Lipids in Health and Disease

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Association between atherogenic index of plasma and infertility: a cross-sectional study based on U.S. women

Zihong Bao[1†], Yanmei Zhang[1†], Ju Zhou[1†] and Zhikun Dai[2*]

Abstract

Background A wealth of evidence indicates that dyslipidemia is associated with endothelial dysfunction, oxidative stress, and inflammation, each of which can impair reproductive function and lead to infertility. The Atherogenic Index of Plasma (AIP) is an innovative lipid biomarker that combines the triglyceride to high-density lipoprotein cholesterol (HDL-C) ratio, providing a more in-depth evaluation of lipid metabolism. This biomarker synthesizes discrete lipid disruptions into a single value, surpassing isolated lipid indicators' diagnostic value. The primary goal of our study was to explore the link between AIP and the incidence of infertility.

Methods Data from the National Health and Nutrition Examination Survey (NHANES) spanning 2013–2018 were subjected to cross-sectional examination. The AIP is determined through the logarithmic transformation (base 10) of the triglyceride-to-HDL-C ratio. To uncover the connection between AIP and infertility, a suite of analytical techniques was employed, encompassing weighted multiple logistic regression, stratified analyses, spline curve modeling, and determination of cutoff values.

Results Among the 1,191 participants, with a weighted mean age of 31.89 years, 12.09% were diagnosed as infertile. The multivariate-adjusted odds ratios for infertility occurrence across the AIP quartiles were 1.00 (reference), 1.96 (95% CI: 1.10–3.49), 2.62 (95% CI: 1.48–4.63), and 2.38 (95% CI: 1.31–4.32), respectively. Subgroup examinations suggest that the association between AIP and infertility remains robust and is not substantially altered by factors including age, marital status, economic status, tobacco use, alcohol intake, and body mass index. Curve fitting and threshold analyses have indicated a positive nonlinear relationship between AIP and infertility, as well as a relatively stable incidence of infertility within the AIP range from -0.21 to 0.22.

Conclusions Incorporating an assessment of AIP into the clinical evaluation could potentially refine the accuracy of risk estimation for infertility patients.

Keywords Atherogenic index of plasma, Infertility, Reproduction, NHANES, Cross-sectional study

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Introduction

Dyslipidemia, featuring lipid abnormalities like increased total cholesterol, low-density lipoprotein cholesterol (LDL-C), or triglycerides (TG), and reduced high-density lipoprotein cholesterol (HDL-C) levels, constitutes a substantial risk element for the development of ischemic heart disease [1]. Emerging research indicates that dyslipidemia plays a role in the development and worsening of diverse conditions, including cardiovascular disorders, metabolic syndrome, non-alcoholic steatohepatitis, diabetes mellitus, and chronic renal disease [2–4]. Nevertheless, the widespread use of individual lipid parameters in clinical settings has limited predictive value. To rectify this gap, Dobiasova and Frohlich proposed the atherogenic index of plasma (AIP) as a measure in the year 2001. The AIP signifies a pioneering development in the evaluation of cardiovascular risk potential, offering a unique and integrative approach that surpasses the limitations of traditional lipid markers. Unlike the conventional markers, AIP provides a comprehensive evaluation of the lipid metabolic state by considering the ratio of triglycerides to HDL-C. This innovative biomarker encapsulates the dynamic balance among different lipid components, providing a more refined insight into atherogenic risk and metabolic well-being [5]. The AIP has emerged as a pivotal element in the development of multiple conditions, including cardiovascular disorders, metabolic syndrome, chronic renal impairment, diabetes mellitus, metabolic-related non-alcoholic fatty liver disease, periodontal disease, obstructive sleep apnea, and male sexual dysfunction.

Infertility is characterized by the inability of a pair to achieve pregnancy following a year of consistent, unprotected sexual activity [6]. In the United States, a considerable 15.5% of women within the childbearing age bracket are affected by infertility, and this is increasing, with an annual rise of 0.37% [7]. This reproductive health challenge can result in a range of adverse outcomes, including psychological stress, social stigmatization, financial burden, and marital discord [8, 9]. Thus, identifying risk factors and developing effective prevention strategies are crucial, and the Centers for Disease Control and Prevention (CDC) has prioritized diagnosing and treating infertility as a major public health concern [10].

Epidemiological research has demonstrated that infertility arises from multiple factors, including obesity, alcohol consumption, smoking, educational attainment, and vascular health, all of which are associated with female infertility [11–14]. Additionally, research has identified a significant correlation between abnormal blood lipid levels (such as HDL-C, LDL-C, TC, and TG) are closely related to decreased female fertility [15, 16]. Nevertheless, traditional methodologies employing single-center, small-sample studies, and individual lipid parameters to assess the interrelationship among lipid levels, vascular health, and female infertility remain contentious and possess limited predictive efficacy. The advent of the AIP introduces a paradigm shift in how we assess the relationship between lipid profiles and reproductive health offering a novel and integrative biomarker that surpasses the limitations of conventional lipid measurements.

The aim of this research was to explore the link between AIP and female infertility via a cross-sectional analysis of the National Health and Nutrition Examination Survey (NHANES) dataset and to assess the clinical relevance of AIP as a probable biomarker for infertility in women.

Materials and methods

Data source

Conducted by the National Center for Health Statistics (NCHS), the National Health and Nutrition Examination Survey (NHANES) offers a comprehensive, multitiered assessment of the health and dietary status of a diverse, nationally representative cohort in the United States. The methodologies and protocols employed in the NHANES were meticulously examined and endorsed by the NCHS's Ethical Review Board for Research, ensuring all procedures were conducted ethically, with each participant granting written informed consent. Adherence to augmented reporting standards was maintained throughout the study's execution. In compliance with the CDC's directives, the statistical assessments were carried out utilizing the proper NHANES survey weights, carefully accounting for the complex nature of multistage cluster sampling designs in the analysis. Additional comprehensive details are available for reference at the following webpage: http://www.cdc.gov/nchs/nhanes/irba98.htm.

Study design and population

This study utilized NHANES data from the 2013–2018 cycles to identify participants. The study excluded participants based on several criteria: being younger than 20 or older than 44 years, a surgical history of hysterectomy or oophorectomy, absence of infertility data, missing records on AIP, and incomplete information on specific confounding factors. Following the implementation of these exclusionary standards, the analytical dataset comprised 1,191 subjects, as detailed in Fig. 1.

Definition of atherogenic index of plasma

The AIP is derived from the logarithmic transformation of the ratio of fasting triglycerides to high-density lipoprotein cholesterol, employing the formula AIP = lg (TG / HDL-C) for its calculation [17]. In adherence to a standardized methodology established by the CDC,

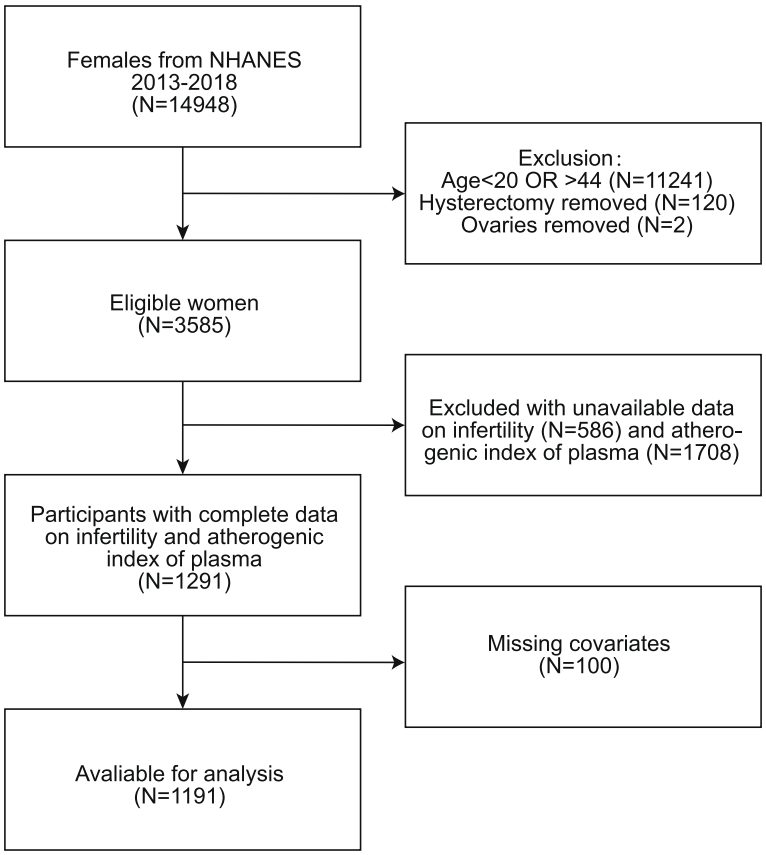

Fig. 1 Flow diagram of the screening and enrollment of study participants

serum HDL-C concentrations were determined via direct immunoassay or precipitation techniques. For the measurement of TG, fasting venous blood samples were obtained from all subjects [18]. Quartiles are commonly used in statistical analysis to divide a dataset into four equal parts, each representing a quarter of the data. In our study, we utilized AIP quartiles to categorize participants into groups with progressively higher AIP values. By examining the prevalence of infertility across these quartiles, we can assess whether there is a gradient of risk associated with increasing AIP levels. The AIP quartiles enable the identification of high-risk subgroups for infertility, guiding the need for targeted interventions and patient risk communication. Those in the highest quartile may benefit from closer monitoring, while lower quartile individuals may require less intensive assessment.

Definition of infertility

Infertility, serving as the key outcome variable, was established from self-declared answers recorded through the Computer Assisted Personal Interview (CAPI) system during sessions at the Mobile Examination Center (MEC) [19]. Participants were deemed to have infertility if they confirmed a year-long effort to conceive without success, as indicated by a favorable outcome to the question "Have you been trying to get pregnant for one year?" Conversely, those who did not report such difficulties were categorized as not infertile.

Covariates

Building upon prior research and clinical insights [20, 21], a comprehensive list of covariates was identified, encompassing age, racial/ethnic background, level of education, marital circumstances, poverty-income ratio (PIR), tobacco use, alcohol intake, physical exercise frequency, total cholesterol levels, menstrual history, history of pelvic inflammatory disease treatment, and the utilization of hormonal pharmaceuticals. The investigative team considered these variables as potential confounders and integrated them into the analytical model to control for their possible influence regarding the relationship between AIP indicators and infertility outcomes. Age was assessed starting from birth up to the baseline period and was divided into two distinct categories: individuals aged 20–30 years and those aged 31–44 years. Data on race/ethnicity were gathered based on self-identification and

classified into five distinct categories: Mexican American, non-Hispanic Black, non-Hispanic White, Other Hispanic, and a Miscellaneous category that included participants of mixed racial backgrounds. Educational qualifications were sorted into three distinct brackets: those with less than a high school diploma, those who have completed high school or obtained an equivalent credential, and those who have pursued education further than high school. Marital status was segmented into three distinct groups: married, never married, and other (encompassing those who are widowed, divorced, or separated). PIR values were categorized into three distinct intervals: below 1.5, ranging from 1.5 to 3.5, and above 3.5, where a higher figure reflects a greater per capita household income. The smoking variable was used to determine if a person had consumed at least 100 cigarettes throughout their life and was classified into two groups: yes (for those who had) and no (for those who had not). The classification of drinkers was based on the consumption of 4 to 5 or more alcoholic beverages per day within the preceding 12-month period. The level of physical activity was evaluated by considering the duration of engagement in moderate-intensity sports, exercise, or leisure pursuits within a standard day, as reported by the participant or study subject.

Statistical analysis

All statistical evaluations were performed with the application of sample weights, stratification, and clustering methodologies to accommodate the intricacies of the survey design, in adherence with NHANES recommendations for employing a weighted approach to mitigate substantial variability within the dataset and to align with the study's complex sampling methodology. The study population's fundamental characteristics were analyzed and presented statistically according to their infertility status. For continuous variables that follow a normal distribution, the data are expressed through means and standard deviations (SD), while categorical variables are depicted by frequency counts and their respective percentage values (%). Categorical variables underwent Chi-square testing, which was modified with Rao and Scott's second-order adjustments; for continuous variables that deviated from a normal distribution, the Wilcoxon rank-sum test was utilized, whereas t-tests were conducted on variables exhibiting a normal distribution pattern.

The investigation employed multiple logistic regression techniques to examine the correlation between AIP and infertility outcomes. The findings derived from the logistic regression analysis are conveyed in terms of odds ratios (OR) along with their corresponding 95% confidence intervals (CI). The study comprised three distinct analytical frameworks: the first, referred to as Model 1, was a baseline unadjusted model; the second, designated as Model 2, factored in variables such as age, ethnicity, marital status, educational attainment, and Personal Income Ratio (PIR); and the third, known as Model 3, expanded upon Model 2 by incorporating additional adjustments for smoking habits, alcohol intake, physical exercise levels, total cholesterol levels, menstrual history, past treatment for pelvic inflammatory disease, and the usage of hormonal contraceptives. Furthermore, to investigate the possible interactions between AIP and infertility, separate subgroup analyses were conducted, each stratified by age, marital status, PIR level, smoking habits, alcohol consumption, and BMI. Additionally, smoothed curve fitting analysis was utilized to investigate potential non-linear associations between the exposure variables and the outcome variables. Threshold effect analysis was utilized to ascertain the presence of a critical value or potential inflection point for AIP, beyond which a marked change in the risk of female infertility occurs. The method typically involves modeling the outcome as a function of the exposure variable and testing for a change in the slope of the relationship at different points. If a significant change in the slope is detected, it suggests the presence of a threshold effect. This can be visualized graphically, with the threshold point identified as the point where the curve representing the association between the exposure and the result changes its direction or steepness.

Statistical computations were carried out utilizing R, version 4.2.0 (R Project for Statistical Computing), in conjunction with the survey package, version 4.11, and EmpowerStats software, version 4.1. Statistical significance was determined by a p-value of less than 0.05.

Results

Baseline characteristics of participants

The current study involved the recruitment of 1,191 female participants, selected according to rigorous inclusion and exclusion standards. On average, these participants were 31.89 ± 7.20 years of age. Among these participants, 12.09% were diagnosed with infertility. The average AIP level, with its standard deviation (SD), was measured at -0.22 (0.32).

Table 1 presents the adjusted baseline characteristics of the participants, stratified by their infertility condition. Significant differences were observed between infertile patients and those without infertility in terms of age, marital status, treatment for pelvic inflammatory disease, and AIP (all $p < 0.05$). The infertile group was more likely to include older women, married, had a history of treatment for pelvic inflammatory disease, and had higher AIP levels, in contrast to the group without infertility.

Table 1 Weighted baseline characteristics of the study population

Characteristics	Total $n=1191$	Non-infertility $n=1047$	Infertility $n=144$	*P* value
Age, mean (SD), year	31.89 (7.20)	31.63 (7.19)	33.79 (6.99)	< 0.001
Age, No. (%)				0.002
20–30	530 (44.50)	483 (46.13)	47 (32.64)	
31–44	661 (55.50)	564 (53.87)	97 (67.36)	
Race/ethnicity, No. (%)				0.913
Mexican American	199 (16.71)	174 (16.61)	25 (17.36)	
Non-Hispanic White	412 (34.59)	359 (34.29)	53 (36.81)	
Non-Hispanic Black	242 (20.32)	212 (20.25)	30 (20.83)	
Other Hispanic	117 (9.82)	105 (10.03)	12 (8.33)	
Other Race	221 (18.56)	197 (18.82)	24 (16.67)	
Marital status, No. (%)				< 0.001
Married	517 (43.41)	429 (40.97)	88 (61.11)	
Never married	377 (31.65)	354 (33.81)	23 (15.97)	
Other	297 (24.94)	264 (25.22)	33 (22.92)	
Education level, No. (%)				0.687
Less than high school	178 (14.95)	153 (14.61)	25 (17.36)	
High school or equivalent	230 (19.31)	203 (19.39)	27 (18.75)	
Above high school	783 (65.74)	691 (66.00)	92 (63.89)	
PIR, No. (%)				0.636
< 1.5	511 (19.75)	453 (43.27)	58 (40.28)	
1.5–3.5	381 (29.41)	330 (31.52)	51 (35.42)	
> 3.5	299 (50.84)	264 (25.21)	35 (24.30)	
Smoked at least 100, No. (%)				0.400
Yes	353 (29.64)	306 (29.23)	47 (32.64)	
No	838 (70.36)	741 (70.77)	97 (67.36)	
Alcohol use, No. (%)				0.052
Yes	79 (6.63)	64 (6.11)	15 (10.42)	
No	1112 (93.37)	983 (93.89)	129 (89.58)	
Physical activity, mean (SD), min	38.91 (31.78)	38.58 (30.42)	41.32 (40.39)	0.850
TC, mean (SD), mmol/L	4.61(0.97)	4.62 (0.98)	4.60 (0.92)	0.669
Regular menstruation, No. (%)				0.510
Yes	1115(93.62)	982 (93.79)	133 (92.36)	
No	76 (6.38)	65 (6.21)	11 (7.64)	
Treated for pelvic inflammatory disease, No. (%)				0.023
Yes	49 (4.11)	38 (3.63)	11 (7.64)	
No	1142 (95.89)	1009 (96.37)	133 (92.36)	
Used hormonal drugs, No. (%)				0.436
Yes	30 (2.52)	25 (2.39)	5 (3.47)	
No	1161 (97.48)	1022 (97.61)	139 (96.53)	
AIP, mean (SD)	-0.22 (0.32)	-0.23 (0.32)	-0.16 (0.31)	0.006
AIP quartile, No. (%)				0.017
Quartile1	297 (24.94)	276 (26.36)	21 (14.58)	
Quartile2	298 (25.02)	261 (24.93)	37 (25.69)	
Quartile3	297 (24.94)	253 (24.16)	44 (30.56)	
Quartile4	299 (25.10)	257 (24.55)	42 (29.17)	

All means and SD for continuous variables and percentages for categorical variables were weighted

Abbreviations AIP Atherogenic index of plasma, *PIR* Poverty income ratio, *SD* Standard deviation, *TC* Total Cholesterol

The association between atherogenic index of plasma and infertility

The findings from the multiple logistic regression analysis, which was adjusted for sample weights and aimed to explore the relationship between AIP and infertility, are represented in Table 2. In the fully adjusted model (model 3), a notable positive association was identified between AIP and infertility (OR = 2.44, 95% CI: 1.34–4.42), which persisted with consistency across different models. Sensitivity evaluations employing AIP quartile categorization were undertaken, and a pronounced positive association between AIP and infertility was noted across all three analytical models (p value < 0.05). Within the fully adjusted analytical framework, the likelihood of infertility increased by 96% in Q2, 162% in Q3, and 138% in Q4, relative to Q1, for every unit increase in AIP (p for trend < 0.05).

Subgroup analyses and additional analyses

Subsequent subgroup examinations suggested variability in the relationship between AIP and infertility, with the connection appearing to be incongruent across different groups, as depicted in Fig. 2. Subgroup investigations indicated that the association between AIP and infertility was most prominent among participants aged 21–30, of other marital statuses, with low PIR, without smoking or drinking habits, and with high BMI levels (p value < 0.05). No significant interactive effects were detected between AIP and the confounding variables (all p for interaction > 0.05).

The application of smooth curve fitting elucidated a nonlinear pattern in the association between AIP and infertility, as illustrated in Fig. 3. Furthermore, employing a two-segment linear regression model, we identified inflection points within the nonlinear relationship between AIP and infertility at -0.21 and 0.22, respectively (Table 3). When AIP values were below -0.21, the odds ratio for infertility was significantly elevated at 18.36 (95% CI: 3.95–85.24), indicating a substantial increase in risk. Conversely, within the range of -0.21 to 0.22, the odds ratio decreased to 0.54 (95% CI: 0.09–3.36), suggesting a relative stability or lower risk of infertility. However, for AIP values exceeding 0.22, the odds ratio increased to 11.82 (95% CI: 1.00–140.72), although this finding narrowly missed statistical significance ($p = 0.050$). This discrepancy could potentially be ascribed to the restricted sample size within the higher AIP range in the present study, which could have influenced the statistical power to detect a significant effect. These inflection points suggest that AIP levels around -0.21 and 0.22 may serve as critical thresholds, with values below -0.21 and above 0.22 potentially marking increased risk strata for infertility.

Discussion

In this comprehensive national investigation, we discovered a considerable positive relationship between AIP levels and the likelihood of infertility, with the effect remaining after adjusting for variables including age, marital status, PIR level, smoking behavior, alcohol use, and BMI. Notably, within the interval of -0.21 < AIP < 0.22, the incidence of infertility remained relatively stable. The results of our study point to AIP levels as a standalone predictive marker for the probability of infertility.

As far as we are aware, this is the initial probe into the correlation between AIP levels and the onset of infertility. Previous researches indicate that abnormal lipid levels and vascular health are critical determinants of adverse pregnancy outcomes [22]. Disturbances in lipid metabolism and atherosclerotic processes can damage the functionality of the ovaries, uterus, and placenta, contributing

Table 2 Association between AIP and Infertility

	Model 1		Model 2		Model 3	
	OR(95%CI)	***P* value**	**OR(95%CI)**	***P* value**	**OR(95%CI)**	***P* value**
AIP	2.03 (1.21–3.41)	0.007	2.03 (1.16–3.55)	0.013	2.44 (1.34–4.42)	0.003
AIP quartiles						
Quartile 1	Reference		Reference		Reference	
Quartile 2	1.86 (1.06–3.27)	0.030	1.84 (1.04, 3.26)	0.036	1.96 (1.10, 3.49)	0.022
Quartile 3	2.29 (1.32–3.95)	0.003	2.40 (1.36, 4.21)	0.002	2.62 (1.48, 4.63)	0.001
Quartile 4	2.15 (1.24–3.73)	0.007	2.14 (1.20, 3.82)	0.010	2.38 (1.31, 4.32)	0.004
P for trend	0.009		0.013		0.005	

Model 1 was the crude model without adjustment for covariates. Model 2 was adjusted for age, race, marital status, education level, PIR. Model 3 was adjusted as for model 2, additionally adjusted for smoking status, alcohol use, physical activity, total cholesterol, menstrual status, treatment of pelvic inflammatory disease, and use of hormonal medications

Abbreviations: *AIP* Atherogenic index of plasma, *OR* Odds ratio, *CI* Confidence interval

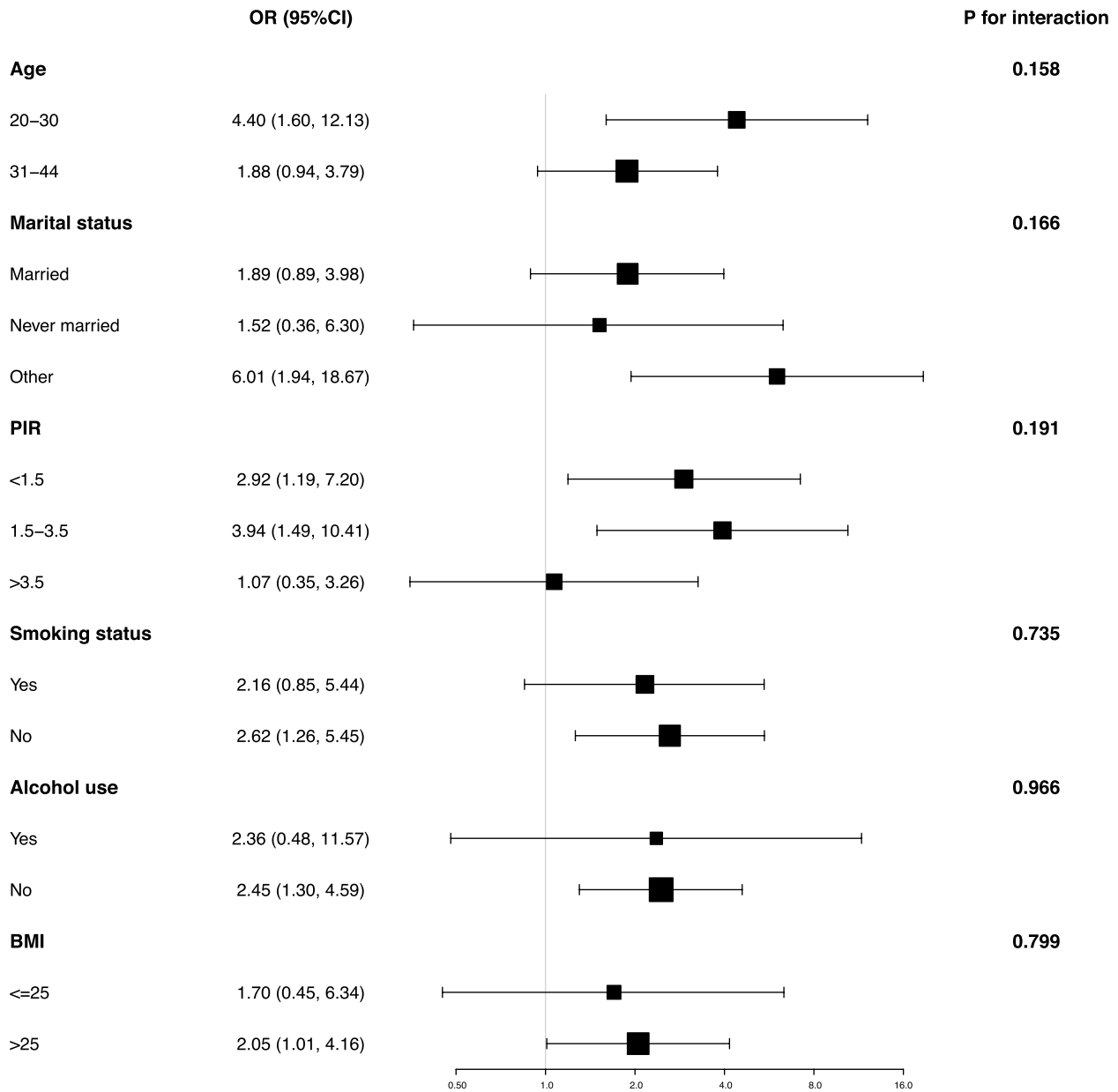

Fig. 2 Subgroup analysis for the association between AIP and infertility

to infertility-associated disorders including conditions like endometriosis, pelvic inflammatory disease, and polycystic ovary syndrome (PCOS) [23–25]. Moreover, the inability to conceive can elicit emotional tension in females, potentially resulting in heightened anxiety and depressive symptoms, which may further compromise endocrine, immune, and reproductive functions, thereby potentially worsening infertility [26, 27]. Our findings align with previous reports of an association between dyslipidemia and female infertility. A forward-looking cohort investigation was carried out by Aleksandra Pirnat and colleagues based on a Norwegian population suggesting that women with poor pre-pregnancy lipid status are at an elevated likelihood of having no children or just a single offspring [28]. An additional cohort investigation conducted by Erica L. Jamro and her team uncovered a correlation, indicating that for every standard increment in serum triglyceride levels, there was a corresponding reduction in the rate of live births [29]. A controlled, randomized, and double-masked clinical trial showed that diminished fertility in females is associated with atypical lipid profiles, including levels of HDL-C, LDL-C, TC, and

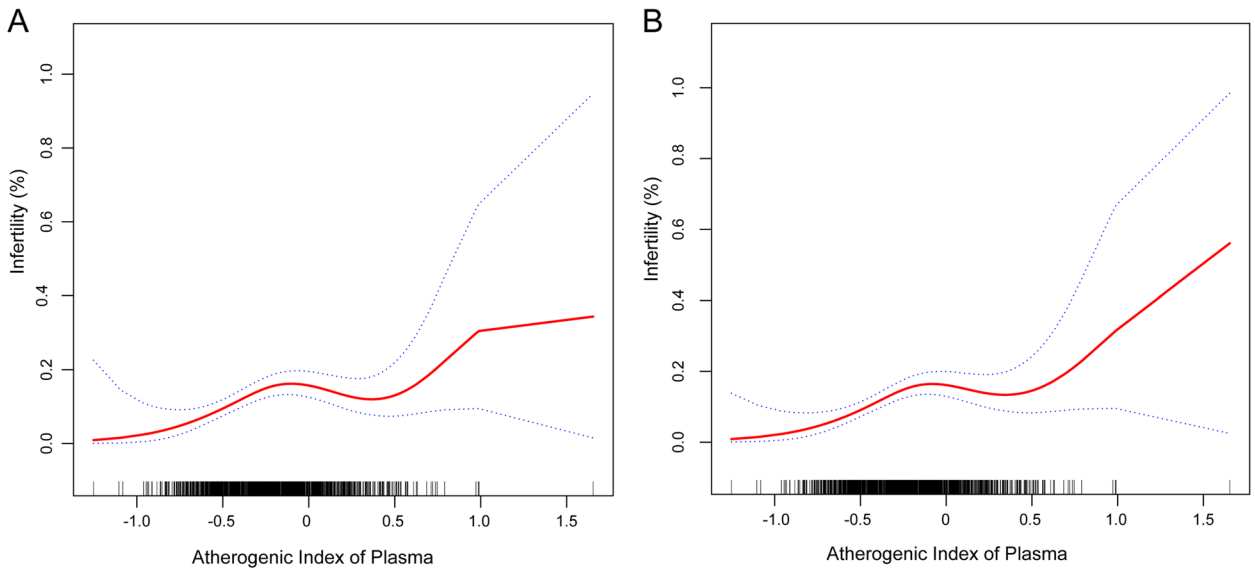

Fig. 3 The Association between Depression and Infertility. The solid line represents the smooth curve fit between variables. Dotted line represents the 95% of confidence interval from the fit. **A** Unadjusted. **B** Age, race, marital status, education level, PIR, smoking status, alcohol use, physical activity, total cholesterol, menstrual status, treatment of pelvic inflammatory disease, and use of hormonal medications were adjusted

Table 3 Threshold effect analysis of AIP on infertility

	Adjusted OR (95% CI)	*P* Value
AIP		
Inflection point	-0.21, 0.22	
AIP < -0.21	18.36 (3.95–85.24)	< 0.001
-0.21 ≤ AIP ≤ 0.22	0.54 (0.09–3.36)	0.511
AIP > 0.22	11.82 (1.00–140.72)	0.050
Log likelihood ratio		< 0.001

Age, race, marital status, education level, PIR, smoking status, alcohol use, physical activity, total cholesterol, menstrual status, treatment of pelvic inflammatory disease, and use of hormonal medications were adjusted

Abbreviations: *AIP* Atherogenic index of plasma, *OR* Odds ratio, *CI* Confidence interval

TG [30]. Hui Wang et al.'s retrospective cross-sectional study revealed that the group with higher HDL concentrations exhibited a 67.0% decrease in the likelihood of female infertility when contrasted with the group possessing lower HDL-C levels, implying an inverse relationship between HDL levels and the incidence of female infertility [31]. Furthermore, A retrospective cohort investigation employing multivariate logistic regression techniques revealed an interesting inverse association between dyslipidemia and the cumulative live birth rate after in vitro fertilization or intracytoplasmic sperm injection (IVF/ICSI) treatments in a patient population devoid of PCOS.

Traditional lipid biomarkers have been extensively utilized to assess risk for various diseases. Nevertheless, their predictive capacity for certain metabolic conditions, such as diabetes mellitus, is limited and fraught with limitations. These markers primarily reflect the levels of individual lipid components, failing to account for the intricate interplay and complex interactions among different lipoproteins. Moreover, they are incapable of distinguishing between the dimensions and concentration of lipoprotein particles, a fact that has been established as a pivotal determinant in cardiovascular disease risk [32]. Additionally, the traditional lipid profile does not afford a comprehensive evaluation of dyslipidemia, as the protective effects of HDL-C can vary considerably among individuals, leading to a suboptimal assessment of lipid abnormalities [33]. AIP serves as a reliable biomarker for both dyslipidemia and atherosclerosis, strongly correlating with cardiovascular disorders and metabolic syndrome [34]. It could thus offer enhanced utility in the evaluation of female reproductive capacity. The AIP is calculated from the logarithmic transformation of the triglyceride to high-density lipoprotein cholesterol ratio, thereby providing a comprehensive evaluation of an individual's blood lipid profile by taking into account the interaction between diverse lipid components [34, 35]. Furthermore, the AIP is regarded as a sensitive indicator of cardiovascular risk, outperforming traditional lipid markers such as TC, LDL-C, HDL-C, and TG in reflecting the levels of atherogenic lipids in plasma [35, 36]. Research indicates that the AIP, as an independent risk factor, can effectively predict the risk of cardiovascular

disease even when other lipid parameters are within normal ranges, highlighting its unique potential in identifying high-risk individuals [35, 37]. This underscores the AIP's broad applicability in assessing overall health and predicting the risk of various diseases. The simplicity of the AIP's calculation, requiring only routine blood lipid test results without additional complex equipment or technology, facilitates its application and dissemination in clinical practice [36]. Therefore, we propose several practical clinical and public health interventions, such as identifying women at risk of infertility based on increased AIP levels for targeted lipid management strategies, integrating AIP assessment into standard preconception care, and establishing standardized AIP screening protocols for women planning to conceive or experience infertility.

The precise mechanism by which the AIP influences female infertility remains unclear However, several potential pathways have been proposed. Firstly, abnormal AIP can disrupt ovarian function by causing mitochondrial dysfunction, reducing follicle count and egg quality, and impairing oocyte maturation and activation [38, 39]. Concurrently, imbalances in lipoprotein cholesterol, critical for steroidogenesis, can negatively affect female fertility [40]. Secondly, oxidative stress is the key factor by which AIP abnormality affects the fertility of women of childbearing age. When lipids accumulate excessively in the body, these lipids may be oxidized to form peroxides, thereby damaging follicles in the ovary and leading to ovulation disorders or a decline in egg quality [41]. Oxidative stress can also reduce endometrial receptivity, making it unfavorable for embryo implantation and thus affecting the success rate of pregnancy [42]. Excessive oxidative stress or a discrepancy between reactive oxygen species (ROS) and the body's antioxidant defense mechanisms can lead to mitochondrial dysfunction, DNA damage, apoptosis, and an exacerbation of the inflammatory response, ultimately resulting in a decline in egg quality and infertility related to endometriosis [38, 43]. Thirdly, Dyslipidemia causes vascular endothelial cells to produce more ROS, impairs the function of vascular endothelial cells, reduces placental vascular density, and consequently decreases the oxygen supply to fetal tissues [44], interferes with blood flow within the placenta [45], and may lead to hypoxia, fetal growth restriction during pregnancy [46]. Fourthly, obesity-related AIP disorders can disrupt the regulatory function of the hypothalamic-pituitary-ovarian axis, leading to hormonal irregularities and affecting the normal processes of ovulation and the menstrual cycle [47]. Moreover, heightened triglyceride concentrations have been linked to an increased incidence of pregnancy-induced hypertensive conditions, gestational diabetes, preeclampsia, and intrahepatic cholestasis [48, 49], adversely affecting maternal and fetal health.

Study strengths and limitations

Our investigation possesses several notable merits. It delivers fresh empirical insights into the connection between AIP and infertility, which may pave the way for innovative approaches in the management and treatment of infertility within a clinical setting. Additionally, our research leverages the strengths of the NHANES database, providing a large, representative sample with rigorous quality control and expert data collection, ensuring the reliability and validity of our findings. The standardized protocols and unified laboratory testing further minimize deviations, enhancing the study's integrity. Nevertheless, certain constraints are inherent in our investigation. Firstly, the evaluation of infertility in our research is predicated on self-reported information, a method that is inherently useful yet potentially subject to distortion from elements like male partner infertility and pregnancy time memory problems, potentially yielding biased outcomes. Concurrently, we are unable to discern whether the infertility cases are primary or secondary. Secondly, although we have controlled for a multitude of confounding factors, residual confounders such as diabetes, hypertension, arrhythmias, and fatty liver disease that might influence lipid abnormalities cannot be entirely excluded. Consequently, additional comprehensive research is warranted to explore the multifaceted effects of baseline and varied AIP scores on female reproductive function. Furthermore, the cross-sectional pattern of the present investigation precludes the demonstration of causative relationships. Hence, a guarded interpretation of the findings is advisable, and longitudinal prospective studies are crucial for elucidating the precise nature of the correlation between AIP and female infertility.

Conclusion

Our investigation has elucidated a substantial association between heightened AIP levels and an increased likelihood of infertility, operating independently of other factors. This discovery highlights AIP's potential significance as a marker for infertility diagnosis. Nevertheless, future longitudinal studies are indispensable to rigorously establish a causative relationship between AIP levels and infertility. These studies will help to confirm the robustness of our findings and potentially contribute to the advancement of more accurate diagnostic methods and personalized treatment strategies within the realm of reproductive health.

Abbreviations

AIP	Atherogenic index of plasma
CAPI	Computer-Assisted Personal Interview
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
MEC	Mobile Examination Center
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
OR	Odds ratio
PCOS	Polycystic ovary syndrome
PIR	Poverty-income ratio
SD	Standard deviations
TG	Triglycerides

Acknowledgements
We extend our sincere gratitude to all the dedicated staff and participants involved in the U.S. National Health and Nutrition Examination Survey (NHANES) for their invaluable contributions to this research endeavor.

Authors' contributions
ZD has full access to all of the data in this study and assumes responsibility for study supervision. ZD, ZB, YZ, JZ conceptualized and designed the study, collected and analyzed data, carried out the initial analyses, and reviewed and revised the manuscript. ZD, ZB, YZ, JZ and acquired, analyzed, and interpreted the data, and drafted the initial manuscript. All authors read and approved the final manuscript.

Funding
The present study was conducted without any external financial support.

Data availability
The datasets utilized in this investigation are accessible in online databases. Detailed information regarding the repositories and the relevant accession numbers can be located at: https://wwwn.cdc.gov/nchs/nhanes.

Declarations

Ethics approval and consent to participate
The NHANES study protocols were granted approval by the National Center for Health Statistics Institutional Review Board, and all participants provided informed written consent. Human study considerations were exempted due to the anonymity of the data.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 3 November 2024 Accepted: 6 February 2025
Published: 14 February 2025

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