

Demographic, lifestyle, and other factors in relation to antimüllerian hormone levels in mostly late premenopausal women

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Fertility and Sterility® Vol. 107, No. 4, April 2017 0015-0282/\$36.00 Copyright ©2017 American Society for Reproductive Medicine, Published by Elsevier Inc. All rights reserved http://dx.doi.org/10.1016/j.fertnstert.2017.02.105 Universitarios de Granada/Universidad de Granada, Granada, Spain; ^r CIBER de Epidemiología y Salud Pública (CIBERESP), Madrid, Spain; ^s Epidemiology and Prevention Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; ^t Department of Epidemiology, Vanderbilt University School of Medicine, Nashville, Tennessee; ^u Department of Pathology, Harvard Medical School, Boston, Massachusetts; ^v Department of Pathology, University of Maryland School of Medicine, Baltimore, Maryland; ^w Cancer Epidemiology Unit, University of Oxford, Oxford, United Kingdom; ^x Danish Cancer Society Research Center, Copenhagen, Denmark; ^y Hellenic Health Foundation, Athens, Greece; ^z World Health Organization Collaborating Center for Nutrition and Health, Unit of Nutritional Epidemiology and Nutrition in Public Health, Department of Hygiene, Epidemiology and Medical Statistics, University of Athens Medical School, Athens, Greece; ^{aa} Department of Epidemiology, Harvard T. H. Chan School of Public Health, Baltimore, Maryland; ^{bb} Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts; ^{cc} Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; ^{dd} Department of Community Medicine, Faculty of Health Sciences, University of Tromsø, The Arctic University of Norway, Tromsø, Norway; ^{ee} Department of Research, Cancer Registry of Norway, Institute of Population-Based Cancer Research, Oslo, Norway; ^{ff} Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; and ⁹⁹ Genetic Epidemiology Group, Folkhälsan Research Center, Helsinki, Finland

Objective: To identify reproductive, lifestyle, hormonal, and other correlates of circulating antimüllerian hormone (AMH) concentrations in mostly late premenopausal women.

Design: Cross-sectional study.

Setting: Not applicable.

Patient(s): A total of 671 premenopausal women not known to have cancer.

Intervention(s): None.

Main Outcome Measure(s): Concentrations of AMH were measured in a single laboratory using the picoAMH ELISA. Multivariableadjusted median (and interquartile range) AMH concentrations were calculated using quantile regression for several potential correlates.

Result(s): Older women had significantly lower AMH concentrations (≥ 40 [n = 444] vs. <35 years [n = 64], multivariable-adjusted median 0.73 ng/mL vs. 2.52 ng/mL). Concentrations of AMH were also significantly lower among women with earlier age at menarche (<12 [n = 96] vs. ≥ 14 years [n = 200]: 0.90 ng/mL vs. 1.12 ng/mL) and among current users of oral contraceptives (n = 27) compared with never or former users (n = 468) (0.36 ng/mL vs. 1.15 ng/mL). Race, body mass index, education, height, smoking status, parity, and menstrual cycle phase were not significantly associated with AMH concentrations. There were no significant associations between AMH concentrations and androgen or sex hormone-binding globulin concentrations or with factors related to blood collection (e.g., sample type, time, season, and year of blood collection).

Conclusion(s): Among premenopausal women, lower AMH concentrations are associated with older age, a younger age at menarche, and currently using oral contraceptives, suggesting these factors are related to a lower number or decreased secretory activity of ovarian follicles. (Fertil Steril® 2017;107:1012–22. ©2017 by American Society for Reproductive Medicine.) **Key Words:** Antimüllerian hormone, demographic, lifestyle, ovarian reserve, reproductive factors

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ntimüllerian hormone (AMH) is a member of the transforming growth factor- β superfamily, produced by the granulosa cells of preantral and small antral ovarian follicles (1–4). Studies show a strong positive correlation between circulating AMH concentrations and the number of follicles (5) and age at menopause (6–8). The correlation of the number of ovarian oocytes retrieved during IVF with AMH is reported to be higher than with FSH, inhibin B, or E₂ (1). Antimüllerian hormone is relatively stable throughout the menstrual cycle (1, 9–14) compared with other ovarian hormones (1). Thus, AMH seems to be a sensitive and stable marker of ovarian reserve in premenopausal women.

Numerous studies have demonstrated that AMH is associated with ovulatory disorders, such as primary ovarian insufficiency, polycystic ovary syndrome (PCOS), and ovarian hyperstimulation syndrome (15, 16). Women with a low AMH concentration respond poorly to fertility treatment (17). Antimüllerian hormone also decreases progressively with increasing age, becoming undetectable a few years before menopause (6–8). Therefore, AMH is a valuable reference in both clinical and research settings for prediction of ovulatory disorders, fertility, and reproductive lifespan. Animal and experimental studies reported that AMH may inhibit the development of cancer, particularly in organs that are of Müllerian origin and/or express AMH receptors (18), whereas recent epidemiologic studies found significant positive associations between AMH concentrations and breast cancer risk (19–21) but not with ovarian or prostate cancer risks (22, 23).

Evidence on individual characteristics associated with AMH has been inconsistent. Some studies have reported significantly lower AMH concentrations associated with oral contraceptive use (9, 24–27), higher body mass index (BMI) (28–33), earlier age at menarche (26, 27, 34, 35), parity (35), alcohol consumption (36), and smoking (27, 37, 38), but these associations have not been consistent in other studies (8–10, 26, 27, 35, 36, 39–44). Many earlier studies included women who were infertile or who had PCOS, which may have influenced associations and reduced

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