

# Predictive value of urinary interleukins (IL-6 and IL-8) for differentiating between asymptomatic and symptomatic bacteriuria in elderly patients

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## Introduction

Urinary tract infections (UTIs) are the main reason for antibiotic prescriptions in the elderly (1). However, asymptomatic carriage of bacteria in the urine (ASB) is also common, with prevalence of 32-50% in women, and 30-34% in men (2).

Accurate diagnosis of UTI (and differentiation from ASB) is complicated by a range of factors (subtle symptoms, poor memory recall, interpretation of complex lab results). Diagnosis of ASB also requires the clinician to 'ignore' the presence of positive urine culture result and pyuria (3).

Consequently, cases of ASB may often be treated unnecessarily with antibiotics (3).

Biomarkers (especially IL6 and IL8) could be a way of quickly differentiating UTI from ASB (and could be incorporated into a POCT in the future)

- Krzemien *et al* (4) – found that IL6 and IL8 levels were higher in febrile UTI vs ASB
- Sunden & Wallt (5) – investigated IL6 and IL8 in urines from 35 elderly patients with ASB and UTI. Urine concentrations of IL6 (but not IL8) shown to differentiate between ASB and UTI

## Methods

Serial urine samples (n=88) were collected from 23 asymptomatic elderly patients in two geriatric wards of a community hospital.

Patients were recruited provided they met the following inclusion criteria: >70 years old, with an expected duration of stay >1 week. The exclusion criteria was a urinary catheter *in situ*, a renal transplant or prostate procedure and patients who had already been in the hospital for 1 week or more.

Upon receipt into the laboratory, samples underwent urinalysis for WBCs, RBCs, and bacteria on a Sysmex UF1000i (Figure 1), and qualitative culture of 10µl on CLED agar. Samples were then tested for IL6 and IL8 biomarkers using a Bio-Plex Pro™ Human Cytokine 2-plex Assay (BioRad) (Figure 1). This kit is designed to detect biomarkers in serum.

## Results

All patients had at least one urine sample which was positive on culture. Biomarker testing on urine samples from a random selection of 14 patients revealed that IL6 and IL8 could be detected in urine samples using this kit, and that there was some association between high IL6/8 levels and the high WBC and bacterial counts.

Based on this, testing was then performed on the remaining samples. Graphs were plotted to compare relationships between the levels of the biomarkers, and the WBCs levels from the urinalysis testing (Figures 2A and B).

The graphs show that the majority of the results cluster close to 0. We believe that these correspond to patients who have ASB. None of these patients were treated.

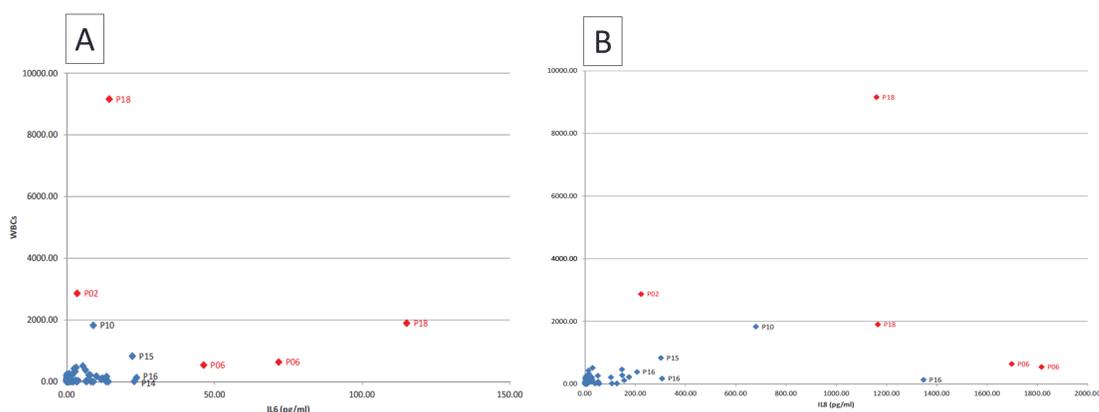


Figure 2: Graph showing the relationships between white blood cell (WBC) counts, and urinary interleukins (in pg/ml) for both A: IL6, and B: IL8.

NB: Shading in red denotes those with strong suspicion of UTI.



Figure 1: A: Dipsticks used in conventional UTI diagnosis, B: the Bio-Plex Pro™ human cytokine 2-plex assay, C: the Sysmex UF1000i analyser

## Aims

To investigate whether urinary interleukins (IL6 and IL8) are useful biomarkers for differentiating between ASB and UTI in elderly patients for whom accurate diagnosis based on clinical symptoms may be difficult.

Table 1: showing the maximum levels of IL6 and IL8 for the patients with elevated biomarker profiles

Patient	Outlier on graph (maximum level of IL in ng/ml)		Suspect UTI?	Antibiotics given?
	IL6	IL8		
P02	Yes (400.5)	Yes (1949.9)	Yes	Yes
P06	Yes (152.6)	Yes (1816.4)	Yes	Yes
P10	Yes (8.95)	Yes (680)	No evidence of UTI	No
P12	Yes (6.77)	Yes (107)	No	No
P14	No	Yes (127)	No	No
P15	Yes (22.2)	Yes (302)	No	No
P16	Yes (23.6)	Yes (1347)	No evidence of UTI	No
P18	Yes (115.05)	Yes (1165)	Yes	Yes
	maximum level of IL in ng/ml (not plotted)		Suspect UTI?	Antibiotics given?
	IL6	IL8		
Control 1	33	1143	Yes	Yes
Control 2	31.81	1750	Yes	Yes
Control 3	3.62	1416.1	Yes	Yes

NB: Pink shaded row is to highlight a patient where the biomarkers suggest UTI, but clinical results are discrepant.

There were several patients where the biomarker values for IL6 and/or IL8 were outliers (according to visual inspection of the graphs) (Table 1).

- Three of these (P02, 06 and 18) subsequently (and independent to our findings) received treatment for UTI.
- From the biomarker values, P16 looks suspect for a UTI, but there was no evidence clinically.

Three urines from known UTI positive patients were anonymised and tested in order to check IL6 and IL8 thresholds (Table 1). Levels are in agreement with our findings.

## Conclusions

Although only a small number of urines have been tested there is some evidence that urinary interleukins (IL-6 and IL-8) may be useful for differentiating between asymptomatic and symptomatic bacteriuria in elderly patients. Additional research is required to define appropriate thresholds of IL6 and IL8 in conjunction with urinalysis findings.