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ARE WE JUSTIFIED IN THE DISMISSING MICROSCOPIC PYURIA OF 1 -9 WBC ML-1 AS NORMAL IN SYMPTOMATIC PATIENTS?

Hypothesis / aims of study

There is growing interest in chronic cystitis in the aetiology of overactive bladder (OAB). The tests used routinely to exclude urinary tract infection (UTI) have been discredited, catalysing a critical analysis of our assumptions. The Kass criterion used for diagnosing UTI is based on data from patients with acute pyelonephritis without justification for application to other symptomatic groups. Urinary dipsticks being calibrated to this criteria, prove particularly misleading. The detection of microscopic pyuria remains the best surrogate marker of infection. The literature recommends the threshold ≥10 wbc μl^{-1} suggestive of pathological pyuria but there are no data to justify this. Thus pyuria in the range 1-9 wbc μl^{-1} merits scrutiny to test its innocence (1). There are other measures of immune activation in the urinary tract suitable as independent arbiters of the true pathology (2). Lactoferrin which chelates iron thereby starving microbes, is elevated in urine in patients with acute UTI. Urothelial cells constitutively express IL-6 and studies show rapid increases in IL-6 after the onset of infection. Urothelial cells when infected with microbes, signal their distress by expressing ATP. We capitalised on the immune properties of these three proteins to scrutinise the significance of pyuria1-9 wbc μl^{-1} and ≥10 wbc μl^{-1}.

Study design, materials and methods

A prospective observational study was conducted from February 2011 to July 2012. Patients presenting with OAB were recruited from incontinence clinics and clean-catch midstream urine samples obtained. Healthy control volunteers were recruited from hospital staff. Light microscopy was performed on fresh urine for leucocytes and urothelial cell counts by blinded investigators. Aliquots of spun urine were frozen at -80°C which were analysed for Lactoferrin and IL6 by high sensitivity ELISA and ATP using a luciferin-luciferase assay.

Results

There were 75 controls (F=49 M=26; Mean age 38.1yrs sd=15.8) and 340 patients (F=314; M=26; Mean age 58.6yrs sd=16.6); 100 patients had OAB no pyuria, 120 had OAB pyuria 1-9 wbc μl^{-1} and 120 OAB ≥ 10 wbc μl^{-1}. Pyuria 1-9 wbc μl^{-1} was clearly associated with inflammatory urinary tract disease. Regression analysis revealed significant associations with urinary lactoferrin ($R= .41$, $t=4$, $p<0.001$) and, IL6 ($R=.42$, $t=3.3$ $p=.001$). ATP reflected only pyuria ≥ 10 wbc μl^{-1}. It seems that pyuria 1-9 wbc μl^{-1} has been overlooked because of spectrum bias between the poles of zero pyuria and pyuria≥ 10 wbc μl^{-1}.

Figure 1: Lactoferrin and pyuria in OAB patients

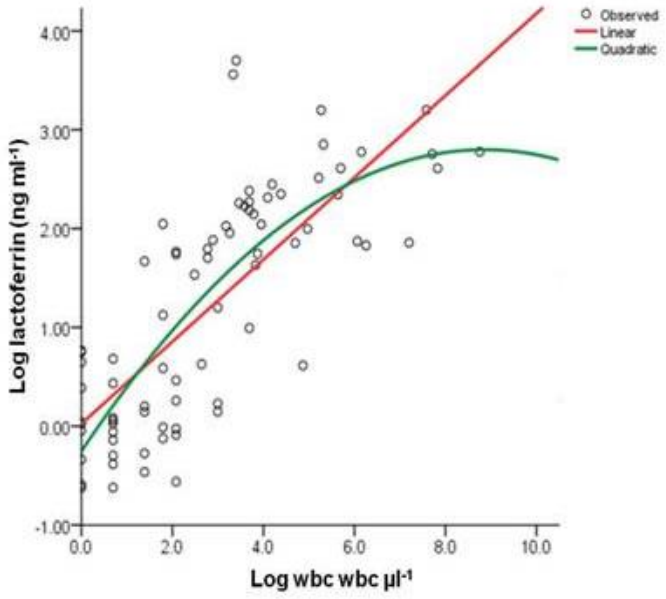
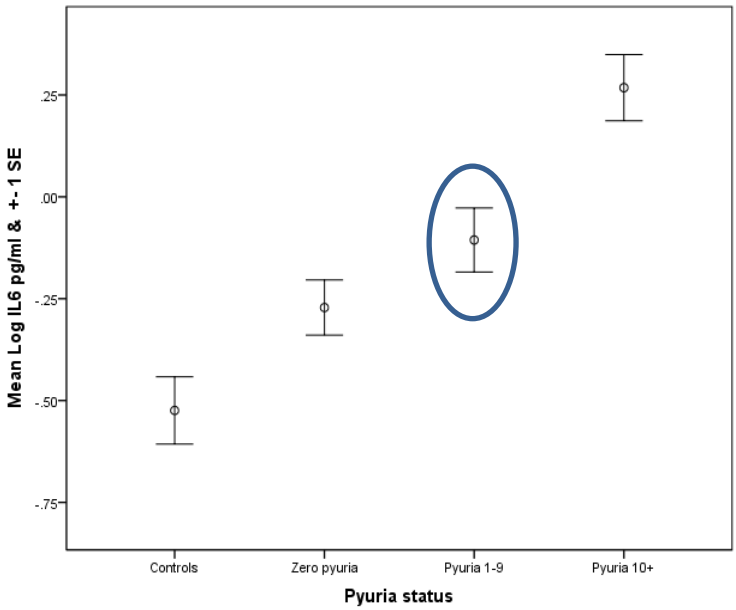


Figure 2: IL6 and pyuria in OAB patients



Interpretation of results

These data support the hypothesis that symptomatic patients with a pyuria1-9 wbc μl^{-1}, have evidence of an inflammatory signal in their urine significantly higher than that of control participants.

Concluding message

It is universally accepted that in all patients presenting with urgency and frequency the exclusion of UTI is mandatory. These data indicate that we need to reassess the implications of pyuria ≤10 wbc μl^{-1} in symptomatic patients as its occurrence may infact be an important marker of significant disease.

References

1. (1) Neurourol Urodyn 2009;28(7):754-5.
2. (2) Eur J Clin Invest. 2008 Oct;38 Suppl 2:29-38

Disclosures

Funding: None **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** This work was conducted with approval from the Whittington and Moorefield's Research Ethical Committee, London. **Helsinki:** Yes **Informed Consent:** Yes