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Research Article

The Association between Serum Albumin and Globulin and All-Cause Mortality of Adults

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Abstract

Background: The relationship between serum albumin and globulin levels and all cause mortality has not been well defined. This study investigated the association between serum globulin and albumin levels with mortality in adults.

Patients and Methods: Public use National Health and Nutrition Examination Survey (NHANES III) data were used. NHANES III complex probabilistic household adult, laboratory and mortality data were merged. Specialized survey analysis software was used. Only sample persons examined in the Mobile Examination Center were included in this study.

Results: There were 2512 sample persons with complete data for all the covariates and were used in this analysis. The univariables odds ratios (95% confidence intervals) were: age 1.00821 (1.00712 - 1.00931); serum albumin concentration 0.852 (0.809 - 0.898); serum globulin concentration 1.089 (1.0465 - 1.1322). After multivariate analysis, the significant variables (Fig. 3), odds ratios (95% confidence intervals) were: age 1.00809 (1.00694 - 1.00925); female relative to male 0.613 (0.384 - 0.978); poverty income ratio 0.869 (0.789 - 0.956); drinking hard liquors 1.0126 (1.00061 1.02471); serum albumin concentration 0.914 (0.846 - 0.988); and serum globulin concentration 1.0503 (1.00612 - 1.09649).

Conclusions: Serum albumin and globulin concentrations were associated with all cause mortality in adults.

Keywords: NHANES III; Serum albumin; Serum globulin; All-cause mortality; Adults

Introduction

Serum albumins have been used as biomarkers in chronic kidney disease [1] and heart disease [2]. Using data from National Health and Nutrition Examination Survey (NHANES), Serum albumin was associated with coronary heart disease and heart disease related mortality [2]. Serum albumin and creatinine ratio was found to predict mortality using NAHNES III data [3]. Serum albumin level was associated with serum acidosis and inflammation in chronic renal disease patients [4]. Albuminuria was also found to be associated with cancer mortality [5]. The relationship between serum albumin levels and all-cause mortality in adults has not been well defined. This study used NHAENS III and NHANES III mortality linked data files to study the association between serum albumin and globulin concentrations and all cause mortality. There is little information on the relationship between serum globulins [6,7] and all-cause mortality. The effect of serum globulin levels on all cause mortality was further studied here. This study was a part of a larger effort to identify potential chemicals with harmful and beneficial health effects. It took

advantage of the vastness of the public use NHANES III (National Health and Nutrition Examination Survey) data to adjust for socio-demographic, health status factors may be confound the effects of serum albumin and globulin concentrations and the mortality of US adults.

Materials and Methods

NHANES and NHANES III

NHANES is a major program of National Center of Health Statistics (a part of Center of Disease Control (CDC) of United States of America) started in 1971. NHANES III is a national study based on a complex, multi-stage probability sampling design. For details of NHANES data and statistical guidance as well as their analysis examples see NHANES website [8]. In brief, NHANES studies were approved by CDC internal institutional review boards. The public use data are made available to the public and researchers. The NHANES sample weights were calculated to represent non-institutionalized general US population to account for non-coverage and non-response. These patients were interviewed at home and examined in mobile examination centers (MEC). This eliminated the cofounding effects of sample persons being too frail, too young or old to go to the MEC for examinations. In this study, NHANES III (conducted between1988 – 1994) household adult data file was merged with NHANES III laboratory data and the NHANES III linked cancer mortality data.

NHNAES III linked mortality

NHANES III participants were followed passively until December 31, 2006 for their mortality data. Detailed information about the data and analysis guidelines are available at their website [9]. In brief, probability matching was used to link NHANES III with National Death Index for vital status and mortality, age 90 years old was censored because they contribute little in person years. NHANES used multiple sources including the use of death certificates and with the National Death Index to ascertain vital status and cause of death.

Statistical analysis

NHANES III employed a complex sampling strategy and analysis [10-13]. Matlab programs (posted on Matlab File Exchange) were developed to convert SAS files provided by NAHNES to STATA programs to download NHANES III data files for further analysis. Specialized survey software is needed for NHANES complex data analysis [14]. STATA 12 (College Station, TX) was among those recommended by CDC to analyze the complex NHANES data and was used in this study. The sampling weight used was WTPFEX6 because only the sample persons had examinations in the MEC were included in this study, SDPPSU6 was used for the probability sampling unit (PSU) and SDPSTRA6 was used to designate the strata for the STATA survey commands. STATA scripts were written for this analysis, and will be submitted for publication separately. Univariate and multivariate logistic regressions [15] were used to study the relationship between serum serum globulin (GBPSI, g/L), and serum albumin (AMPSI, g/L) and all cause in adults (17 years or older). The status of mortality was coded as a binary outcome (1= death, 0 = otherwise). Linearized Taylor Standard Error estimation was used. The covariates and the corresponding NHANES III codes used were: MXPAXTMR (age at the MEC final examination in months), HSSEX (sex, _IHSSEX_1 = male, female as the reference group when applicable), HAM6S (weight in lbs without clothes), DMPMETRO (urban rural residence status), _IDMPMETRO_2 (rural residence, urban residence was used as the reference group), DMARETHN (race and ethnicity, _IDMARETHN_2 = non-Hispanic black, _IDMARETHN_3 = Mexican Americans, _IDMARETHN_4 = others, non-Hispanic white was used as the reference group), DMPPIR (poverty index ratio), HAN6JS (alcohol consumption, number of hard liquor drinks per month), and HAR4S (smoking, number cigarettes per day). For STATA analyses, only the patients without missing values for all of WTPFEX6, SDPPSU6, SDPSTRA6, MXPAXTMR, HSSEX, DMPMETRO, HAM6S, DMARETHN, DMPPIR, HAR4S, HAN6JS, AMPSI and GBPSI were included in this study. Further, these additional NHANES III codes considered not eligible: HAM6S (888), HAM6S (999), DMPPIR (888888), the numerator of DMPPIR was the midpoint of the observed family income category in the Family Questionnaire variable:HFF19R, and the denominator was the poverty threshold, the age of the family reference person, and the calender year in which the family was interviewed, HAR4S (666), HAR4S (777), HAR4S (888), HAR4S (999), HAN6JS (888), HAN6JS (999), not in BMI > 15 & BMI < 50, AMPSI (888), GBPSI (888), youth sample persons and incomplete mortality data. A total of 2512 sample persons with complete data were analyzed in this study.

Results

The general characteristics of the NHANES III linked mortality data were as follows. There were 20024 cases in NHANES III linked mortality data file included in this study. 13944 cases were not available in the public use file to protect the privacy of youth subjects. 26 cases in the NHANES III linked dataset did not have mortality data. All cause mortality (5291 deaths out of 33994 subjects, uod_113 codes were used to determine the cause of death) was used as the binary outcomes for this analysis. The NHANES III adult data file and the NHANES III linked mortality file were merged according to the SEQN number provided by NHANES III to uniquely identify the cases. All the results were obtained by using survey command taking into account the primary sampling unit and stratification variables and the weights assigned to the sample persons examined in the MEC. Thus these results were representative of the US population.

There were 2512 sample persons (Table 1) had complete data and were used in this analysis. The univariables (S.E.) were: the risk of death (S.E.) (IndicatorDeath), 0.147,

(0.129-0.165); body mass index (BMI), 25.231 (24.940-25.522); age (MXPAXTMR), 474.180 (464.512-483.847); sex (HSSEX), 1.446 (1.425-1.467); urbanicity (DMPMETRO), 1.563 (1.433-1.692); race (DMARETHN), 1.374 (1.278-1.469); poverty income ratio (DMPPIR), 2.737 (2.551-2.923); smoking (cigarettes per day) (HAR4S), 19.584 (18.479-20.689); drinking hard liquors (drinks per month) (HAN6JS), 2.802 (2.089-3.514); follow up in months (permth_exm) 163.387 (158.824-167.949); serum albumin level (umol/L) (AMPSI) 41.582 (41.141 -42.023); serum globulin concentration (umol/L) (GBPSI), 31.040 (30.536-31.544).

For univariate analysis, the significant univariates (Fig. 2), odds ratios (95% confidence intervals) were: age 1.00821 (1.00712-1.00931); serum albumin concentration 0.852 (0.809-0.898); serum globulin concentration 1.089 (1.0465 -1.1322). For multivariate analysis, the significant variables (Fig. 3), odds ratios (95% confidence intervals) were: age 1.00809 (1.00694-1.00925); female relative to male 0.613 (0.384-0.978); poverty income ratio 0.869 (0.789- 0.956); drinking hard liquors 1.0126 (1.00061-1.02471); serum albumin concentration 0.914 (0.846-0.988); serum globulin concentration 1.0503 (1.00612-1.09649).

Discussion

The relationship between serum albumin and globulin levels and all cause mortality has not been well defined. Although albumin serum level has been associated with mortality related to heart disease [2] and cancer [5]. Serum globin is a large family of globular functional serum proteins [16]. There is little information on the relationship between serum globulin and mortality [6,7]. This study investigated the association between serum globulin and albumin levels with mortality in adults. The NHANES III data and HNAHES III linked mortality data were taken to represent US non-institutionalized population as designed by NHANES. There were 2512 sample persons (Table 1) had complete data and were used in this analysis. This study had a long follow up time of 163 months (Table 1). From the univariate analysis (Table 2), this study found significant association between age of the subject, serum albumin and globulin concentrations and all cause mortality in adults.

Table 1

	Mean	Linearized Std. Err.	[95% Conf. Interval]	
Indicator Death	0.1467653	0.0090606	.1285378	.1649929
BMI	25.23112	0.1446976	24.94002	25.52221
MXPAXTMR	474.1798	4.805605	464.5121	483.8474
HSSEX	1.446128	0.0105629	1.424878	1.467378
DMPMETRO	1.562798	0.064464	1.433114	1.692483
DMARETHN	1.373806	0.0474796	1.278289	1.469322
DMPPIR	2.73682	0.0924366	2.550862	2.922779
HAR4S	19.58398	0.5494216	18.47869	20.68927
HAN6JS	2.801754	0.3540962	2.089404	3.514103
permth_exm	163.387	2.267935	158.8245	167.9495
TPPSI	72.62067	0.218112	72.18189	73.05946
AMPSI	41.58208	0.2194896	41.14053	42.02364
GBPSI	31.03954	0.2505498	30.5355	31.54358

Table 1. Baseline characteristics of serum albumin and globulin and covariables of adult all-cause mortality. Indicator Death: 0=alive, 1=dead. Linearized Taylor Standard Error estimation was used. The NHANES III codes used were: body mass index, MXPAXTMR (age at the MEC final examination), HSSEX (sex), AMPSI (serum albumin concentration in S.I. units), GBPSI (serum albumin concentration in S.I. units),DMPMETRO (urban rural residence status), HAM6S (weight in lbs without clothes), DMARETHN (race and ethnicity), DMPPIR (poverty index ratio), HAN6JS (alcohol consumption), HAR4S (smoking), and permth_exm (months of follow up from MEC examination). n = 2512 samples.

Table 2

IndicatorDeath	Odds Ratio	Linearized Std. Err.	t	P>|t|	[95% Conf. Interval]	
BMI	1.012644	0.0167891	0.76	0.452	.9794256	1.046989
MXPAXTMR	1.008214	0.0005457	15.11	0	1.007116	1.009312
HSSEX	0.8279532	0.120299	-1.3	0.2	.6181043	1.109047
DMPMETRO	1.281079	0.1671808	1.9	0.064	.9852798	1.665682
DMARETHN	1.046702	0.0826259	0.58	0.566	.8930066	1.226849
DMPPIR	0.9369329	0.0327065	-1.87	0.068	.8733931	1.005095
HAN6JS	1.014256	0.0085381	1.68	0.099	.9972238	1.031578
HAR4S	1.006592	0.006029	1.1	0.278	.9945359	1.018794
AMPSI	0.8520222	0.0220691	-6.18	0	.8087619	.8975966
GBPSI	1.088527	0.0213031	4.33	0	1.046503	1.132238

Table 2. Univariate analysis of socio-economic and serum albumin and globulin factors of all cause mortality. Indicator Death: 0=alive, 1=dead. Linearized Taylor Standard Error estimation was used. The NHANES III codes used were: body mass index, MXPAXTMR (age at the MEC final examination), HSSEX (sex), AMPSI (serum albumin concentration in S.I. units), GBPSI (serum globulin concentration in S.I. units), DMPMETRO (urban rural residence status), HAM6S (weight in lbs without clothes), DMARETHN (race and ethnicity), DMPPIR (poverty index ratio), HAN6JS (alcohol consumption), HAR4S (smoking), and permth_exm (months of follow up from MEC examination). n = 2512 samples.

All of the univariables were used in the final multivariate analysis so as not to miss the potentially important predictors. For multivariate analysis (Table 3), this study found that the significant predictors of all cause mortality in adults were age, female sex (relative to males), poverty income ratio, drinking hard liquors, serum albumin and globulin concentration. Previous studies have found racial disparities [17,18] and the adverse effects of smoking and drinking [19]. This study found an increased risk of mortality with drinking and lower poverty income ration. After adjusting for all the covariates, serum globulin and albumin levels remained an independent risk factor of adult all cause mortality.

Table 3

IndicatorDeath	Odds Ratio	Std. Err.	Linearized t	P>|t|	[95% Conf. Interval]	
BMI	1.00112	0.0187618	0.06	0.953	.9640786	1.039584
MXPAXTMR	1.008092	0.0005745	14.14	0	1.006937	1.009249
_IHSSEX_2	0.6132621	0.1424138	-2.11	0.041	.3843752	.9784458
_IDMPMETRO_2	1.312836	0.2008741	1.78	0.082	.965005	1.786042
_IDMARETHN_2	1.064784	0.2054743	0.33	0.746	.7222105	1.569855
_IDMARETHN_3	0.5825249	0.1755566	-1.79	0.079	.3176944	1.068118
_IDMARETHN_4	0.7059258	0.2147134	-1.14	0.258	.3828418	1.301663
DMPPIR	0.8686943	0.0413115	-2.96	0.005	.789438	.9559077
HAN6JS	1.012587	0.0059889	2.11	0.04	1.00061	1.024707
HAR4S	0.9942541	0.0078206	-0.73	0.467	.9786449	1.010112
AMPSI	0.9142072	0.0350771	-2.34	0.024	.846296	.9875681
GBPSI	1.050333	0.0224562	2.3	0.026	1.006115	1.096495
_cons	0.0282851	0.0574659	-1.75	0.086	.0004748	1.684989

Table 3. Multivariate analysis of socio-demographic factors, serum albumin and globulin levels and all cause mortality. Indicator Death: 0=alive, 1=dead. Linearized Taylor Standard Error estimation was used. The NHANES III codes used were: BMI (body mass index), HSSEX (_IHSSEX2 =female, using male as the reference group), AMPSI (serum albumin concentration in S.I. units), GBPSI (serum globulin concentration in S.I. units), MXPAXTMR (age at the MEC final examination), HAM6S (weight in lbs without clothes), DMPMETRO (urban rural residence status, _IDMPMETRO_2=rural residence, urban residence used as the reference group), DMARETHN (race and ethnicity, _IDMARETHN_2=non-Hispanic black, _IDMARETHN_3 =Mexicans, _IDMARETHN_4=others, non-Hispanic white used as the reference group), DMPPIR (poverty index ratio), HAN6JS (alcohol consumption), and HAR4S (smoking). n=2512 samples.

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