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The correlation between serum alkaline phosphatase and grip strength in middle-aged and elderly people: NHANES 2011–2014

Ziyi Zhang^{1†}, Jiajie Zhou^{1†}, Anpei Ma², Honggu Chen³, Bo Wang¹ and Guoyang Zhao^{1*}

Abstract

Background Serum alkaline phosphatase (ALP) plays a crucial role in bone and muscle health. Previous studies have demonstrated that serum alkaline phosphatase (ALP) is closely associated with muscle mass. Nevertheless, the association between serum alkaline phosphatase (ALP) and grip strength remains unclear. Therefore, the present study focused on exploring the association of serum ALP with grip strength in middle-aged and elderly people.

Methods We conducted a cross-sectional study using data from the National Health and Nutrition Examination Survey conducted from 2011 to 2014. A total of 3514 participants (1891 males and 1623 females) aged 40–80 years were included in this study. Serum ALP and pelvic grip strength were analyzed as independent and dependent variables, additional variables were the possible impact modifiers. weighted generalized linear models and stratified analysis by gender, age group, and race were applied to assess the relationship between serum ALP and grip strength. Smooth curve fitting and threshold effect analysis/saturation effect analysis were used to analyze the nonlinear relationship between the 2 variables.

Results In the gender-stratified subgroup analysis, we observed an inverse association between serum ALP and grip strength in both male and female. When stratified by age group, the association remained significant among participants 40–59 years of age, but not among those ≥ 60 years old. When stratified by race, the association remained significant among Non-Hispanic White and Non-Hispanic Black. It is noteworthy that serum ALP and grip strength showed a significant negative correlation among female aged 40–59 years, but not among female aged ≥ 60 years. Additionally, Smooth curve fitting showed that serum ALP had a nonlinear relationship with grip strength in male aged 40–59 years and male aged over 60 years, the inflection points are 54 IU and 97 IU respectively.

Conclusion Our study revealed an inverse relationship between serum ALP and grip strength, this finding offers new insights and avenues for understanding how serum alkaline phosphatase affects skeletal muscle health.

Keywords Serum alkaline phosphatase, Grip strength, Sarcopenia, NHANES

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Background

Sarcopenia represents a progressive and generalized skeletal muscle disorder entailing the accelerated depletion of muscle mass and function, which is associated with augmented adverse outcomes such as falls, functional deterioration, frailty, and mortality [1]. Sarcopenia is correlated with a multitude of factors, including age-related inflammation, inactivity, poor nutrition, and chronic diseases [2]. Grip strength constitutes an essential factor in the diagnosis of sarcopenia [3], as muscle strength is not solely dependent on mass [4]. Lower handgrip strength in healthy adults predicts an elevated risk of functional limitations and disabilities in later life, as well as all-cause mortality [5]. Considering the high prevalence and severe implications of sarcopenia, there is an immediate and compelling urgency to investigate the mechanisms influencing grip strength.

Alkaline phosphatase (ALP) is an enzyme present in diverse tissues throughout the body. The majority of ALP in serum (over 80%) originates from the liver and bones, with a minor portion coming from the intestines [6]. ALP plays a significant role in inflammation and metabolic syndrome [4], and elevated ALP is invariably associated with adverse outcomes [7]. A large cohort study demonstrated that higher serum total ALP levels were significantly associated with the incidence of hip fractures [8]. Basic research suggests that tissue nonspecific alkaline phosphatase (TNAP) functions within bone and muscle progenitor cells to impact ATP production and mitochondrial respiration [9], but the exact physiological function of ALP remains largely unknown.

In relation to the musculoskeletal system, some researchers have discerned a positive association between serum alkaline phosphatase (ALP) and a low muscle mass index [10]. Nevertheless, the effect of serum ALP on grip strength remains uncharted. Hence, we initiated this research endeavor to investigate the interrelationship between serum ALP and grip strength within the US population.

Methods

Study population

The National Health and Nutrition Examination Survey (NHANES) is a biennial nationwide study that recruits a representative sample of the general population in the United States. Our analysis uses data collected from 2011 to 2014, representing 2 dataset cycles of NHANES. In the 2011–2014 NHANES, Of 29,902 participants, we excluded 12,513 individuals aged < 40 years, 747 with missing data for serum ALP, 1727 with missing grip strength data, 54 with missing BMI data, 307 with cancer. Individuals fulfilling any of the following criteria were also excluded: pregnancy ($n=5$), a history of hand surgery ($n=291$), liver disease ($n=278$), neoplastic disease

($n=632$), thyroid disease ($n=521$). Additionally, 653 with missing data for relevant covariates. Finally, 3514 participants were included in this study. Flowchart illustrating the exclusion criteria is provided in Fig. 1.

Measurement of serum alkaline phosphatase

In this investigation, serum ALP was designated as the exposure variable. From 2011 to 2014, the DxC800 system adopted a kinetic rate methodology employing a 2-Amino-2-Methyl-1-Propanol (AMP) buffer for the measurement of ALP activity in serum or plasma. In the reaction, ALP catalyzes the hydrolysis of the colorless organic phosphate ester substrate, p-Nitrophenylphosphate, to the yellow-colored product, p-Nitrophenol, and phosphate. This reaction transpires at an alkaline pH of 10.3. The system monitors the rate of alteration in absorbance at 410 nm within a fixed-time interval. This rate of change in absorbance is directly proportional to the ALP activity in the serum. Detailed information about serum alkaline phosphatase can be found in the National Health and Nutrition Examination Survey: Laboratory Procedure Manual at <http://www.cdc.gov/nchs/nhanes/>.

Measurement of grip strength

The grip strength data was collected using the Takei Digital Grip Strength Dynamometer (Model T.K.K.5401). A proficient examiner elaborated and demonstrated the protocol to the participant. Subsequently, the examiner adjusted the grip size of the dynamometer to match the participant's hand size and requested the participant to squeeze the dynamometer for a practice attempt. After the practice session, the participant was instructed to employ one of their hands to squeeze the dynamometer with maximal force. Subsequently, the test was repeated for the opposite hand, with each hand undergoing three trials. Detailed guidelines for implementation are outlined in the NHANES Muscle Strength Procedures Manual. The total grip strength was calculated as the sum of the maximum readings from each hand and expressed in kilograms.

Covariates

As stated on the NHANES website, qualified personnel at all study sites adhered to standardized protocols for data collection. During household interviews, information regarding sociodemographic factors such as age, gender, and race/ethnicity was gathered. Based on prior literature, the following variables were selected as covariates. The demographic variables encompassed gender (male or female), age groups (40–59 years, ≥ 60 years), race (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Asian, Other Race), education level (less than high school, high school or equivalent, college or above), marital status (married/

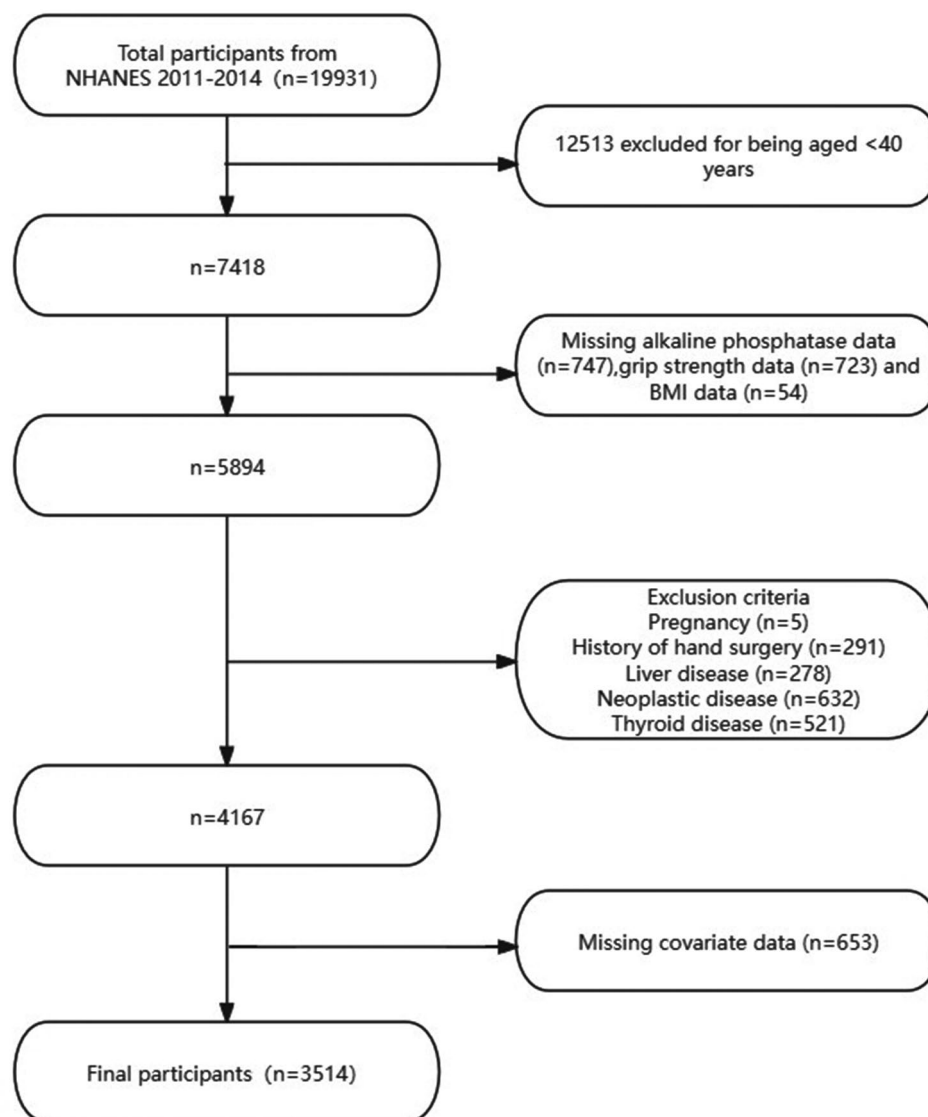


Fig. 1 Flowchart of the study participants included in NHANES 2011–2014

living with partner, widowed/divorced/separated/never-married), with ratio of family income to poverty (FIPR) categorized as <1.3, 1.3–3.5, > 3.5 [11]. We also incorporated smoking status, drinking status, and physical activity as lifestyle variables. Individuals who had smoked more than 100 cigarettes over their lifetime were categorized as smokers, and those who had not were designated as non-smokers [12]. Drinking status was categorized as “drinker” if the participant reported having more than 12 alcoholic beverages in the past year and “nondrinker” otherwise [13]. Physical activity was divided into work activities and recreational activities in accordance with the survey collection, with three levels: vigorous, moderate, and none [14]. We further included hypertension, diabetes, and high cholesterol status as risk variables. The determination of high blood pressure and high

cholesterol status was based on the NHANES questionnaire data. Diabetes was defined as having a history of diabetes, a fasting blood glucose level ≥ 7.0 mmol/L, or a glycosylated hemoglobin (HbA1c) > 6.5%. In addition, this study also considered body mass index (BMI) to correct for grip strength.

Statistical analysis

The statistical analyses were conducted using R 3.4.3 (<https://www.r-project.org/>) and EmpowerStats 2.0 (<http://www.empowerstats.com>), $P < 0.05$ was considered statistically significant. Continuous variables encompassed in this study were delineated as means along with standard errors, whilst categorical variables were depicted by the actual number in conjunction with weighted percentages. The NHANES sample weights

Table 1 Characteristics of participants enrolled in study (*n* = 3514)

Variables	Mean (SD) or <i>N</i> (%)
Gender, <i>n</i> (%)	
Male	1891 (53.813)
Female	1623 (46.187)
Age group, <i>n</i> (%)	
40–59 years	2058 (58.566)
≥ 60 years	1456 (41.434)
Race ethnicity, <i>n</i> (%)	
Mexican American	396 (11.269)
Other Hispanic	341 (9.704)
Non-Hispanic White	1384 (39.385)
Non-Hispanic Black	905 (25.754)
Other Race	488 (13.887)
Education level, <i>n</i> (%)	
Less than high school	810 (23.051)
High school or equivalent	808 (22.994)
College or above	1896 (53.956)
Marriage status, <i>n</i> (%)	
Married/living with partner	2183 (62.123)
Widowed/divorced/separated/ never married	1331 (37.887)
PIRR, <i>n</i> (%)	
<1.3	1042 (29.653)
1.3–3.5	1233 (35.088)
> 3.5	1239 (35.259)
Smoking status, <i>n</i> (%)	
Smoker	1633 (46.471)
Non-smoker	1364 (53.529)
Drinking status, <i>n</i> (%)	
Drinker	2582(73.478)
Non-drinker	932 (26.522)
Work activity status, <i>n</i> (%)	
Vigorous	592 (16.847)
Moderate	665 (18.924)
None	2257 (64.229)
Recreational activity status, <i>n</i> (%)	
Vigorous	606 (17.814)
Moderate	1033 (29.397)
None	1855 (52.789)
Hypertension, <i>n</i> (%)	
Yes	1536 (43.711)
No	1978 (56.289)
High cholesterol status, <i>n</i> (%)	
Yes	1537 (43.739)
No	1977 (56.261)
Diabetes, <i>n</i> (%)	
Yes	738 (21.002)
No	2776 (78.998)
BMI	29.299 ± 6.749
Serum alkaline phosphatase, (IU/L, mean ± SD)	68.391 ± 22.008
Comprehensive grip strength (Kg, mean ± SD)	70.479 ± 21.207

Continuous Variables: Presented as means with standard errors (SE), **Categorical Variables:** Displayed as counts (*n*) and percentages (%). FIPR family income to poverty ratio, BMI body mass index

Table 2 Relationship between concentrations of serum alkaline phosphatase and grip strength in all participants

	Model A β (95% CI) <i>P</i> value	Model B β (95% CI) <i>P</i> value	Model C β (95% CI) <i>P</i> value
Alkaline phosphatase (IU/L)	-0.11 (-0.149, -0.080) < 0.001	-0.053(-0.073, -0.032) < 0.001	-0.049(-0.069, -0.029) < 0.001
Model A was not adjusted			
Model B was adjusted for BMI, gender, age, race, education level, marital status, and PIRR			
Model C was adjusted for BMI, gender, age, race, education level, marital status, and PIRR, smoking status, drinking status, work activity status, recreational activity status, and hypertension, high cholesterol status, diabetes			

were used as recommended by the NCHS. Generalized weighted linear Model was performed to investigate the association between serum alkaline phosphatase and grip strength. Subgroup analyses stratified by age group, gender, and race were also performed. In addition, smooth curve fitting were used to explore nonlinear relationships, and in the presence of nonlinearity, a two-segment linear regression model was used to determine the inflection point.

Results

Characteristics of the study population

Detailed baseline characteristics of the participants are summarized in Table 1. A total of 3514 participants were involved, encompassing 1891 males (53.813%) and 1623 females (46.187%), with a larger proportion being within the 40–59 years age group (58.566%). The majority of participants had a college education or higher (53.956%), with a predominant representation of non-Hispanic White individuals (39.385%). The average level of grip strength was 70.479 ± 21.207 Kg. The mean concentration of serum ALP was 68.391 ± 22.008 IU/L.

Relationship between serum ALP and grip strength

Table 2 presents the association between serum ALP and grip strength in three multivariate linear regression models, we reveal the negative correlation between serum ALP and grip strength in Model A (β = -0.115, 95% CI -0.149, -0.080, *P* < 0.001). This inverse relationship remained evident in Model B (β = -0.053, 95% CI -0.073, -0.032, *P* < 0.001) and Model C (β = -0.049, 95% CI -0.069, -0.029, *P* < 0.001).

In subgroup analysis stratified by gender, the association between serum ALP and grip strength remained significant in both male and female. In subgroup analysis stratified by age group, the association between serum ALP and grip strength remained significant in 40–59 years old. Among participants aged ≥ 60 years, the association between serum ALP and grip strength remained significant in model A and model B, but not among Model C (β = -0.024, 95% CI -0.057, -0.009, *P* = 0.155).

In subgroup analysis stratified by race, the association between serum ALP and grip strength remained significant among Non-Hispanic White (Model C: $\beta = -0.058$, 95% CI -0.091, -0.024, $P < 0.001$) and Non-Hispanic Black (Model C: $\beta = -0.058$, 95% CI -0.097, -0.020, $P = 0.003$), but not among Mexican American, Other Hispanic and Other Race. (Table 3)

Further analysis found that serum ALP and grip strength were significantly negatively correlated in male (40–59 years) ($\beta = -0.078$, 95% CI -0.125, -0.032, $P = 0.001$) and female (40–59 years) ($\beta = -0.080$, 95% CI -0.108, -0.052, $P < 0.001$), there was no correlation between serum ALP and handgrip strength in participants aged ≥ 60 years, regardless of gender. (Table 4)

Nonlinear relationship between serum ALP and grip strength

Smooth curve fitting revealed relationship between serum ALP and grip strength in all participants (Fig. 2), Fig. 3 revealed relationship between serum ALP and grip strength by gender and age group. Further analysis revealed a nonlinear relationship between serum ALP and grip strength in both male (40–59 years) and female (≥ 60 years) (Fig. 4). In male (40–59 years) participants, when serum ALP was < 54 IU, each unit increase in serum ALP was associated with a 0.498 unit decrease in grip strength. When serum ALP > 54 IU, there was no significant association with grip strength (Fig. 4a; Table 5). In male (40–59 years) participants, when serum ALP was < 97 IU, there was no significant association with grip strength. When serum ALP > 97 IU, each unit increase in serum ALP was associated with a 0.211 unit decrease in grip strength (Fig. 4a; Table 6). Figure 4b revealed relationship between serum ALP and grip strength in Female (40–59 years) and Female (≥ 60 years). Figure 5 revealed relationship between serum ALP and grip strength by race.

Discussion

The association between serum ALP and grip strength has thus far been inadequately explored. Our results showed that serum ALP were negatively associated with grip strength in both male and female after adjusting for potential confounding variables. Comparable to our findings, A cross-sectional study in South Korea showed that both male and female serum ALP were positively correlated with low skeletal muscle mass index (LSMI). To the best of our knowledge, this study represents the first exploration of the complex connections between serum ALP and grip strength among middle-aged and elderly people.

Muscle health holds a crucial position in physical function and metabolism [15]. Muscle function constitutes an important indicator for predicting the outcome of sarcopenia [16]. Besides primary aging, other secondary

Table 3 Stratified analysis of the correlation between serum alkaline phosphatase and grip strength

	Model A β (95% CI) <i>P</i> value	Model B β (95% CI) <i>P</i> value	Model C β (95% CI) <i>P</i> value
Subgroup analysis stratified by gender			
Male	-0.106 (-0.144, -0.068) < 0.001	-0.070 (-0.103, -0.036) < 0.001	-0.058 (-0.091, -0.024) < 0.001
Female	-0.071 (-0.095, -0.046) < 0.001	-0.034 (-0.055, -0.012) 0.002	-0.034 (-0.055, -0.013) 0.002
Subgroup analysis stratified by age group			
40–59 years	-0.103 (-0.148, -0.059) < 0.001	-0.094 (-0.122, -0.067) < 0.001	-0.089 (-0.117, -0.062) < 0.001
≥ 60 years	-0.115 (-0.165, -0.065) < 0.001	-0.034 (-0.067, -0.001) 0.041	-0.024 (-0.057, -0.009) 0.155
Subgroup analysis stratified by race			
Mexican American	-0.072 (-0.163, 0.020) 0.125	-0.048 (-0.104, 0.007) 0.090	-0.039 (-0.095, 0.017) 0.174
Other Hispanic	-0.148 (-0.252, -0.044) 0.005	-0.034 (-0.097, 0.028) 0.285	-0.028 (-0.090, 0.034) 0.378
Non-Hispanic White	-0.127 (-0.186, -0.067) < 0.001	-0.059 (-0.092, -0.026) < 0.001	-0.058 (-0.091, -0.024) < 0.001
Non-Hispanic Black	-0.121 (-0.182, -0.061) < 0.001	-0.061 (-0.100, -0.022) 0.002	-0.058 (-0.097, -0.020) 0.003
Other Race	0.025 (-0.062, 0.112) 0.570	-0.003 (-0.054, 0.048) 0.916	-0.003 (-0.048, 0.054) 0.911

Model A was not adjusted

Model B was adjusted for BMI, gender, age, race, education level, marital status, and PIRR

Model C was adjusted for BMI, gender, age, race, education level, marital status, and PIRR, smoking status, drinking status, work activity status, recreational activity status, and hypertension, high cholesterol status, diabetes

In the subgroup analysis stratified by gender, age group and race, the model was not adjusted for gender, age or race

Table 4 Stratified examination of the relationship between serum alkaline phosphatase and grip strength based on gender (age group)

Subgroup	β (95% CI)	<i>P</i> value
Male (40–59 years)	-0.078 (-0.125, -0.031)	0.001
Male (≥ 60 years)	-0.036 (-0.088, 0.016)	0.173
Female (40–59 years)	-0.080 (-0.108, -0.052)	< 0.001
Female (≥ 60 years)	0.013 (-0.024, 0.050)	0.485

BMI, race, education level, marital status, and PIRR, smoking status, drinking status, work activity status, recreational activity status, and hypertension, high cholesterol status, diabetes were adjusted

causes like malnutrition, endocrine disorders, inflammation, etc., may contribute to the acceleration of muscle loss, ultimately resulting in a decrease in muscle strength [17]. Sarcopenia is common among the elderly but can also be witnessed in middle-aged people [18]. Paying attention to skeletal muscle health in middle-aged people

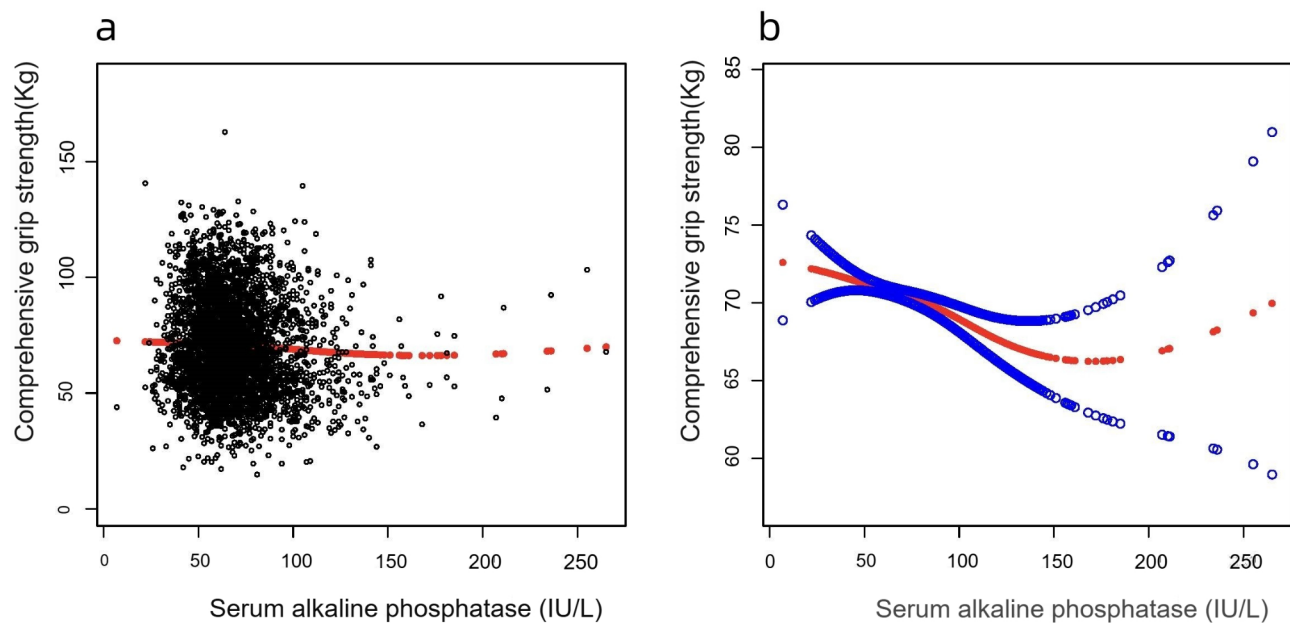


Fig. 2 The association between serum alkaline phosphatase and grip strength. **(a)** Each black dot signifies an individual sample. **(b)** The solid red line illustrates the smoothed fitting curve among the variables, while the blue band represents the 95% confidence interval associated with the fit. (BMI, gender, age, race, education level, marital status, and PIRR, smoking status, drinking status, work activity status, recreational activity status, and hypertension, high cholesterol, diabetes were adjusted)

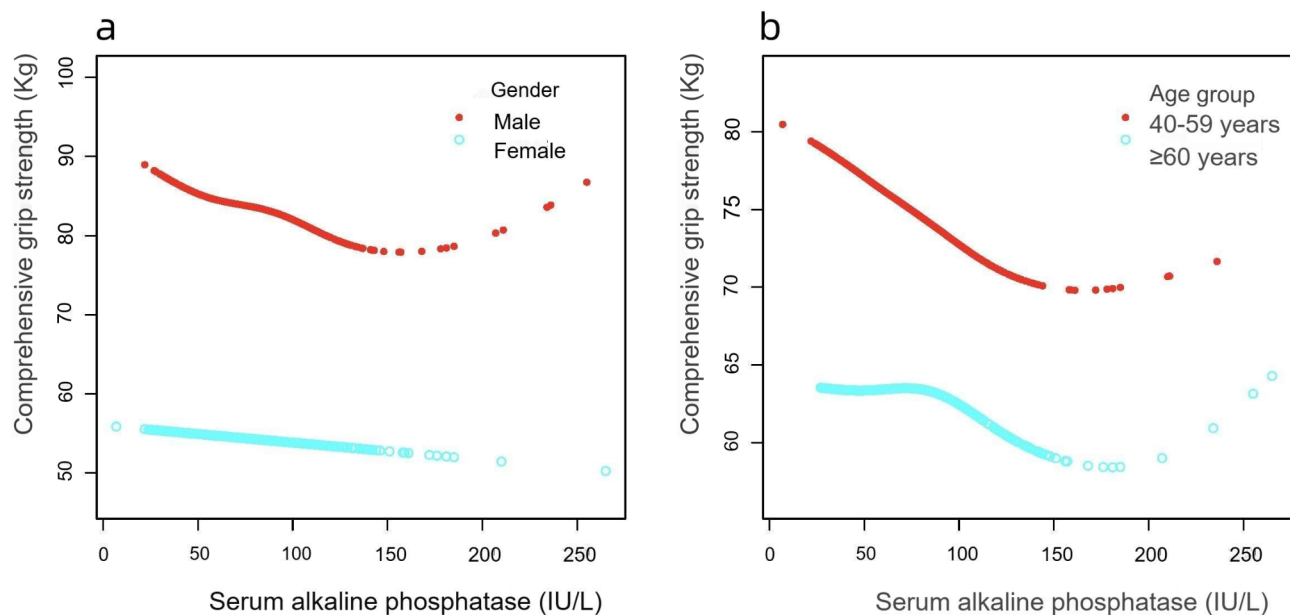


Fig. 3 **(a)** The association between serum alkaline phosphatase and grip strength by gender. **(b)** The association between serum alkaline phosphatase and grip strength by BMI, gender, age, race, education level, marital status, and PIRR, smoking status, drinking status, work activity status, recreational activity status, and hypertension, high cholesterol status, diabetes were adjusted were adjusted. In the subgroup analysis stratified by gender and age group, the model was not adjusted for gender or age

is of critical importance for preventing sarcopenia in the elderly. Serum ALP is a ubiquitous membrane-bound glycoprotein present in nearly all tissues of the body [19], notably elevated levels are found in the liver, kidneys, bile ducts, bones [7]. It has been demonstrated that

increased plasma levels of serum ALP have been associated with a worse prognosis in several types of diseases [20], such as renal osteodystrophy [7] and stroke [21]. In humans, four distinct isoenzymes of alkaline phosphatase are expressed: tissue-nonspecific ALP, intestinal

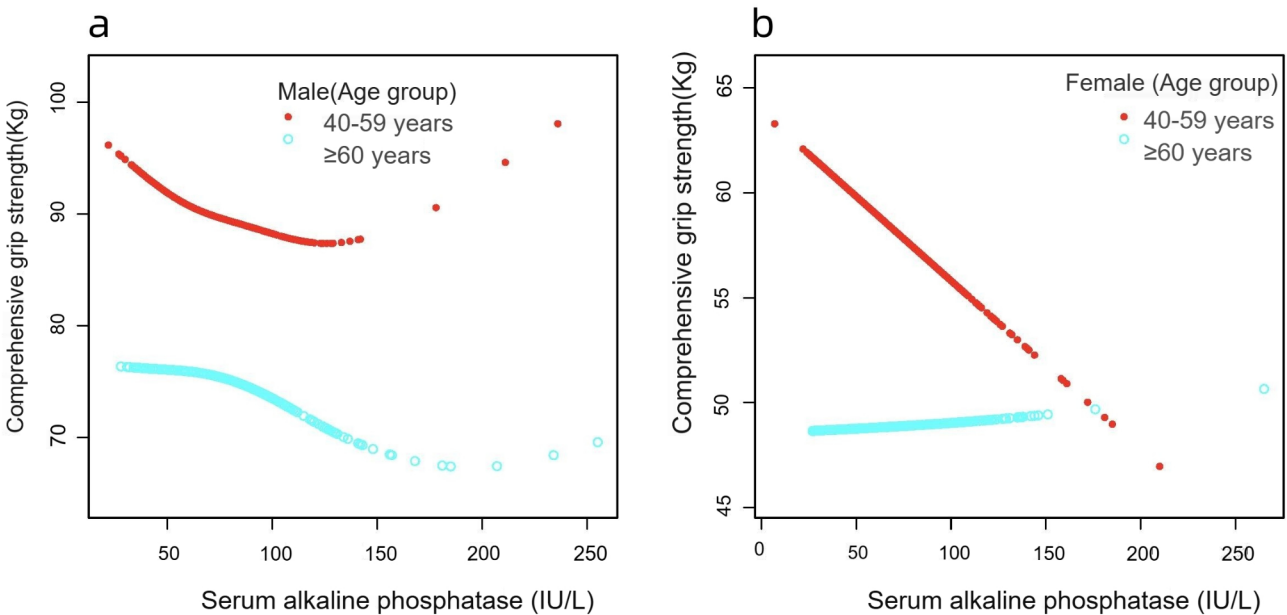


Fig. 4 The association between serum alkaline phosphatase and grip strength by gender (age group). **(a).**Male **(b)** Female BMI, race, education level, marital status, and PIRR, smoking status, drinking status, work activity status, recreational activity status, and hypertension, high cholesterol status, diabetes were adjusted were adjusted

Table 5 Saturation effect analysis of serum alkaline phosphatase on combined grip strength in male (40–59 years) using the two-piecewise linear regression model

Male(40-59y)	Combined grip strength/weight Adjusted β (95% CI) P value
Turing points(K)	54
< K effect	-0.498 (-0.691, -0.304) < 0.001
> K effect	-0.007 (-0.063, 0.049) 0.799
likelihood-ratio test	< 0.001

BMI, race, education level, marital status, and PIRR, smoking status, drinking status, work activity status, recreational activity status, and hypertension, high cholesterol status, diabetes were adjusted

Table 6 Threshold effect analysis of serum alkaline phosphatase on combined grip strength in male (≥ 60 years) using the two-piecewise linear regression model

Male(40-59y)	Combined grip strength/weight Adjusted β (95% CI) P value
Turing points(K)	97
< K effect	0.020 (-0.046, 0.086) 0.548
> K effect	-0.211 (-0.350, -0.072) 0.003
likelihood-ratio test	0.007

BMI, race, education level, marital status, and PIRR, smoking status, drinking status, work activity status, recreational activity status, and hypertension, high cholesterol status, diabetes were adjusted

ALP, placental ALP, and germ cell ALP [7]. ALP plays a significant role in muscle metabolism. Tissue-nonspecific alkaline phosphatase (TNALP) is the predominant isoenzyme of alkaline phosphatase in the human body. Basic research has discovered that TNAP deficiency can alter mitochondrial activity, reduce muscle strength, and hamper bone mineralization and trabecular formation of

bone marrow stromal cells [9]. Simultaneously, increased basal mitochondrial respiration might induce chronic oxidative stress, leading to superoxide production and inducing muscle pathology [22]. Moreover, Clinical research indicates that in patients undergoing hemodialysis, there is an inverse relationship between the levels of ALP and their muscle mass, strength, and overall physical function [23].

A substantial cohort study identified a significant association between elevated serum total ALP levels and the incidence of hip fractures [8]. A single-center cohort study demonstrated that elevated serum bone-specific ALP levels were correlated with fracture risk, and hemodialyzed patients with increased b-AP had an elevated fracture risk [24]. The study by Xiao Song Cheng et al. revealed that serum ALP levels in young and middle-aged individuals were negatively correlated with pelvic bone density [25]. In states of diminished bone density, osteoblasts are activated and produce a substantial quantity of bone alkaline phosphatase, thereby resulting in a significant increase in serum ALP levels [26]. Lower bone density might indirectly impact muscle function, leading to a reduction in muscle strength. The effect of ALP on bone and mineral homeostasis is a double-edged sword. ALP can enhance bone mineralization, but it may also induce vascular calcification [27], which may have a negative influence on skeletal muscle health [28]. The specific mechanisms underlying this relationship call for further meticulous and profound exploration.

ALP levels are intimately related to nutritional status and chronic inflammation. Seok Hui Kang et al.

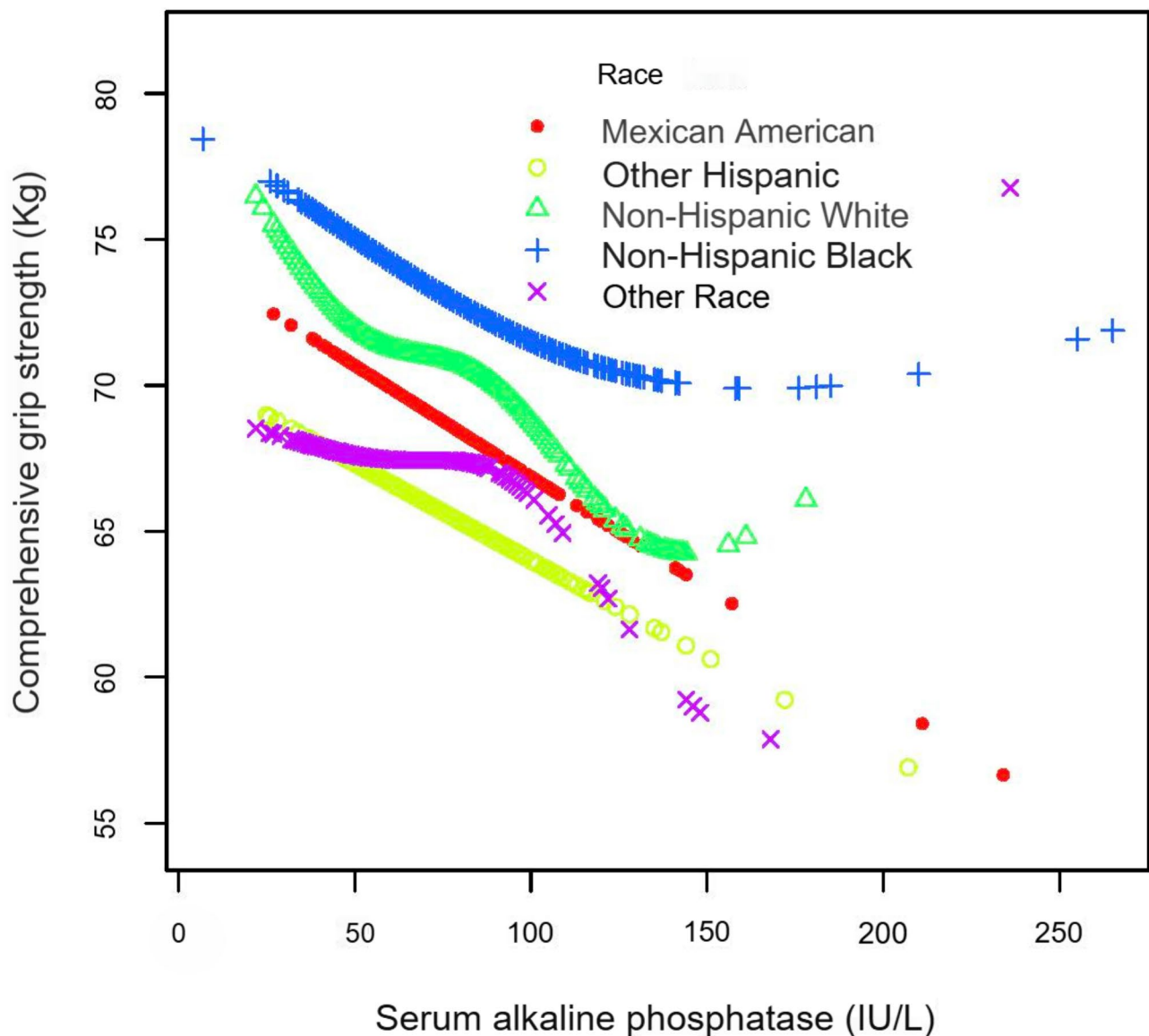


Fig. 5 The association between serum alkaline phosphatase and grip strength by BMI, gender, age, education level, marital status, and PIRR, smoking status, drinking status, work activity status, recreational activity status, and hypertension, high cholesterol status, diabetes were adjusted were adjusted

discovered a negative correlation between ALP levels and PhA [23]. The phase angle (PhA), a well-acknowledged nutritional indicator associated with healthy cell membranes, exhibits excellent accuracy in reflecting muscle mass and can also be employed as a facile indicator for gauging muscle mass [29]. Kim et al. found that ALP is closely associated with metabolic or nutritional disorders, and serum ALP levels showed a positive correlation with body fat mass among the general population in Korea [30]. Fermín Sánchez de Medina et al. suggested that ALP seems to be related to the inflammatory process and its regulation [31]. The activity of ALP is influenced by oxidative stress in both in vitro and in vivo conditions [32]. ALP can be utilized as a comprehensive marker of

nutritional status and inflammation [33]. Elevated serum total ALP levels correlate with higher serum C-reactive protein (CRP) levels and increased mortality in the general population [34]. Experimental studies have shown that inflammatory cytokines can activate numerous molecular pathways associated with skeletal muscle atrophy, resulting in muscle atrophy [35]. Additional studies are essential to explore the adverse effects of this process on muscle function.

Moreover, such association was influenced by gender, age, and ethnicity. When stratified by race, the association remained significant among non-Hispanic whites and non-Hispanic blacks, but not among Mexican American, Other Hispanic and Other Race, which may

be related to potential confounding factors. When stratified by age group, the association remained significant for participants aged 40–59 years, but not in participants aged ≥ 60 years. It is worth noting that further analysis showed that serum ALP was significantly negatively correlated with grip strength in women aged 40–59 years, but not in women aged ≥ 60 years, which may be related to the increase in serum alkaline phosphatase in elderly women after menopause. Bashu Dev Pardhe et al. found that compared with premenopausal women, estradiol levels in postmenopausal women decreased significantly, while alkaline phosphatase (ALP) levels increased significantly [36]. Estrogen is conducive to maintaining the dynamic balance of bone resorption and bone formation [37]. Serum alkaline phosphatase (ALP) is a biochemical indicator reflecting bone formation [38]. The increase in serum alkaline phosphatase after menopause may be due to the increase in compensatory bone formation caused by the hyperresorption of bone [39–40]. Although ALP is a well-established marker of bone diseases, but it is not specific only for bone. Increased levels of hepatic alkaline phosphatase in elderly men and increased levels of bone alkaline phosphatase in postmenopausal women [41]. Serum ALP level was positively and independently associated with metabolic syndrome (MetS), suggesting that serum ALP level may be a useful additional measure in assessment of MetS [42]. Zhang L et al. found that the liver enzyme levels of patients with metabolic syndrome were much higher than those in healthy people, and ALP levels were significantly associated with the risk of MetS [43].

A large-scale population-based study showed that Muscle strength is inversely associated with MetS and its separate components [44]. In addition, ALT levels within the normal range are associated with metabolic syndrome and its components, liver enzyme levels may change when early metabolic disorders occur without deviating from the normal range [45]. The above factors may be related to the nonlinear relationship between serum ALP and grip strength in male over 60 years old. The specific mechanisms of these relationships need further detailed and in-depth exploration.

Limitation

There were some limitations in our study. Firstly, due to the cross-sectional nature of this study, no causal relationship between serum ALP and grip strength could be concluded. Secondly, data on muscle mass were not available in this study, so the relationships between muscle mass and serum ALP could not be investigated. Finally, Although many covariates were controlled in the analysis, the presence of some other potential confounders may still bias the results. Therefore, more research and exploration in this field are still needed.

Conclusions

The present study revealed an inverse relationship between serum ALP and grip strength in middle-aged and elderly people, especially in female, male aged 40–59 years, Non-Hispanic White and Non-Hispanic Black. This discovery provides new clues and orientations for the mechanism of the influence of serum ALP on skeletal muscle health.

Abbreviations

ALP	Alkaline Phosphatase
FIPR	Family income to poverty ratio
BMI	Body mass index
PhA	Phase Angle
TNALP	Tissue-nonspecific alkaline phosphatase
LSMI	Low skeletal muscle mass index
NHANES	National Health and Nutrition Examination Survey
MetS	Metabolic syndrome

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Author contributions

ZYZ, JJZ, contributed to the study design and writing of the manuscript. APM, HGC, BW and contributed to data collection, analysis, and writing of the manuscript. G.Y.Z. project administration, supervision. All authors read and approved the final manuscript.

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Data availability

The datasets generated and/or analysed during the current study are available in the Health and Nutrition Examination Survey (NHANES) during 2013–2014, at <http://www.cdc.gov/nchs/nhanes/>.

Declarations

Ethics approval and consent to participate

The ethics review board of the National Center for Health Statistics approved all NHANES protocols, and each participant signed written informed consent.

Consent for publication

Not applicable.

Clinical trial number

Not applicable.

Competing interests

The authors declare no competing interests.

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