ELEVATED UREA IN THE ELDERLY: AGE OR RENAL FUNCTION? – A DATABASE ANALYSIS

Chung JZY, Jones GRD
Chemical Pathology, SydPath, St Vincent’s Hospital, Sydney, Australia.
jchungzy@gmail.com

Introduction

- Increasing age is known to be associated with elevations in serum urea in adults.
- Consideration has been given to the use of age-related reference intervals for urea.
- However, it is unknown whether the age-related increase in urea is due to the increased prevalence of reduced renal function in the elderly population, or is an unrelated age effect.
- We investigated the relationship between urea, age and eGFR from samples processed over a 15 month period.

Aim

- To elucidate the relationship between urea, age, and eGFR.

Methods

- An extract was performed on the SydPath database to retrieve results from all samples processed between August 2011 and January 2013 for which analyses for both urea and creatinine had been performed.
- The data was filtered to exclude patients under 18 years of age.
- Both inpatients and outpatients were included in the study.
- Results of 272,102 urea and creatinine determinations were obtained from samples representing 79,887 patients.
- Estimated Glomerular Filtration Rate (eGFR) was calculated using the CKD-EPI formula.
- Serum urea concentrations were separately graphed as functions of eGFR and age. Centiles were determined from binned data.
- Serum urea concentrations were sub-stratified according to eGFR. For each stratification, median urea concentrations were determined for selected age bins and overlaid on the graph showing urea as a function of age.

Results

- A strong inverse relationship between urea and eGFR was demonstrated (Figure 1).
- Urea concentrations were also positively associated with age on a population level (Figure 2).
- When stratified according to eGFR, this relationship was no longer apparent, that is, urea was not associated with age for a given eGFR (Figure 3). This is illustrated by the flat profiles of the median lines for each eGFR stratification.

Discussion

- The observed increase in urea with decreasing eGFR is not surprising. Note that patients with known dialysis were not excluded from this study.
- The increase in urea with age has been characterised in this population which comprises both outpatients and hospital inpatients.
- 25% of patients older than 60 have urea concentrations above the SydPath upper reference limit (8.5 mmol/L), rising to 50% in patients older than 83.
- The disappearance of the age-related increase in urea when stratified for eGFR suggests that the age-related increase in urea can be completely accounted for by the age-related decline in renal function.
- Although renal function is the major determinant, many extra-renal factors also influence serum urea concentration, including dietary protein intake and total body protein turnover. These factors may also vary with age. Note is again made of the study population, which included hospital inpatients.
- Since renal function is more directly related to serum urea than age per se, consideration may be given to two dimensional reference intervals whereby the reference limits of urea can be constructed as a function of eGFR.
- An eGFR-related reference interval may be derived by generating a graph similar to Figure 1 using data collected from a reference population. Appropriate upper and lower reference limits may be derived from appropriate centiles corresponding to defined eGFR bins. It would also be possible to observe the distribution of urea values corresponding to individual eGFR bins.
- By way of example, using the data derived from the present study population, the 90th centile of urea was 9.2 mmol/L for the defined eGFR bin 60-90 mL/min/1.73m², compared to 13.2 mmol/L for eGFR 45-60 mL/min/1.73m² and 18.2 mmol/L for eGFR 30-45 mL/min/1.73m² (Figure 1).
- Age-related reference limits for urea are still considered reasonable, whereby age functions as a surrogate marker for renal function.

Conclusion

- The observation of elevated urea in the elderly population may be completely accounted for by considering the age-associated decline in renal function.
- On a population level, urea levels are associated with decreasing eGFR in a relationship that is otherwise largely independent of age.