Review Article:

Assessment of correlation between urinary secretary IgA (sIgA) levels and different types of urinary tract infection (UTI) in various age groups

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ABSTRACT

Urinary tract infections (UTIs) currently rank among the most prevalent infectious diseases worldwide, with chronic and recurrent infections being especially problematic. Urinary secretory IgA (sIgA) in mucosal surface is an important immunological defense in preventing bacterial adherence to periurethral epithelia and uroepithelial. This is a thematic review describing and focusing on a central element which is taken into consideration from different point of views .So, the present study surveyed a brief consideration of assessment correlation between urinary sIgA levels and urinary tract infection (UTI) in various age groups. In children with anatomic abnormalities, higher rates of sIgA was seen compared to children without anatomic abnormalities. The interesting point was that children with recurrent UTI with normal urinary tract had lower levels of sIgA compared to the control group. Also, no remarkable difference of the sIgA concentration rate was seen in healthy and rUTI children who had no bacteriuria; yet, it was considerably higher in children with bacteriuria. It was proven that locally synthesized sIgA was low in patients' urine with recurrent UTI, independent of the presence or absence of bacteriuria. UTI did not interfere with sIgA secretion as shown by high sIgA in patients with upper UTI. Low urinary sIgA may illustrate one factor predisposing to recurrent UTI. The outcomes displayed that the existence of sIgA is associated with the UTI in children as well as in adults; however, sIgA showed to be manipulative to the infective agent and can also be applied to recognize infection type . Therefore, evaluation of urine antibody levels can provide another marker of host responses to infection, which can be used either as a simple screening test or could be beneficial to facilitate along with other experiments in establishing an assessment.

Keywords: Urinary Secretary IgA (sIgA) Levels; Urinary tract infection (UTI); Children; Adults; Pyelonephritis; Cystitis

INTRODUCTION

Urinary tract infections (UTIs) currently rank among the most prevalent infectious diseases worldwide, with chronic and recurrent infections being especially problematic .The primary etiologic agents associated with UTIs are strains of uropathogenic *Escherichia coli* (UPEC). Nonetheless, some bacteria especially UPEC isolates, express a wide spectrum of virulence and fitness factors that aid in successful colonization of the mammalian urinary tract. These microorganisms can in fact invade a number of host cell types, including the terminally differentiated superficial facet cells and less mature intermediate and basal epithelial cells that comprise the stratified layers of the bladder urothelium. Host cell invasion is proposed to facilitate both the establishment and persistence of them within the urinary tract. Moreover, pathogenic extraintestinal isolates harbor specialized virulence factors, *i.e.*, traits that confer pathogenic potential, which are infrequent among commensal isolates.

Urinary tract infections (UTIs) occur when pathogen enters the urethra and goes up into the higher parts. If the infection only stays in the bladder, the UTI is entitled as "cystitis" but if it

goes up to the kidney it is called "pyelonephritis". These infections are among the widespread ones among children and adults [1-3].

sIgA in children

Immunoglobulin A (IgA, also referred to as sIgA) is an antibody that plays a critical role in immune function in the mucous membranes. More IgA is produced in mucosal linings than all other types of antibody combined; between three and five grams are secreted into the intestinal lumen each day [4, 5]. This accumulates up to 15% of the total immunoglobulin produced in the entire body [6].

IgA has two subclasses (IgA1 and IgA2) and can exist in a dimeric form called secretory IgA (sIgA). In its secretory form, IgA is found in mucous secretions, including tears, saliva, sweat, colostrum and secretions from the genitourinary tract, gastrointestinal tract, prostate ,and respiratory epithelium. It is also found in small amounts in blood. The secretory component of sIgA protects the immunoglobulin from being degraded by proteolytic enzymes, thus sIgA can survive in the harsh gastrointestinal tract environment and provide protection against microbes that multiply in body secretions [7] . sIgA can also inhibits inflammatory effects of other immunoglobulins [8] . Several studies have manifested that every changes in sIgA levels may be associated with UTI. Finding rapid techniques to diagnose the patients with UTI is so important. The existence of sIgA in urine is not only one of the factors related to being infected, but also an indicator for the sort of infection. The assessment of urine antibody levels can be used either as a simple screening test or could be useful as an assistant along with other tests for a proper diagnosis. It should be noted that this conclusion can be true for both children and adults.[9] Fliedner M et.al demonstrated that in younger children, UTIs were frequently associated with anatomic abnormalities. Notably, they had higher rates of sIgA than children without anatomic abnormalities. And yet, the interesting point is that children who had a history of recurrent UTI with normal urinary tract without symptoms and bacteriuria had lower levels of sIgA than in controls. So, it was concluded that low urinary sIgA values may be a marker for recurrent symptomatic bacteriuria in girls with normal urinary tract"[10]. The study of Teodosio M et.al claimed that the bacteriuria was the element which made the difference. This study was conducted on healthy children and children with history of recurrent UTI (rUTI). It was observed that there were no remarkable differences of the sIgA concentration rate between healthy and rUTI children who had no bacteriuria, but it was considerably higher in children with bacteriuria, as compared to healthy, as well as to children without bacteriuria. No difference between children with anatomic abnormalities and normal ones was found. Conversely, it was noted that a previous study suggests a sIgA deficiency in children with rUTI who had no bacteriuria. [11]

sIgA in Adults

In Floege J et.al study, it was demonstrated that in a group of patients with acute UTI, sIgA level was increased interestingly in normal women who did not have symptomatic problem at the time of study but had rUTI with or without urological problem [12]. In another research on "bacterial adherence and humoral immune response", patients with recurrent UTI had a slightly higher concentration of urinary sIgA, almost the same as in controls [13]. Another study on "the role of humoral immune response and bacterial adherence in the pathogenesis of symptomatic and asymptomatic UTI in women showed sIgA level was increased in women with symptomatic UTI [14]. Remarkably, lower urinary sIgA were detected in women with acute UTI. Comparably, low sIgA was found in UTI women with and without urethral narrowing. Low urinary sIgA were also found, however, in asymptomatic women with a history of UTI without bacteriuria at the time of the study and in women with an acute bacteriuria without a history of UTI. Enhancement of urinary sIgA level was percieved in persons with tube nephrostomy,and were invisible in all bacteriuric persons without nephrostomy and exist in all with nephrostomy.Women with an acute offensive form of UTI without a history of UTI as well as those who possessed low urinary sIgA. Given their young age, such probands may demostrate women susceptible to recurrent UTI who had experienced their first attack; yet, this presumption remains theoretical. Every storing and processing of urine sample may cause a variable detriment of

sIgA. Several artifacts is thought and deprived by suitable procedures. First, urinary sIgA in women pertain on the phase of the cycle. The change of sIgA amount with the menstrual cycle is much greater than the mistake of replicate modules which do not overpass 10%. However, low urinary sIgA in recurrent UTI cannot be pertained to the clustering of UTI occurrence at the menstrual period, whereas the occurrence is allocated indiscriminately to the menstrual cycle . Urinary sIgA decrease by water polyuria is excluded by the finding of low urinary sIgA when considered for urinary creatinine. It is improbable that other proteins interpose with the attempt in women with UTI, whiles low concentration urinary diffusion plates for IgG and transferrin is examined routinely and these consistently fail to show IgG presence or transferrin in persons with nephrostomy. Finally, urinary bacteria can cause the consumption of sIgA by proteolytic cleavage. Conatminated urine with Escherichia coil (10^5 cfu/ml) with incubation for 24 hr at 37°C failed to reduce sIgA to 15%, while the sIgA amount of noninfected urine under the identical conditions changed by no more than 3%.

Riedasch G et.al, showed that the presence of low urinary sIgA could be the cause or the consequence of urinary tract infection. Likewise, luminal infections (negative antibody coating) could interfere with local sIgA synthesis. No change of sIgA synthesis in experimental bladder infections was established, and sIgA levels were low in acutely symptomatic urinary tract infection without antibody-coated bacteria; yet, they were consistently elevated in patients with nephrostomy and antibody-coated bacteria [15].

Differences between Pyelonephritis and Cystitis

It is possible to differentiate pyelonephritis from cystitis by measuring the levels of sIgA. An obvious change has been seen in pyelonephritis patients compared to normal controls but levels in cystitis patients were the same as in healthy people. It can be related to differential secretion of sIgA by upper and lower urinary tract mucosa when exposed to infectious agents [16]. In contrast, Greenwell D et.al, showed a rise in sIgA level in lower UTI without any sIgA level change in upper UTI. In nephrostomy or ureterostomy, sIgA levels could even be zero. Consequently, sIgA level increase happened faster when patients had recurrent UTI [17]. Glycosaminoglycans (GAGs) are heteropolysaccharides in mammalian tissue and consist of repeated disaccharide units with mono-sulfated or non-sulfated monosaccharaides. GAGs are important components of the extracellular matrix (ECM) with several physiological roles, in the recognition, migration, adhesion, proliferation and differentiation processes [18]. Glycosaminoglycan helps sIgA in urinary tract fight against infections. In an analysis on urinary glycosaminoglycan and sIgA in patients who had renal transplantation and UTI when cyclosporine was taken, it was noted that both elements had been reduced in UTI [19]. Immunoglobulin A nephropathy (IgA N) is the most important glomerulonephritis in the world and can lead to a complete renal failure after 20-25 years and patients must be continuously assessed. As renal biopsy is an invasive method, scientists suggested sIgA as a biomarker for evaluation of kidney injury in IgAN. It was noted that high levels of urinary sIgA can be a reliable parameter. The more noticeable the kidney injury is, the higher the occurrence of urinary sIgA gets. This assessment can be used in the monitoring processes [20]. In patients with bacteriuria, urinary sIgA in upper UTI was higher than in patients with unchallenging lower UTI. [21]

CONCLUSION

Some investigators inquired the changes in sIgA, IgA, and free secretory component at first years life in respect to age, sex, and infants' nourishing practice. When healthy children were checked in contrast to those with acute and recurrent UTI, acute UTI remarkably eventuated in raised sIgA, IgA, and free secretory component compared to controls [22]. So, sIgA in urine is not only associated with UTI in children but seems to address the infective agent and could then be used to recognize infection type [23]. Other scientists illustrated that female children with symptomatic UTI with normal urinary tracts had remarkably higher sIgA excretion amount compared to controls or girls without symptoms, and urinary sIgA excretion amount were exclusively highest in children with symptomatic UTI who owned an abnormal

urinary tract [24] .This agrees with previous observations of those who found higher urinary sIgA in UTI of children with severe anatomic derangements of urinary tracts [15]. Furthermore, it was concluded from another study that low urinary sIgA may also represent an important predisposing factor to recurrent UTI [25] .

The effect of malnutrition on IgA has been established albeit in animal studies. [26-28] In one of the studies, the results suggested that protein deprivation resulted in a reversible reduction in the IgA response to antigens [26]. Similarly, other researchers specifically demonstrated that the protein deprivation in mice is accompanied by the stimulation of Lyt-2+ suppressor T cells which suppress IgA response after oral antigenic exposure [27]. In addition, the findings from a relevant study showed that dietary protein played a significant, site-specific role in the developmental expression of the secretory immune system, as severe protein malnutrition dramatically suppressed this immune component in the rat models [28]. The pattern of UTI etiologic agents is similar in malnourished and non-malnourished children; transferrin levels are generally reduced in self-assembled monolayers, leading to free, unbound iron in circulation. This is thought to provide a milieu for Gram-negative organisms to thrive, resulting in Gram-negative sepsis and subsequently UTI through the hematogenous route [29].

Urinary sIgA concentrations, as measured by immunodiffusion, were not different from control women and women with recurrent UTI; yet, this technique of slgA measurement does not reliably exclude sIgA loss. In general, evidence suggests that sIgA levels increase in children with UTI and increases in children with rUTI bacteriuria; in rUTI with no bacteriuria sIgA levels do not change. In both acute and symptomatic UTI, the sIgA levels are higher but in rUTI it is slightly lower than normal. In asymptomatic rUTI, the sIgA levels are normal, too. While it is suggested that in pyelonephritis sIgA levels rise and in cystitis they are normal, there exists a controversy because in some studies it has been concluded that UTI related to lower parts leads to higher levels of sIgA and no change can be seen in UTI related to higher parts. In nephrostomy sIgA level can even be zero. In the cases of bacteriuria, sIgA levels in UTI related to upper parts are higher than lower parts. Glomerulonephritis can lead to high levels of sIgA while renal transplantation when taking cyclosporine will lead to lower levels of sIgA. In this study, an in-depth examination of principles and procedures was provided through evaluation of relevant objectives. The central element was taken into considerations from different point of views. It was noted that the evaluation of urine antibody levels can provide another marker of host responses to infection, which can be used either as a simple screening test or could be beneficial to facilitate the establishing an assessment along with other experiments. It is worth mentioning that sIgA levels vary in different types of UTI and various age groups.

"The authors declare no conflict of interest"

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