Value of B_2 - microglobulin in Localization of urinary tract infection

THESIS

SUBMITTED IN PARTIAL FULFILMENT

OF MASTER DEGREE OF

INTERNAL MEDICINE

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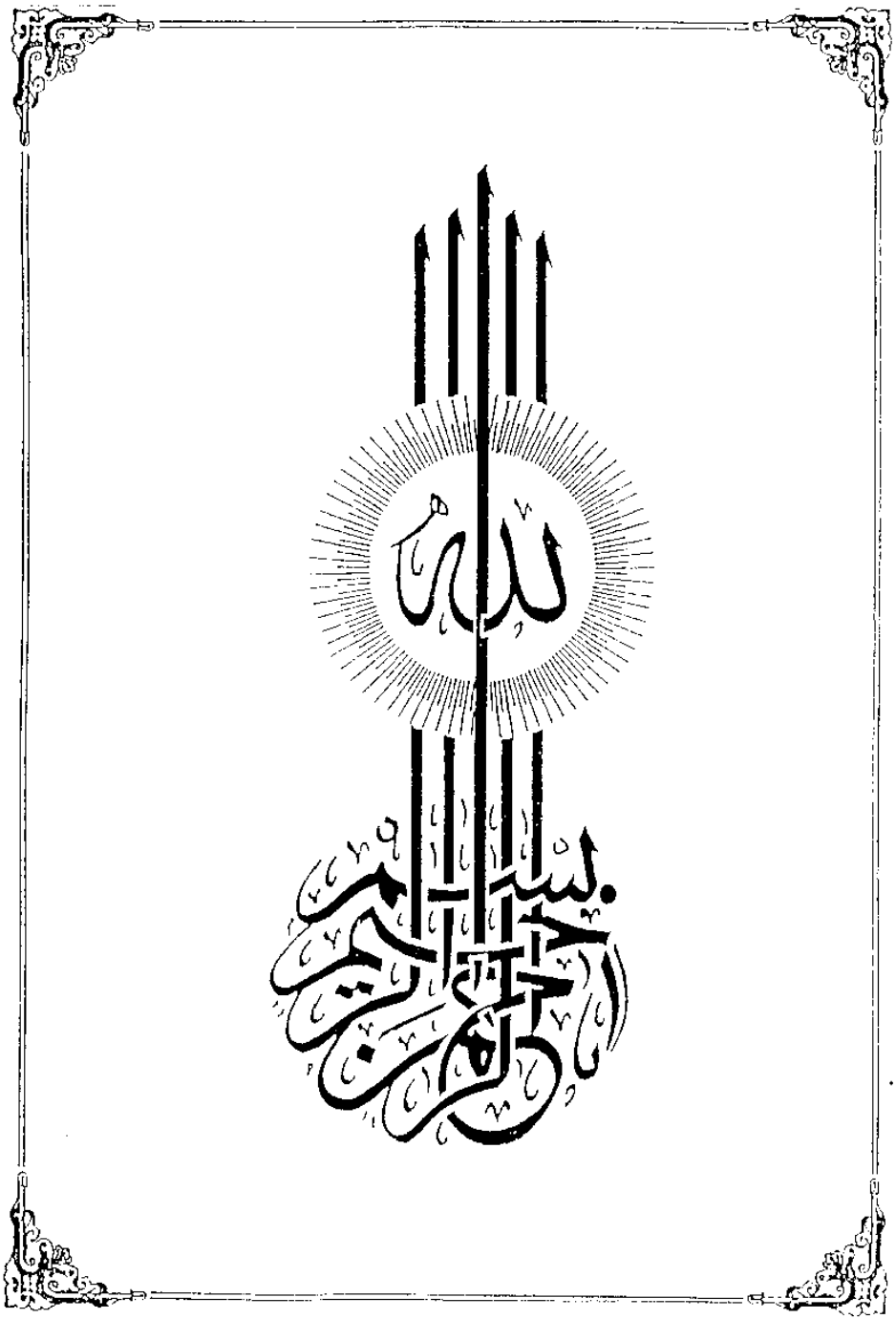
1987



Acknowledgement

I wish to express my deepest gratitude and sincere thanks to Prof. Wahid El-Said, Prof. of internal medicine and nephrology, faculty of medicine, Ein Shams University, for his constant help, faithful guidance and helpful criticism.

My sincere appreciation to Dr. Alaa Abdel Rahman lecurer of internal medicine, faculty of medicine, Ein Shams University for his help, advice and encouragement.

My deepest thanks to Dr. Basima Mahmoud lecurer of clinical pathology, faculty of medicine, Ein Shams University, not only for her supervision but also for her continous guidance and endless encouragment.

Finally, my deepest thanks to my colleagues for their continous assistance and support.

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(1987)

Contents

INTRODUCTION

Infection of the urinary tract is common in nearly all branches of medicine. The ability of the clinician to distinguish between kidney infection and infection restricted to the bladder on the basis of presenting signs and symptoms is quite limited. Not only will many patients with renal infection present only with symptoms referable to the lower urinary tract (dysuria, frequency and urgency.), but also some patients with bladder infection will complain of flank pain, fever and systemic symptoms usually associated with pyelonephritis. **(Sanford, 1976)**.

In addition, patients with so called acute uretheral syndrome (Symptomatic abacteruria) will have simillar symptoms in the face of urine cultures showing insignificant or no growth of bacteria. **(Gallagher et al., 1965)**.

So, better techniques of infection localization are clearly required to fairly evaluate the hypothesis that the site of infection affects the clinical course and response to therapy **(Sanford,1976)**.

Since the first technique for localization of urinary tract infection has been developed by **Stamey et al. (1965)** many techniques were introduced to reach the most precise and least invasive method for localization of urinary tract infection. **(Rubin et al, 1986)**.

Recently, many workers investigated urinary ß2-microglobulin level in urinary tract infection but the results remain unconclusive.

Schardjin et al, (1979) demonstrated significant increase in urinary excretion of $ß_2$ microglobulin in patients with clinical pyelonephritis while its level was normal in patients with uncomplicated cystitis. On the other hand **Sandberg et al, (1985)** studied urinary excretion of $ß_2$-microglobulin in upper and lower urinary tract infection and they suggested that urinary excretion of $ß_2$-microglobulin has little value in localization of urinary tract infection. Moreover, **Hemmingsen and Skaarup (1977)** found that the urinary excretion of this protein increased also in patients with fevers of non-renal infection.

The aim of this work is to assess the level of urinary excretion of $ß_2$-microglobulin in patients with upper, lower urinary tract infection and in patients with fevers of non-renal infection.

REVIEW OF LITERATURE

Localization of Urinary Tract Infection (UTI)

Pathologically, there is a major difference between renal and bladder infections. Broadly, infection within the bladder primarily involves the superficial mucosa and little immunologic responses to such superficial infection is present. In contrast, renal infection is a deep tissue infection in which a significant immunologic response is a rule. **(Hepinstall, 1974)**

Clinical significance of localization of UTI :

Clinically, evidence that such distinctions are of practical importance comes from two sources : firstly, after analysis of the pattern of recurrence in those patients with recurrent bacteruria, and secondly, after analysis of response to antimicrobial agents in patients whose infection has been localized to appropriate anatomic site., **(Fang et al., 1979).**

Turck et al, (1966) have clearly demonstrated - on the basis of careful bilateral catheterization - that the great majority of relapsing UTI occur in patients with upper UTI, whereas the great majority of reinfections occur with infections restricted to the bladder. **Ronald et al, (1976)**, recorded 92% cure in patients with lower UTI by a single dose of 500 mg of intramuscular Kanamycin. **Fang et al (1978)**, recorded 100% cure in patients with lower UTI treated by a single dose of 3gm. amoxacillin. **Turck (1979)** reported that patients

with true relapsing infections (i.e those with renal infection) will have a good cure rate if treated for six weeks.

Unfotunately, currently prescribed antimicrobial regimens lasting 7-14 days if used without localization of UTI, will be too long for cases of lower UTI and do not provide adequate treatment for a significant number of renal parenchymal infections. **(Fang et al., 1978)**

Thus, localization of the site of UTI appears to play a useful role in expecting the prognosis and deciding the proper antimicrobials for use. **(Fang et al,1979).**

Urinary tract infection and renal failure :

Over the past three decades the major question dominating the field of urinary tract infection has been, "What is the contribution of such infections to the development of chronic renal failure ?". The question was initially posed because of the frequent demonstration at autopsy or at the time of transplantation of the pathologic changes of chronic pyelonephritis even in patients without a clearcut history of documented UTI. However, in recent years at least three different lines of evidence have developed, demonstrating that adult UTI is essentially never the primary cause of chronic renal failure **(Fang et al., 1979).**

(1) The pathologic changes of chronic pyelonephritis are caused by a number of different processes, ranging from chronic analgesic

abuse and other intoxications to long standing ischaemia. Therefore, the term used to describe these pathologic findings is "interstitial nephritis" and only in these cases of interstitial nephritis in which a clearcut evidence of infection is present, the diagnosis of chronic pyelonephritis is made. **(Hepinstall 1976).**

(2) Long term studies of both adult males and females with chronic pyelonephritis or recurrent bacteruria have not demonstrated progressive renal damage in absence of significant anatomical defect. **(Asscher et al., 1969, Freeman et al, 1975).**

(3) A retrospective study of 100 consecutive cases of renal failure caused by chronic interstitial nephritis seen at a major centre failed to reveal a single case in which infection is the primary cause. **(Murray & Goldberg 1975)** However, in the presence of the conditions given in table "1" particularly vesicoureteral reflux and obstruction, infection was thougnt to play an important secondary role. **(Fang et al ., 1979).**

.Analgesic abuse.	.Nephrolithiasis.	.Radiation
.Hypertension	.Hypercalcaemia.	.Lead nephropathy
.Renal vascular dis.	.Hypokalaemia.	.Balkan nephropathy.
.Obstruction.	.Sickle cell anaemia	

. Table "1"

Etiologies of chronic interstitial nephritis **(Quoted from Fang et al., 1979).**

Given this body of evidence, then, the major value in the study of localization of UTI today is the prognostic outcome and clinical management. **(Rubin et al., 1986).**

Techniques for localization of UTI

Invasive techniques :

Stamey et al., (1965) described an accurate method for the localization of UTI based on bilateral ureteral catheterization and quantitative bacterial counts on bladder and serial ureteric specimens.

The technique is at times technically difficult and too invasive for general application, nevertheless, it is the only direct method for localization of UTI and it is still considered as the standard against which all other methods of localization must be compared. **(Rubin et al 1986)**.

In an effort to employ a less invasive technique **Fairely et al., (1967,1971)** used " the bladder washout test" in which the bladder is emptied through a uretheral catheter, then irrigated by 40 ml of 0.2 % neomycin, then emptied and washed out with 2 litres of sterile saline solution, then 3 timed specimens are collected at ten minutes time intervals, bacterial counts are done on all specimens. Patients with lower UTI will have sterile urine during collection period following the washout, while patients with renal infection will have bacteria in the post - wash samples.

Some authors suggest that misleading results may be obtained due to transient vesicoureteral refulx in severe cystitis, with false

positive results in such patients **(Turck, 1975)**. Others, point out that a constant outflow of bacteria into the renal pelvis is required if counting of bacteria in ureteral urine is to be used as an indication of renal infection, which is not always the case as bacteruria usually occurs intermittently **(Kass and Zinner, 1969)**. In addition, unilateral renal involvement can not be distinguished from bilateral involvement. **(Fang et al ., 1979)**.

Still, in practical term, since it is easy to perform, safe, inexpensive and does not require an expert cystoscopist, it has now replaced the ureteral catheterization technique as the method against which all non-invasive techniques are compared. **(Rubin et al., 1986)**.

Non-invasive techniques:

Urinary concentrating ability:

Patients with upper UTI differ from those with lower urinary tract infection in that, they often have an abnormality in renal concentrating ability. The inability to concentrate urine is most obvious when maximal urinary concentrating ability is measured **(Kaitz 1961)**. **Kaitz and london (1964)** proved that normal concentrating ability is uncommon in the presence of significant pyelonephritis. **Clark et al., (1969)** demonstrated that renal and not bladder bacteruria is associated with decreased urinary concentrating ability. A typical result was reported by **Ronald et al., (1969)** in a group of 38 patients whose infection was directly localized