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The association between fat distribution and α1-acid glycoprotein levels among adult females in the United States

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Abstract

Background

Visceral fat accumulation and obesity-induced chronic inflammation have been proposed to be an early marker for multiple disease states, especially in women.

Nevertheless, the potential impact of fat distribution on α1 acid glycoprotein (AGP), a marker of inflammation, remains unclear. This research was in order to investigate the relationships among obesity, fat distribution, and α1 acid glycoprotein levels.

Methods

A cross-sectional observational investigation was performed using blood samples of adult females recruited through the National Health and Nutrition Examination Survey from 2015 to 2018. Serum levels of AGP were measured using the Tina-quant Alpha-1-Acid Glycoprotein Gen.2 assay. Based on the fat distribution data obtained from dual-energy X-ray absorptiometry assessments, we used Body Mass Index (BMI), total percent fat (TPF), android percent fat (APF), gynoid percent fat (GPF), android fat/gynoid fat ratio (AGR), visceral percent fat (VPF), subcutaneous percent fat (SPF), visceral fat/subcutaneous fat ratio (VSR) and as dependent variables. To investigate the link between fat distribution and AGP, we used multivariate linear regression analysis. Furthermore, sensitivity analysis was also performed.

Results

The present study included amount of 2295 participants. After adjusting for covariates, BMI, TPF, APF, GPF, VPF, and SPF were found to be positively correlated with AGP levels (BMI: β=23.65

95%CI:20.90-26.40; TPF: β=25.91 95%CI:23.02-28.80; APF: β=25.21 95%CI:22.49-27.93; GPF: β=19.65 95%CI:16.96-22.34; VPF: β=12.49 95%CI:9.08-15.90; SPF: β=5.69 CI:2.89-8.49; AGR: β=21.14 95%CI:18.16-24.12; VSR: β=9.35 95%CI:6.11-12.59, all *P*<0.0001). The above indicators all had a positive dose-response relationship with AGP. In terms of fat distribution, both AGR and VSR showed positive associations with AGP (*P* for trend<0.0001). In particular, when in comparison to individuals in tertile 1 of AGR, participants in tertiles 2 and 3 had 13.42 mg/dL (95% CI 10.66-16.18) and 21.14 mg/dL (95% CI 18.16-24.12) higher AGP level, respectively. Participants in the highest tertile of VSR were mor probably to exhibit a 9.35 mg/dL increase in AGP when compared to those in the lowest tertile (95% CI 6.11-12.59).

Conclusions

Overall, this study revealed a positive dose-dependent relationship between fat proportion/distribution and AGP levels in women. These findings suggest that physician can associate the abnormal serum AGP and obesity and allow timely interventions.

Keywords

α1-acid glycoprotein, obesity, fat distribution, inflammation

Introduction

In the United States, 38% of adult women are obese(1). Obesity ,once believed to be just a metabolic abnormality ,has been shown to demonstrate mutual causality with non-specific immune (2–7). As a result of obesity, women are more vulnerable to fertility problems in addition to metabolic problems including type Ⅱ diabetes and heart disease.(8). Furthermore, the importance of fat distribution is gaining more attention. Accumulation of fat in the abdominal region is linked to health issues related to obesity and even all-cause mortality(9–11). Conversely, fat tissue gathering in the lower body (gluteofemoral

region) has been linked to protective lipid and glucose profiles, along with a decreased risk of cardiovascular and metabolic diseases in population studies(12,13). Get the whole picture of the correlation between body status and fat distribution is vital for health maintenance. In addition, fat distribution is not uniform between men and women. Men and postmenopausal women often exhibit android obesity (14,15). This body habitus is also known as an apple-shaped body, due to increased fat in the trunk whilst the limbs tend to be thin. Women of childbearing age usually demonstrate gynoid shaped (16). In other words, their bodies seem to have a pear shape due to enhanced fat deposition in the hip and thighs. Differences between these forms of fat distribution are also related to disease predisposition. Excess fat accumulation in the android region is believed to be linked with a higher likelihood of developing cardiovascular disease, hypertension, hyperlipidemia, insulin resistance, and type 2 diabetes.(17), whereas gynoid fat accumulation is linked to a lower likelihood of developing metabolic and cardiovascular conditions (18). In pre-menopausal women altered fat distribution is crucial since android fat accumulation is correlated to a raised prevalence of female infertility(19).

Systemic and tissue-specific chronic inflammation is an ordinary characteristic of obesity(20). Many findings have suggested that the chronic inflammation caused by fat accumulation differs according to tissue type and distribution. Soo Lim et al. noted that visceral fat in specific tissues released unique inflammatory mediators(21),whilst Marial et al. suggested that trunk higher fatty deposits and inflammation were positively correlated(22). In women, the release of IL-6 from gluteal and femoral adipose tissue is significantly lower than that from abdominal subcutaneous fat(23).Therefore fat distribution strongly correlates to inflammation, with gynoid fat demonstrating a more beneficial inflammatory profile compared to android fat.

Alpha-1-acid glycoprotein (AGP) is a protein that is produced throughout the body in response to inflammation in the liver and peripheral tissues (24).Elevated levels of AGP can be observed in inflammatory patients(25,26) which have also been reported to be a good indicator of inflammation in patients with polycystic ovary syndrome (PCOS), especially those with infertility (27). One study, having

reported on the association between obesity and AGP, found that the association was stronger in women (28). Indeed, Prioreschi *et* al also demonstrated that fat accumulation was positively associated with AGP levels in South African women (29)further noting (20) that both the trunk/limb ratio and android/ gynoid ratio were positively associated with AGP. More evidence is needed to prove the relationship between AGP and fat distribution, especially in larger populations, so as to better clarify the association among obesity, fat distribution and inflammatory states. The association betwixt AGP in blood and fat distribution is explained in this study for the first times using data gathered from the National Health and Nutrition Examination Survey (NHANES).

To examine the correlation betwixt obesity and fat distribution in NHANES female participant using dual-energy X-ray absorption (DXA) scans is the objective of this research which was to provide worthwhile insights into the health consequences of fat distribution on inflammation and related issue in a wider population.

Methods

2.1 Participant Selection

Initiated in 1999, the National Health and Nutrition Examination Survey (NHANES) is an ongoing initiative that evaluates people's nutritional status and general health throughout the United States. Orchestrated by the Centers for Disease Control and Prevention (CDC), this comprehensive survey merges detailed interviews with thorough physical assessments (For more details: http://www.cdc.gov/nchs/nhanes.htm). The interview portion probes into various domains such as demographics, socioeconomic factors, dietary habits, and health-related concerns. Meanwhile, the examination component encompasses a wide range of evaluations including medical and dental check-ups, physiological measurements, and extensive laboratory analyses, all carried out by trained healthcare professionals. The National Center for Health Statistics' Ethics Review Board (Protocol #2011-17 continuation) granted approval for all involved procedures, ensuring that every participant provided

consent in writing prior to participation.

In this study, because AGP data were only available for NHANES survey cycles 2015-2016 and 2017-2018, we selected these cycles. Only women 18 to 49 years of age were included for analysis which included 19225 participants.

Missing data on α1-acid glycoprotein (AGP); BMI; or fat distribution (android percent fat [APF], gynoid percent fat [GPF], visceral adipose tissue mass [VF] and subcutaneous fat [SF]) were exclude. Finally, a total of 2295 participants were taken in.

2.2 Ethical Considerations

Each participant gave written agreement prior to participation, in accordance with the procedure approved by the Research Ethics Review Board of the National Center for Health Statistics(30). The NHANES is committed to maintaining strict confidentiality standards and has robust measures in place to safeguard participant anonymity. Given that the current research involved secondary analysis of de-identified data, and that the NHANES dataset is publicly accessible(31), there was no necessity for an institutional review board assessment for this study(30).

2.3 Measurement of α1-acid glycoprotein (AGP)

The assessment of α1-acid glycoprotein (AGP) was conducted using the Tina-quant Alpha-1-Acid Glycoprotein Gen.2 assay, which operates on the immunological agglutination principle. This process involves the formation of an antigen/antibody complex when anti-Alpha-1-acid glycoprotein antibodies interact with antigens present in the test specimen. This complex leads to agglutination, the intensity of which is quantified turbidimetrically (Refer to: AAGP2 Tina-quant α1-Acid Glycoprotein Gen.2 [package insert]. Indianapolis, IN. Roche Diagnostics. 2014-11, V 9.0.). Each testing sequence included serum quality control (QC) pools from Roche or were generated internally to guarantee accuracy, processed in duplicate. These QC samples were then assessed against predefined standards using a robust multi-rule quality control scheme(32). Data acquisition occurred post-completion of all laboratory analyses. The

research team accessed the NHANES database, extracted the pertinent data, and meticulously documented the corresponding measurements.

2.4 Measurement of fat distribution

The computation of Body Mass Index (BMI, kg/m2) involved dividing the individual's weight (in kilograms) by the square of their height (in meters), with the result rounded off to one decimal point. This data collection took place at the Mobile Examination Center (MEC), conducted by skilled health technicians.

As far as body composition analysis goes, dual-energy x-ray absorptiometry (DXA) is the most widely accepted technique. (33). Get a comprehensive DXA scans of the entire body at the NHANES mobile examination center (MEC). When conducting the scanning procedure, utilize the Hologic APEX software for precise demarcation of the Android and Gynoid (A/G) areas. The bottom trunk section has been specifically labeled as the Android region, with two different lines denoting its borders: a lower line aligning with the pelvic horizontal cut and an upper line automatically positioned above this cut line by the software. The Gynoid region was determined with respect to the Android region's height. Establish the maximum boundary of the Gynoid region as 1.5-ford the height of the Android region beneath the pelvic line. Conversely, set up the lower bound of the Gynoid area at a distance ensuring the vertical span between the two Gynoid lines was exactly double as high as the Android region. The Hologic program carefully placed these demarcating lines to ensure precision and consistency in delineating these essential anatomical regions(34). The mass of visceral adipose tissue within the abdomen was measured at the approximate level between the L4 and L5 vertebrae. The mass of subcutaneous adipose tissue outside the abdomen was measured at the approximate level between the L4 and L5 vertebrae. We obtained the records of total percent fat (%, TPF), android percent fat (%, APF), and gynoid percent fat (%, GPF) from NHANES, According to the data for total fat (g), android fat mass (g), subcutaneous fat mass (g), visceral adipose tissue mass (g), and subcutaneous fat mass (g), we calculated android fat/gynoid fat ratio (%, AGR),: visceral fat/total fat (%, VPF), subcutaneous fat/total fat (%, SPF), visceral fat/subcutaneous fat

ratio (%, VSR).

2.5 Covariates

The study recorded demographic variables such as age, race (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Other race), education (Less than high school, High school or GED General educational development, Above high school), marital status (Live alone, Living with a partner) and income-to-poverty ratio. Biochemical parameters included serum albumin (g/dL), total cholesterol (mg/dL), triglycerides (mg/dL), Energy intake (kcal). The questionnaire-based variables encompassed disease state such as hypertension or not, high cholesterol level or not, diabetes or not, and lifestyle factors such as physical activity (Vigorous, Moderate, Less than moderate) and smoking status.

2.6 Data Analyses

Our analysis followed the recommendation of NHANES on the complex sampling design and weights.

Descriptive statistics were employed for data representation, with continuous variables typically represented by the weighted median and standard deviation (SD), while categorical variables are often depicted using weighted frequency(percentage). Student 2-tailed t-test or Mann-Whitney U test is utilized to test continuous variables, while chi-square or Fisher exact test is utilized to test categorical variables.

Applying multivariate linear regression model to explore fat distribution's connection with AGP, including an unadjusted model (non-adjusted); a minimally adjusted model (adjust I; adjusted only for age, race, education, marital status, and income: poverty ratio); and a fully adjusted model (adjust II; adjusted for age, race, education, marital status, and income: poverty ratio, smoking status, hypertension or not, high cholesterol level or not, diabetes or not and serum albumin, total cholesterol, triglycerides)(35–37). Calculate β and it's 95% confidence intervals (95%CI) to represent the estimated effect value. We used the tertile of exposure as ordinal categorical variables (first to third, with the first tertile set as the reference values) to examine possible trends in this relationship.

To account for missing covariates data, we employed multiple imputation in the R MI procedure

involving 5 replications and a chained equation approach method. (38,39), to performed sensitivity analyses (n=3015).

Data analysis was conducted using R (version 4.3.0; The R Foundation) and Empower (X&Y Solutions Inc) software(40). The distinction is statistically significant at $p<0.05$.

Results

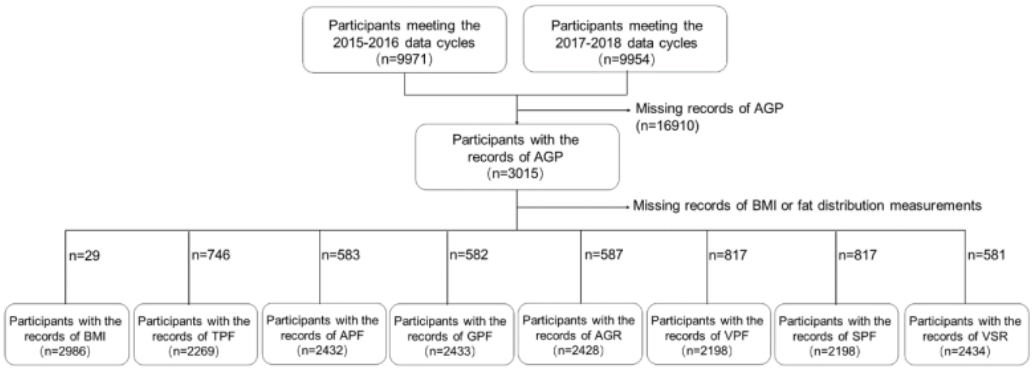
3.1 Population characteristics

In the midst of those recruited, only 2295 female participants successfully passed all screenings (Figure 1). The characteristics of participants classified by AGP were reported in Table 1(line 482). These included average age, average AGP level, BMI, total percent fat, android percent fat, gynoid percent fat, AGR, subcutaneous percent fat, visceral percent fat, VSR, total cholesterol, triglycerides, C-reactive protein, albumin.

The present study confirmed the findings that AGP showed the highest content with increasing age and BMI. We divided BMI into three ranges for statistical analysis, and the results showed that BMI > 30 (obese group) showed the highest AGP levels (percentage 64.41%). Similarly, fat distribution indicators showed the same trend (all $P<0.05$). Experimental results found clear support that higher BMI and fat mass are associated with higher AGP content.

Moreover, higher levels of total cholesterol, triglycerides and lower albumin were observed in this population. AGP levels were higher in smokers, when compared to non-smoker. More detailed data can be found in Table 1.

Fig. 1



Flowchart outlining the eligibility and disqualification criteria for female American adults participating in 2015-2016 and 2017-2018 National Health and Nutrition Examination Survey of the United States. Abbreviations: AGP: α1 acid glycoprotein; BMI: Body Mass Index; TPF: Total Percent Fat (%); APF: Android percent fat (%); GPF: Gynoid percent fat (%); AGR: Android/Gynoid ratio (%); VPF: Visceral percent fat (%); SPF: Subcutaneous percent fat (%); VSR: Visceral/Subcutaneous ratio (%).

3.2 Multivariate regression analysis

Table 2 demonstrates the correlation betwixt AGP level and fat distribution through the utilization of multivariable linear regression analysis. BMI, TPF, APF, GPF, AGR, VPF, SPF and VSR showed positive correlations with AGP level (BMI: all P values < 0.0001) after adjusting for all covariates (BMI: β=1.31, 95%CI: 1.18-1.45; TPF: β=1.72, 95%CI: 1.55-1.89; APF: β=1.30, 95%CI: 1.17-1.43; GPF: β=1.59, 95%CI: 1.39-1.79; AGR: β=0.62, 95%CI: 0.53-0.71; VPF: β=8.58, 95%CI: 5.90-11.25; SPF: β=2.79, 95%CI: 1.48-4.11; VSR: β=0.41, 95%CI: 0.26-0.57; all P values < 0.0001). When all the exposures were divided into three quantiles, pronounced dose-response relationships between BMI, TPF, APF, GPF, AGR, VPF, SPF, VSR and AGP levels were observed.

Further analysis showed that, AGP's effect size (β) had an 9.55 mg/dL and 23.65 mg/dL increase in the second and third quantiles of BMI, respectively compared to the first quantile (P<0.0001). Similarly significant positive dose-response relationships were found for both total fat percent (TPF) and part fat percent (APF, GPF, VPF, SPF), whose quartiles 2 and 3 having meaningful higher AGP than that of quartile 1.

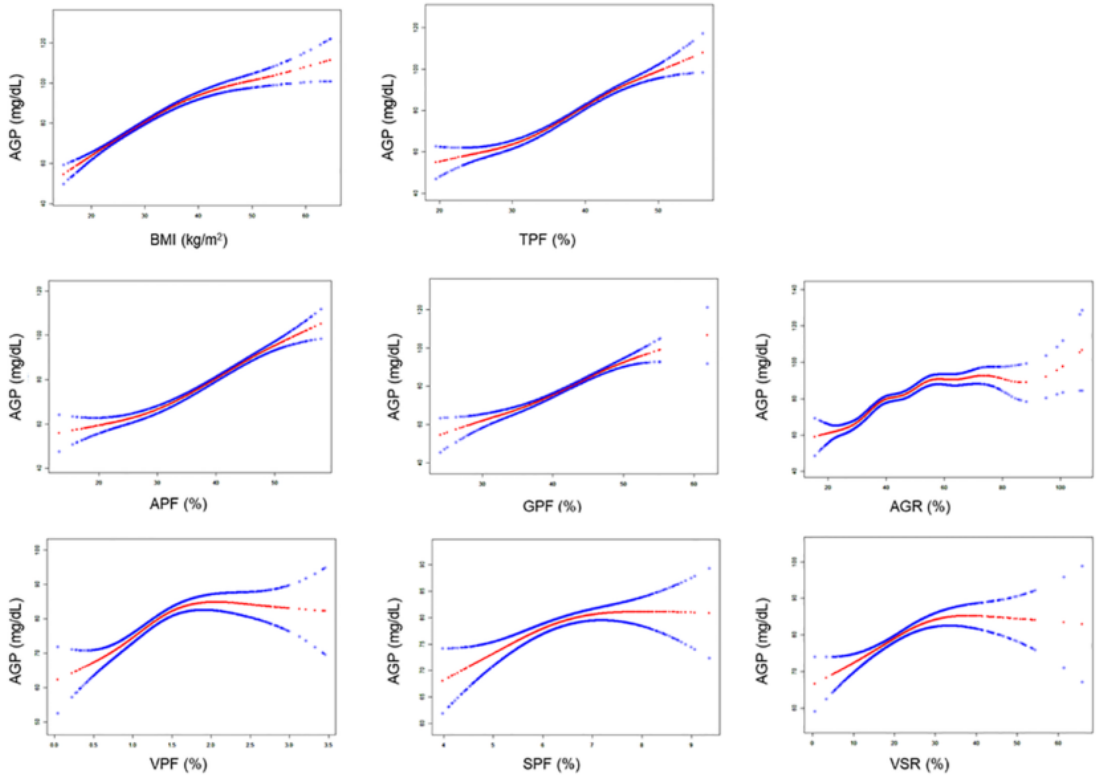
As mentioned above, there was a concentration response relationship between android/gynoid fat ratio

(AGR) or visceral/subcutaneous fat ratio (VSR) and AGP. The second and third quantiles of AGR had an increase in AGP compared to the first quantile (quantile 2: β=13.42, 95%CI: 10.66-16.18, *P*<0.0001; quantile 3: β=21.14, 95%CI: 18.16-24.12, *P*<0.0001), whilst the third quantile of VSR also had an increase in AGP (quantile 3: β=9.35, 95%CI: 6.11-12.59, *P*<0.0001).

Similar to analysis results, the link between AGP and BMI, TPF, APF, GPF, AGR, VPF, SPF, VSR was further confirmed in smooth curve fitting in Figure 2 which is positive and monotonic. It suggested that the increase in the ratio of android fat to gynoid fat was accompanied by increasing AGP accumulation. In the same vein, the increased ratio of visceral fat to subcutaneous fat was accompanied by an increase AGP accumulation.

In sensitivity analysis, the association between AGP and BMI, TPF, APF, GPF, AGR, VPF, SPF, VSR was robust after inclusion of participants missing confounders by multiple imputation (Supplemental Table 1).

Fig. 2



a–d The red line depicts the fitted smooth curve of the variable, while the space between the two blue lines illustrates the 95% confidence interval (CI).

Discussion

In this study, the increased BMI and excess fat accumulation were meaningful connected with increased α1-acid glycoprotein concentrations in adult females after full adjustment for covariates. Furthermore, in terms of fat distribution, APF, GPF, VPF, and SPF were found to be positively associated with AGP levels. So as to investigate the influence of different fat distributions on AGP, we took android/gynoid ratio and visceral/subcutaneous ratio as research objects and found that both showed an increasing trend.

There is a multifactorial and single effect relationship between obesity, inflammation, and chronic disease(2–7). During chronic inflammation, inflammatory cells such as neutrophils and monocytes infiltrate adipose tissue(41). What's more, enlarged adipocytes are more likely to enter a stressed state and release chemokines such as TNF- α and IL-6, which mediate immune cell infiltration(42).Given that

gynoid fat distribution is a protective factor in females, it is relatively less likely to cause inflammation. AGP, an abundant human plasma glycoprotein is an inflammatory marker, whose serum levels can reach up to 5 times during inflammatory events (45).A different angle on the relationship between obesity and inflammation is provided by the findings, which showed that fat was associated with an increase in AGP.. Consistent with the results, study has indicated that higher levels of inflammatory markers such as IL-6, TNF- α , and leptin are present in the blood of overweight and obese individuals, including adults and children.(46) Furthermore, Palaniswamy *et* al. have argued that an increase in BMI and fat accumulation led to increases in inflammatory markers, including AGP(28) Significantly, these results support their findings. However, for as much as we know, this is the first anthropometric study in which the risk of obesity and fat distribution on health is evaluated in a population of only women using AGP levels. The relationship between obesity and AGP has been previously studied with data suggesting that obesity is accompanied by an increase of AGP index(28,47,48). Furthermore, Prioreschi *et* al. emphasized that accumulation of android fat in South African women is probably to source an increase in AGP(29);with Black South African women gain extra fat around their abdomens. The data indicate that the distribution of AGP levels differs according to race. Mexican American and other Hispanic groups had the largest number of people with moderate AGP levels, accounting for 21.18% and 14.74% of the total population, respectively Non-Hispanic Whites accounted for with high AGP levels, indicating a greater incidence of obesity among this group. Similarly, the proportion of non-Hispanic Black people with high APG levels was the largest(22.50%).In contrast, the total number of individuals with low AGP levels was higher in other ethnic groups. One study shown that the prevalence of obesity increased between 2017 to 2018 in both non-Hispanic Whites and non-Hispanic Blacks (49).This data provides the basis for our view. The reason for the differences in obesity levels among ethnic groups may be related to sociodemographic status(50). Thus, we hypothesized that it similarly affected serum AGP levels.

The present study confirmed findings that an increase in visceral and android fat increases the risk of adverse outcomes and elevated APG. Similar to our conclusions, it has been proven that differences in fat

distribution lead to altered metabolism and increased risk of metabolic diseases (51).Android adipocytes tend to increase in size and become more sensitive to lipolytic stimuli. Additionally android fat discharges more lipolysis products into the systemic circulation than gynoid fat. On the contrary, gynoid fat can better retain fatty acids and other lipolysis products, which play a protective role in metabolism (36,52).Android obesity, also known as abdominal obesity, is harmful to women, since it can lead to abnormal hormone levels(53) and may be related to some forms of female infertility. Abdominal obesity not only causes hypothalamic-pituitary-gonadal axis dysfunction in women with ovulatory dysfunction, but also has toxic effects on reproductive tissue due to excessive fatty acid degradation. This leads to germ cell damage and a chronic low-grade inflammatory state (54–56).Intriguingly, Broughton *et* al. point out that obese women remain infertile even in the absence of ovulatory dysfunction, and it appears that obesity has an effect on the outcome of assisted reproductive technology (57). As we have previously described, AGP has been reported to be an excellent mmarker of inflammation in patients with PCOS, particularly in those with concurrent infertility. A promising research direction may be the potential association between female infertility and AGP. In short, the results further clarify the association between adiposity, fat distribution and AGP, consistent with previous findings of others group. We also provide support for the aassociation of inflammation related disease due to differences in fat distribution and suggest that AGP should be considered an essential disease marker in women.

When compared to subcutaneous fat, visceral fat is mostly composed of larger and dysfunctional adipocytes, and is associated with high levels of fatty acid degradation and adipokine secretion leading to inflammation (58–61). AGP glycoforms are altered during inflammation, rendering AGP a potential detection index for some diseases (44).As a result of this experiments, we concluded that accumulation of visceral fat related to an increase in AGP. Previous studies have demonstrated that fatty acids and cytokines released from visceral fat lead to insulin resistance (62–64).Due to its unique anatomical location, primary hepatic insulin resistance caused by visceral fat may be the cause of glucose metabolic dysfunction in patients (65).We hypothesized that the reason for increased AGP was related to changes in the cellular environment of the liver. Additionally, females as a group, demonstrate differences in visceral

fat production. As previously mentioned, women of childbearing age whose estrogen antagonizes the production of visceral fat(14), therefore, visceral obesity is more usual in men and postmenopausal women. Similarly, visceral fat deposition occurs in women with abnormally high androgen levels (66). Moreover, estrogen itself reduces AGP synthesis (67). Thus, we speculate that the result of decompensated estrogen action is the accumulation of visceral fat in women of childbearing age. In summary, visceral adiposity produces higher levels of AGP. In women the detrimental effects of elevated AGP are related to the endocrine system which will be the focus of future research.

Study strengths and limitations

Although this study used NHANES data to analyze the correlation between fat distribution and the serum AGP level for the first time, several limitations should be noted. To begin with, we only analyzed the adult female population, and the representativeness of the sample needs to be improved. Therefore, whether the findings can be extrapolated to other, larger populations (males, adolescents, and the elderly) need to be confirmed. In the second place, due to the cross-sectional nature of this study, it is not feasible to definitively determine the causal link between obesity and AGP. There are various reasons for changes in AGP levels, and different conformations of AGP have different physiological functions (68). It is too simple to use AGP as an inflammatory marker and the correlation between obesity and levels of inflammation requires more detailed and diverse indicators. It is worth mentioning that other markers such as C-reactive protein (CRP), Adiponectin, serum inerleukin-6, FGF and TGF(69–73)have been repeatedly reported to have a strong relationship between adipose and obesity, which also supports this conclusion. Finally, there are different types of adipose cells, each with its own function and importance(74,75). We also need to conduct animal studies to extract fat cells from different parts. They are analyzed structurally and functionally, and their functions and roles are understood at the transcriptome level.

Conclusions

The study found that there is a correlation between fat distribution and AGP levels in adult North American females. Android fat and visceral fat will become our focus in future research. It is essential to prevent the transition to tissue-specific obesity in overweight individuals. It is worth to note that obesity should be considered when abnormal serum AGP levels are found during physical examination. Good control of body fat, especially visceral fat, is benefit to improve the AGP-related inflammation. Recognizing differences in fat deposition helps to identify obese individuals at risk for inflammation in order to implement early interventions in those at extreme risk. The results cast a new light and insights into discrimination of women at risk for bad metabolic health.

List of Abbreviations

AGP: α 1 acid glycoprotein

AGR: android fat/gynoid fat ratio

APF: android percent fat

BMI: Body Mass Index

CAD: coronary artery disease

DXA: Dual-energy x-ray absorptiometry

GPF: gynoid percent fat

MEC: Mobile Examination Center

NHANES: National Health and Nutrition Examination Survey

PCOS: polycystic ovary syndrome

QC: quality control

SF: subcutaneous fat

SPF: subcutaneous percent fat

TPF: total percent fat

VPF: visceral percent fat

VF: visceral adipose tissue mass

VSR: visceral fat/subcutaneous fat ratio

Table 1. Study population characteristics categorized by α1 acid glycoprotein (AGP).

Table 2. The correlation between adipose distribution and Alpha-1-acid glycoprotein (AGP) levels in adult women in the United States as observed in the National Health and Nutrition Examination Survey conducted between 2015 and 2018.

Table 1. Study population characteristics categorized by α1 acid glycoprotein (AGP).

Variables	Total (n = 2295)	AGP (mg/dL)			*P* Value
		Low (n=1004)	Middle (n=1002)	High (n=1009)	
AGP (mg/dL), Mean ± SD	77.73 ± 24.05	53.13 ± 8.87	75.21 ± 5.73	104.71 ± 16.74	<0.001
Age (year), Mean ± SD	28.84 ± 11.40	27.39 ± 10.85	29.20 ± 11.49	30.71 ± 11.43	<0.001
BMI (kg/m^2), n (%)					-
<25	1274 (32.85%)	547 (55.36%)	319 (32.29%)	122 (12.35%)	
25-30	1309 (33.75%)	280 (28.06%)	412 (41.28%)	306 (30.66%)	
>30	1295 (33.39%)	128 (12.80%)	298 (29.80%)	574 (57.40%)	

Total Percent Fat (%), Mean ± SD	37.32 ± 6.81	32.87 ± 5.80	37.96 ± 5.74	41.54 ± 5.61	<0.001
Android Percent Fat (%), Mean ± SD	37.26 ± 8.70	31.78 ± 7.61	37.84 ± 7.54	42.47 ± 6.96	<0.001
Gynoid Percent Fat (%), Mean ± SD	41.19 ± 5.52	38.26 ± 5.19	41.68 ± 4.77	43.80 ± 4.83	<0.001
AGR (%), Mean ± SD	41.11 ± 13.51	34.56 ± 10.80	41.45 ± 12.85	48.31 ± 13.57	<0.001
Subcutaneous Percent Fat (%), Mean ± SD	6.38 ± 0.87	6.22 ± 0.87	6.44 ± 0.89	6.51 ± 0.81	<0.001
Visceral Percent Fat (%), Mean ± SD	1.26 ± 0.53	1.11 ± 0.47	1.27 ± 0.53	1.44 ± 0.55	<0.001
VSR (%), Mean ± SD	19.62 ± 8.19	17.75 ± 6.98	19.78 ± 8.10	22.15 ± 9.20	<0.001
Total Cholesterol(mg/dL), Mean ± SD	177.88 ± 37.16	176.45 ± 38.61	176.72 ± 34.75	180.90 ± 38.35	0.012
Triglycerides (mg/dL), Mean ± SD	110.90 ± 75.05	95.63 ± 67.33	112.19 ± 76.93	128.05 ± 76.16	<0.001
Albumin (g/dL), Mean ± SD	4.15 ± 0.38	4.20 ± 0.41	4.18 ± 0.35	4.07 ± 0.34	<0.001
Energy intake (kcal), Mean ± SD	1880.80 ± 832.88	1951.37 ± 819.37	1873.27 ± 798.85	1845.20 ± 817.27	0.014
ratio of family income to poverty (%), Mean ± SD	2.28 ± 1.59	2.56 ± 1.65	2.27 ± 1.56	2.08 ± 1.51	<0.001
Smoke, n (%)					-
Yes	783 (26.06%)	154 (20.18%)	197 (25.99%)	306 (37.55%)	
No	2222 (73.94%)	609 (79.82%)	561 (74.01%)	509 (62.45%)	
Hypertension, n (%)					-
Yes	456 (13.71%)	67 (7.90%)	115 (13.50%)	168 (18.69%)	
No	2869 (86.29%)	781 (92.10%)	737 (86.50%)	731 (81.31%)	
High cholesterol level, n (%)					-
Yes	413 (12.42%)	94 (11.08%)	109 (12.79%)	140 (15.59%)	
No	2912 (87.58%)	754 (88.92%)	743 (87.21%)	758 (84.41%)	

Diabetes, n (%)					-
Yes	151 (3.90%)	18 (1.81%)	44 (4.46%)	61 (6.17%)	
No	3718 (96.10%)	974 (98.19%)	943 (95.54%)	927 (93.83%)	
Physical Activity, n (%)					-
Vigorous	561 (16.15%)	124 (13.93%)	154 (17.68%)	173 (18.89%)	
Moderate	869 (25.02%)	231 (25.96%)	214 (24.57%)	248 (27.07%)	
Less than moderate	2043 (58.83%)	535 (60.11%)	503 (57.75%)	495 (54.04%)	
Education, n (%)					-
Less than high school	1427 (36.41%)	360 (35.93%)	385 (38.50%)	330 (32.74%)	
High school or GED General educational development	667 (17.02%)	144 (14.37%)	166 (16.60%)	202 (20.04%)	
Above high school	1825 (46.57%)	498 (49.70%)	449 (44.90%)	476 (47.22%)	
Marital status, n (%)					-
Married or living with partner	2116 (63.26%)	560 (66.83%)	514 (60.97%)	548 (61.57%)	
Living alone	1229 (36.74%)	278 (33.17%)	329 (39.03%)	342 (38.43%)	
Race, n (%)					-
Mexican American	722 (18.39%)	170 (16.93%)	226 (22.55%)	197 (19.52%)	
Other Hispanic	427 (10.87%)	94 (9.36%)	136 (13.57%)	95 (9.42%)	
Non-Hispanic White	1125 (28.65%)	299 (29.78%)	270 (26.95%)	373 (36.97%)	
Non-Hispanic Black	912 (23.22%)	186 (18.53%)	203 (20.26%)	225 (22.30%)	
Other Race	741 (18.87%)	255 (25.40%)	167 (16.67%)	119 (11.79%)	

348 Table 2. The correlation between adipose distribution and Alpha-1-acid glycoprotein (AGP)
349 levels in adult women in the United States as observed in the National Health and Nutrition
350 Examination Survey conducted between 2015 and 2018..

Exposure	Non-adjusted		Adjust I[a]		Adjust II[b]	
	β (95%CI)	*P* value	β (95%CI)	*P* value	β (95%CI)	*P* value
BMI (kg/m2)**						
Continuous	1.43 (1.33, 1.52)	<0.0001	1.37 (1.26, 1.48)	<0.0001	1.31 (1.18, 1.45)	<0.0001
Tertile:						
13.8-23.6	ref		ref		ref	
23.7-30.5	11.97 (10.09, 13.85)	<0.0001	11.31 (9.09, 13.53)	<0.0001	9.55 (6.93, 12.17)	<0.0001
30.6-72.6	26.47 (24.57, 28.36)	<0.0001	25.75 (23.47, 28.04)	<0.0001	23.65 (20.90, 26.40)	<0.0001
P for trend		<0.0001		<0.0001		<0.0001
TPF (%)						
Continuous	1.88 (1.75, 2.00)	<0.0001	1.93 (1.78, 2.07)	<0.0001	1.72 (1.55, 1.89)	<0.0001
Tertile:						
15 – 34.4	ref		ref		ref	
34.5 – 40.8	14.40 (12.33, 16.47)	<0.0001	15.41 (12.99, 17.83)	<0.0001	13.15 (10.38, 15.92)	<0.0001
40.9 - 56.1	28.80 (26.73, 30.87)	<0.0001	29.43 (26.97, 31.89)	<0.0001	25.91 (23.02, 28.80)	<0.0001
P for trend		<0.0001		<0.0001		<0.0001
APF (%)						
Continuous	1.43 (1.34, 1.53)	<0.0001	1.47 (1.37, 1.58)	<0.0001	1.30 (1.17, 1.43)	<0.0001
Tertile:						
11.9 - 33.8	ref		ref		ref	
33.9 – 42	13.47 (11.46, 15.48)	<0.0001	14.84 (12.50, 17.18)	<0.0001	12.70 (10.05, 15.36)	<0.0001
42.1 - 58.8	28.39 (26.38, 30.40)	<0.0001	28.98 (26.65, 31.31)	<0.0001	25.21 (22.49, 27.93)	<0.0001
P for trend		<0.0001		<0.0001		<0.0001
GPF (%)						
Continuous	1.82 (1.66, 1.98)	<0.0001	1.78 (1.60, 1.96)	<0.0001	1.59 (1.39, 1.79)	<0.0001
Tertile:						
16.6 – 39	ref		ref		ref	
39.1 – 43.8	12.22 (10.10, 14.34)	<0.0001	12.83 (10.42, 15.25)	<0.0001	10.91 (8.25, 13.58)	<0.0001
43.9 - 61.9	23.07 (20.94, 25.19)	<0.0001	22.50 (20.05, 24.94)	<0.0001	19.65 (16.96, 22.34)	<0.0001
P for trend		<0.0001		<0.0001		<0.0001
AGR (%)						
Continuous	0.75 (0.69, 0.81)	<0.0001	0.75 (0.68, 0.82)	<0.0001	0.62 (0.53, 0.71)	<0.0001
Tertile:						
15.37 – 33.67	ref		ref		ref	
33.68 – 45.16	13.34 (11.24, 15.43)	<0.0001	15.25 (12.82, 17.68)	<0.0001	13.42 (10.66, 16.18)	<0.0001
45.17 - 107.47	24.76 (22.67, 26.86)	<0.0001	26.10 (23.58, 28.62)	<0.0001	21.14 (18.16, 24.12)	<0.0001
P for trend		<0.0001		<0.0001		<0.0001
VPF (%)						

Continuous	11.43 (9.65, 13.20)	<0.0001	12.53 (10.17, 14.89)	<0.0001	8.58 (5.90, 11.25)	<0.0001
Tertile:						
0.039 – 0.96	ref		ref		ref	
0.97 - 1.39	8.00 (5.66, 10.34)	<0.0001	9.06 (6.28, 11.84)	<0.0001	7.80 (4.71, 10.89)	<0.0001
1.40 – 4.22	14.53 (12.21, 16.85)	<0.0001	16.72 (13.62, 19.82)	<0.0001	12.49 (9.08, 15.90)	<0.0001
P for trend		<0.0001		<0.0001		<0.0001
SPF (%)						
Continuous	3.74 (2.62, 4.86)	<0.0001	3.75 (2.51, 4.99)	<0.0001	2.79 (1.48, 4.11)	<0.0001
Tertile:						
3.95 – 6.00	ref		ref		ref	
6.01 – 6.75	5.63 (3.25, 8.01)	<0.0001	6.11 (3.45, 8.77)	<0.0001	4.89 (2.06, 7.73)	0.0007
6.76 - 9.36	7.49 (5.11, 9.87)	<0.0001	7.80 (5.16, 10.44)	<0.0001	5.69 (2.89, 8.49)	<0.0001
P for trend		<0.0001		<0.0001		<0.0001
VSR (%)						
Continuous	0.62 (0.51, 0.73)	<0.0001	0.65 (0.50, 0.79)	<0.0001	0.41 (0.26, 0.57)	<0.0001
Tertile:						
0.53 – 15.35	ref		ref		ref	
15.36 - 21.28	3.22 (0.95, 5.49)	0.0055	3.48 (0.79, 6.17)	0.0113	2.69 (-0.30, 5.67)	0.0777
21.29 – 65.83	11.42 (9.16, 13.67)	<0.0001	12.18 (9.19, 15.18)	<0.0001	9.35 (6.11, 12.59)	<0.0001
P for trend		<0.0001		<0.0001		<0.0001

[a]Model I: Adjust for: age; race; education; marital status; ratio of family income to poverty.

[b]Model II: Adjust for: age; race; education; marital status; ratio of family income to poverty; physical activity; energy intake(kcal); smoke status; hypertension or not; high cholesterol level or not; diabetes or not; albumin (g/dL); total Cholesterol(mg/dL); triglycerides (mg/dL).

Abbreviations: AGP: α1 acid glycoprotein; BMI: Body mass index; TPF: Total Percent Fat (%); APF: Android percent fat (%); GPF: Gynoid percent fat (%); AGR: Android/Gynoid ratio (%); VPF: Visceral percent fat (%); SPF: Subcutaneous percent fat (%); VSR: Visceral/Subcutaneous ratio (%).

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