Study of the Diagnostic Relevance of Pyuria 1n Hemodialysis Patients

Thesis for Complete Fulfillment of Master Degree in Internal Medicine

Submitted by

Manar Ahmed Mohammed Hussein

M.B.B.Ch, Cairo University.

Under Supervision of

Prof. Dr. Ahmed Hamza Dorgham

Professor of Internal Medicine

Cairo University

Prof. Dr. Azza Abd-EIRahman EIShamaa

Professor of Nephrology

Theodor Bilharz Research Institute.

Dr. Dalia Roshd Abd-EIRahman

Lecturer of Internal Medicine

Cairo University

Cairo University

2008

Abstract

Urinary Tract Infection is a common Cause Of Morbidity and Mortality inhemodialysis Patients . The Urinary Tract is Often Overlooked as a source Of infection .The Value Of Pyuria as a marker .

The Current Study Was Performed To Assess The Value Of Pyuria as a Marker For Urinary Tract infection .

The Current Study Was Performed an 30 Patients an Regular Hemodialysis and 10 Healthy Volunteers Age and Sex Matched served as Control .

The Current Study Concluded that Pyuria is a common Finding in Hemodialysis Patients and it does not always indicate Urinary Tract Infection and Urine Culture Shoud be done To Hemo Dialysis Patients every three minths .

Key Words :

Pyuria – Hemodialysis – Urinary tract infection .

Table Of Contents

List of Tables

List of Figures

List Of Abbreviations

C	**Cytosine**
CNF	**Cytotoxic Necrotizing Factor**
CRF	**Chronic Renal Failure**
DNA	**Deoxyribonucleic Acid**
dNTPS	**Deoxynucleotide triphosphates**
E.coli	**Escherichia Coli**
ESRD	**End Stage Renal Disease**
G	**Guanine**
GAG	**Glucoseaminoglycan**
HIV	**Human Immunodeficiency Virus**
Hpf	**High Power Field**
ICU	**Intensive Care Unit**
IgA	**Immunoglobulin A**
IL	**Interleukin**
KDa	**Kilodalton**
L.E	**Leukocyte Esterase**
LPs	**Lipopolysaccharides**
PAIs	**Pathogenicity Associated Islands**
PCR	**Polymerase Chain Reaction**
PMNs	**Polymorph Nuclear Leukocytes**
RBC	**Red Blood Cell**
r.P.M	**Run Per minute**
T.B	**Tuberculosis**
THP	**Tammhorsefall Proteins**
TLRS	**Toll Like Receptors**
UPEC	**Uropathogenic Escherichia Coli**
UTI	**Urinary Tract Infection**
WBC	**White Blood Cells**
Z.N	**Ziehl-Neelsen**

Acknowledgment

First and foremost, I thank God for helping and guiding me in accomplishing this work.

I would like to express my sincere gratitude to ***Prof. Dr. Ahmed Hamza Dorgham,*** Professor of internal medicine, faculty of medicine, Cairo University, for his great support and stimulating views. His active, persistent guidance and overwhelming kindness have been of great help throughout this work.

A special tribute to ***Prof. Dr. Azza Abd-ElRahman ElShamaa***, Professor and head of the Nephrology Department in Theodor Bilharz Research institute for her supervision and advice.

I must extend my warmest gratitude to ***Dr. Dalia Roshd Abd-ElRahman,*** Lecturer of internal medicine and nephrology, faculty of medicine, Cairo University, for her great help and faithful advice.

I would like to extend my deep gratitude to ***Prof. Dr. Mohammed Aly Saber,*** *supervisor* of the Biotechnology unit in Theodor Bilharz Research institute for his supervision and advice

I would like to extend my deep gratitude to ***Dr.Emam Wakid,*** assistant professor of Nephrology, in Theodor Bilharz Research institute for his supervision and advice.

I must express my deepest gratitude to ***Dr.Laila Abu-alfadl,*** assistant professor of Microbiology in Theodor Bilharz Research institute for her great help and cooperation.

A special tribute to ***Dr. Ihab El-Dabaa*** assistant professor and head of Biochemistry Department in Theodor Bilharz Research institute for his great help and faithful advice.

To My Father and Mother,,

My Husband,,

My Sister and brothers,,

My Senior Staff and Colleagues in the Nephrology,

Microbiology , and Biochemistry Departements in THeoder

Bilharz Research Institute ,,

And all Patients ,,

Thank You…

Introduction

Infection is a common cause of morbidity and mortality in hemodialysis patients. The severity of infection related hospitalizations can vary greatly. At one extreme are patients who die, require an intensive care unit (ICU) stay, or have a prolonged admission, whereas at the other extreme are patients with relatively mild illness who can be discharged home after a brief hospitalization **(Allon et al, 2005).**

It worth nothing to know that urinary infection is the presence of microbial pathogens within the normally sterile urinary tract. Infections are overwhelmingly bacterial, although fungi, viruses, and parasites are also occasionally pathogens. Urinary infection is the most common bacterial infection in humans and can be either symptomatic or asymptomatic. Symptomatic infection is associated with a wide spectrum of morbidity, from mild irritative voiding symptoms to bacteremia, sepsis, and occasionally death. Asymptomatic urinary infection is the isolation of bacteria from urine in quantitative counts consistent with infection, but without localizing genitourinary signs or symptoms, and with no systemic symptoms attributable to the infection **(Nicolle, 2005).**

(Fasolo et al, 2006) stated that dialysis dependent patients are more susceptible to urinary tract infections (UTI), and UTIs are an important cause of morbidity and mortality in these patients. When undiagnosed and

untreated, significant complications may occur, leading to the need for drainage procedures, nephrectomy, or death.

Delayed diagnosis is a relevant issue because the urinary tract is often overlooked as a source of infection in hemodialysis patients, especially because UTI symptcms are mostly related to voiding, which is reduced or absent in these patients.When diagnosed these infections are easily treatable, and early treatment prevents future complications **(Hyodo et al, 2005).**

The value of pyuria as a marker of UTI in hemodialysis patients is controversial, some authors claim that the presence of pyuria in dialysis patients is not indicative of infection because of several clinical factors, including the presence of low urine volume, bladder stasis, and the underlying etiology of kidney disease, as many conditions leading to terminal renal failure are associated with sterile pyuria owing to chronic parenchymal inflammation **(Wah et al, 2006).**

While several studies raised the impression that pyuria is not an accurate marker of infection, **(Orlowska et al, 2002)** have defended pyuria as a good marker for UTI in patients on continuous ambulatory peritoneal dialysis.

Aim of the Work

To assess pyuria as a marker of urinary tract infection in hemodialysis patients.

Chapter 1

Urinary Tract Infection:

Bacterial Virulence &Host Defense

The urinary tract is a complicated epithelium-lined tube with an opening to the body surface, making it susceptible to infection by exogenous organisms. Indeed urinary tract infections (UTIs), which are almost caused by colonic organisms in the normal host, may be the most common bacterial infection of humans (**Nicoll LE., 2003**).

In the course of producing, storing, and voiding urine, the urinary tract is continually flushed, and infecting organisms are usually recovered by the clinician or investigator in a voided urine specimen. This fortunate situation allows for relatively easy assessment of bacteriuria, which always accompanies UTIs. Bacteria generally manifests in one of three clinical presentations, the first category is asymptomatic bacteriuria, in which bacteria may be limited to the bladder or may be found in both the bladder and kidney, the second is cystitis, a syndrome characterized by dysuria, frequency, and urgency of urination, sometimes with lower abdominal pain and hematuria, the third is acute pyelonephritis, which is clinically indicated by flank pain and fever and complicated by bacteremia in about 30% of the cases **(Weissman, 2007).**

The most common uropathogen is ***Escherichia coli*** (*E.coli*), which can cause acute cystitis or pyelonephritis in the normal urinary tract (i.e., one without structural or functional abnormalities, or prior

instrumentation) after entering the bladder through the urethra **(Weissman, 2007).**

Strains of E.coli colonize the colon of human newborns soon after birth; this organisms and a succession of different *E.coli* (some transient, some more persistent), inhabit this site for the rest of the individuals life. Some of these strains may colonize periurethral areas and enter the bladder. Those that do and persist without symptoms are similar in their characteristics to the spectrum of *E.coli* colonizing the gut. However those that enter and elicit symptoms are not a random sample of fecal *E.coli*, but rather a subset of strains (the uropathogenic *E.coli* UPEC) that differ from the majority of fecal strains in that they are more likely to possess a variety of putative virulence factors, including polysaccharide capsules, adhesins, siderophores, and cytotoxins **(Marrs et al., 2002).**

A large proportion of UTIs are caused by a limited number of UPEC "clones" that typically derive from phylogenetic groups B2 and D, more than groups A and B1**(Johnson et al., 2001).** Although virulence factor carriage remains a better predictor of experimental virulence than does phylogenetic background, the concentration of virulence factors in strains from groups B2 and D suggests the evolution of certain *E.coli* well equipped for production of extraintestinal disease **(Johnson et al., 2002).**

Uropathogenic E.coli are, those, defined not only by their source (they are cultured from the urine or blood of individuals with symptomatic UTI), but also by the presence of putative virulence factors; however mere association does not establish whether these factors are truly involved in infection. The concept of molecular Koch's postulates

has been very useful for determining whether a putative virulence factor is indeed important for infection. According to these postulates, a factor is considered a virulence determinant if the following three conditions are met: (a) the factor is associated with virulent strains, (b) inactivation of the gene encoding the factor results in attenuation of virulence in a relevant animal model, and (c) virulence is restored when the gene encoding the factor is reintroduced to the mutant (**Weissman, 2007).**

Studying model UPEC strain 536, Hacker and colleagues noted the spontaneous deletion of chromosomal regions leading to simultaneous loss of multiple, distinct virulence-associated phenotypes. Further characterization of the deleted segments led to the discovery of horizontally mobile, virulence factor-rich clusters of DNA that they termed "pathogenicity associated islands" (PAIs). PAIs are 10 to 200 kb in size, carry virulence genes, are inserted near or within tRNA genes, contain insertion sequences or other mobile genetic elements, and have a G+C content different from the rest of the chromosome**.** The contribution of mobile genetic elements to the emergence of pathogenic strains from commensal population has been highlighted by the recent publication of several bacterial chromosomal sequences. The chromosomes of these model strains differ not only in size, but also in content (**Schmidt et al., 2004).**

The host-pathogen interactions that lead to urinary tract disease are initiated upon attachment of bacteria to epithelial cells. This type of adherence is a highly specific phenomenon; tropism for and within the urinary tract is mediated by molecular interactions between adhesins on the bacterial surface and complementary receptors on the epithelial cell membrane **(Hung et al., 2007).**