ASYMPTOMATIC BACTERIURIA IN CHRONIC HEMODIALYSIS PATIENTS

Thesis

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INTRODUCTION

Urinary tract infections (UTI) are among the most common bacterial infections in humans. UTIs may be acute, symptomatic infections of varying severity and localization, and also be sporadic, recurrent or chronic infections. Chronic infections that involve the upper urinary tract remain a major cause of renal disease ***(Kunin, ١٩٨٧).***

Paradoxically, the most common form of UTI is asymptomatic bacteriuria (ABU). ABU patients may carry more than $١٠^{٥}$ colony forming units (CFU)/ml of urine for months or years without developing symptoms or sequels ***(Lindberg et al., ١٩٧٨).***

Asymptomatic bacteriuria (ABU) is commonly detected at screening of defined populations or at follow-up visits after a first symptomatic infection ABU is quite frequent, occurring in about ١%of girls, ٢–١١% of pregnant women and up to ٢٠% of elderly men and women ***(Kunin, ١٩٨٧).***

E. coli is the causative organism in at least ٩٠ % of cases of asymptomatic bacteriuria. Strains of *E. coli* that invade the urinary tract are not merely the most prevalent components of the fecal flora, but rather are specific clones that possess a variety of virulence characteristics that facilitate intestinal

carriage, persistence in the vagina and then ascension and invasion of the urinary tract ***(Svanborg–Eden et al., ١٩٨٨).***

Patients with diabetes have an increased risk of infections with the urinary tract being the most prevalent infection site. In fact, a ١٩٤٠ autopsy study showed that ١٨% of the subjects with diabetes had a urinary tract infection (UTI). Many UTIs are asymptomatic, and whether symptomatic UTIs are preceded by asymptomatic bacteriuria (ASB) is not known In contrast with men, a higher prevalence of ASB has been found in women with diabetes than in women without the disease ***(Carton et al., ١٩٩٢.; Pozzilli and Leslie, ١٩٩٤).***

From ٢ to ١١% of pregnant women have asymptomatic bactetiuria in the first trimester, a prevalence similar to that in age-matched nonpregnant women. If asymptomatic bacteriuria in pregnancy is not treated, ٢٠ to ٣٠% of women develop acute pyelonephritis, usually at the end of the second trimester or early third trimester. Stasis in the genitourinary tract secondary to hormonal changes in pregnancy, as well as pressure at the pelvic brim by the fetal head, result in obstruction and symptomatic infection. Acute pyelonephritis in later stages of pregnancy is dangerous for the fetus, as it is associated with premature labor and delivery ***(Patterson et al., ١٩٩٧a).***

Patients with end-stage renal disease on hemodialysis have documented defects in their immune responses, and infections contribute significantly to their morbidity and

mortality. ***Chaudhry et al. (١٩٩٣)*** found that thirty-one percent of asymptomatic hemodialysis patients had significant pyuria (> ١٠ white blood cells per high-power field) and ٢٥% had bacteriuria of pathologic dimensions, (> ١٠٠٠٠٠/mL of a single microorganism). Their results demonstrate that the urinary tract, even in ESRD patients on hemodialysis, may represent a significant reservoir for infection ***(Chaudhry et al., ١٩٩٣).***

The presence of inflammation in hemodialysis patients , chronic or episodic, has been found to be associated with increased mortality risk. The causes of inflammation are *multifactorial* and include patient-related factors, such as underlying disease, co-morbidity, oxidative stress, infections, obesity, and genetic or immunologic factors, or on the other side, HD-related factors, mainly depending on the membrane biocompatibility and dialysate quality. The adequate knowledge of these causes and their prevention or treatment if possible may contribute to improving the inflammatory state of patients who are on HD and possibly their mortality ***(Jaar et al., ٢٠٠٠; Vaziri, ٢٠٠٤).***

AIM OF THE WORK

To study prevalence of asymptomatic bacteriuria and its possible correlation with C-reactive protein level as marker of chronic inflammatory state in hemodialysis patients

ASYMPTOMATIC BACTERIURIA

Urinary tract infections (UTI) are among the most common bacterial infections in humans**.** UTIs may be acute, symptomatic infections of varying severity and localization, and also be sporadic, recurrent or chronic infections. Chronic infections that involve the upper urinary tract remain a major cause of renal disease ***(Kunin, 1987).***

Paradoxically, the most common form of UTI is asymptomatic bacteriuria (ABU). ABU patients may carry more than $١٠^{٥}$ colony forming units (CFU)/ml of urine for months or years without developing symptoms or sequels ***(Lindberg et al., 1978).***

The history of quantitative bacteriology of reasonably aseptically collected urine as an aid to the diagnosis of urinary tract infections was initially described by **Marple** in **١٩٤٠.** This concept was resurrected by ***Sanford et al. (1956) and by Kass and Finland (2002).***

These studies described a method for quantitative bacterial counts, using an agar pour plate technique as part of the procedure for urine cultures. They also demonstrated that contamination of the urine should be distinguished from 'true' bacteriuria by quantitation of the numbers of bacteria in the urine; and that large numbers of bacteria in the urine

suggested that bacteria had actually multiplied within the urinary tract ***(Sanford et al., 1956; Kass and Finland, 2002).***

During the ensuing four decades, many investigators applied the basic concept of quantitative bacteriology of the urine not only to the diagnosis of urinary tract infections, but to the prognostic value of effective antibacterial treatment of urinary tract infections. Numerous methods of quantitative and semiquantitative bacteriology of urine have been developed and applied to patients with urinary tract infection. Fifty years ago, **Kass** and other investigators first proposed and validated the use of the quantitative urine culture for the microbiological diagnosis of UTI ***(Kass, 1957 & 1962).***

Asymptomatic patients from whom bacteria were isolated in quantitative counts of $\geq 10^5$ colony-forming units (CFU)/mL in a voided urine specimen had the same organisms consistently isolated in paired specimens obtained by urinary catheterization. When lower quantitative counts of bacteria were isolated from voided specimens, the paired catheterized specimens were usually negative. The lower quantitative counts in voided specimens were interpreted as contamination. Widespread acceptance and application of the quantitative urine culture identified several patient populations who were clinically asymptomatic but had a high prevalence of positive urine cultures ***(Kunin, 1966).***

These included, among others, pregnant women, individuals with urological abnormalities and patients with indwelling urethral catheters. Pyelonephritis was recognized as an important problem for pregnant women, and many early studies evaluated the impact of treatment of asymptomatic bacteriuria on pyelonephritis in pregnancy. These studies consistently documented that treatment of asymptomatic bacteriuria substantially decreased the risk of pyelonephritis later in pregnancy. The clear and consistent benefits of treatment of bacteriuria in this population were interpreted to be generally applicable, leading to endorsement of treatment of asymptomatic bacteriuria for other patient groups ***(Kass, 1962).*** The conceptual framework for clinicians was that asymptomatic bacteriuria was consistently harmful in all populations and warranted antimicrobial treatment. The following several decades saw advances in understanding through critical clinical evaluation in selected patient populations. In particular, observations from long-term cohort studies and prospective randomized comparative trials in defined populations with asymptomatic bacteriuria have addressed appropriate management.

Urine culture

The diagnosis of asymptomatic bacteriuria in women requires at least two consecutive voided specimens with similar organism(s) isolated in sufficient quantitative counts ***(Rubin et al., 1992).*** This definition is derived from studies

reporting that an initial voided urine specimen with a quantitative count of ≥١٠٥ CFU/mL of organisms was confirmed only ٨٠% of the time in a second specimen obtained within ١ week. A third voided specimen was consistent with the first two specimens ٩٥% of the time ***(Kunin, 1966).***

The observation of only ٨٠% positive concordance of the second specimen has been interpreted as contamination of the initial specimen. In fact, *transient bacteriuria* is common in young women, and the finding of ٢٠% of women with negative cultures on the second specimen probably reflects transient bacteriuria identified on the initial specimen, rather than contamination ***(Hooton et al., 2000).***

While two consecutive voided specimens with ≥١٠٥ CFU/mL of the same organism isolated is the recommended standard for diagnosis in women, alternative definitions have been used in some studies. Bacteriuria has been identified with only a single specimen ***(Hooton et al., 2000),*** or requiring as many as three consecutive specimens with consistent microbiological results ***(Evans et al., 1978).***

Obviously, studies that define bacteriuria with only a single voided specimen report a higher prevalence of asymptomatic bacteriuria than those requiring *persistent bacteriuria* from two or more specimens. For men, a single voided specimen with a quantitative count of a potential