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Donors at risk: haematuria

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GUIDELINES

No recommendations possible based on Level I or II evidence

SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

- **The discovery of microscopic haematuria in potential donors needs further investigation to determine if this is clinically significant. Underlying urological and renal disease should be excluded before proceeding to donation.**
- **No recommendations regarding potential donors with thin basement membrane disease (TBMD) can be made.**

IMPLEMENTATION AND AUDIT

Short- and long-term living kidney donor outcomes need to be closely monitored.

BACKGROUND

Microscopic haematuria is commonly encountered in potential kidney donors. The implications of this vary greatly. It may signify a false positive result or be a transient insignificant finding. However, it may also signify the presence of important underlying pathology in the donor.

The aim of this guideline is to provide guidance regarding the investigation and further assessment of these prospective donors. There is no good data regarding the long-term outcome for donors with what is judged to be 'benign haematuria'.

SEARCH STRATEGY

Databases searched: MeSH terms and text words for kidney transplantation were combined with MeSH terms and text words for living donor, and combined with MeSH terms and text words for haematuria. The search was carried out in Medline (1950 – January Week 2, 2008). The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline.
Date of searches: 15 January 2008.

WHAT IS THE EVIDENCE?

There are no studies that have properly examined the issue of microscopic haematuria in potential donors. Thus, there is very little evidence on which to base strong recommendations regarding this issue. General population studies demonstrate that microscopic haematuria is a common and often 'benign' or transient disorder in otherwise normal individuals. In most of these studies, extensive investigations have not been performed to delineate any underlying pathology and the implications of kidney donation have not been examined or clearly defined.

Asymptomatic microscopic haematuria is found in up to 21% of the general community.[1–3] This should be investigated in all potential live donors to exclude significant urological disease and underlying renal pathology. The prevalence of haematuria depends on the clinical scenario e.g. haematuria as an isolated finding is very common whereas persistent haematuria is less often encountered (serial measures >3 months). Persistent microscopic haematuria is observed in up to 3% of the general population.[4]

One possible cause of incidentally discovered haematuria, is underlying mild IgA disease. A report by Suzuki *et al.* reported that latent IgA mesangial 'disease' was diagnosed in approximately 16% of live kidney donors and deceased donors considered to be otherwise normal.[5] The long-term implications of live donation in these individuals has not been specifically studied.

Case reports exist regarding donors with known underlying glomerular pathology.[6–8] In most cases these people are highly motivated to donate, have good renal function, and minimal pathology at the time of assessment. It is not possible to make formal recommendations based on the strength of these reports.

Both microscopy and dipstick (reagent strip) urine testing are recommended. Reagent strips can be very useful tools, however, these may produce false positive but uncommonly, false negative findings. Because erythrocytes can lyse in the urine over time, the processing of fresh samples for microscopy is essential. For this reason, negative results by microscopy need to be interpreted with some caution. If cells have lysed then urine microscopy may be negative and reagent strip testing may be positive. It is recommended that

microscopy with centrifugation (examination of urine sediment) is performed. Specimens that are not examined by centrifugation are not reliable at excluding microscopic haematuria.

A minimum of two reagent dipstick and two microscopy tests is recommended to increase the possibility of detecting intermittent haematuria. If these tests are positive, then a further 3 specimens need to be analysed over 2–3 months to determine if the haematuria is 'persistent'. Persistent microscopic haematuria requires full urological evaluation to exclude major pathology such as malignancy or stones, and may require a renal biopsy to exclude underlying significant renal disease.

The likely diagnoses in patients with microscopic haematuria include: thin basement membrane disease (TMBD), IgA nephropathy and hereditary nephritis.[5,9–11] Acceptance of individuals with TBMD as live donors remains a controversial clinical issue for which there is limited long-term data. There is general consensus that patients with TBMD who have risk factors for progressive disease, such as proteinuria, hypertension, or overt renal insufficiency, should not be donors. In addition, detailed assessment of the potential donor's family history, presence of haematuria in family members, and extrarenal manifestations of Alport syndrome may help identify potential donors at risk of having underlying subclinical disease.

SUMMARY OF THE EVIDENCE

There are no studies that have properly examined the issue of haematuria in live kidney donors. Most of our information comes from studies of the incidence of haematuria in the general population and from the known pathological associations with this finding. Case reports exist in the literature, describing donors with known glomerular abnormalities with good short-term outcomes for donor and recipient. No large, prospective, controlled studies have been performed.

WHAT DO THE OTHER GUIDELINES SAY?

British Transplant Society / British Renal Association:
An extensive, 100-page document has been produced outlining similar issues to those discussed here. The full version of these British Live Donor Guidelines is available at: www.bts.org.uk and at www.renal.org

- Persistent microscopic haematuria in the potential living donor requires full investigation to identify an underlying cause, up to and including renal biopsy if there is no obvious urological explanation. Where there is insufficient evidence to quantify the risks following histological diagnoses of renal pathology, donation is not recommended.
- Advice from a clinical geneticist is recommended when a diagnosis of thin membrane disease is made as new data is being generated all the time.

The Amsterdam Forum:
A short manuscript outlining similar issues to those discussed here.

Isolated microscopic hematuria (defined as 3–5 urinary sediment red blood cells (RBCs)/HPF) may not be a contraindication to donation. RBCs with glomerular origin have a dysmorphic appearance observed by phase-contrast microscopy and automated RBC analysis. Patients with persistent microscopic hematuria should not be considered for kidney donation unless urine cytology and a complete urologic work up are performed. If urological malignancy and stone disease are excluded, a kidney biopsy may be indicated to rule out glomerular pathology such as IgA nephropathy.

European Renal Association-European Dialysis and Transplant Association:
(Nephrol Dial Transplant 2000): Exclusion criteria include: 'reduced GFR (in comparison to normal range for age), proteinuria >300 mg/day, microhematuria (except when a urologic evaluation and possible kidney biopsy are normal), or hypertension without good control'.

SUGGESTIONS FOR FUTURE RESEARCH

1. Prospective, controlled studies on long-term living kidney donor outcomes, including an assessment of the utility of tests for haematuria and outcomes of donors with isolated urinary abnormalities such as microscopic haematuria.
2. Registry for living kidney donors. Including practice patterns on selection of living kidney donors.

CONFLICT OF INTEREST

John Kanellis has no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by CARI.

Frank Ierino has no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by CARI.

REFERENCES

1. Mohr DN, Offord KP, Owen RA *et al*. Asymptomatic microhematuria and urologic disease. A population-based study. *JAMA* 1986; **256**: 224–29.
2. Messing EM, Young TB, Hunt VB *et al*. Home screening for hematuria: results of a multiclinic study. *J Urol* 1992; **148**: 289–92.
3. Froom P, Gross M, Ribak J *et al*. The effect of age on the prevalence of asymptomatic microscopic hematuria. *Am J Clin Pathol* 1986; **86**: 656–57.
4. Jaffe JS, Ginsberg PC, Gill R *et al*. A new diagnostic algorithm for the evaluation of microscopic hematuria. *Urology* 2001; **57**: 889–94.
5. Suzuki K, Honda K, Tanabe K *et al*. Incidence of latent mesangial IgA deposition in renal allograft donors in Japan. *Kidney Int* 2003; **63**: 2286–94.
6. Yachnin T, Iaina A, Schwartz D *et al*. The mother of an Alport's syndrome patient: a safe kidney donor? *Nephrol Dial Transplant* 2002; **17**: 683–84.
7. Sessa A, Pietrucci A, Carozzi S *et al*. Renal transplantation from living donor parents in two brothers with Alport syndrome. Can asymptomatic female carriers of the Alport gene be accepted as kidney donors? *Nephron* 1995; **70**: 106–9.

8. Sukai K, Muramatsu M, Oriwara H *et al*. Living related kidney transplantation in a patient with autosomal recessive Alport syndrome. *Clin Transplant* 2003; **17**(Suppl 10): 4–8.
9. Murakami S, Igarashi T, Hara S *et al*. Strategies for asymptomatic microscopic hematuria: a prospective study of 1,034 patients. *J Urol* 1990; **144**: 99–101.
10. Topham PS, Harper SJ, Furness PN *et al*. Glomerular disease as a cause of isolated microscopic haematuria. *Q J Med* 1994; **87**: 329–35.
11. Sobh MA, Moustafa FE, el-Din Saleh MA *et al*. Study of asymptomatic microscopic hematuria in potential living related kidney donors. *Nephron* 1993; **65**: 190–5.