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Urinary Tract Infections in Infants and Children in Developing Countries in the Context of IMCI

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URINARY TRACT INFECTIONS

CAH

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Introduction

Urinary tract infections (UTI) are a common cause of febrile illness in young children. Due to lack of overt clinical features in children less than two years, appropriate collection of urine samples and basic diagnostic tests at first-level health facilities in developing countries, UTI are not generally reported as a cause of childhood morbidity. UTI are not included in the current Integrated Management of Childhood Illness (IMCI) algorithm as the main focus has been preventing mortality and severe morbidity by identifying children at risk of serious diseases including malaria, measles, meningitis, pneumonia, diarrhoeal diseases and malnutrition. Some countries have included assessment and management of dengue or streptococcal sore throat in the IMCI algothrim. However, in many countries without malaria and with a high measles vaccine coverage, the fever box of the IMCI algorithm provides limited guidance for health workers in first-level health facilities.

Several years ago, South Africa suggested including UTI identification in IMCI based on dipstick urinalysis for leucocytes and nitrites but this approach has been largely discarded. Oman, with basic laboratory facilities at primary health care level decided to include UTI management in its IMCI adaptation through screening febrile or symptomatic children with urine microscopy and referring those with urine white cells of 20 per cubic mm or more for paediatric consultation (personal communication).

The studies included in this review were identified by a search on Medline and PubMed of the relevant scientific literature published in English from 1966 to the present. UTI in children was linked with the following keywords: developing countries, IMCI, epidemiology, aetiology, risk factors, diagnosis, symptoms, signs, diagnosis, urinalysis, treatment, prevention, prognosis, urinary tract abnormalities, vesico-ureteric reflux, acute pyelonephritis, renal scarring, hypertension, renal imaging, chronic renal failure, reflux nephropathy and end stage renal failure. Additional material was obtained from other sources including internet searches and personal communication.

Extensive research has been conducted in developed countries on the epidemiology, risk factors, aetiology, diagnosis, treatment, prognosis and prevention of UTI in children. Initially this review will summarize relevant UTI literature from developed countries as in comparison fewer studies have assessed its importance in developing countries. Next, findings from UTI studies in children from developing countries will be presented. Subsequently the information will be combined and possibilities for UTI identification and management in first-level health facilities through IMCI will be suggested while indicating difficulties. Finally, necessary research questions will be suggested.

Review of urinary tract infection in children in *developed* countries

EPIDEMIOLOGY, AETIOLOGY AND RISK FACTORS

Urinary tract infections (UTI) are one of the most common bacterial infections seen in children. It has been estimated that UTI are diagnosed in 1% of boys and 3-8% of girls. In the first year of life UTI is more prevalent in boys with rates of 2.7% compared with 0.7% in girls (Riccabona 2003). Most infections in boys occur in the first three months of life (Roberts and Akintemi 1999; Schalger 2001) but by school age, the rate has decreased in boys and increased in girls (Riccabona 2003). Studies have shown a 10-12 fold increased risk of UTI in uncircumcised boys (Roberts and Akintemi 1999; Wiswell 2000). The reported rate of recurrent UTI is around 12-30% with risk greater in infants < 6 months, severe vesico-ureteric reflux and abnormal nuclear renal scans at time of first infection (Panaretto, Craig et al. 1999).

UTI has accounted for febrile presentations in 7.5% of 442 infants <8 weeks, 5.3% of 945 infants <1 year, 4.1% of 501 children <2 years and 1.7% of 664 children <5 years (Schalger 2001). The Pediatric Research in Office Settings (PROS) Network of the American Academy of Pediatrics study showed UTI in 9% of 3066 febrile infants, ≤ 3 months and 10% of these had bacteraemia (Newman, Bernzweig et al. 2002). Meningitis has been reported in 3-5% of infants in the first month of life with bacteraemic UTI (Wiswell 2000).

Gram negative organisms are those most commonly isolated from urine samples of children with uncomplicated UTI with *Escherichia coli* (*E. coli*) accounting for 70 to 90% of infections (Schalger 2001; Riccabona 2003).

Surveys have demonstrated bacteriuria in asymptomatic children of all ages from premature infants to school age children. It is now accepted that asymptomatic bacteriuria does not present a risk to a child of any age and screening for bacteriuria in the asymptomatic child is not indicated (Roberts and Akintemi 1999; Liao and Churchill 2001).

DIAGNOSIS OF UTI

Clinical predictors of UTI

Few studies have assessed the frequency, sensitivity, specificity and predictive value of symptoms and signs associated with UTI in children (American Academy of Pediatrics 1999; Roberts and Akintemi 1999). Fever is the commonest symptom of UTI in infants and the presence of another source of fever on clinical examination does not exclude UTI (Shaw, Gorelick et al. 1998). In infants and young children symptoms and signs of UTI tend to be non-specific. Older children may have symptoms including loin or abdominal pain, frequency, dysuria, urgency, hesitancy, enuresis and haematuria (Steele 1999). The 1999 American Academy of Pediatrics practice parameter, based on the accompanying technical report, recommended that UTI should be considered in any child younger than two years of age with unexplained fever. (American Academy of Pediatrics 1999; Downs 1999).

A study of 2411 febrile children with a rectal temperature ≥ 38.5°C, (males up to one year and females up to two years) showed a UTI prevalence of 3.3% overall. Higher prevalence occurred in children with malodorous urine

or haematuria (8.6%), abdominal or suprapubic tenderness (13.2%), children who appeared ill (5.7%) or had fever of ≥ 39°C (3.9%) though these signs were uncommonly elicited. Symptoms of vomiting, diarrhoea, irritability and poor feeding were common in febrile children with UTI but equally common in those febrile due to other causes (Shaw, Gorelick et al. 1998). The PROS study showed fever ≥38°C of duration ≥24 hours also to be a predictor of UTI (OR=1.8, 95% C.I.=1.2-2.8) (Newman, Bernzweig et al. 2002). A UK study has reported that a history of urine smell was unlikely to be of benefit in UTI diagnosis (Struthers, Scanlon et al. 2003). Studies have shown no difference in clinical symptoms in children with bacteraemic and non-bacteraemic UTI (Bachur and Caputo 1995; Honkinen, Jahnukainen et al. 2000).

Acute pyelonephritis is a UTI with systemic features including fever, vomiting, abdominal or loin pain, and lethargy (Craig and Hodson 2004). Nuclear renal scans have suggested that the majority of febrile young children with UTI will have acute pyelonephritis (Shaw, Gorelick et al. 1998; Wiswell 2000). Available studies with data to assess fever as a marker of pyelonephritis (defined by a positive scan) provide a wide range of sensitivity (53% to 84%) and specificity (44% to 92%) (American Academy of Pediatrics Committee on Quality Improvement 1999). Diagnosing acute pyelonephritis using clinical and laboratory parameters are unreliable in children particularly those less than two years (Riccabona 2003).

Viral and yeast infections and inflammation of the external genitalia with vulvitis, and vaginitis may present with frequency and dysuria. Schistosomiasis presents with frequency, dysuria and haematuria, is more prevalent in older children > 10 years of age but heavy worm loads usually occur in younger age groups.

Laboratory diagnosis of UTI

Urine obtained by suprapubic aspirate (SPA) or transurethral catheter in young children is unlikely to be contaminated and is the preferred specimen for documenting UTI. SPA is considered the gold standard for diagnosing UTI. A catheter urine specimen when compared to SPA, has a sensitivity of 95% and specificity of 99%. Cultures of urine specimens obtained by a bag applied to the perineum are 100% sensitive but have specificity between 14-84%. The definitive diagnosis of UTI in young children requires semi-quantitative culture of urine obtained by SPA or catheterisation. The method of urine collection determines the number of colony forming units that are significant as the distal urethra may be colonized by the same bacteria that cause UTI (American Academy of Pediatrics 1999).

Urine culture results can take 24 to 72 hours to become available. Urine screening tests have been investigated in many settings to assist the presumptive diagnosis and treatment of UTI. Urinalysis using rapid dipstick tests for leucocyte esterase and nitrite or identification of leucocytes or bacteria on urine microscopy has been studied. No element of the urinalysis or combination of elements is as sensitive and specific as a semi-quantitative urine culture for diagnosing UTI. Dipstick tests for blood and protein have a poor sensitivity and specificity with respect to screening for UTI (American Academy of Pediatrics 1999).

A meta-analysis published in 1999 concluded both Gram stain and dipstick analysis for nitrite and leucocyte esterase performed similarly in detecting UTI in children and were superior to microscopic analysis for pyuria (Gorelick and Shaw 1999). A 2002 meta-analysis combining a multi-variant approach concluded pyuria ≥ 10 per high power field with bacteriuria (any) to be best for assessing the risk of UTI in children of all ages. This group was unable to definitively assess the combinations of rapid test dipsticks including leucocyte esterase and nitrite, as they stated the number of studies assessing these markers were small. The method of urine sampling and

centrifugation affected the performance of the tests. This group also concluded that pyuria alone showed the lowest performance in all age groups, particularly with a non-sterile specimen (Huicho, Campos-Sanchez et al. 2002). Despite this studies have generally shown that a negative dipstick urinalysis can exclude UTI in children particularly over two years (Wiggelinkhuizen, Maytham et al. 1988; Armengol, Hendley et al. 2001; Doley and Nelligan 2003).

Sensitivity and specificity of components of urinalysis

Test	Sensitivity % (range)	Specificity % (range)
Leukocyte esterase	83 (67-94)	78 (64-92)
Nitrite	53 (15-82)	98 (90-100)
Leukocyte esterase or nitrite positive	93 (90-100)	72 (58-91)
Microscopy: WBC	73 (32-100)	81 (45-98)
Microscopy: bacteria	81 (16-99)	83 (11-100)
Leukocyte esterase or nitrite or microscopy positive	99.8 (99-100)	70 (60-92)

Source: American Academy of Pediatrics 1999; Downs 1999

TREATMENT

Children with uncomplicated UTI are likely to respond to amoxycillin, sulphonamides, trimethoprim-sulfamethoxazole (cotrimoxazole) or cephalosporins, as these antibiotics are concentrated in the lower urinary tract. Parenteral antibiotics should be considered in children who are toxic, vomiting or dehydrated, or who have an abnormal urinary tract (Riccabona 2003). A recent article has reviewed the evidence for treatment of acute pyelonephritis. The authors state that oral antibiotics, chosen to cover local uropathogens are as safe and effective as intravenous antibiotics in children with a clinical diagnosis of acute pyelonephritis and intravenous antibiotics should be reserved for those who are seriously ill or have persistent vomiting (Craig and Hodson 2004).

Resistance rates to commonly prescribed antibiotics for urinary *E. coli* isolates have been reported as ampicillin (39-45%), trimethoprim-sulpamethoxaole (14-31%), nitrofurantoin (1.8-16%) and fluoroquinolones (0.7-10%) (Riccabona 2003). Studies from Israel and UK of community-acquired UTI over 5-10 years have shown a generalized decrease in bacterial sensitivity to common oral antibiotics including cotrimoxazole and cephalexin (Ladhani and Gransden 2003; Prais, Straussberg et al. 2003).