



REVIEW ARTICLE

RISK FACTORS, PATHOPHYSIOLOGY AND CLINICAL PRESENTATION IN ASYMPTOMATIC BACTERIURIA - A REVIEW

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ABSTRACT

Asymptomatic bacteriuria is the presence of at least 10^5 colony forming units/ml of one or two bacterial species in a clean-voided midstream urine sample from an individual without any symptoms of urinary tract infections. The prevalence of asymptomatic bacteriuria is influenced by various risk factors. In the present review, an attempt has been made to review the various risk factors associated with asymptomatic bacteriuria, pathophysiology of asymptomatic bacteriuria and its clinical presentation.

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INTRODUCTION

Bacteriuria literally means 'bacteria in urine'. It is defined as multiplication of bacteria in urine within the renal tract. The term significant bacteriuria was introduced by Kass (1956). According to Kass criteria, a count greater than 100000 bacteria per ml ($>10^5$) in a suitably collected and well transported mid-stream sample of urine is considered as significant bacteriuria (Kass, 1956). The term asymptomatic bacteriuria (ASB) or asymptomatic urinary tract infection (UTI) means an isolation of specified quantitative count of bacteria ($>10^5$ bacteria/ml) in an appropriately collected urine specimen obtained from a person without symptoms or signs of UTI (Colgan et al., 2006). The term ASB has also been defined in different ways by different workers. Delzell et al. defined ASB as persistent, actively multiplying bacteria of more than or equal to 100,000 colony forming unit per ml of urine without any symptoms of urinary tract infections, which include lower abdominal pain, burning micturation, fever, dysuria, frequency, urgency, supra pubic discomfort, offensive smelling urine, strangury, urge incontinence and nocturia. Antony et al. (2007) stated that ASB is a microbiological diagnosis based on the isolation of a specified quantitative count of bacteria in a clean catch midstream urine from persons without signs or symptoms, who are referable for urinary tract infection (Antony et al., 2007).

But Whalley et al. in 1967 found that although ASB is generally defined as true bacteriuria in the absence of symptoms of acute urinary-tract infection, many women with ASB may experience occasional episodes of dysuria, urgency and frequency retrospectively (Whalley, 1967).

Risk factors predisposing to asymptomatic bacteriuria

The important factors predisposing to asymptomatic bacteriuria are as follows:

Age: Population studies throughout the world have shown a rise in the prevalence of asymptomatic bacteriuria with age. The prevalence increases with advancing age from ~ 1% among school girls to > 20% among healthy women \geq 80 years of age (Nicolle, 2003). ASB is rare in healthy young men, however its prevalence in men increases substantially after the age of 60 years with further increase to 6-15% in men above 75 years of age (Nicolle, 2003 and Nicolle et al., 2005).

Sex: The prevalence of ASB varies widely with sex. It is more common in women than men and it is rare in healthy young men. The prevalence of bacteriuria among young women is strongly associated with sexual activity. In men, the prevalence of ASB increases substantially after the age of 60 years when there is prostatic hypertrophy or other abnormalities of urinary tract (Nicolle et al., 2005).

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Diabetes Mellitus: In diabetic patients, there is increased prevalence of perineal colonization by potential pathogens. Presence of glucose in urine increases the frequency and severity of infection in diabetes. It is evident from the earlier studies that hyperglycemia and subsequent glucosuria create optimal conditions for bacterial colonization in the urinary tract, which can make diabetic individuals more prone to ASB or UTI. Global prevalence of ASB in diabetic female ranges from 9 – 27% and is usually correlated with duration of diabetes and presence of long-term complications of diabetes, rather than with metabolic parameters of diabetic control, whereas in diabetic men it ranges from 0.7 – 11%. The prevalence of ASB is about three times higher in diabetic women than in non-diabetic women (less than 10%). Diabetic men do not appear to have an increased prevalence of bacteriuria, compared with non-diabetic men (Zhanel *et al.*, 1991 and Sharma *et al.*, 2011). Renko *et al.* 2011 in a systematic review and meta-analysis found that ASB was more common in patients with diabetes than healthy controls. The prevalence of ASB was higher in both women and men as well as in children and adolescents with diabetes than in healthy controls. They concluded that the prevalence of ASB is higher in all patients with diabetes compared with control subjects.¹⁰ Geerlings *et al.* carried out a study to find out the prevalence of and risk factors for ASB in women with and without diabetes. A total of 636 non-pregnant women with diabetes (type 1 and type 2), who were 18-75 years of age and had no abnormalities of the urinary tract, and 153 women without diabetes (control subjects) were included. They found that the prevalence of ASB was 26% in the diabetic women and 6 % in the control subjects. The prevalence of ASB was 29% in women with type 2 diabetes. They concluded that prevalence of ASB increases in women with diabetes (Geerlings *et al.*, 2000).

Pregnancy: It is one of the most important predisposing factors for ASB. The frequency of bacteriuria increases by about 1% during pregnancy. The prevalence of ASB in pregnancy ranges from 1.9 - 9.5%. Women with ASB in early pregnancy have a 20-30 fold increased risk of developing pyelonephritis. These women are also more likely to experience premature delivery and to have infants with low birth weight. The antimicrobial therapy of ASB during pregnancy reduces risk of development of pyelonephritis (Nicolle, 2003 and Nicolle *et al.*, 2005; Stenqvist *et al.*, 1989 and Smaail, 2001).

Structural/Neurological Abnormalities of Urinary Tract

The structural/neurological abnormalities of urinary tract that are associated with “residual urine” increase the chances of ASB. These include:

- **Neurogenic bladder:** The neurogenic bladder dysfunction is the most important predisposing factor for ASB. Patient with neurogenic bladder, especially patients with spinal cord injuries, may need long term catheterization and hence, carry the risk of ASB.
- **Instrumentation and surgery:** Catheterization increases the risk of ASB in hospitalized patients. Patients undergoing any surgical procedures or manipulation of the genitourinary tract carry the risk of ASB. Patients undergoing hemodialysis have a prevalence of ASB of 28%. Patients with short-term indwelling urethral catheters acquire bacteriuria at the rate of 2 – 7% per day.

- **Obstruction:** Obstruction because of urethral stricture, calculus formation (stones in the urinary tract), prostatic hypertrophy, tumour and pregnancy predisposes to ASB.
- **Immunosuppression:** Patients receiving immunosuppressive agents such as steroids and cytotoxic drugs are more prone to ASB. Immunosuppressive agents increase the risk of ASB and favour infection of the kidneys by unusual microbes such as Salmonella, Serratia, Candida and Nocardia.

Other Factors

Factors such as low socio-economic status, sickle cell trait and grand multi-parity predispose to ASB. Physical impairment, mental decline, including dementia, etc. also predispose to ASB. Women who use spermicides for birth control have an increased vaginal pH and increased colonization with uropathogens, particularly *E. coli* (Smaail *et al.*, 2001; Sampson and Gravett, 1999; Wesley, 2002; Gupta *et al.*, 2000; Park, 2013; Drekonja and Johnson, 2008 and Roberts, 1991).

Pathophysiology of Asb

Many conditions common to elderly, contribute to dysfunction of the urinary system and ASB. Bacteria gain access to the urinary tract by the ascending route of infection in which bacteria from the fecal flora spread to the perineum and then ascend up into the bladder. Most people are able to eliminate these bacteria with the help of first line of defense, but in some individuals this defense is weaker; hence they develop ASB. Various predisposing factors such as aging, physical impairment, mental decline, including dementia, diabetes mellitus, lead to the development of ASB, most likely by resulting in incomplete bladder emptying. Other conditions such as prostate enlargement and bladder prolapse, hamper the flow of urine and increase the risk of ASB. Decreased prostatic secretions and inability to acidify urine, have also been suggested in the pathophysiology of ASB. Additionally, estrogen deficiency enhances colonization of the vaginal introitus and has been proposed as a potential risk factor for ASB (Park *et al.*, 2013).

Over 50% of men and women with diabetes have bladder dysfunction, mainly adult patients are affected with this complication. The average urinary flow was significantly higher in diabetics than in healthy controls. The longer time of the voiding sensation can lead to higher volume of urine fraction which results in increased bladder capacity. Hyperglycaemia diminishes the detrusor contractibility of the bladder, therefore the amount of residual urine increases, this retention may promote bacterial colonization of the urinary tract (Ueda *et al.*, 1997). The prevalence of ASB among patients with diabetes has been correlated with several clinical characteristics. It is evident that hyperglycaemia and subsequent glycosuria present optimal circumstances to bacterial colonization in the urine and urinary tract, which can make diabetic patients susceptible to ASB or UTI.

Clinical presentation in Asb

Asymptomatic infections are unnoticeable by the patients due to lack of any clinical signs and symptoms. Such symptomless infection of urinary tract is known as covert or asymptomatic bacteriuria.

ASB is common but its prevalence varies widely with age, gender and presence of genitourinary abnormalities or underlying diseases. Asymptomatic infections are equally important as symptomatic infections in regards to health hazard because asymptomatic bacteriuria is one of the common problems seen in diabetic patients preceding symptomatic UTI. The extent of ASB in diabetics may be the guide to prevent further complications in them. As ASB is associated with active disease process in kidney, it can develop cystitis and pyelonephritis, and might go to renal failure, if left untreated (Park, 2013 and Longo *et al.*, 2012).

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