Reviewer’s report

Title: Exclusion of pregnancy in dialysis patients: diagnostic performance of human chorionic gonadotropin

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Reviewer: Andrea G. Kattah

Reviewer's report:

This is a study looking at the diagnostic performance of hcg for the diagnosis pregnancy in women on dialysis. The goal was to determine what level of hcg would rule out pregnancy in women on dialysis to help in the provision of care, in particular anesthesia and procedures. 71 consecutive dialysis patients ages 18 to 50 years of age at dialysis units in Vienna Austria were recruited. Samples were collected before dialysis for hCG, FSH, LH and AMH. They determined whether women were fertile or infertile based on gynecologic history and hormonal profile and presented hCG cut-offs in fertility and infertility.

Some thoughts for the authors to consider:

1. One major question I have that is not clear in the text is what the 'definition' of fertility or infertility are. The others reference two articles in the methods, but one is a review on menopause and CKD and the other is a consensus statement on reproductive aging, which reviews the different stages of menopause in a presumably non-CKD population. Do the authors mean infertile to mean menopausal? One easy and acceptable way to assess fertility is by the presence/absence of menstrual periods in a woman not on contraception, but it is not clear to me if this is the standard that was used. Also, menopausal should be clearly defined (absence of periods or by FSH status). If readers are to interpret different hCG levels in infertile vs. fertile dialysis patients, knowing what fertile and infertile means is critically important. Do providers need to draw an HCG, AMH, LH and FSH prior to a procedure to correctly rule out pregnancy?

2. Once the authors explain and justify how they determined fertility status, I think a table with the hormone levels in the two groups, rather than a Table with them all lumped together would be useful (Table 3 could be divided into the two groups).

3. Hormones fluctuate dramatically during the month in young, premenopausal women with ongoing menses, and so the authors should describe when they drew the hormones. Was it at random or at a specific point in the menstrual cycle for women with continued periods. AMH and hCG would not be expected to fluctuate, but FSH and LH would and this could affect the results, particularly if fertility status was based on an FSH concentration.

4. Were any of these women on hormonal contraception? How do the authors think that would impact hormone levels?
5. In the discussion, the authors cite work showing that women on dialysis go into menopause 4.5 years earlier than healthy women. However, this is a point of controversy, as many women on dialysis labeled as 'menopausal' will have the return of periods after transplant or even after intensive dialysis. Determining who is truly menopausal and who has hypothalamic dysfunction due to advanced kidney disease is more complicated and I think the authors have the ability to use their data to see if there are distinct subsets of women in their population. When with marked elevations in FSH and no periods vs. those with only mild elevation in FSH/LH and no periods, who may simply have secondary amenorrhea. At a minimum, a discussion of this is warranted if the authors do not have the numbers to subset out different populations.

6. Would suggest that in the conclusion of the discussion, the authors state clearly what cut-off should be used. If they are saying less than 5 is definitive, but if higher than that, providers need to know whether someone is fertile or not. If infertile, 14 is fine, but if fertility status is unknown, best to go with 25. Is this correct?

7. In Table 4, what does current menstrual cycle mean? Patient 7, for example, has a current menstrual cycle, but also premature ovarian failure? Also, I do not think the Study ID should be included in the Table. Definitions of premature menopause and cut-offs used should be included in methods and in the Table legend.

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