

Pathogenesis of Urinary Tract Infection in the Intensive Care Unit: A Quick Review

Namrita Malhan¹, Ankur Sinha^{2*}, Ravikaran Patti² and Yizhak Kupfer³

¹Department of Dental Surgery, Sri Aurobindo Institute of Medical Sciences, India

²Department of Medicine, Maimonides Medical Center, USA

³Divisions of Pulmonary Medicine and Critical Care Medicine, Maimonides Medical Center, USA

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*Corresponding author

Ankur Sinha, Resident, Department of Internal Medicine, 4802 10th avenue, Brooklyn, NY 11219, United States of America, Tel: 267-916-7785; Email: ansinha@maimonidesmed.org

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Abstract

Urinary Tract Infection (UTI) has been one of the pivotal agents of morbidity in the Intensive Care Unit (ICU) worldwide. UTI's in the ICU cause significant mortality and increase the length of ICU stay, thereby increasing the bane on healthcare costs worldwide. We aim to review literature and elaborate on the several factors leading to the causation of UTI's in the ICU.

Introduction

Urinary Tract Infection (UTI) has been one of the pivotal agents of morbidity in the Intensive Care Unit (ICU) worldwide. Richards et al reported UTI's to be the commonest form of nosocomial infection in both medical and surgical ICU [1]. Apart from significantly increasing healthcare costs and length of hospital stay [2], UTI's in the hospital-based setting have shown to increase mortality [3].

ICU acquired UTI is defined as a positive urine culture that is first identified on day 3 of ICU admission or later; this also includes positive urine cultures within 48 hours of discharge from the ICU. A positive urine culture is the presence of more than 10^3 colony forming units per milliliter (CFU/ml) with no more than two bacterial species in catheterized patients, and more than 10^5 CFU/ml in non catheterized individuals [5].

We will review the multitude of factors that lead to the causation and disease progression of UTI's in patient's that are critically ill.

Classification

UTI's can be classified into categories based on the presence or absence of an invasive catheter, anatomical defects in the urinary tract, comorbidities, and based on the source of the disease. This classification can aid clinicians in covering appropriate pathogens while treating patients empirically. Figure 1 depicts the classification of UTI.

Complicated UTIs are associated with the comorbidities that reduce urine output (like renal stones, anatomic abnormalities or presence of foreign bodies in urinary tract). There is increased chances of therapy failure. It is frequently associated with multiple drug resistant uropathogens.

Immunology

Severe illness as is the case in most patients in the intensive care unit has profound effects on the body's immune function. The basic foundation of our body's immune function is laid on the interdependence and communication between several cell types. The steps involved in this process are 1. Antigen recognition / Phagocytosis, 2. Antigen presentation and 3. Activation of innate immune response.

Sepsis is characterized by a host response to infection that leads to organ dysfunction [4]. Over the years the pathogenesis of sepsis has been studied, and it was well recognized that sepsis has an initial pro-inflammatory phase followed by a long-standing phase of immunosuppression [5,6] (Figure 2). With better management of the initial phase of sepsis due to strict resuscitation policies, this immunosuppressive phase has become more evident. More recent studies suggest that the phase of immunosuppression may actually be simultaneous with the phase of inflammation, although these findings remain controversial [7].

Several factors contribute to the phase of immunosuppression like markedly decreased cytokine function [8], programmed cell death or apoptosis of immune cells through mitochondrial pathways

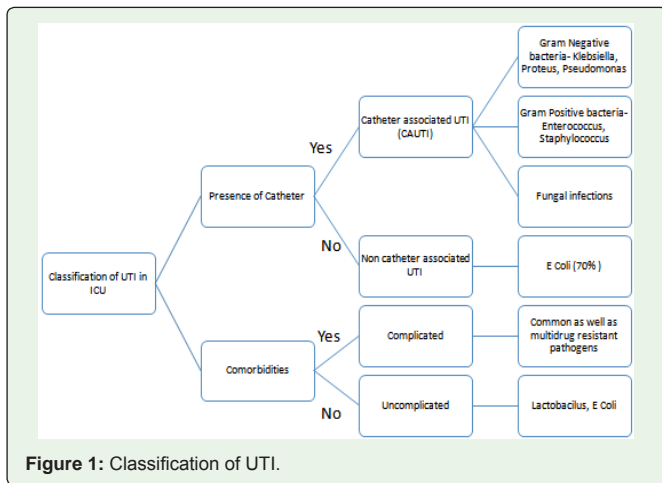


Figure 1: Classification of UTI.

and death receptor pathways [9], impaired neutrophil function with loss of chemotaxis, impaired monocyte function with decreased ability to release cytokines, decreased number of Natural Killer cells (NK cells) and T cell exhaustion. Figure 2 summarizes the various immune dysfunctions evident in patients with sepsis [10-13].

Host factors

Several host specific factors contribute as risk for UTI. Advancing age leads to increased incidences of UTI, this is due to several factors like commonly encountered debilitating diseases, decreased host defense, increased colonization of gram negative organisms on epidermis, changes in pelvic musculatures, reduced bladder efficiency in women, and benign prostrate hypertrophy in men [14].

Women are clearly at higher risks of developing UTIs due to several factors like – shorter urethra as compared to males and the moist environment around urethra. Moreover, the most significant factor is the small distance between anus and urethral meatus because rectal flora is the most common source of uropathogens. Vaginal microflora can also be the source of uropathogens specifically with alterations in pH, leading to changes in concentration of normal vaginal commensal organisms [15]. Use of spermicidal cream can increase the colonies of pathogens in vaginal microflora, which in turn increases risk of UTI.

Anatomical or pathological obstruction of the urinary tract ultimately leads to pooling of urine and stasis. This pooling of urine acts as a medium for pathogens to grow, is resistant to host immune system as well as a barrier to antibiotic penetration [16].

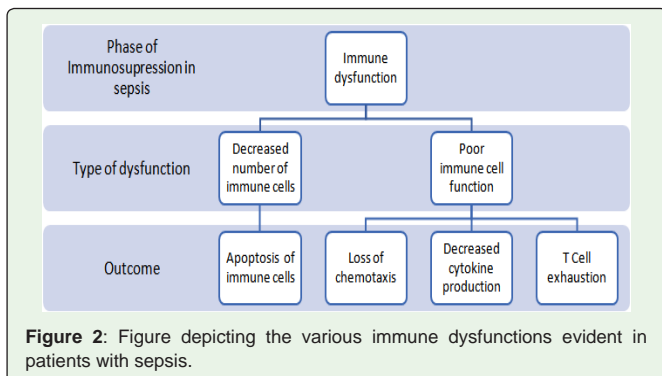


Figure 2: Figure depicting the various immune dysfunctions evident in patients with sepsis.

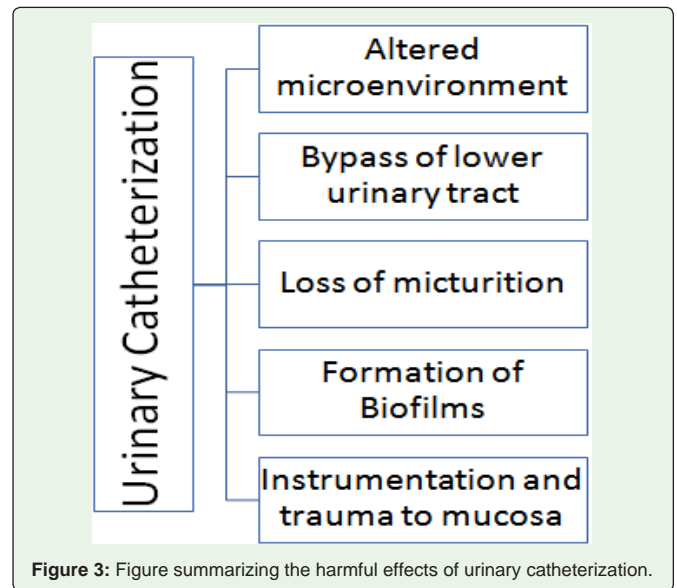


Figure 3: Figure summarizing the harmful effects of urinary catheterization.

Catheterization

Catheter Associated Urinary Tract Infections (CAUTI) are one of the commonest complications associated with ICU stay and may be associated with increased mortality regardless of the severity of co-morbidities [17]. The length of urinary catheterization plays an important role as well, with almost 95% of CAUTI's being associated with long term indwelling catheters in the ICU [18].

The basic pathophysiology of increased risk of infection with catheterization is an alteration of the microenvironment. Catheters serve as a nidus for microbes to anchor, and can weaken important host defenses. One of the most important mechanisms of protection is the length of urethra, which is bypassed because of catheterization [17,18]. The process of bladder contraction and micturition with

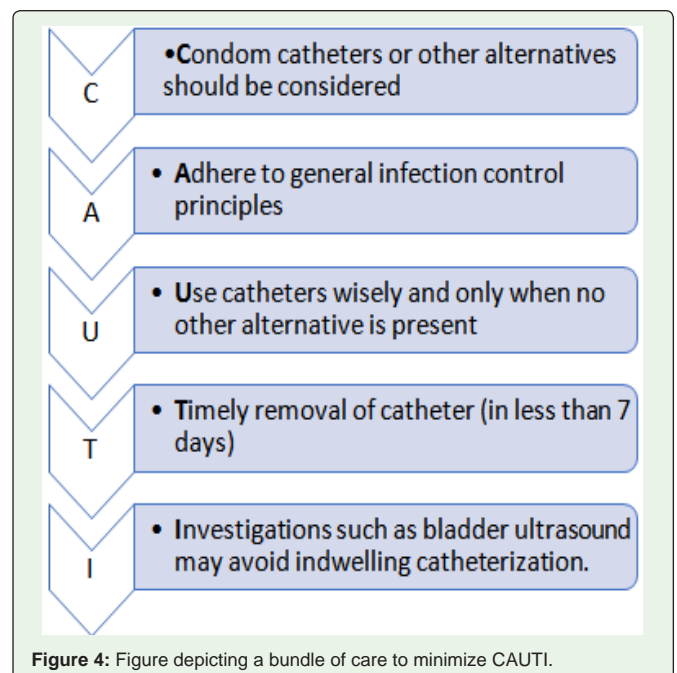


Figure 4: Figure depicting a bundle of care to minimize CAUTI.

the formation of an outflow urine stream hampers microorganisms from anchoring in the urinary tract, this mechanism is redundant in catheterized individuals [17,18].

Both inner and outer walls of the catheter form a favorable base for formation of “Biofilms”. These biofilms are clusters of microorganisms engulfed in extracellular matrix [19]. Biofilms are a relatively safe environment for microbes because of poor penetration of antibiotics into the biofilm, and slower growth of organisms in the biofilm. Many antibiotics that target cell replication cycle fail to provide relief of infection due to this slow growth [20]. Only strict indications should define the use of indwelling catheters and every measure should be taken to minimize the use of catheters when not indicated. Figure 3 summarizes the harmful effects of urinary catheterization.

Microbial invasion is usually endogenous, and primarily from intestinal tract and perineum. On rare occasions, like via contaminated hands of health care personnel the microorganisms may be exogenous [21].

Prevention of CAUTI

The incidence of CAUTI has been on a steady decline and this is due to national guidelines on infection prevention and control [22]. We suggest a simple bundle of care that can minimize CAUTI (Figure 4).

To conclude, these interventions, although simple require strong motivation and collaboration amongst ICU staff. Participation of healthcare personnel with a common goal of improving outcomes remains key. Strict adherence to guidelines requires “culture change”, which remains a challenge.

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