HHS Public Access

Author manuscript

Fertil Steril. Author manuscript; available in PMC 2019 November 01.

Published in final edited form as:

Fertil Steril. 2018 November ; 110(6): 1145–1153. doi:10.1016/j.fertnstert.2018.06.037.

Dietary factors and serum Anti-Mullerian hormone concentrations in late premenopausal women

Chelsea Anderson, MPH[1], **Yong-Moon Mark Park, PhD**[2], **Frank Z. Stanczyk, PhD**[3], **Dale P. Sandler, PhD**[2], and **Hazel B. Nichols, PhD**[1]

[1]Department of Epidemiology, University of North Carolina, Chapel Hill, North Carolina

[2]Epidemiology Branch, National Institute of Environmental Health Sciences, Research Triangle Park, NC

[3]Departments of Obstetrics and Gynecology and Preventive Medicine, University of Southern California Keck School of Medicine, Los Angeles, CA

Abstract

Objective: To study associations between dietary factors and circulating anti-Mullerian hormone (AMH) concentrations among late premenopausal women.

Design: AMH concentrations were measured in serum samples collected at enrollment from 296 women (aged 35–45 years) in the Sister Study cohort. Usual dietary intakes in the past 12 months were assessed using a validated food frequency questionnaire. Dietary exposures of interest included macronutrients, dietary fat subtypes, fiber, and glycemic index. Multivariable linear regression was used to evaluate associations between dietary variables and serum AMH concentrations. We also used nutrient density models to examine isocaloric replacement of macronutrients.

Setting: N/A

Patients/Animals: Women aged 35–45 years

Interventions: N/A

Main outcome measures: Serum AMH concentrations (ng/ml)

Results: AMH concentrations were positively associated with percentage of energy from carbohydrates (β per 5% calories=0.141 [95% CI: 0.023, 0.259]; p-trend=0.019), and inversely associated with percentage of energy from fat (β per 5% calories=−0.152 [95% CI: −0.299, −0.004]; p-trend=0.044). In analyses of dietary fat subtypes, AMH decreased with increasing monounsaturated fatty acids (p-trend=0.082) and polyunsaturated fatty acids (p-trend=0.043), particularly ω−6 fatty acids (p-trend=0.044), while no strong trend was observed for saturated fatty acids. Protein and alcohol intake were not strongly associated with AMH.

Corresponding author: Hazel B. Nichols, Assistant Professor, Department of Epidemiology, University of North Carolina Gillings School of Global Public Health, 2104F McGavran-Greenberg Hall, 135 Dauer Drive, Chapel Hill, NC, USA 27599-7435, Phone: (919) 966-7456, hazel.nichols@unc.edu.

Conflict of Interest: None

Conclusions: Our cross-sectional analyses in a sample of late premenopausal women suggest that dietary fat intake may be inversely associated with circulating AMH concentrations. Further research in prospective studies is warranted to evaluate dietary factors as potential modifiers of ovarian reserve.

Capsule:

In this cross-sectional analysis in a sample of late premenopausal women, findings suggest that dietary fat intake may be inversely associated with circulating AMH concentrations.

Keywords

Anti-mullerian hormone; diet; premenopausal women

Introduction

The reproductive lifespan in women is characterized by a gradual depletion of the ovarian oocyte pool, or the ovarian reserve, ultimately leading to the onset of menopause.(1) Anti-Müllerian hormone (AMH), a dimeric glycoprotein produced by the granulosa cells of preantral and small antral ovarian follicles, has emerged as a marker of ovarian reserve in premenopausal women, with circulating AMH concentrations positively correlated with the number of remaining antral follicles.(2–4) AMH remains relatively stable throughout the menstrual cycle, in contrast to other ovarian hormones, and has been used clinically to predict time to menopause in late reproductive age women(5, 6) and response to ovarian stimulation in women undergoing in vitro fertilization.(7, 8)

Though age is undoubtedly the strongest predictor, other lifestyle and environmental factors may also modify ovarian reserve. Diet has been hypothesized to affect reproductive function in women through a number of diverse mechanisms including altered menstrual cycle length and subsequent rate of follicular depletion, or follicular atrophy induced by diet-associated inflammation or oxidative stress.(9) In studies of mice, exposure to excess dietary fat has been associated with a decrease in primordial follicles and an increase in follicular atresia, potentially contributing to a shortening of the reproductive lifespan in females.(10–15) In contrast, other evidence from murine studies suggests that a diet rich in ω−3 fatty acids could help to delay ovarian aging.(16) However, limited research has investigated relationships between dietary factors and measures of ovarian aging in humans. One study reported an inverse association between serum follicle-stimulating hormone (FSH) concentrations, a marker of ovarian reserve, and dietary fiber intake in women, though another study found no significant association.(17, 18) Others have reported nonsignificant associations between dietary fats, including ω−3 fatty acids, and circulating FSH concentrations.(17, 19) However, FSH is a less accurate and sensitive marker than AMH, and levels vary substantially across the menstrual cycle, making it a less useful marker for studies in which blood collection is not timed to the menstrual cycle phase.(20) To our knowledge, only one previous observational study in humans has investigated associations between AMH and dietary factors, finding no significant relationships for dietary fiber or percent of calories from any macronutrient. However, their analyses were limited to a relatively narrow range of dietary exposures.(21) Therefore the objective of this cross-

sectional study was to examine associations between dietary factors and serum AMH concentrations among late premenopausal women. Given the positive association between AMH concentrations and time to menopause,(5, 6) factors that modify AMH concentrations may be of interest to women in this age group.

Materials and methods

Study population

Participants included in these analyses were controls in a case-control study of AMH and breast cancer risk nested within the prospective Sister Study cohort.(22) The Sister Study was initiated to identify genetic and environmental risk factors for breast cancer and enrolled over 50,000 women from the U.S. and Puerto Rico between 2003 and 2009. All Sister Study participants were themselves free of breast cancer at enrollment but had a sister with a previous breast cancer diagnosis. Sociodemographic information, smoking status, and reproductive history were collected from enrollment questionnaires. Blood samples were collected by trained phlebotomists during an enrollment home visit, shipped overnight to the Sister Study biorepository, where they were processed and aliquoted and stored at −80˚C in liquid nitrogen vapor phase. At the enrollment home visit, standardized protocols were used by trained study personnel to measure blood pressure, height, weight, and waist circumference. The study was approved by the Institutional Review Board of the National Institute of Environmental Health Sciences, the National Institutes of Health, and the Copernicus Group, and all participants provided written informed consent.

Sister Study participants were eligible to be selected for the control sample if they were ages 35 to 54 years, premenopausal, had at least one intact ovary, and had a serum sample archived from enrollment. Women were considered premenopausal if they reported at least one menstrual cycle within the 12 months prior to enrollment. Those aged 54 years and younger whose only reason for not experiencing menses was hysterectomy (without bilateral oophorectomy) were also considered premenopausal. A total of 916 women, who remained free of breast cancer as of December 31, 2012, had serum samples analyzed for AMH and were selected as control participants. For these analyses, we excluded women older than 45 years at enrollment (N= 597) because >10% of those aged 46–54 years had samples with nondetectable AMH values. Women with a self-reported diagnosis of polycystic ovarian syndrome (PCOS) or missing PCOS information (N=13) were excluded, since PCOS is associated with elevated AMH concentrations,(2) and may be managed through lifestyle changes, including dietary modification strategies.(23) We also excluded those missing a food frequency questionnaire (FFQ) (N=8) and those with implausible values for total energy intake (<500 or >5000 kcal/day; N=2). Final analyses thus included 296 women.

Dietary assessments

Usual dietary intake for the previous 12 months was measured at enrollment using a modified 1998 Block 109-item FFQ.(24) This instrument assesses both the portion size and frequency of consumption for listed foods. Dietary exposures examined in these analyses included macronutrient intake, dietary fat subtypes, fiber, glycemic index, and glycemic load.

Laboratory assays

Assays of AMH concentrations in serum samples were performed at the Reproductive Endocrine Research Laboratory at the University of Southern California Keck School of Medicine. An Ultrasensitive AMH ELISA kit (Ansh Labs, Webster TX) was used to measure AMH. The interassay coefficients of variation for the Ultrasensitive AMH ELISA are 4.6%, 4.8%, and 2.0% at 0.346, 0.715, and 1.85 ng/ml, respectively. When AMH values were below the limit of detection of this instrument (<0.07 ng/ml), the picoAMH ELISA kit (Ansh Labs), was used. The picoAMH ELISA has a limit of detection of 0.003 ng/ml, and interassay coefficients of 4.5%, 2.2%, and 3.8% at 22.6, 86.5, and 373 pg/ml, respectively. A total of 12 samples had undetectable concentrations using the picoAMH.

Statistical analysis

AMH samples that were undetectable with the picoAMH ELISA were imputed as half of the limit of detection (0.0015 ng/ml). Participant characteristics were tabulated according to quartiles of untransformed serum AMH concentrations. Because AMH concentrations were skewed, values were log-transformed to approximate a normal distribution, and log-transformed values were used in all further statistical analyses. Geometric means of AMH according to quartiles of dietary variables were calculated using generalized linear models. Dietary variables, evaluated individually as exposures in separate regression models, included percentages of calories from macronutrients (carbohydrates, fat, protein, alcohol), total carbohydrates (g/day), fiber (g/day), total sugars (g/day), glycemic index, glycemic load, total fat (g/day), saturated fat (g/day) monounsaturated fat (g/day), polyunsaturated fat (g/day), ω−3 fatty acids (g/day), ω−6 fatty acids, the ratio of ω−6 to ω−3 fatty acids, long-chain ω−3 fatty acids (g/day), and short chain ω−3 fatty acids (g/day). Tests for trend were performed by including the continuous linear term for each dietary variable in separate linear regression models. We conducted both age-adjusted and multivariable-adjusted analyses. Multivariable models were adjusted for total energy intake (kcal/day) and characteristics associated with AMH concentrations in previous studies, including age (years), body mass index (BMI; kg/m^2), current smoking (yes/no), and current oral contraceptive use (yes/no).(25–28) In sensitivity analyses, we excluded women who reported current use of oral contraceptives (N=42), those with a unilateral oophorectomy (N=17), and those who were current smokers (n=32).

As a secondary analysis, we analyzed associations between AMH and percent energy from macronutrients (fat, carbohydrates, protein, and alcohol) using multivariable nutrient density models.(29) With log-transformed AMH as the dependent variable, each possible combination of three macronutrients was entered together in a separate linear regression model, with the fourth macronutrient omitted. In these models, parameter estimates for each of the 3 included macronutrients are interpreted as the effect of substituting calories from that macronutrient for equal energy from the omitted macronutrient. For example, with separate terms in the model for total energy, percent energy from protein, percent energy from carbohydrate, and percent energy from alcohol, the coefficient for percent energy from carbohydrate represents the effect of substituting energy from carbohydrates for energy from fat, holding constant energy from protein and alcohol.(29) All analyses were conducted

using SAS software, version 9.4 (SAS Institute, Cary, NC). Two-sided p-values < 0.05 were considered statistically significant.

Results

Women included in these analyses were predominately non-Hispanic white (87%), with a median age of 42.8 years (IQR: 40.6, 44.6) and a median BMI of 25.0 kg/m^2 (IQR: 22.3, 28.9). The majority had at least a Bachelor's degree (57%), were not current smokers (89%), and were not currently using oral contraceptives (86%). Participant characteristics according to quartiles of AMH concentrations are shown in Table 1. The overall median of untransformed AMH concentrations was 0.93 ng/ml (IQR: 0.28, 2.23). Compared to women in the lower three quartiles of AMH, women in the highest quartile were more likely to be less than 40 years old and to have a BMI less than 25.0 kg/m^2. They were also less likely to have had a hysterectomy or unilateral oophorectomy.

The overall geometric mean AMH concentration was 0.62 ng/ml (95% CI: 0.50, 0.77). In multivariable-adjusted models, serum AMH concentrations increased with increasing carbohydrate intake, both in grams per day (β per 10 g/day=0.061 [95% CI: 0.006, 0.116]; p-trend=0.031) and as a proportion of total energy (β per 5% calories=0.141 [95% CI: 0.023, 0.259]; p-trend=0.019) (Table 2). Glycemic load was also positively associated with AMH concentrations (β per 5 units=0.051 [95% CI:0.008, 0.094]; p-trend=0.020). Glycemic index, total sugars, and dietary fiber intake were not strongly associated with AMH. Percentages of energy from protein and alcohol were also not associated with AMH.

Inverse associations were observed between AMH concentrations and total fat intake as a percentage of energy (β per 5% calories= −0.152 [95% CI:−0.299, −0.004]; p-trend=0.044; Table 2) and in grams per day (β per 10 g/day= −0.141 [95% CI: −0.295, 0.012]; p-trend=0.071; Table 3) in multivariable-adjusted models. In analyses of dietary fat subtypes, grams per day of both monounsaturated fatty acids (MUFAs; p-trend=0.082) and polyunsaturated fatty acids (PUFAs; p-trend=0.043) were inversely associated with AMH. No strong trend was observed for grams per day of saturated fatty acids, although the AMH concentration for the highest quartile of saturated fatty acids was approximately half that in the lowest quartile. AMH concentrations appeared to decrease with increasing ω−6 and ω−3 fatty acid intakes, though the trend was stronger for ω−6 (p-trend=0.044) than ω−3 (p-trend=0.136). In general, adjustment for energy contributed the most to observed differences between age-adjusted and multivariable-adjusted models. Findings were similar when women currently taking oral contraceptives, those who had a unilateral oophorectomy, and those who were current smokers were excluded (*data not shown*).

In nutrient density models, replacing energy from carbohydrates with energy from fat was associated with lower AMH concentrations (β = −0.034, p=0.025) (Supplementary Table 1). Replacing energy from fat with energy from carbohydrates was positively associated with AMH (β = 0.032; p=0.034). The magnitude and direction of association were similar, though not statistically significant, when energy from fat was replaced with energy from protein (β = 0.035, p=0.387). Other substitutions of macronutrients were not strongly associated with AMH concentrations.

Discussion

Modifiable exposures such as diet may affect reproductive function in women, yet few studies have examined associations between dietary factors and markers of ovarian reserve. In our cohort of late premenopausal women, AMH concentrations were positively associated with total carbohydrate intake and inversely associated with total fat intake. In analyses of dietary fat subtypes, modest inverse associations with AMH were observed for intakes of both MUFAs and PUFAs. Other dietary factors, such as protein intake and glycemic index, were not strongly related to AMH concentrations.

High dietary fat intake has been speculated to compromise reproductive function in women, with potential direct effects on ovarian morphology and function.(10) Some, though not all, studies in animal models have observed decreases in the number of primordial, primary, secondary, and antral follicles following exposure to a high-fat diet,(11–14, 30–35) an association potentially mediated by increased inflammation.(12) Others have also found that a high fat diet may increase follicular atresia.(11, 13, 15) However, a study in mice found no significant differences in serum AMH concentrations between those fed a low-fat or high-fat diet, suggesting that granulosa cell function may not be altered by high fat intake.(12) Studies of dietary fat and markers of ovarian reserve in humans are more limited. In a report from the BioCycle Study, a prospective observational study of healthy premenopausal women (N=259 women aged 18 to 44 years, mean=27 years) without a known diagnosis of PCOS, serum AMH concentrations were not associated with macronutrient intakes, including percent calories from fat.(21) Dietary assessment in their study was performed using multiple 24-hour dietary recalls, and blood samples used to measure AMH concentrations were collected several times throughout the menstrual cycle. Although distributions of macronutrient intakes in the BioCycle report were similar to those in our cohort, our analyses, in a narrower age-range of women suggested inverse associations between AMH concentrations and dietary fat intake, both as a proportion of total energy and in total grams per day.

In our cohort, both PUFAs and MUFAs, but not saturated fats, were modestly inversely associated with AMH concentrations. Relationships between subtypes of dietary fat and AMH were not evaluated in the BioCycle study report.(21) However, in a separate report from the same cohort, specific types of fat were not strongly associated with serum FSH concentrations.(19) While studies of fat subtypes and ovarian reserve markers remain limited, one prospective study of 3,115 premenopausal Japanese women (aged 35–56 years at dietary assessment) found that higher intakes of PUFAs and MUFAs were modestly associated with an earlier onset of menopause,(36) consistent with lower age-specific AMH concentrations.

Associations did not appear to differ substantially between ω−3 and ω−6 PUFAs in our analyses. These results are consistent with a possible detrimental effect of higher dietary ω −6 fatty acids, but do not support the hypothesis that a diet rich in ω−3 fatty acids may delay ovarian aging.(16) The proposed biological mechanisms relating ω −3 fatty acids to ovarian reserve are not well-established, but are thought to involve reductions in inflammation and oxidative stress.(37) We are not aware of any prior observational studies that have examined

associations between AMH and dietary ω−3 fatty acids. However, in a small trial of 15 obese and 12 normal weight women, one month of ω−3 fatty acid supplementation did not result in a change in AMH concentrations, but did result in a reduction in FSH in normal weight women.(37) While our cross-sectional analyses do not support a positive association between dietary ω−3 fatty acid and serum AMH concentrations, larger prospective studies, with multiple biomarkers of ovarian reserve, may be needed to clarify associations with PUFA subtypes.

In our cohort, AMH concentrations increased with grams per day of carbohydrates and percent of energy from carbohydrates. These factors were not significantly associated with AMH concentrations in the report from the BioCycle Study.(21) Consistent with our results, one study of Chinese women aged 40 to 70 reported that higher carbohydrate intake was modestly associated with a later age at natural menopause.(38) Although the biological basis for our findings is not immediately clear, observed associations with carbohydrate intake could be largely explained by an AMH-lowering effect of dietary fat, since carbohydrate and fat intake as a proportion of total energy were strongly inversely correlated in our sample (*data not shown*). In our nutrient density models, replacing energy from fat with either carbohydrates or protein was positively associated with AMH (though the association with protein was not statistically significant). Conversely, substituting fat for carbohydrates was associated with lower AMH, while substituting protein for carbohydrates had no effect.

Dietary fiber has been of interest as a potential modifier of female reproductive hormones, given several previous reports of inverse associations between fiber intake and estrogen concentrations in women.(18, 39–43) Consistent with findings from the BioCycle study,(21) dietary fiber was not strongly associated with AMH in our analyses. Two prior studies have investigated relationships between fiber intake and FSH in premenopausal women, with conflicting results. Higher dietary fiber intake was associated with significantly lower serum FSH concentrations in the BioCycle Study,(18) but was not associated with plasma FSH in a study of 393 premenopausal Japanese women.(17) Though research to date is limited, it is possible that dietary fiber may affect some reproductive hormone concentrations, but not strongly influence AMH levels in premenopausal women.

Our study is among the first to examine associations between dietary factors and AMH concentrations in women, and was also able to account for other factors related to AMH levels, such as BMI and oral contraceptive use. However, due to the cross-sectional design, we cannot interpret our findings as causal. We were also limited to the evaluation of recent dietary intake, as comprehensive information on childhood or young adult diet was not available. It is possible that early-life dietary exposures may also influence AMH concentrations among late premenopausal women. Dietary assessment via FFQ may also result in some degree of measurement error, though we do not expect that this error would be differential with respect to AMH concentrations. In addition, women in our cohort were 35–45 years of age, predominately non-Hispanic white, and all had a family history of breast cancer. Thus, our findings may not be generalizable to younger women or those of other racial or ethnic groups.

Conclusions

Findings from this cross-sectional study of late premenopausal women suggest that dietary fat intake may be inversely associated with circulating AMH concentrations. Further research in prospective studies is warranted to evaluate dietary factors as potential modifiers of ovarian reserve.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

This research was supported in part by the Intramural Research Program of the National Institutes of Health, National Institute of Environmental Health Sciences (Z01-ES044005) and the Avon Foundation (02-2012-085). C.A. was supported by the UNC Lineberger Cancer Control Education Program (T32 CA057726).

References

1. Broekmans FJ, Soules MR, Fauser BC. Ovarian aging: mechanisms and clinical consequences. Endocr Rev 2009;30:465–93. [PubMed: 19589949]
2. Broekmans FJ, Visser JA, Laven JS, Broer SL, Themmen AP, Fauser BC. Anti-Mullerian hormone and ovarian dysfunction. Trends Endocrinol Metab 2008;19:340–7. [PubMed: 18805020]
3. Hansen KR, Hodnett GM, Knowlton N, Craig LB. Correlation of ovarian reserve tests with histologically determined primordial follicle number. Fertil Steril 2011;95:170–5. [PubMed: 20522327]
4. Visser JA, Schipper I, Laven JS, Themmen AP. Anti-Mullerian hormone: an ovarian reserve marker in primary ovarian insufficiency. Nat Rev Endocrinol 2012;8:331–41. [PubMed: 22231848]
5. Freeman EW, Sammel MD, Lin H, Gracia CR. Anti-mullerian hormone as a predictor of time to menopause in late reproductive age women. J Clin Endocrinol Metab 2012;97:1673–80. [PubMed: 22378815]
6. Broer SL, Eijkemans MJ, Scheffer GJ, van Rooij IA, de Vet A, Themmen AP et al. Anti-mullerian hormone predicts menopause: a long-term follow-up study in normoovulatory women. J Clin Endocrinol Metab 2011;96:2532–9. [PubMed: 21613357]
7. La Marca A, Sighinolfi G, Radi D, Argento C, Baraldi E, Artenisio AC et al. Anti-Mullerian hormone (AMH) as a predictive marker in assisted reproductive technology (ART). Hum Reprod Update 2010;16:113–30. [PubMed: 19793843]
8. Broer SL, Mol B, Dolleman M, Fauser BC, Broekmans FJ. The role of anti-Mullerian hormone assessment in assisted reproductive technology outcome. Curr Opin Obstet Gynecol 2010;22:193–201. [PubMed: 20407372]
9. Moslehi N, Mirmiran P, Tehrani FR, Azizi F. Current Evidence on Associations of Nutritional Factors with Ovarian Reserve and Timing of Menopause: A Systematic Review. Adv Nutr 2017;8:597–612. [PubMed: 28710146]
10. Hohos NM, Skaznik-Wikiel ME. High-Fat Diet and Female Fertility. Endocrinology 2017;158:2407–19. [PubMed: 28586412]
11. Wang N, Luo LL, Xu JJ, Xu MY, Zhang XM, Zhou XL et al. Obesity accelerates ovarian follicle development and follicle loss in rats. Metabolism 2014;63:94–103. [PubMed: 24135502]
12. Skaznik-Wikiel ME, Swindle DC, Allshouse AA, Polotsky AJ, McManaman JL. High-Fat Diet Causes Subfertility and Compromised Ovarian Function Independent of Obesity in Mice. Biol Reprod 2016;94:108. [PubMed: 27030045]
13. Ma X, Hayes E, Prizant H, Srivastava RK, Hammes SR, Sen A. Leptin-Induced CART (Cocaine- and Amphetamine-Regulated Transcript) Is a Novel Intraovarian Mediator of Obesity-Related Infertility in Females. Endocrinology 2016;157:1248–57. [PubMed: 26730935]

14. Sohrabi M, Roushandeh AM, Alizadeh Z, Vahidinia A, Vahabian M, Hosseini M. Effect of a high fat diet on ovary morphology, in vitro development, in vitro fertilisation rate and oocyte quality in mice. Singapore Med J 2015;56:573–9. [PubMed: 26512150]
15. Jungheim ES, Schoeller EL, Marquard KL, Louden ED, Schaffer JE, Moley KH. Diet-induced obesity model: abnormal oocytes and persistent growth abnormalities in the offspring. Endocrinology 2010;151:4039–46. [PubMed: 20573727]
16. Nehra D, Le HD, Fallon EM, Carlson SJ, Woods D, White YA et al. Prolonging the female reproductive lifespan and improving egg quality with dietary omega-3 fatty acids. Aging Cell 2012;11:1046–54. [PubMed: 22978268]
17. Tsuji M, Tamai Y, Wada K, Nakamura K, Hayashi M, Takeda N et al. Associations of intakes of fat, dietary fiber, soy isoflavones, and alcohol with levels of sex hormones and prolactin in premenopausal Japanese women. Cancer Causes Control 2012;23:683–9. [PubMed: 22399233]
18. Gaskins AJ, Mumford SL, Zhang C, Wactawski-Wende J, Hovey KM, Whitcomb BW et al. Effect of daily fiber intake on reproductive function: the BioCycle Study. Am J Clin Nutr 2009;90:1061–9. [PubMed: 19692496]
19. Mumford SL, Chavarro JE, Zhang C, Perkins NJ, Sjaarda LA, Pollack AZ et al. Dietary fat intake and reproductive hormone concentrations and ovulation in regularly menstruating women. Am J Clin Nutr 2016;103:868–77. [PubMed: 26843151]
20. Jamil Z, Fatima SS, Ahmed K, Malik R. Anti-Mullerian Hormone: Above and Beyond Conventional Ovarian Reserve Markers. Dis Markers 2016;2016:5246217. [PubMed: 26977116]
21. Sjaarda LA, Schisterman EF, Schliep KC, Plowden T, Zarek SM, Yeung E et al. Dietary Carbohydrate Intake Does Not Impact Insulin Resistance or Androgens in Healthy, Eumenorrheic Women. J Clin Endocrinol Metab 2015;100:2979–86. [PubMed: 26066675]
22. Nichols HB, Baird DD, Stanczyk FZ, Steiner AZ, Troester MA, Whitworth KW et al. Anti-Mullerian hormone concentrations in premenopausal women and breast cancer risk. Cancer Prev Res (Phila) 2015;8:528–34. [PubMed: 25873369]
23. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet 2013;113:520–45. [PubMed: 23420000]
24. Block G, Hartman AM, Dresser CM, Carroll MD, Gannon J, Gardner L. A data-based approach to diet questionnaire design and testing. Am J Epidemiol 1986;124:453–69. [PubMed: 3740045]
25. Jung S, Allen N, Arslan AA, Baglietto L, Brinton LA, Egleston BL et al. Demographic, lifestyle, and other factors in relation to antimullerian hormone levels in mostly late premenopausal women. Fertil Steril 2017;107:1012–22.e2. [PubMed: 28366409]
26. Dolleman M, Verschuren WM, Eijkemans MJ, Dolle ME, Jansen EH, Broekmans FJ et al. Reproductive and lifestyle determinants of anti-Mullerian hormone in a large population-based study. J Clin Endocrinol Metab 2013;98:2106–15. [PubMed: 23533229]
27. Marsh EE, Bernardi LA, Steinberg ML, de Chavez PJ, Visser JA, Carnethon MR et al. Novel correlates between antimullerian hormone and menstrual cycle characteristics in African-American women (23–35 years-old). Fertil Steril 2016;106:443–50.e2. [PubMed: 27114331]
28. Bernardi LA, Carnethon MR, de Chavez PJ, Ikhena DE, Neff LM, Baird DD et al. Relationship between obesity and anti-Mullerian hormone in reproductive-aged African American women. Obesity (Silver Spring) 2017;25:229–35. [PubMed: 27925445]
29. Hu FB, Stampfer MJ, Rimm E, Ascherio A, Rosner BA, Spiegelman D et al. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. Am J Epidemiol 1999;149:531–40. [PubMed: 10084242]
30. Fernandez MO, Sharma S, Kim S, Rickert E, Hsueh K, Hwang V et al. Obese Neuronal PPARgamma Knockout Mice Are Leptin Sensitive but Show Impaired Glucose Tolerance and Fertility. Endocrinology 2017;158:121–33. [PubMed: 27841948]
31. Lai H, Jia X, Yu Q, Zhang C, Qiao J, Guan Y et al. High-fat diet induces significant metabolic disorders in a mouse model of polycystic ovary syndrome. Biol Reprod 2014;91:127. [PubMed: 25100714]

32. Balasubramanian P, Jagannathan L, Mahaley RE, Subramanian M, Gilbreath ET, Mohankumar PS et al. High fat diet affects reproductive functions in female diet-induced obese and dietary resistant rats. J Neuroendocrinol 2012;24:748–55. [PubMed: 22192683]
33. Wu S, Divall S, Nwaopara A, Radovick S, Wondisford F, Ko C et al. Obesity-induced infertility and hyperandrogenism are corrected by deletion of the insulin receptor in the ovarian theca cell. Diabetes 2014;63:1270–82. [PubMed: 24379345]
34. Brothers KJ, Wu S, DiVall SA, Messmer MR, Kahn CR, Miller RS et al. Rescue of obesity-induced infertility in female mice due to a pituitary-specific knockout of the insulin receptor. Cell Metab 2010;12:295–305. [PubMed: 20816095]
35. Tortoriello DV, McMinn J, Chua SC. Dietary-induced obesity and hypothalamic infertility in female DBA/2J mice. Endocrinology 2004;145:1238–47. [PubMed: 14670988]
36. Nagata C, Wada K, Nakamura K, Tamai Y, Tsuji M, Shimizu H. Associations of physical activity and diet with the onset of menopause in Japanese women. Menopause 2012;19:75–81. [PubMed: 21926924]
37. Al-Safi ZA, Liu H, Carlson NE, Chosich J, Harris M, Bradford AP et al. Omega-3 Fatty Acid Supplementation Lowers Serum FSH in Normal Weight But Not Obese Women. J Clin Endocrinol Metab 2016;101:324–33. [PubMed: 26523525]
38. Dorjgochoo T, Kallianpur A, Gao YT, Cai H, Yang G, Li H et al. Dietary and lifestyle predictors of age at natural menopause and reproductive span in the Shanghai Women's Health Study. Menopause 2008;15:924–33. [PubMed: 18600186]
39. Rose DP, Goldman M, Connolly JM, Strong LE. High-fiber diet reduces serum estrogen concentrations in premenopausal women. Am J Clin Nutr 1991;54:520–5. [PubMed: 1652197]
40. Goldin BR, Woods MN, Spiegelman DL, Longcope C, Morrill-LaBrode A, Dwyer JT et al. The effect of dietary fat and fiber on serum estrogen concentrations in premenopausal women under controlled dietary conditions. Cancer 1994;74:1125–31. [PubMed: 8039147]
41. Bagga D, Ashley JM, Geffrey SP, Wang HJ, Barnard RJ, Korenman S et al. Effects of a very low fat, high fiber diet on serum hormones and menstrual function. Implications for breast cancer prevention. Cancer 1995;76:2491–6. [PubMed: 8625075]
42. Woods MN, Barnett JB, Spiegelman D, Trail N, Hertzmark E, Longcope C et al. Hormone levels during dietary changes in premenopausal African-American women. J Natl Cancer Inst 1996;88:1369–74. [PubMed: 8827014]
43. Monroe KR, Murphy SP, Henderson BE, Kolonel LN, Stanczyk FZ, Adlercreutz H et al. Dietary fiber intake and endogenous serum hormone levels in naturally postmenopausal Mexican American women: the Multiethnic Cohort Study. Nutr Cancer 2007;58:127–35. [PubMed: 17640158]

Table 1.

Study participant characteristics of 296 premenopausal women according to quartile of anti-Mullerian hormone (AMH)

	AMH			
	Quartile 1 (<0.28 ng/ml)	**Quartile 2 (0.28–0.92 ng/ml)**	**Quartile 3 (0.93–2.22 ng/ml)**	**Quartile 4 (≥2.23 ng/ml)**
	N(%)	**N(%)**	**N(%)**	**N(%)**
Age, years				
<40	2 (3)	11 (15)	22 (30)	27 (36)
40–44	42 (58)	46 (61)	37 (50)	44 (59)
45	29 (40)	18 (24)	15 (20)	3 (4)
Race/ethnicity				
Non-Hispanic white	63 (86)	62 (83)	66 (89)	66 (89)
Non-Hispanic black	5 (7)	6 (8)	4 (5)	2 (3)
Hispanic	3 (4)	5 (7)	3 (4)	4 (5)
Other	2 (3)	2 (3)	1 (1)	2 (3)
Education				
Less than Bachelor's degree	14 (19)	11 (15)	8 (11)	10 (14)
Bachelor's degree	22 (30)	23 (31)	20 (27)	19 (26)
Higher than Bachelor's degree	37 (51)	41 (55)	46 (62)	45 (61)
Body mass index, kg/m^2				
<25.0	30 (41)	36 (48)	38 (51)	43 (58)
25.0–29.9	25 (34)	26 (35)	19 (26)	14 (19)
≥30.0	18 (25)	13 (17)	17 (23)	17 (23)
Current smoker				
No	63 (86)	71 (95)	61 (82)	69 (93)
Yes	10 (14)	4 (5)	13 (18)	5 (7)
Currently using oral contraceptives				
No	56 (77)	65 (87)	68 (92)	65 (88)
Yes	17 (23)	10 (13)	6 (8)	9 (12)
Hysterectomy				
No	63 (86)	68 (91)	67 (91)	68 (92)
Yes	10 (14)	7 (9)	7 (9)	6 (8)

	AMH			
	Quartile 1 (<0.28 ng/ml)	Quartile 2 (0.28–0.92 ng/ml)	Quartile 3 (0.93–2.22 ng/ml)	Quartile 4 (≥2.23 ng/ml)
	N(%)	N(%)	N(%)	N(%)
Unilateral oophorectomy				
No	66 (90)	72 (96)	68 (92)	73 (99)
Yes	7 (10)	3 (4)	6 (8)	1 (1)
Total energy intake, kcal/day (quartiles)				
<1233.9	23 (32)	20 (27)	16 (22)	15 (20)
1233.9–1527.4	13 (18)	21 (28)	18 (24)	22 (30)
1527.5–1979.6	19 (26)	17 (23)	22 (30)	16 (22)
≥1979.7	18 (25)	17 (23)	18 (24)	21 (28)

Table 2.

Geometric means of AMH (95% CI) according to quartiles of macronutrient intake and carbohydrate measures *a,b*

	Age-adjusted	Multivariable adjusted *c*
% calories from carbohydrates		
<41.25	0.41 (0.28, 0.61)	0.41 (0.27, 0.61)
41.25–47.34	0.64 (0.43, 0.95)	0.66 (0.45, 0.98)
47.35–51.84	0.77 (0.52, 1.15)	0.76 (0.51, 1.13)
≥51.85	0.71 (0.48, 1.06)	0.71 (0.48, 1.05)
β per 5% calories (95% CI)	0.134 (0.015, 0.253)	0.141 (0.023, 0.259)
p-value	0.027	0.019
% calories from fat		
<32.25	0.65 (0.44, 0.98)	0.64 (0.43, 0.96)
32.25–36.59	0.74 (0.49, 1.11)	0.78 (0.52, 1.16)
36.60–40.39	0.54 (0.36, 0.80)	0.55 (0.37, 0.82)
≥40.40	0.56 (0.37, 0.83)	0.53 (0.36, 0.79)
β per 5% calories (95% CI)	−0.139 (−0.286, 0.009)	−0.152 (−0.299, −0.004)
p-value	0.065	0.044
% calories from protein		
<13.40	0.58 (0.39, 0.87)	0.60 (0.40, 0.90)
13.40–15.44	0.63 (0.42, 0.94)	0.63 (0.42, 0.93)
15.45–17.09	0.61 (0.41, 0.92)	0.60 (0.40, 0.90)
≥17.10	0.65 (0.44, 0.96)	0.64 (0.43, 0.95)
β per 5% calories (95% CI)	0.031 (−0.316, 0.379)	0.000 (−0.344, 0.345)
p-value	0.859	0.999
% calories from alcohol		
<0.40	0.67 (0.45, 1.01)	0.72 (0.47, 1.09)
0.40–1.69	0.70 (0.47, 1.05)	0.67 (0.45, 1.00)
1.70–5.94	0.64 (0.43, 0.95)	0.62 (0.42, 0.92)
≥5.95	0.48 (0.32, 0.72)	0.49 (0.33, 0.73)
β per 5% calories (95% CI)	−0.123 (−0.292, 0.046)	−0.119 (−0.289, 0.050)
p-value	0.154	0.167
Total carbohydrates (g/day)		
<138.40	0.51 (0.34, 0.76)	0.42 (0.26, 0.68)
138.40–175.54	0.53 (0.36, 0.79)	0.48 (0.32, 0.73)
175.55–232.69	0.69 (0.46, 1.03)	0.67 (0.45, 1.00)
≥232.70	0.78 (0.53, 1.17)	1.07 (0.61, 1.86)
β per 10g (95% CI)	0.017 (−0.008, 0.042)	0.061 (0.006, 0.116)
p-value	0.189	0.031
Fiber (g/day)		
<10.70	0.64 (0.43, 0.95)	0.84 (0.53, 1.33)
10.70–13.94	0.81 (0.54, 1.21)	0.92 (0.61, 1.37)

	Age-adjusted	Multivariable adjusted [c]
13.95–19.94	0.57 (0.38, 0.85)	0.51 (0.34, 0.75)
≥19.95	0.49 (0.33, 0.73)	0.37 (0.23, 0.60)
β per 5g (95% CI)	0.003 (−0.124, 0.131)	−0.048 (−0.238, 0.142)
p-value	0.959	0.622
Total sugars (g/day)		
<60.40	0.43 (0.29, 0.63)	0.41 (0.26, 0.63)
60.40–80.44	0.62 (0.42, 0.92)	0.58 (0.39, 0.86)
80.45–112.04	0.66 (0.44, 0.98)	0.66 (0.44, 0.98)
≥112.05	0.83 (0.56, 1.24)	0.94 (0.60, 1.49)
β per 5g (95% CI)	0.015 (−0.006, 0.036)	0.020 (−0.008, 0.048)
p-value	0.156	0.162
Glycemic index		
<51.65	0.47 (0.32, 0.71)	0.44 (0.30, 0.66)
51.65–53.73	0.78 (0.52, 1.16)	0.78 (0.53, 1.16)
53.74–55.74	0.58 (0.39, 0.86)	0.59 (0.40, 0.88)
≥55.75	0.69 (0.46, 1.02)	0.71 (0.48, 1.05)
β per 1 unit (95% CI)	0.012 (−0.039, 0.063)	0.023 (−0.028, 0.074)
p-value	0.646	0.372
Glycemic load		
<62.94	0.45 (0.30, 0.68)	0.42 (0.26, 0.66)
62.94–82.41	0.71 (0.47, 1.05)	0.64 (0.42, 0.97)
82.42–109.13	0.69 (0.45, 1.00)	0.67 (0.45, 0.99)
≥109.14	0.69 (0.46, 1.02)	0.81 (0.48, 1.35)
β per 5 units (95% CI)	0.019 (−0.005, 0.044)	0.051 (0.008, 0.094)
p-value	0.122	0.020

[a] Geometric means of AMH were estimated using generalized linear regression models; p-values are from tests of linear trend with dietary exposures modelled as continuous variables

[b] AMH values are presented in ng/ml

[c] Adjusted for age, body mass index, energy intake, smoking, and current use of oral contraceptives

Table 3.

Geometric means of AMH (95% CI) according to quartiles of dietary fat measures [a,b]

	Age-adjusted	Multivariable adjusted [c]
Total fat (g/day)		
<45.59	0.61 (0.41, 0.91)	0.82 (0.49, 1.37)
45.59–62.52	0.63 (0.42, 0.94)	0.71 (0.47, 1.07)
62.53–84.70	0.71 (0.48, 1.06)	0.67 (0.45, 1.00)
≥84.71	0.53 (0.35, 0.79)	0.37 (0.21, 0.67)
β per 10g (95% CI)	−0.010 (−0.073, 0.053)	−0.141 (−0.295, 0.012)
p-value	0.760	0.071
Saturated fat (g/day)		
<13.38	0.68 (0.46, 1.02)	0.84 (0.50, 1.38)
13.38–18.91	0.54 (0.36, 0.81)	0.57 (0.38, 0.87)
18.92–25.17	0.67 (0.45, 1.00)	0.66 (0.45, 0.99)
≥25.18	0.59 (0.39, 0.88)	0.46 (0.25, 0.82)
β per 5g (95% CI)	0.009 (−0.091, 0.108)	−0.066 (−0.298, 0.166)
p-value	0.866	0.577
Monounsaturated fat (g/day)		
<17.81	0.64 (0.43, 0.95)	0.89 (0.54, 1.48)
17.81–24.97	0.64 (0.43, 0.96)	0.75 (0.49, 1.13)
24.98–32.86	0.69 (0.46, 1.03)	0.67 (0.45, 1.00)
≥32.87	0.51 (0.34, 0.76)	0.32 (0.18, 0.58)
β per 5g (95% CI)	−0.015 (−0.094, 0.065)	−0.150 (−0.320, 0.019)
p-value	0.720	0.082
Polyunsaturated fat (g/day)		
<10.54	0.62 (0.42, 0.93)	0.85 (0.52, 1.37)
10.54–14.25	0.77 (0.52, 1.15)	0.86 (0.57, 1.30)
14.26–19.56	0.60 (0.40, 0.90)	0.58 (0.39, 0.86)
≥19.57	0.51 (0.34, 0.75)	0.34 (0.20, 0.59)
β per 5g (95% CI)	−0.047 (−0.174, 0.081)	−0.244 (−0.480, −0.008)
p-value	0.473	0.043
Total ω−3 fatty acids (g/day)		
<1.01	0.65 (0.43, 0.97)	0.82 (0.51, 1.30)
1.04–1.41	0.72 (0.48, 1.08)	0.77 (0.51, 1.16)
1.42–1.94	0.52 (0.35, 0.78)	0.49 (0.33, 0.73)
≥1.95	0.59 (0.40, 0.88)	0.47 (0.28, 0.78)
β per 1g (95% CI)	−0.078 (−0.329, 0.172)	−0.300 (−0.695, 0.095)
p-value	0.539	0.136
Total ω −6 fatty acids (g/day)		
<9.38	0.58 (0.39, 0.86)	0.80 (0.49, 1.29)
9.38–12.62	0.82 (0.55, 1.23)	0.91 (0.60, 1.37)
12.63–17.45	0.62 (0.42, 0.93)	0.60 (0.40, 0.89)

	Age-adjusted	Multivariable adjusted [c]
≥17.46	0.49 (0.33, 0.73)	0.33 (0.19, 0.58)
β per 1g (95% CI)	−0.011 (−0.039, 0.018)	−0.053 (−0.105, −0.001)
p-value	0.465	0.044
Ratio of ω −6 to ω −3 fatty acids		
<8.09	0.52 (0.35, 0.77)	0.49 (0.33, 0.74)
8.09–8.98	0.63 (0.42, 0.94)	0.68 (0.46, 1.02)
8.99–10.28	0.62 (0.41, 0.92)	0.63 (0.42, 0.93)
≥10.29	0.72 (0.48, 1.08)	0.69 (0.46, 1.02)
β per 1 unit (95% CI)	0.010 (−0.091, 0.110)	0.014 (−0.085, 0.114)
p-value	0.850	0.776
Long chain ω −3 fatty acids (g/day)		
<0.05	0.66 (0.44, 1.00)	0.73 (0.48, 1.11)
0.05–0.07	0.66 (0.44, 0.97)	0.67 (0.45, 0.98)
0.08–0.14	0.60 (0.40, 0.89)	0.57 (0.38, 0.84)
≥0.15	0.56 (0.38, 0.83)	0.53 (0.35, 0.80)
β per 0.1g (95% CI)	−0.093 (−0.278, 0.092)	−0.135 (−0.328, 0.059)
p-value	0.324	0.172
Short chain ω−3 fatty acids (g/day)		
<0.95	0.70 (0.47, 1.04)	0.86 (0.54, 1.38)
0.95–1.29	0.70 (0.47, 1.04)	0.74 (0.49, 1.11)
1.30–1.83	0.48 (0.32, 0.72)	0.46 (0.31, 0.68)
≥1.84	0.62 (0.42, 0.93)	0.49 (0.30, 0.83)
β per 1g (95% CI)	−0.068 (−0.333, 0.197)	−0.270 (−0.687, 0.146)
p-value	0.612	0.203

[a] Geometric means of AMH were estimated using generalized linear regression models; p-values are from tests of linear trend with dietary exposures modelled as continuous variables

[b] AMH values are presented in ng/ml

[c] Adjusted for age, body mass index, energy intake, smoking, and current use of oral contraceptives