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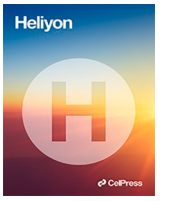

Serum albumin levels and stress urinary incontinence in females: A retrospective study based on NHANES 2007–2016

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ABSTRACT

Background: Serum albumin (sAlb) is an essential indicator of human physiological function. However, the correlation between the concentration of sAlb and stress urinary incontinence (SUI) remains poorly understood.

Methods: The sAlb was measured using the bichromatic digital endpoint method. The SUI was assessed according to information from the National Health and Nutrition Examination Survey (NHANES) questionnaire. Univariate and multivariate logistic regression analyses of the potential correlation between sAlb and stress incontinence were performed. Subgroup analysis was also conducted according to body mass index (BMI).

Results: After adjusting for potential key confounders, sAlb was found to have a significant association with SUI in adult females, and higher sAlb levels were associated with a lower risk of SUI (OR = 0.849; 95 % CI: 0.724–0.994; $P = 0.042$). Furthermore, subgroup analysis indicated that sAlb was associated with reduced SUI risk only in the subgroup with a body mass index (BMI) $\geq$ 30 (OR = 0.762; 95 % CI: 0.595–0.975; $P = 0.030$).

Conclusion: Female SUI was correlated with sAlb concentration, and a lower risk of SUI was seen in those with greater sAlb levels. These findings provide new insights into SUI prevention.

1. Introduction

Urinary incontinence is a common disorder among females, which imposes a huge psychological burden on fellow females and adds to the socioeconomic pressure [1]. Stress urinary incontinence (SUI) stands out as one of the prevalent forms characterized by the inadvertent discharge of urine resulting from heightened intra-abdominal pressure attributed to physical activity. Statistically, stress incontinence deeply affects 10%–40 % of women [2]. Current treatments for SUI involve lifestyle changes, physical therapy, pharmacological interventions, and surgical treatment [3,4]. These treatments may improve the symptoms of the patient to some extent.

Serum albumin (sAlb) is the predominant protein in the circulatory system. The sAlb has several functions and is characterized by its elevated abundance, predominantly synthesized within the hepatic tissue [5,6]. Beyond its pivotal function in upholding colloid osmotic pressure, sAlb actively contributes to various metabolic processes [7]. Additionally, it is an important indicator for assessing nutrition and can reflect the recent nutritional status of the body [8]. Furthermore, sAlb usually has important antioxidant effects. Recent evidence has emerged that sAlb is closely associated with various diseases, including cardiovascular diseases and tumors [9,10].

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A study from Taiwan has suggested that cirrhosis and overactive bladder (OAB) patients had low sAlb [11]. Furthermore, diminished sAlb levels have been observed to be linked to perioperative complications of SUI [12]. However, the association between sAlb and the risk of SUI remains unknown. Subsequently, this research aimed to assess the correlation between sAlb and SUI and hopefully provide novel perspectives on treating and managing patients afflicted with SUI.

2. Materials and methods

2.1. Study participants

The National Health and Nutrition Examination Survey (NHANES, https://www.cdc.gov/nchs/nhanes/) is a complimentary and public database dedicated to collecting information about population health and nutrition-related information [13]. This database is available for public access and does not require ethical permission. This study is a cross-sectional study and all information was derived from selected data from the NHANES database from 2007 to 2016. Detailed information on SUI, sAlb, and related covariates was provided in these cycle years. Participants who did not answer the questionnaire about stress incontinence and those without sAlb data were excluded. Fig. 1 shows the detailed information about the participants in a flowchart.

2.2. SAlb testing and SUI definition

Herein, sAlb was identified as the independent variable. The albumin concentration was measured using DcX800, based on the principle that albumin can bind to Bromocresol Purple (BCP) to form a complex. Stress incontinence was assessed by trained

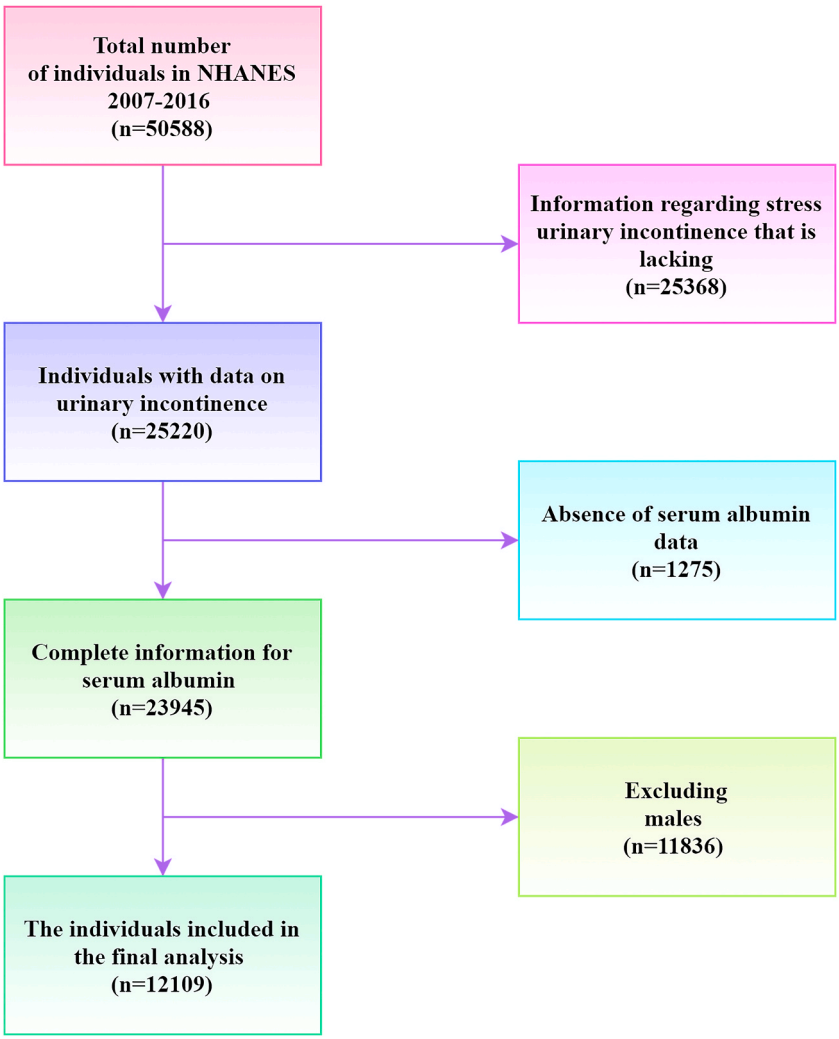

Fig. 1. Description of the research process.

Table 1
Demographic features of included individuals.

	SUI		*P* Value
	Yes	No	
Participants (n)	4970	7139	
Age, Mean±SD	53.15 ± 15.92	47.38 ± 18.41	< 0.001
BMI, n (%), kg/m2			< 0.001
< 25	1126 (22.7)	2443 (34.2)	
25–30	1414 (28.5)	2025 (28.4)	
≥30	2383 (47.9)	2616 (36.6)	
missing	47 (0.9)	55 (0.8)	
Race, n (%)			< 0.001
Non-Hispanic White	2358 (47.4)	2814 (39.4)	
Non-Hispanic Black	741 (14.9)	1711 (24.0)	
Other Hispanic	590 (11.9)	817 (11.4)	
Other races	1281 (25.8)	1797 (25.2)	
Alcohol use, n (%)			0.108
yes	3036 (61.1)	4253 (59.6)	
no	1929 (38.8)	2883 (40.4)	
missing	5 (0.1)	3 (0)	
Hypertension, n (%)			< 0.001
yes	2452 (49.3)	2709 (37.9)	
no	2472 (49.7)	4315 (60.4)	
missing	46 (0.9)	115 (1.6)	
Smoking, n (%)			< 0.001
never	2998 (60.3)	4733 (66.3)	
former	1052 (21.2)	1227 (17.2)	
current	917 (18.5)	1174 (16.4)	
missing	3 (0.1)	5 (0.1)	
Depression, n (%)			< 0.001
yes	780 (15.7)	627 (8.8)	
no	4142 (83.3)	6450 (90.3)	
missing	48 (1.0)	62 (0.9)	
Diabetes, n (%)			< 0.001
yes	779 (15.7)	736 (10.3)	
no	4055 (81.6)	6253 (87.6)	
borderline	130 (2.6)	146 (2.0)	
missing	6 (0.1)	4 (0.1)	
Family poverty ratio, n (%)			0.711
< 1.3	1566 (31.5)	2204 (30.9)	
1.3–3.5	1668 (33.6)	2458 (34.4)	
≥3.5	1324 (26.6)	1871 (26.2)	
missing	412 (8.3)	606 (8.5)	
Vaginal deliveries, n (%)			< 0.001
yes	3887 (78.2)	4433 (62.1)	
no	632 (12.7)	1247 (17.5)	
missing	451 (9.1)	1459 (20.4)	
Cesarean deliveries, n (%)			< 0.001
yes	956 (19.2)	1412 (19.8)	
no	1495 (30.1)	1751 (24.5)	
missing	2519 (50.7)	3976 (55.7)	
Macrosomia, n (%)			< 0.001
yes	789 (15.9)	919 (12.9)	
no	3554 (71.5)	4382 (61.4)	
missing	627 (12.6)	1838 (25.7)	
hysterectomy, n (%)			< 0.001
yes	1345 (27.1)	1415 (19.8)	
no	3617 (72.8)	5701 (79.9)	
missing	8 (0.2)	23 (0.3)	
Level of education, n (%)			< 0.001
less than high school	1342 (27.0)	1588 (22.2)	
high school	1069 (21.5)	1536 (21.5)	
higher than high school	2552 (51.3)	4010 (56.2)	
missing	7 (0.1)	5 (0.1)	
sAlb (g/dL), Mean±SD	4.15 ± 0.34	4.18 ± 0.33	< 0.001

SUI, stress urinary incontinence; BMI, body mass index; sAlb, serum albumin; SD, standard deviation.

interviewers through questionnaires. The SUI was determined by typical symptoms, with urine overflow occurring with varying degrees of increased abdominal pressure (coughing, lifting, or exercise) [14].

2.3. Covariates

The NHANES provides information on age, race (non-Hispanic White, non-Hispanic Black, other Hispanic, or other races), education (less than high school, high school, higher than high school, or missing), family poverty ratio (<1.3, 1.3–3.5, ≥3.5, or missing), body mass index (BMI) (<25, 25–30, ≥30, or missing), smoking (never, former, current, or missing), and hysterectomy (yes, no, or missing) [15,16]. Both diabetes (yes, no, borderline, or missing) and hypertension (yes, no, or missing) were assessed with questionnaire information [17]. Depression was assessed mainly using PHQ-9; a score ≥10 was considered as depression, and vice versa [16]. Individuals having ≥12 drinks per year were defined as alcohol use. A vaginal birth count of 0 was defined as having no history of vaginal birth, and a vaginal birth count ≥1 was considered a vaginal birth [18]. A history of macrosomia delivery was defined as having delivered a baby weighing >9 pounds.

2.4. Statistical analysis

All analyses were performed using SPSS26 and Stata15. Categorical variables were represented as frequency distributions. Continuous variables were expressed as mean ± standard deviation. Herein, sAlb was analyzed as a continuous and categorical variable, respectively [19]. The weighted logistic regression was employed to determine the relationship between sAlb and SUI in women. Similarly, the relationship between sAlb and moderate/severe SUI was investigated using logistic regression. The multifactorial logistic regression model included significant univariate or clinically relevant covariates. Moreover, a subgroup analysis was performed to assess the association between sAlb and SUI, grouped using BMI. Statistical significance was attributed to $P < 0.05$.

3. Results

3.1. Characteristics of the population included in the analysis

A total of 12,109 female participants were included in the final analysis during five consecutive cycles of the NHANES survey from 2007 to 2016 (Table 1). Of these participants, 4970 reported SUI conditions. This study found that sAlb was lower in stress incontinence patients than in participants without stress incontinence (4.15 ± 0.34 vs. 4.18 ± 0.33). Compared with participants without SUI, patients with SUI were older (53.15 ± 15.92 vs. 47.38 ± 18.41), had a higher prevalence of diabetes mellitus (15.7 vs. 10.3), and had a higher prevalence of depression (15.7 vs. 8.8). Moreover, patients with SUI usually had a higher percentage of vaginal deliveries

Table 2
Association between covariates and SUI in females.

Variable	Univariable	*P* value
	OR (95%CI)	
Age	1.023 (1.020–1.025)	< 0.001
BMI, kg/m2		
25-30 (**vs.** BMI < 25)	1.419 (1.251–1.609)	< 0.001
≥30 (**vs.** BMI < 25)	1.994 (1.777–2.237)	< 0.001
Race		
Non-Hispanic Black (**vs.** Non-Hispanic White)	0.524 (0.470–0.586)	< 0.001
Other Hispanic (**vs.** Non-Hispanic White)	0.764 (0.668–0.874)	< 0.001
Other races (**vs.** Non-Hispanic White)	0.818 (0.733–0.913)	< 0.001
Alcohol use	1.072 (0.974–1.179)	0.156
Hypertension	1.661 (1.508–1.828)	< 0.001
Smoking		
former (**vs.** never)	1.323 (1.171–1.494)	< 0.001
current (**vs.** never)	1.180 (1.042–1.336)	0.009
Depression	1.786 (1.543–2.068)	< 0.001
Diabetes	1.899 (1.642–2.196)	< 0.001
Family poverty ratio		
1.3–3.5 (**vs.** < 1.3)	1.005 (0.900–1.124)	0.923
≥3.5 (**vs.** < 1.3)	1.080 (0.961–1.213)	0.199
Vaginal deliveries	1.796 (1.567–2.059)	< 0.001
Cesarean deliveries	0.765 (0.664–0.880)	< 0.001
Macrosomia	1.084 (0.944–1.245)	0.252
hysterectomy	1.556 (1.390–1.741)	< 0.001
Level of education		
high school (**vs.** less than high school)	0.855 (0.746–0.979)	0.023
higher than high school (**vs.** less than high school)	0.798 (0.713–0.893)	< 0.001

Weighted logistic regression analysis: Univariable, not adjusted.
SUI, stress urinary incontinence; OR, odd ratio; BMI, body mass index.

compared with participants without SUI (78.2 vs. 62.1).

3.2. Logistic regression analysis

First, we performed a univariate analysis. Table 2 demonstrates strong correlation between SUI and the following: age (OR = 1.023; 95 % CI: 1.020–1.025), depression (OR = 1.786; 95 % CI: 1.543–2.068), diabetes (OR = 1.899; 95 % CI: 1.642–2.196), vaginal deliveries (OR = 1.796; 95 % CI: 1.567–2.059), cesarean deliveries (OR = 0.765; 95 % CI: 0.664–0.880), and hysterectomy (OR = 1.556; 95 % CI: 1.390–1.741).

In a multifactorial regression analysis adjusted for age, BMI, race, alcohol use, hypertension, smoking, depression, diabetes mellitus, family poverty ratio, vaginal delivery, cesarean delivery, macrosomia, history of hysterectomy, and education, sAlb remained an independent factor and was a protective factor for SUI (OR = 0.849; 95 % CI: 0.724–0.994; $P = 0.042$). Specifically, the risk of SUI decreased by 15.1 % for each 1 g/dL increase in sAlb. Furthermore, we transformed albumin concentration into a categorical variable to investigate the correlation. The outcomes indicated that those in tertile 1 for sAlb had a higher risk of developing SUI compared with tertile 3. Moreover, we found that the lower the sAlb level, the higher the risk of developing SUI (OR = 1.167; 95 % CI: 1.021–1.333; $P = 0.024$) (Table 3).

Subsequently, we further explored the relationship between sAlb and moderate/severe SUI. The findings suggested a 23.7 % reduction in moderate/severe SUI risk for each 1 g/dL increase in sAlb (OR = 0.763; 95 % CI: 0.592–0.982; $P = 0.036$). Concurrently, an increased risk of moderate/severe SUI was observed in the lower sAlb population (tertile 1) compared with the higher sAlb population (tertile 3) (OR = 1.257; 95 % CI: 1.035–1.527; $P = 0.021$) (Table 4).

3.3. Subgroup analysis

The SUI usually increases in prevalence as BMI increases. Consequently, a subgroup analysis was performed to assess the association between sAlb and SUI in participants with different BMIs. The outcomes demonstrated that sAlb was only associated with reduced SUI risk in the subgroup with a BMI ≥30 (Table 5).

4. Discussion

SUI is a common condition that afflicts many women. Current research on influencing factors is highly interesting. Available evidence supports older age, obesity, and history of hysterectomy as risk factors for female SUI [20–22]. Simultaneously, numerous factors can potentially influence SUI, emphasizing the importance of identifying and intervening in these SUI-related factors. Similarly, due to the abundant role of sAlb, numerous studies have explored its relevance to disease. A more comprehensive meta-analysis showed a strong correlation between low sAlb and cardiovascular diseases [23]. Additionally, results from clinical trials in the United States have shown that low sAlb levels are associated with poor survival in patients with heart failure [24]. However, few sAlb is in relation to SUI in women. Accordingly, we investigated the association between the sAlb and SUI based on the NHANES database.

The outcomes of this cross-sectional study, conducted with a large sample from the NHANES database, demonstrated that increased sAlb levels were still significantly associated with a reduced risk of SUI in females after adjusting for multiple covariates. Notably, this study is the first to address the relationship between sAlb and SUI in women.

Some studies have concentrated on the correlation between albumin and overactive bladder (OAB). Liu et al. [25] observed that sAlb was significantly lower in OAB patients than in non-OAB individuals. Another research investigated 168 patients with cirrhosis, and it was observed that sAlb levels in these patients were significantly linked to nocturia and urge incontinence [11]. Additionally, a prospective cohort study found that sAlb was negatively related to incontinence-associated dermatitis [26]. These studies have suggested that lower sAlb may contribute to developing urinary incontinence. However, the sample sizes of the few available studies were small, and they mostly focused on OAB. Compared with these studies, the present study concentrated on the correlation between sAlb and SUI in women. Herein, we further clarified the correlation between sAlb and the risk of SUI and moderate/severe SUI.

Table 3
Association between sAlb and SUI in females.

Variable	Univariable		Multivariable	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value
sAlb (g/dL)				
continuous variable	0.739 (0.643–0.850)	< 0.001	0.849 (0.724–0.994)	0.042
categorical variable				
Tertile 1 (<4)	1.307 (1.159–1.473)	< 0.001	1.167 (1.021–1.333)	0.024
Tertile 2 (4–4.3)	1.057 (0.949–1.177)	0.315	0.957 (0.852–1.074)	0.454
Tertile 3 (≥4.3)	1.000 (Reference)		1.000 (Reference)	

Weighted logistic regression analysis: Univariable, not adjusted; Multivariable, adjusted for age, BMI, race, alcohol use, hypertension, smoking, depression, diabetes, family poverty ratio, vaginal deliveries, cesarean deliveries, macrosomia, hysterectomy, level of education (Categorical variables (covariates) used no or lowest rank as the reference value.).
SUI, stress urinary incontinence; sAlb, serum albumin; OR, odd ratio; BMI, body mass index.

Table 4
Association between sAlb and moderate/severe SUI in females.

	Univariable		Multivariable	
Variable	OR (95%CI)	*P* value	OR (95%CI)	*P* value
sAlb (g/dL)				
continuous variable	0.591 (0.479–0.731)	<0.001	0.763 (0.592–0.982)	0.036
categorical variable				
Tertile 1 (<4)	1.600 (1.339–1.910)	<0.001	1.257 (1.035–1.527)	0.021
Tertile 2 (4–4.3)	1.210 (1.018–1.437)	0.031	1.029 (0.858–1.234)	0.757
Tertile 3 (≥4.3)	1.000 (Reference)		1.000 (Reference)	

Weighted logistic regression analysis: Univariable, not adjusted; Multivariable, adjusted for age, BMI, race, alcohol use, hypertension, smoking, depression, diabetes, family poverty ratio, vaginal deliveries, cesarean deliveries, macrosomia, hysterectomy, level of education (Categorical variables (covariates) used no or lowest rank as the reference value.).
SUI, stress urinary incontinence; sAlb, serum albumin; OR, odd ratio; BMI, body mass index.

Table 5
Weighted subgroup analysis.

	OR	95%CI	*P* value
BMI (kg/m2)			
< 25	1.044	0.770-1.416	0.780
25–30	0.913	0.684-1.218	0.536
≥30	0.762	0.595-0.975	0.030

OR, odd ratio; BMI, body mass index.
adjusted for age, race, alcohol use, hypertension, smoking, depression, diabetes, family poverty ratio, vaginal deliveries, cesarean deliveries, macrosomia, hysterectomy, level of education (Categorical variables (covariates) used no or lowest rank as the reference value.).

The mechanisms by which sAlb reduces the risk of SUI are incompletely understood. However, several potential mechanisms may exist. First, sAlb is an important transport carrier involved in transporting many hormones in the body, including estrogen [27,28]. Several studies have suggested that estrogen is significantly associated with the risk of urinary incontinence and that topical estrogen use also improves the symptoms of urinary incontinence [29,30]. Second, pelvic floor muscle hypofunction is a common cause of SUI [31,32]. Sarcopenia is significantly associated with urinary incontinence [33]. Furthermore, a survey from Japan demonstrated that trunk muscle mass was correlated with the status and severity of SUI [34]. Moreover, sAlb levels are positively correlated with muscle mass and strength. This explains why low sAlb is associated with an increased risk of SUI [35–37]. Finally, Wilke et al. systematically summarized the role of oxidative stress in SUI. The results presented a significant increase in oxidative stress-related markers in patients with SUI compared with controls [38]. Moreover, a community survey from Japan confirmed that advanced glycation end products (AGEs), oxidative stress markers, were significantly associated with lower urinary tract symptoms [39]. This implies that oxidative stress may be a potential mechanism of SUI. Conversely, sAlb, as an important antioxidant, indirectly acts by enhancing the antioxidant system in the body and directly reducing the oxidative properties of polyvalent metal ions by binding [27,40].

This study has several strengths. First, it is the first to examine the relationship between sAlb and SUI in females. Second, this research was based on the NHANES database, which provided a large sample size. However, there are still certain limitations. Although we adjusted for relevant confounding variables as much as possible, it is possible that certain variables were omitted from our analysis. Furthermore, due to its cross-sectional nature, this study may have some shortcomings in exploring causality. Therefore, further prospective studies are necessary.

5. Conclusion

Briefly, sAlb levels are associated with SUI in females, and the risk of SUI decreases as sAlb levels increase.

Data Availability

All data used in this research were obtained from the public data available in the NHANES database (https://wwwn.cdc.gov/nchs/nhanes/Default.aspx).

Ethical statement

This database is available for public access and does not require ethical permission.

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CRediT authorship contribution statement

Mingming Xu: Writing – original draft, Conceptualization. **Hang Zhou:** Methodology, Data curation. **Yang Pan:** Methodology, Data curation. **Zhunan Xu:** Methodology, Data curation. **Xiaoqiang Liu:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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