INVESTIGATING THE UTILITY OF ANTI-MÜLLERIAN HORMONE IN YOUNG WOMEN WITH CHRONIC KIDNEY DISEASE

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OBJECTIVES

Women with chronic kidney disease (CKD) have menstrual and gonadal dysfunction mainly manifesting as hormonal imbalance. AMH plays a critical role in folliculogenesis, with circulating levels directly reflecting the number of developing preantral follicles and indirectly the number of primordial follicles in the ovaries[1].

The aims of this study were to:

A. measure serum AMH concentrations in women of childbearing age with CKD
B. explore potential factors affecting AMH and
C. compare AMH levels with age-matched healthy controls

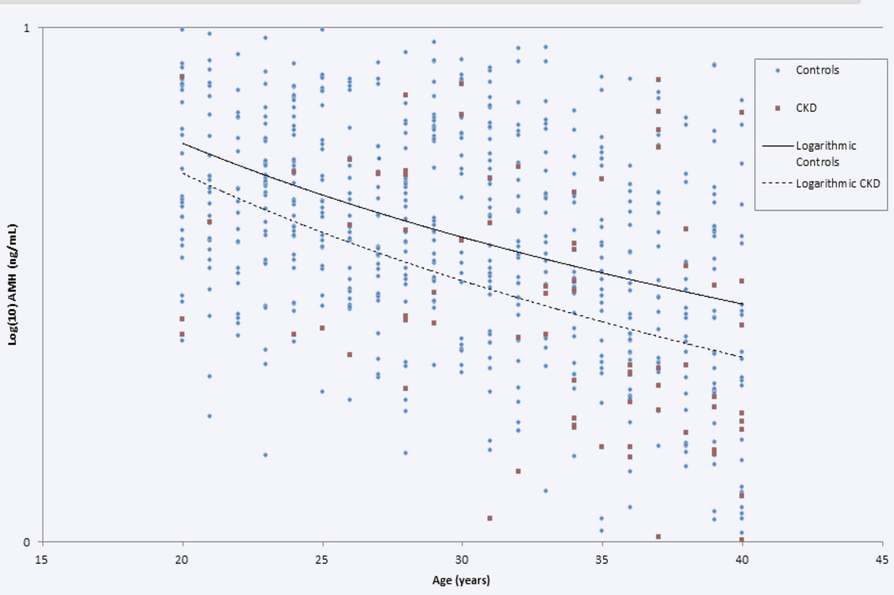

Figure 1. Log AMH levels in young women with CKD (n=77) compared to AMH levels in a cohort of 600 age-matched healthy women (p<0.001, two-sample z-test). Data are log-transformed.

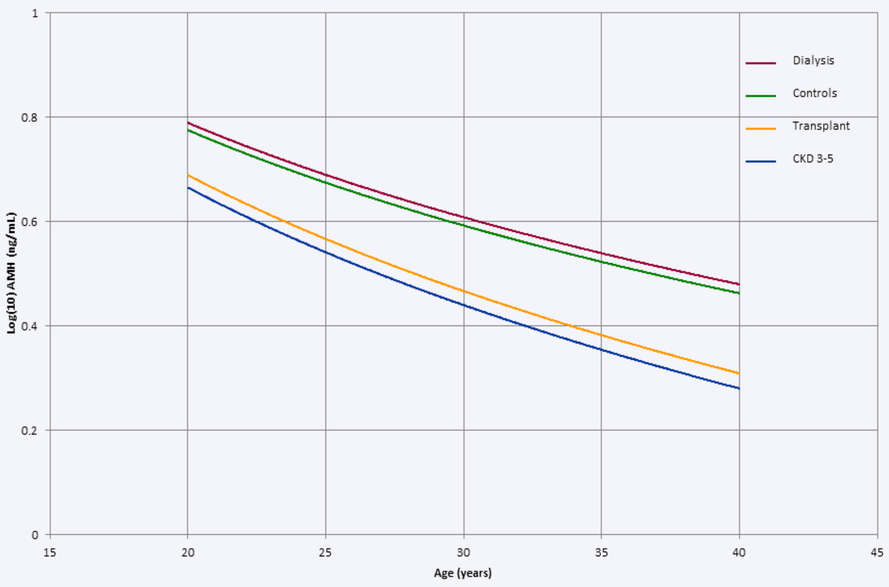

Figure 2. Age-related distribution of serum log AMH levels in women of reproductive age with CKD stages 3-5 (n=26), on HD (n=26), kidney transplant recipients (n=25) and healthy controls (n=600). Data are log-transformed.

METHODS

- Single-centre cohort study of all women aged 18-40 years attending renal services between August 1, 2015 and March 31, 2016 in our catchment area (serving a population of approximately 1.5 million).
- We measured serum AMH levels in 3 distinct groups of patients; women with CKD stages 3-5, women on haemodialysis (HD), and kidney transplant recipients.
- AMH levels from a multicentre study using the same assay in 600 age-matched healthy women with regular menstrual cycles, not on contraception were used as the reference group[2].
- AMH was measured on first thaw of stored samples using an automated method on a clinically validated platform (e411, Roche Diagnostics, Burgess Hill, UK)[3].
- For all comparisons, values of AMH were log transformed to normalise their distribution and were analysed as continuous variables.
- Correlation analyses were performed to assess the relationship between log transformed AMH and each predictor variable. Variables tested were age, weight, alcohol and smoking history, eGFR, CKD group, cause of established renal failure (ERF), biochemical parameters (reproductive hormones, thyroid hormones and CRP), day of menstrual cycle, presence or not of menstrual periods, and medications potentially related to follicular growth (contraceptives, steroids, cyclophosphamide).

RESULTS

- We measured AMH levels in 77 women of childbearing age who were attending the renal services and fulfilled the study entry criteria. Twenty-six had CKD stages 3-5, 26 were on HD, and 25 had a kidney transplant.
- Mean age of the enrolled participants was 32.9 (SD 5.4) years, 38 (49.3%) had regular menstrual periods, and approximately a third were on hormonal contraception. More than half had previous successful pregnancies and 18 (23.4%) had at least one miscarriage in the past. Six women (7.8%) had a history of PCOS.
- Median AMH was higher in HD patients (2.9, IQR 1.1-5.2ng/mL) compared to CKD stages 3-5 patients (1.6, IQR 0.7-2.2ng/mL) and transplant patients (1.5, IQR 1.0-4.2ng/mL).
- When multiple linear regression analysis was performed, there was an average 4% (95%CI 0.02 to 0.06, p<0.001) decrease in AMH level per year increase in age when accounting for the CKD group. Patients on HD had higher AMH levels by 53% (95%CI 0.20 to 0.98, p=0.002) compared to CKD patients, following adjustment for age. No differences were found between the other CKD groups. The multiple regression model fit was R-squared=0.24 (Table 1).
- Women with CKD had substantively lower AMH levels than healthy women (1.7, IQR 0.9-3.8ng/mL vs 3.0, IQR 1.9-5.0ng/mL, p<0.001) (Figure 1).
- When stratified by CKD group, in comparison with healthy age-matched women controls, AMH was lower in women with CKD stages 3-5 (1.6 vs 3.0ng/mL, p<0.001) and women with a kidney transplant (1.5 vs 3.0ng/mL, p<0.001) but not in women on HD (2.9 vs 3.0, p=0.27) (Figure 2).

Table 1. Covariates associated with AMH levels

Covariate	Multiple linear regression		
	Ratio of geometric means (Bootstrap 95%CI)	p-value	R-square
Age (each additional year)	-0.04 (-0.06 to -0.02)	<0.001	0.24
CKD group			
CKD (reference)	1.0	-	
HD	0.53 (0.20 to 0.98)	0.002	
Transplant	0.06 (-0.18 to 0.36)	0.70	

AMH, anti-Müllerian hormone; CI, confidence interval; CKD, chronic kidney disease; HD, haemodialysis.

CONCLUSIONS

- In women of reproductive age with CKD or a renal transplant, AMH exhibits a similar age-related decline but age-specific values are lower than equivalent healthy controls.
- For women on HD circulating AMH concentrations are higher, suggesting a disruption of folliculogenesis or impaired clearance.
- AMH evaluation may be a useful biochemical test in estimating the reproductive lifespan in women with CKD not treated with dialysis, pursuing preconception counselling.
- Further research is warranted to investigate the direct impact of uraemia on ovarian follicles and AMH production.

References

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