

Reviewer's Comments:

- 1) Do you know what type, i.e. MPGN, Membranous, FSGS, ?HIV?
- 2) I would conduct an ANOVA test to report the differences in frequency among cases and controls. Include the p value.
- 3) While you did enroll patients, this study is not prospective in its design because you already knew the outcome (ESRD). You therefore cannot determine incident ESRD. All you can say is whether there is an association or not. You can perhaps say that the validation of this association may facilitate further research in inflammation and offer therapeutic incites towards ESRD.
- 4) In Figure 1 please Include the number of patients in each of these subgroups.
- 5) In Table 2 please include OR for row Genotype/Alele G.
- 6) Table 3 is very confusing. Why are there 3 columns of p values.? Please conduct ANOVA and include one p value for each of these predictors.
- 7) In the discussion, I would first say that the frequency of Genotype polymorphisms was higher among the ESRD patient population.
- 8) In the discussion, please elaborate why age is such a significant predictor to patients with ESRD and TNF-Alpha polymorphism.
- 9) In the discussion, be careful correlation is not the same as saying associated. Correlations are reported with a correlation coefficient.
- 10) In a separate paragraph include limitations. Please include the typical limitations with case control studies including sampling bias, low sample size and unmeasured confounding.
- 11) Conclusions should be more robust. Why is it important and what are the future implications?

Author's Feedback:

- 1) Our patient population comprised of MGN (n=36), RPGN (n=30), polycystic (n=6), IgA (n=18) and Idiopathic (n=6). Since all these forms are categorized under glomerulonephritis, we clubbed these 96 patients under the said category.
- 2) The difference in frequency among cases and controls is stated as indicated. P value is also given.
- 3) We have eliminated the prospective. The study is designated as hospital based case-control study. Also corrections have been made regarding the association and not determination of incident ESRD.
- 4) Figure 1 represents the histogram in which data is expressed as percentage for visual comprehension. The number of patients in subgroups is shown in Table 2. Representing number of patients in figure 1 would result in repetition of data in Figure 1 and Table 2.
- 5) In Table 2 include OR for Allele G has been included (G is actually referant allele there).
- 6) In Table 3 we earlier calculated significance of different parameters across three different genotypes, however in order to eliminate confusion we have conducted ANOVA and included the single p value for each parameter.
- 7) In the discussion, we have mentioned the higher frequency of genotype among the ESRD patient population.
- 8) Response to why age is such a significant predictor to patients with ESRD and TNF-Alpha polymorphism:

Age differences in the prognostic significance of eGFR observed here probably reflect a variety of different phenomena. The lower incidence of ESRD among older compared with younger patients with similar levels of eGFR is likely due, at least in part, to their greater competing risk for death. Other considerations include the greater likelihood that older patients are long-term CKD survivors and thus by definition have nonprogressive or slowly progressive disease. Differences in outcomes may also reflect age differences in the underlying cause of low eGFR. Perhaps in older patients, low eGFR functions more commonly as a “marker” for a variety of other age-related coexisting comorbid conditions and thus tends to be a better predictor of “global” health outcomes (e.g., mortality) than of more “specific” renal outcomes. In contrast, in younger patients, perhaps low eGFR results more frequently from a single disease affecting the kidney and thus may better predict renal outcomes. An additional consideration is that some loss of GFR is believed to occur as part of “normal” aging.

With respect to TNF-Alpha polymorphism:

Because TNF- α AA genotype is associated with an increased expression of TNF- α levels, carriers of AA genotype may experience an exacerbated inflammatory response that would in turn result in worsening of the inflammation and rapid progression of disease.

9) In the discussion, correlation has been modified and the term association is used instead.

10) Limitations of study have been included.

11) Conclusions have been made more robust and specific.