Analysis of Serum Anti-Mullerian Hormone Values for Puerto Rican Women Presenting to a Fertility Center

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Objective: To characterize the AMH levels in Puerto Rican women presenting to a fertility clinic.

Methods: This was a cross-sectional study involving the acquisition of measured AMH levels from patient records dating October 2012- October 2014 (N=250). AMH levels determined by laboratory values were obtained. Data were stratified by age groups (25-29, 30-35, 35-39, 40+). Each dataset was represented as an AMH value at a single time point to determine median, mean and standard deviation for each group. Percentage of change for values were calculated comparing to previous corresponding age group and each group to 25-29 (subset 1) to evaluate declining trend.

Results: A total of 250 records were evaluated. The data was segregated into 4 different age groups and their means, medians, and standard deviations were calculated individually. Age group 25-29 AMH values with a mean of 4.94, a standard deviation of 3.17, and a median of 4.75. Age group 30-34 AMH values: mean 4.30, standard deviation 5.63, and median 3.2. Age group 35-39 AMH values: mean 2.58, standard deviation 4.83, median 1.3. Age group 40 + AMH values: mean 1.29, standard deviation 1.54, median 0.85. Results showed a reduction of 47.7% and 73.8% when values of AMH were calculated for ages 35-39 and 40+ and compared to 25-29 years, respectively.

Conclusion: The results demonstrate AMH levels among Puerto Rican women presenting to a fertility clinic supporting a decline of AMH with advancing age. [*P R Health Sci J 2019;38:262-265*]

Key words: AMH Levels, Fertility, Puerto Rican Women

Anti-Müllerian Hormone (AMH) belongs to the growth and differentiation regulating transforming growth factor-β (TGF-β) super-family. AMH or Müllerian Inhibiting Substance is a glycoprotein secreted by granulosa cells of the gonads (1,2). AMH was named given its function in fetal gender differentiation. It induces regression of the embryonal Müllerian ducts (3). By the 36th week of gestation, AMH is expressed in the ovarian granulosa cells. In the ovaries, AMH inhibits both the recruitment of resting primordial follicles and the antral follicle's sensitivity to follicle-stimulating hormone (FSH). The expression of AMH is most significant in granulosa cells from preantral and small antral follicles and diminishes gradually in larger antral follicles (4-9). From here we can conclude that AMH is expressed in stages of folliculogenesis that are independent of the hormone cycle for the most part. The mechanism of regulation for ovarian AMH production is currently unknown (10-13). The plasma AMH level in females starts low in the first month of life; it then suffers a dramatic increase during childhood leading until puberty. After the age of 20, AMH plasma levels slowly decrease and purportedly fall to undetectable levels around menopause (14-17).

AMH can be used as a marker to determine ovarian reserve in adult women. The AMH plasma level correlates positively with the number of ovarian antral follicles and negatively with the woman's age (13,14). This correlation gives use to AMH concentration as a possible biomarker to determine ovarian age. Raised AMH concentrations have been associated with Polycystic Ovarian Syndrome (PCOS); which is characterized by small antral follicles, and a lack of follicular maturation (14-16).

The role of Anti-Müllerian hormone (AMH) and its significance has been extensively studied with the intent to discover measures of ovarian dysfunction and reserve. A decrease in AMH levels usually occurs with aging, suggesting a progressive drop in the cells of the early stages of folliculogenesis.

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The author/s has/have no conflict/s of interest to disclose.

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Based on this finding, AMH has been proposed as a biomarker to assess follicular aging and ovarian reserve (15-17). Studies have been conducted to describe the tendency of AMH and its age-specific rate of decline in different populations. Furthermore, it has been determined that hormone levels might vary depending on ethnicity; there are no studies done among Puerto Rican women describing such hormone. AMH levels have shown cyclic tendencies following follicle development and possible pathologic processes, but it is the biomarker of choice for clinical evaluation, independent of cycle date (17-20). The goal of this study will be to characterize the rate of decline and establish the general tendencies for the decline of AMH in the Puerto Rican women population. Results will be sued to curtail the treatment of fertility further and vary gynecologic diagnosis that is present within populations and serve as well to extrapolate data for the treatment of women with general-like characteristics elsewhere. Future work will compare the data gathered from this study to other factors used in the treatment of the general female population by establishing tendencies in the relations between said factors.

Materials and Methods

Medical records and documented antimüllerian hormone levels from 250 women born in Puerto Rico or of Puerto Rican descent currently residing in Puerto Rico presenting to a fertility clinic were analyzed. Before commencing study, IRB approval was obtained. Using statistical analysis, an AMH nomogram was established to understand the specific age-related decline of AMH in this population. Inclusion criteria consisted of all patients evaluated at a fertility clinic between October 2012-October 2014 who had their AMH levels documented. Records must have indicated patients' age and AMH levels as reported by laboratory test performed at a private laboratory adjacent to the clinic. All patient data gathered was limited to patient's assisting said laboratory, standards for measurements included were from 0.01ng/ml-8.0ng/ml. An absence of other data points will not be an exclusion criterion. The exclusion criteria consisted of patients who presented for evaluation and had no AMH levels on their laboratory data, patients who had their laboratory studies done in another non-referral lab, the presence of other data will not constitute for inclusion into the study. No data regarding diagnosis or reason for the visit was gathered.

Any personal identifying data was not collected, and any further personal identifying information was removed before statistical analysis. The AMH levels as determined by their laboratory values were obtained from records of women who presented to a fertility clinic. It is important to state that not all patients presenting to the clinic had fertility problems, were seeking help with fertility issues, or had previous issues with AMH levels. AMH levels are ordered as routine laboratory studies for all women presenting to this clinic as a standard of care. Patients were divided by age groups {(25-29), (30-35), (35-39), (40+)}. Each data point was represented as an AMH value at a single time point to determine median, mean, and standard deviation at each age group. Percentage of change for AMH values datasets were calculated by comparison to their corresponding younger age group and each age group to 25-29 to evaluate declining trend.

Table 1. Statistical distribution of Anti-Mullerian hormone levels. Mean, standard deviation, median, and margin of error given for individual age.

Age	Number of participants per age group	Mean AMH level	Standard deviation or AMH value	Margin of error	Median AMH level value
25	14	4.60	2.82	25.336	4.6
26	3	4.36	3.43	8.521	4.7
27	7	5.93	5.18	4.791	5.5
28	8	3.71	2.36	1.973	2.9
29	12	5.39	2.27	1.442	5.18
30	12	6.63	9.61	6.105	3.35
31	15	4.43	3.93	2.269	3.65
32	18	5.65	7.71	3.834	3.1
33	13	3.38	2.43	1.468	3.3
34	24	2.55	1.59	0.671	2.5
35	21	2.67	2.44	1.111	2.2
36	12	4.06	7.22	4.587	1.3
37	17	3.23	7.53	3.876	1.1
38	21	1.85	2.62	1.193	0.99
39	18	1.73	3.45	1.716	0.42
40	12	1.25	1.42	0.902	0.56
41	10	0.96	0.76	0.544	0.8
42	6	2.52	2.9	3.043	1.49
43	3	1.90	1.57	1.648	1.2
44	3	0.83	0.33	0.820	0.72
45	3	0.49	0.36	0.894	0.45
46	1	0.24			0.24
47	0				
48	1	0.85			0.85

Results

AMH data values calculated for each age group are outlined here. For age group 1 (25-29yrs, 38 participants): mean value 4.94, STD 3.2. Age group 2 (30-34yrs, 81 participants): mean value 4.3, STD 5.7. Age group 3 (35-39yrs, 89 participants):

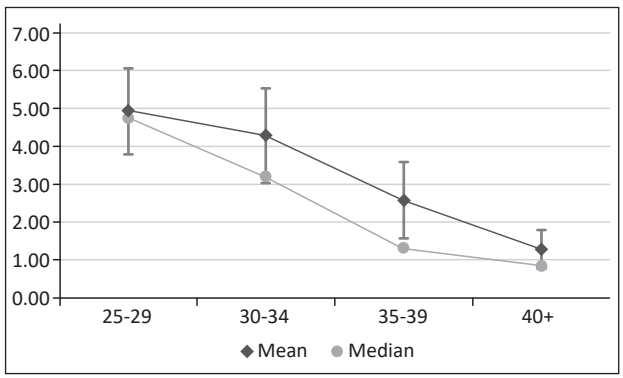

Figure 1. Mean AMH levels and age group median AMH levels versus Age Groups for the sample collected.

mean value 2.5, STD 4.9. Age group 4 (40+yrs, 42 participants): mean value 1.29, STD 1.5. AMH level change between groups was calculated as a percentage of change. Results showed a reduction of 47.7% and 73.8% of AMH values calculated for age groups 3 and 4 when compared to age group 1, respectively.

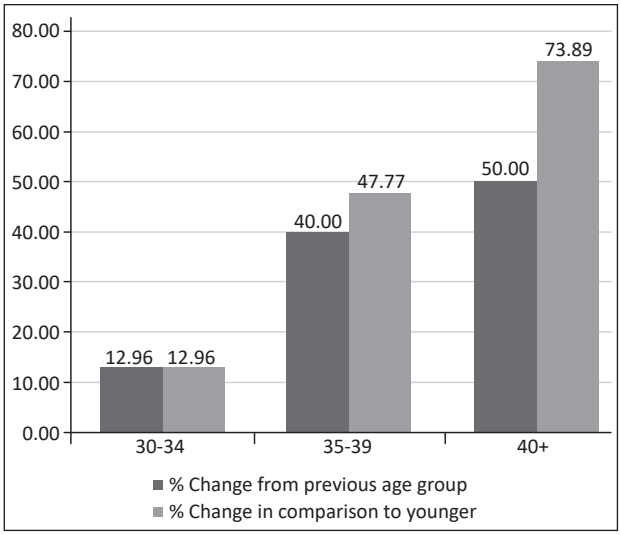

Figure 2. Percent changes between age groups and when compared to the previous younger age group.

Discussion

To establish an AMH nomogram for the Puerto Rican female population, we performed a cross-sectional study including statistical analysis of 250 patient records. AMH variations due to cyclic variation and present female status (pre- or post-menopause) were not taken into account. For age group one we found an average value of 4.49, which decreased to 4.3 in the age group 2, then further decreased by age group 3 to 2.5, and lastly to an average of 1.29 for age group 4. These variations show a steady decline in AMH levels throughout populations consistent with higher age and what has been previously studied in the literature.

The most significant difference between averages between the following groups can be found between age group 2 and 3 (difference of 1.8); this is consistent with previously established reproductive age parameters. This result further indicates that AMH therapy should be a consistent factor in reproductive treatment for women in the age group 3 and above. This study also establishes the trend that by age 35 AMH values half dropped approximately by half their peak values. By perimenopausal age, the decline is almost to a quarter of the original levels. This observation directly correlated with the decline in reproductive function observed and established in the literature.

Studies have demonstrated an independent effect over AMH levels in varying ethnicities (11-12, 21-22). In comparison to women of White ethnicity, Hispanic women tended to have lower AMH levels after controlling for other factors; Hispanic women also had lower AMH values than women of Black ethnicity (11, 21-22). The data in our study correlates with decreasing AMH values with increasing age. Mean values of AMH correlate closely with other values presented in previous studies comparing AMH values from varying female ethnicities. It is essential to recognize the decreased AMH levels of Hispanic women and by extension Puerto Rican women given the association with premature ovarian failure and correlation between AMH and menopause. It can be stipulated that given the causal relationship of AMH to ovarian reserve, women of Hispanic ethnicity may pertain to having a lower ovarian reserve and should, therefore, be followed more closely when considering fertility studies and procedures.

In summary, the present study establishes and demonstrates the correlation of AMH levels amongst Puerto Rican women presenting to a fertility clinic. The established nomogram will serve to curtail fertility treatment more specifically to the population, and the established values can be extrapolated to other similar populations. Comparison of AMH levels between our study and previous studies of Hispanic populations coincide reaffirming a direct effect of ethnicity over AMH levels. Limitations of this study include its population of women presenting to a fertility clinic and lack of correlation to other related variables. Further work should develop the relationship between the established nomogram and other reproductive factors as well as clinical history and diagnosis.

Resumen

Objetivo: Caracterizar niveles de AMH en mujeres puertorriqueñas que acuden a una clínica de fertilidad. Métodos: se adquirió los niveles de AMH de registros de pacientes que datan entre octubre 2012 a octubre de 2014 (N = 250). Los datos se estratificaron por grupos de edad (25-29, 30-35, 35-39, 40+). La data se representó como un valor de AMH dado un tiempo único para determinar mediana, media y desviación estándar por grupo. El porcentaje de cambio para valores se calculó comparando el grupo de edad correspondiente anterior y contra subconjunto 1 para evaluar la tendencia decreciente. Resultados: se evaluaron un total de 250 registros. Los datos se segregaron en 4 grupos por edades diferentes y se calculó la media, mediana y desviacion estándar individualmente. Los valores del subconjunto 1 obtuvo una media de 4.94, desviación estándar de 3.17 y mediana de 4.75. Valores del subconjunto 2: media 4,30, desviación estándar 5,63 y mediana de 3,2. Valores del subconjunto 3: media 2.58, desviación estándar 4.83, mediana 1.3. Valores del subconjunto 4: media 1,29, desviación estándar 1,54, mediana 0,85. Los resultados mostraron una reducción de 47.7% y 73.8% dado las medidas calculadas para subconjunto 3 y 4 en comparación con subconjunto 1, respectivamente. Conclusión: Los resultados demuestran que niveles de AMH entre mujeres puertorriqueñas representadas en una clínica de fertilidad apoyan la teoría de disminución de AMH con el avance de la edad.

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