMS.REC.1394.318).

Consent to publish

Not applicable.

Availability of data and materials

All the information on how to access the RaNCD, with a list of current proposals and papers currently under preparation, can be found on our website: www.persiancohort.com

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

PJ and MM wrote much of the manuscript and performed all statistical analysis and generated figures and tables. FN,BH,YP,MSH and ES contributed their nephrology expertise and provided significant contributions to the literature review and collaborated in the writing of the manuscript. All authors have read and approved of this statement.

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Figures

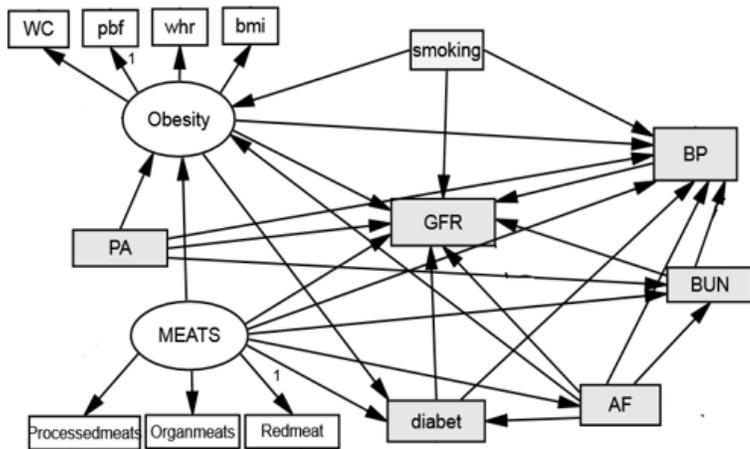


Figure 1
 The conceptual model diagram for risk factors relationship with glomerular filtration rate Note. BUN, blood urea nitrogen; PA, physical activity; BP, blood pressure; AF, atherogenic factor, WHR; waist to hip ratio ; BMI, body mass index; PBF, percent body fat

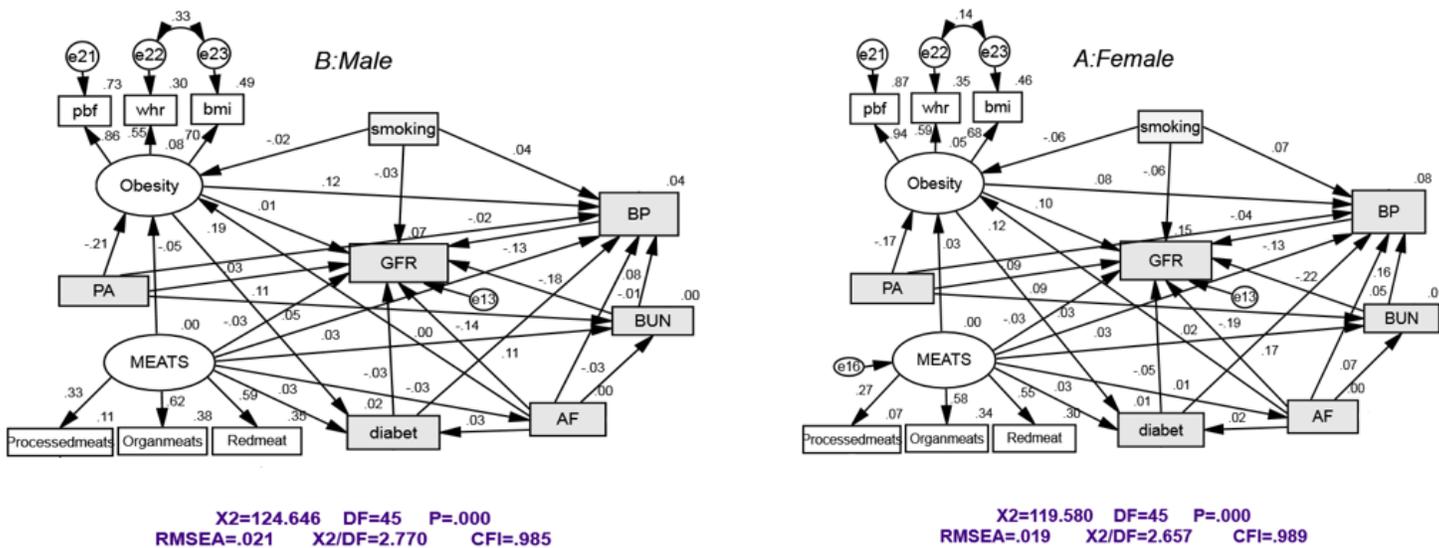


Figure 2
 part A and B: shows structural equation models for assessing direct and indirect effects on GFR for both females and males by standardized path coefficient and goodness of fit indices. "e" represent the errors Note. BUN, blood urea nitrogen; PA, physical activity; BP, blood pressure; AF, atherogenic factor WHR, waist to hip ratio ; BMI, body mass index; PBF, percent body fat