Associations Between Physical Activity and Age-Related Anti-Mullerian Hormone Decline: Insights from All of Us Research Program

Article type: Short Communication

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Acknowledgments: We gratefully acknowledge All of Us participants for their contributions, without whom this research would not have been possible. We also thank the National Institutes of Health's All of Us Research Program for making available the participant data examined in this study.

Financing: Not applicable

Conflict of Interest: None to report

Author Contributions: PC: Conceptualization, data curation, methodology, writing – original draft, writing – review & editing, project administration; RL: Conceptualization, writing – original draft, writing – review & editing; MZ: conceptualization, data curation, software, formal analysis, writing – original draft, writing – review & editing; REL: writing – original draft, writing – review & editing; SS: Conceptualization, data curation, methodology, writing – original draft, writing – review & editing, project administration, supervision.

Manuscript word count: 1685

Abstract word count: 216

Number of figures and tables: 2

Accepted, in-press

ABSTRACT

Background: Anti-mullerian hormone (AMH) is used to measure ovarian reserve and female fertility levels. Physical activity is thought to influence fertility and warrants further investigation, especially using objective measures.

Methods: Using the All of Us Research Program dataset, the relationship between normal age-based decline in AMH and levels of physical activity were examined. Inclusion criteria were: ≥ 1 AMH test in electronic health record, AMH level < 7 ng/ml, and ≥ 30 days of valid Fitbit data within 1 year prior to AMH test. Final dataset included 24 participants.

Results: Generalized linear regression models were fitted between log transformed AMH level and daily average activity intensity minutes (sedentary, lightly active, fairly active and very active) and daily step counts. Daily average of "very active" minutes showed a trend towards a positive effect on preventing the decline of AMH levels (B = 0.02 (95% CI 0-0.04), p = 0.136), though results were not statistically significant.

Conclusion: Despite its small sample size, this study is one of the first to report a positive correlation, approaching significance, between objectively measured physical activity and preserving AMH, suggesting that daily high intensity physical activity may extend ovarian reserve. Further studies, with large, diverse samples are needed to provide clearer numbers for optimal engagement in physical activity and AMH level for fertility.

Keywords: Fitbit, fertility, fecundity, women, exercise

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INTRODUCTION

Infertility is a prominent issue for women and their partners. Nearly 14% of premenopausal women in the United States have impaired fecundity, the physiological ability to produce a child.[1] Impaired fertility is not only associated with reduced fecundity (e.g., disruption of ovarian function, fallopian tube obstruction, physical characteristics of uterus)[2] but also with social factors, such as prolonged times of unwanted non-conception (i.e., postponing pregnancy).[3,4] For women seeking to conceive, fertility can be evaluated via physical exams, laboratory tests, and/or imaging. Often, anti-mullerian hormone (AMH; produced by the granulosa cells of antral follicles), a marker of ovarian reserve, is used to predict age-based decline in fecundity and prediction of the response during ovarian stimulation in treating infertility. Serum AMH levels increase in childhood, reaching their maximum around age 15, remaining stable until around age 25, and then progressively decline to menopause.

In addition to age and other biological factors, many lifestyle behaviors (e.g., physical activity, smoking, and alcohol) are believed to influence ovarian reserve. With regards to physical activity, consensus regarding its influence on fertility remains somewhat unclear, with studies reporting contradicting findings (i.e., positive, negative, or no relationship).[5,6] For example, results of a systematic review by Hakimi and Cameron posit the presence of a U-shaped association between physical activity and ovulation, suggesting that moderate physical activity can assist women in maintaining optimal hormonal balance and regular ovulation.[7] These results are supported by findings from Kiranmayee et al., who reported that self-reported regular, physical activity was associated with improved age-specific levels of ovarian reserve markers, including AMH.[8] Findings from another systematic review and meta-analysis (all self-reported measures of physical activity) support the possibility that vigorous physical activity may negatively impact fertility, but contradict aforementioned reports by concluding no association between moderate physical activity and fertility.[9] A third systematic review, which reported mixed findings, also highlighted the need for additional research using objective measures of physical activity (e.g., activity tracking devices) and fertility (e.g., serum AMH) in lieu of previously relied upon subjective instruments.[6]

The All of Us Research Program (AoURP) dataset provides a unique opportunity to retrospectively study the effects of physical activity on fertility using wearable and clinical data. Run by the National Institutes of Health, AoURP aims to collect health-related information (e.g., electronic health records, genomics, physical measures, participant surveys and wearables) from 1 million or more Americans, with a particular focus on populations typically underrepresented in biomedical research. This study analyzed the AoURP dataset to examine the relationship between normal age-based decline in AMH and varying levels of physical activity.

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METHODS

Study Population

The study population was sourced from the National Institutes of Health AoURP database (dataset v7; R2022Q4R9), available to authorized users on the Research Workbench. All participants provided written informed consent at the time of study enrollment, and institutional review board approval was obtained for primary data collection.[10,11] To preserve participant privacy, data provided to researchers through the Researcher Workbench undergoes extensive de-identification and data transformation procedures. Secondary analysis of the de-identified data was considered not human subjects research by the Henry Ford Health Institutional Review Board. All aspects of the project adhered to the tenets of the Declaration of Helsinki.

Among 409,420 participants enrolled as of February 15, 2024, participants needed to meet the following criteria to be included in the current sample: a) 1+ AMH test records in their electronic health records (Logical Observation Identifiers Names and Codes 38376-8), b) normal AMH level range (< 7ng/ml)[12], and c) 30+ days of valid Fitbit data (more than 10 hour heart rate data at given day)[13,14] within 1 year prior to AMH test date.

Statistical Analysis

For participants with multiple AMH test results, the earliest test result was used for the following analysis. AMH test results were log-transformed with *log* (*AMH*+1). Daily average minutes were calculated for four different activity intensity measurements, based on metabolic equivalents (METS), from Fitbit activity summary table: sedentary (< 1.5 METS), lightly active (1.5-3.0 METS), moderately-fairly active (3.0-6.0 METS), and very active (> 6 METS). Daily average steps count was also calculated for valid days within a year prior to AMH test date.[13-17]

To explore the potential association between physical activity and AMH, a series of generalized linear regression models (GLM) were fitted between log transformed AMH level and the four daily average activity intensity minute measurements and daily step counts. Each model was adjusted for the age when AMH was tested (AMH age). All statistical analysis codes were edited and executed with R 4.0.1 in AoURP Workbench. GLMs were built in the pre-installed "stats" package.

RESULTS

Within the AoURP dataset (V7: R2022Q4R9) dataset, 1381 participants had AMH test results and 14,947 participants had Fitbit data. Of which, 71 participants had both AMH test results and Fitbit data. After removing participants whose AMH test result values were abnormal (> 7 ng/ml) or missing, 60 participants remained. Participants without 30+ days of valid Fitbit data within 1 year prior to their AMH test date were then removed, resulting in a final sample of 24 participants from 6 different states. The majority of participants were White and from Pennsylvania. See Table 1 for further cohort characteristics.

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Results of the GLMs are presented in Table 2. Despite a limited sample size, results of the GLMs suggest that a unit increase of daily average of "very active" minutes has a positive effect, approaching significance, on preventing the decline of AMH level (*B* = 0.02, 95% CI 0-0.04, *p* = 0.136). Age, a known factor to cause AMH decline, was negatively associated with AMH in all 6 models.

DISCUSSION

Here, we describe preliminary findings regarding the association of age-based decline in AMH and levels of physical activity among women using a AoURP dataset. AMH has long been a biomarker used to predict ovarian reserve. Given that many women are waiting longer to pursue motherhood and that AMH levels naturally decline starting in a women's mid-twenties, it is important to understand how other factors, such as modifiable lifestyle behaviors, can influence AMH levels and fertility. The aim in presenting these preliminary results is to encourage other researchers to explore the use of objective physical activity to better understand the relationship between normal age-based decline in AMH.

Despite a small sample, there was a positive correlation, approaching significance, between daily average of very active minutes and preserving AMH, suggesting that daily high intensity physical activity may extend ovarian reserve. We present these results for illustrative purposes only. Many studies have demonstrated a link between physical activity and fertility with inconclusive results or have focused on extreme/unhealthy amounts of strenuous physical activity and negative outcomes on female reproductive health.[5-9] Moreover, much of the literature has utilized self-reported measures of physical activity (e.g., computing outcome variables of minutes/week physical activity intensity) or fertility,[5,6] and/or measured fertility via time to pregnancy or probability of conception through retrospective comparison.[5,6,9] Self-reported data tends to overestimate physical activity due to social desirability bias (e.g., participants may overestimate their activity levels to appear healthier or more active than they are).[18,19] Recall bias is another limitation of self-reported data as participants might forget or fail to accurately recall the intensity, duration, or frequency of their physical activity, leading to inaccurate reporting, especially over longer periods.[18] Thus, in addition to our sample being too small to conduct further analyses, it is difficult to compare our results (which utilized objectively measured, daily physical activity and AMH as a measure of fertility) to previous reports, based on the aforementioned methodological differences.

In terms of practical recommendations, based on our findings, it might be beneficial for women, particularly those concerned with fertility and ovarian reserve, to incorporate regular, vigorous physical activity into their routines. However, we caution that more research is needed to determine the ideal intensity, duration, and frequency of physical activity necessary to see meaningful changes in AMH and fertility outcomes. Given the methodological limitations of prior studies that relied on self-reported physical activity, our study, which uses objectively measured activity data, provides a valuable contribution to the

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literature. It suggests that higher intensity activity could be beneficial for maintaining ovarian reserve, but more studies are needed to establish clear guidelines and causal relationships. For now, these results should be seen as exploratory, and future research should focus on expanding the sample size and further investigating the effects of different types of physical activity on fertility biomarkers like AMH.

Limitations

Although the AoURP builds a biomedical dataset from a diverse group of participants from across the United States, a limitation of the current study is the small homogenous (White and predominantly from Pennsylvania) sample - skewing results/restricting generalizability, limiting external validity, and reducing the statistical power of findings. It should also be noted that, although we adjusted the GLM for age, other factors (e.g., body mass index and ethnicity) were not adjusted for in this analysis because of the sample's small and homogenous nature. A major strength of the current study was the objective measure of physical activity; future studies should consider supplying the wearable device to participants, so ownership is not a barrier,[20,21] resulting in a more robust dataset. An additional limitation to note is that an AMH test is likely only requested/conducted if a person was having fertility issues, resulting in a sampling bias. Lastly, the majority of the data in the current study came from obese women, which may influence the relationship between physical activity and fertility.[6] Thus, a future consideration in studies with larger samples is to further explore the influence of overweight/obesity with physical activity on fertility.

Conclusion

Although AMH levels begin their natural decline in a woman's mid-twenties, many women are choosing to delay motherhood until later. Preliminary findings suggest a potential link between physical activity and AMH preservation, though larger studies are needed to confirm this association. More robust research is also needed to determine what level of preservation is needed to ensure significantly higher fecundity. Additionally, future studies (controlled, intervention-based) with large, diverse samples are also needed to provide clearer understanding and identify optimal physical activity engagement (e.g., time, intensity, and frequency) to support the preservation of AMH and increase chances of fertility.

SUMMARY – ACELERATING TRANSLATION

Title: Can Physical Activity Help Preserve Fertility? Exploring the Role of Exercise in Anti-Müllerian Hormone (AMH) Levels

Main Problem to Solve: Many women are choosing to delay motherhood until later in life. However, female fertility naturally declines with age, making it more difficult to conceive. One common way to assess fertility is by measuring anti-müllerian hormone (AMH), which reflects the number of eggs (ovarian

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reserve) a woman has. Despite this, there is limited understanding of how lifestyle factors—like physical activity—may influence AMH levels and, by extension, fertility.

Aim of the Study: To examine whether there is a relationship between objectively measured physical activity (using Fitbit devices) and AMH levels in women. This could help determine whether exercise plays a role in preserving ovarian reserve and potentially supporting fertility.

Methodology: The study used data from the National Institutes of Health "All of Us" Research Program, which collects medical and lifestyle data from a diverse U.S. population. Eligible participants were women with at least one recorded AMH test, AMH levels within the normal range (less than 7 ng/ml), and at least 30 days of valid Fitbit data within one year prior to their AMH test. The final sample included 24 participants.

Researchers analyzed the relationship between AMH levels and daily physical activity intensity—categorized as sedentary, lightly active, moderately active, and very active—as well as total daily step count. Generalized linear regression models were used to examine the relationship, adjusting for participant age.

Results: The analysis suggested a positive trend between the number of "very active" minutes per day and higher AMH levels, indicating that more intense daily physical activity may help slow the natural decline in ovarian reserve. While this finding did not reach statistical significance—likely due to the small sample size—it still provides a meaningful signal worth investigating further. As expected, age showed a negative association with AMH levels across all models.

Conclusion: This is one of the first studies to explore the relationship between physical activity and AMH using objective data from wearable devices, rather than self-reported questionnaires. The preliminary results suggest that vigorous daily physical activity could help preserve ovarian reserve, and thus support fertility.

While the findings are promising, they are based on a small, relatively homogenous group (mostly White women from Pennsylvania), which limits how broadly the results can be applied. Larger studies with more diverse populations are needed to confirm these findings and determine the optimal type, intensity, and duration of physical activity to support AMH levels and fertility.

In practical terms, women who are concerned about their fertility might benefit from incorporating regular, high-intensity exercise into their routines. However, more research is needed to provide specific guidance. These results should be considered exploratory and used to guide future studies focused on identifying lifestyle strategies to support reproductive health.

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Table 1**:** All of Us Research Program Dataset Cohort Characteristics

Cohort Characteristics	**Mean (SD)**
AMH age* (years)	35.23 (4.70)
AMH (ng/ml)	2.30 (2.05)
BMI (kg/m²)	34.70 (10.74)
Sedentary minutes/day	808.14 (180.85)
Light active minutes/day	202.11 (50.11)
Moderate-fairly active minutes/day	12.10 (8.18)
Very active minutes/day	14.14 (9.96)
Daily steps	6897.51 (2578.99)

AMH, anti-mullerian hormone; BMI, body mass index; SD, standard deviation.

*The age when AMH was tested.

Table 2: Results of Generalized Linear Regression Models between Log Transformed Anti-Mullerian Hormone (AMH) Level and Fitbit Daily Average Activity Intensity Minutes[17] and Daily Step Counts, Adjusted for AMH Age (Age in Years When AMH Was Tested) in an All of Us Research Program Dataset (N=24)

Activity	**Main Effect (95%CI)**	**P-value**	**Age Effect (95%CI)**	**P_val_age**
Sedentary minutes/day	0 (0-0)	0.440	-0.09 (-0.14 to -0.05)	0.001
Lightly active minutes/day	0 (0-0)	0.979	-0.09 (-0.14 to -0.04)	0.003
Moderate-fairly active minutes/day	0.01 (-0.02 to 0.03)	0.678	-0.09 (-0.13 to -0.04)	0.001
Very active minutes/day	0.02 (0-0.04)	0.136	-0.09 (-0.13 to -0.05)	0.001
Daily steps/1000	0.04 (-0.05 to 0.12)	0.375	-0.08 (-0.13 to -0.03)	0.003

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