Reviewer’s report

Title: The Increasing Rates of Acute Interstitial Nephritis in Australia: A Single Centre Case Series

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Reviewer: Cynthia Nast

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This study examines the incidence and causes of acute interstitial nephritis over time in a single center to corroborate the recent findings of the Australian Institute of Health and Welfare report on acute kidney injury, which found an increase in acute interstitial nephritis and pyelonephritis in women under 55 years of age. In this single center, the rate of acute interstitial nephritis increased from 2000-03 to 2012-15, with an increase in women with AIN. The authors suggest this is due to an increase in immune-mediated AIN, which is more common in women less than 55 year old. They also found that those with antibiotic and PPI/H2 blocker associate AIN were older than those with other etiologies of AIN.

COMMENTS

1. Inclusion of cases with acute tubular necrosis in addition to acute interstitial nephritis should be done, as ATN may accompany interstitial nephritis and may be why the renal function was not worse in their AIN only patients. By excluding those with concomitant ATN and AIN due to the causes assessed in this study, the data may be skewed. It would be informative to include AIN cases with and without ATN.

2. The authors need to address the possibility of a change in practice patterns or in referring entities (such as a rheumatology clinic) over the time of the study to exclude the possibility that the reported increase in women with autoimmune AIN is due to the patient population and not a true increase in incidence. The number of men and women getting renal biopsies during the different time periods should be added as the denominator to ensure the increase in women with AIN is not reflective of an increase in women getting renal biopsies.

3. The authors focus on autoimmune disease, but do not address the fact that NSAID-induced AIN was not identified prior to 2008. The authors should address why this occurred and if this fact contributed to the increase in AIN in women as they report that, in the later years of the study, NSAIDs were being used by younger patients relative to the other medications studies.
4. Figure 2 is unnecessary as it is largely redundant with figure 3. Figure 2 should be deleted and replaced with a figure showing the incidence of the different causes of AIN over time and by gender.

5. On page 9, lines 56 - 58 the manuscript states "Patients who received steroid treatment had on average lower serum creatinines compared to those who did not receive treatment." The authors need to address why this was the case, as it seems that higher creatinine levels would prompt steroid therapy. Was this because those with higher creatinines had more fibrosis?

6. While the authors acknowledge the small numbers in their study, this really does preclude meaningful statistical analysis and any solid conclusions. These data can be expanded as noted in comment 1 above and with data from other institutions.

7. Dyslipidaemia data are missing from Table 1. The meaning of 15< in the UPC column in Table 2 is unclear. The AKI severity grading are provided in Table 2 and should be deleted from Table 3.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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