Effect of diabetes on occurrence of urinary tract infection and asymptomatic bacteriuria among diabetic and ketacidosis patients in Egypt

N.N. Adly, Y.M. Ragab, A.M. Hashem, A.K. Ahmady

Cairo University Egypt
Corresponding author's E-mail:Nermin_Nader@hotmail.com

Abstract

Diabetic patients have a higher risk of infections which is the leading trigger of diabetic ketoacidosis. The second most common infection in diabetics is urinary tract infection (UTI). Elevation of glucose level induces an inflammatory process within numerous tissues in the body leading to disturbance in cytokines level and oxidative stress. This study is divided into two parts, firstly it was to investigate the prevalence of asymptomatic bacteriuria (ASB) and urinary tract infections in 84 Type 1 diabetes patients, 63 Type 2 diabetes patients and 57 ketoacidotic patients, and to determine the uropathogens responsible for ASB and UTIs as well as their antimicrobial susceptibility pattern. The second part is to determine the level of IL-1β, IL-6 and superoxide dismutase (SOD) in blood samples of diabetic and ketoacidotic patients. Escherichia coli was the most common isolated bacterial uropathogen followed by Enterococcus faecalis, Staphylococcus saprophyticus and Pseudomonas aeruginosa. These isolates showed 100% sensitivity to cephalothin, imipenem, linezolid, teicoplanin, ceftobiprole and piperacillin-tazobactam. Upon examining cytokines level in diabetic patients, results showed higher levels of IL-1β and IL-6 than control samples, indicating inflammation and disturbance in the regulation of metabolic, regenerative, and neural processes, while SOD examination showed lower levels than control samples, indicating both micro- and macrovascular diabetic complications.

Keywords: Urinary tract infection, asymptomatic bacteriuria, diabetes, IL-1β, IL-6, superoxide dismutase.

INTRODUCTION

Diabetes has interested medical authors for over 3 millenia since the ancient Egyptians who discovered this disease in 1862 AD (Poretsky, 2002). According to WHO, diabetes mellitus is the ninth leading cause of death worldwide. Good diabetes management has been shown to reduce the risk of complications (Stratton et al., 2000) otherwise it may lead to microvascular and macrovascular damage (King et al., 1999) as well as microbial infections (Joshi et al., 1999) especially urinary tract infection (Chitã et al., 2013), accounting for nearly 25% of all infections in the elderly and affecting mainly children and women (Buonanno and Damweber, 2006). Hirji et al. (2012a) reported a 60% increase in the risk of urinary tract infection in diabetic patients. UTI is of great concern since it is considered as a precipitating factor of diabetic ketoacidosis (DKA) together with pneumonia (Koul, 2009). DKA can be developed in less than 24 hours and it is the most severe acute metabolic complication of diabetes mellitus (Umpierrez et al., 1996) as it causes 70% of diabetes-related fatalities (Flaws, 2002). Elevation of glucose level induces an inflammatory process within numerous tissues in the body (Wellen and Hotamisligil, 2005). Therefore, cytokines reflect the presence and intensity of inflammation, and they have long been used as a clinical guide to diagnosis and management (Gabay, 2006). The main cytokines involved in the pathogenesis of diabetes as well as ketoacidosis are IL-1, TNF-α, and IL-6 (Alexandraki et al., 2006; Stewart, 2006). Interleukin 1 (IL-1), is a key mediator of inflammation (Mandrup-Poulsen, et al., 2010) while IL-6 plays roles in the immune system and inflammation (Guzmán et al., 2010).

Oxidative stress may constitute the key and common event in the pathogenesis of secondary diabetic
complications (Moussa, 2008). It occurs due to both hyperglycemia (de Carvalho Vidigal et al., 2012) and ketosis (Jain and McVie, 1999). Superoxide overproduction is considered as a major pathogenic pathway in diabetic vascular complications (Brownlee, 2005).

SOD is the major antioxidant enzyme for superoxide removal, (Vaziri et al., 2003), and the front line for defense against reactive oxygen species (ROS) (Apel and Hirt, 2004).

The aim of this study was firstly to determine uropathogenic pattern and UTI percentage in urine samples obtained from T1DM, T2DM and ketoacidotic patients as well as the antibiotic sensitivity patterns of the pathogens concerned. The second aim was to determine the level of IL-1β, IL-6, and SOD in blood samples obtained from the three mentioned groups; T1DM, T2DM and ketoacidotic patients.

**METHODOLOGY**

This study was done on three groups of patients’ type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM) and DKA patients.

**Bacteriological urine samples analysis**

**Samples collection**

A total of 84 urine samples of T1DM patients and 57 samples of ketoacidotic patients were collected from children department and intensive care unit in National Diabetes & Endocrinology Institute- Kasr El Ainy- Cairo, Egypt, respectively. A number of 63 samples of T2DM patients were collected from a private clinical laboratory, Giza. Urine samples were obtained by clean voided mid-stream technique or from urethral catheter as in case of DKA patients.

**Urine analysis and microscopy**

Urine samples collected were tested by dipstick method for glucose in T1DM and T2DM patients, and for both glucose and ketones in ketoacidotic patients. Each sample was tested microscopically for pus cells and for the initial count of organism by pour plate technique. Samples showing pyuria and bacteriuria as well as positive urine glucose test in T1DM, T2DM patients and positive urine glucose and ketone test in ketoacidotic patients were subjected to a sequence of identification steps.

**Biochemical investigation**

One ml of each selected sample was added to each of lactose broth and trypticase soya broth. After incubation for 24 hr at 37°C, 0.1ml from the lactose broth was streaked on MacConkey agar and EMB, and 0.1ml from trypticase soya broth was streaked on Mannitol salt agar, Cetrimide agar, Nutrient agar and Sabouraud dextrose agar + chloramphenicol. After incubation at 37°C for 24 hr, growing organism was checked for colony morphology, gram reaction and motility; then subjected to a sequence of identification tests including: catalase, oxidase, coagulase, indole, methyl red, Voges-Proskauer, triple sugar iron, germ tube, citrate utilization test, urease test, and novobiocin sensitivity test.

**Antibiotic sensitivity tests**

Each isolated organism was tested for antibiotic sensitivity according to Kirby Bauer method (Bauer et al., 1966). Tested antibiotics included: Ampicillin 10 μg, Ampicillin+ Sulbactam 10/10 μg, Piperacillin 100 μg, Cefepime 30 μg, Aztreonam 30 μg, Imipenem 10 μg, Meropenem 10 μg, Vancomycin 30 μg, Norfloxacin 10 μg, Ofloxacin 5 μg, Gentamicin 10 μg, Linezolid 30 μg, Methicillin 5 μg, Cefaclor 30 μg, Oxacillin 1 μg, Cloxacillin 5 μg, Cefotaxime 30 μg, Penicillin 10 U, Amoxicillin 25 μg, Teicoplanin 30 μg, Cephalothin 30 μg, Cefalexin 30 μg, Cefadroxil 30 μg, Ciprofloxacin 5 μg, Piperacillin + tazobactam 100/10 μg, Polymyxin B 300 U, Erythromycin 15 μg and Clindamycin 2 μg that were all obtained from Bioanalyse Co. (Turkey). Ceftobiprole 30 μg, Novobiocin 5 μg, Voriconazole 1 μg, Fluconazole 25 μg and Nystatin 100 U were obtained from Becton Dickinson (USA).

**Immununological assay of IL-1β, IL-6, and SOD in Serum by ELISA**

**Samples collection**

Blood samples were collected from patients of T1DM, T2DM and ketoacidotic patients for serum level assay of IL-1β, IL-6, and superoxide dismutase (SOD) by the use of ELISA. Samples were collected from T2DM patients at diabetes clinic, El Kasr El Ainy hospital. T1DM blood samples were collected from Diabetes and Endocrinology department as well as Abo El Reesh pediatric hospital. DKA blood samples were collected from intensive care unit of Diabetes and Endocrinology department and Abo El Reesh pediatric hospital.

**Samples immunoassay**

Each sample collected from the groups of volunteers was tested first for blood glucose by Accucheck blood glucose test strips. Normal control blood samples were collected from Abo El Reesh pediatric hospital and Kasr El Ainy...
Table 1. Mean age of the study population

<table>
<thead>
<tr>
<th>Type of patients</th>
<th>No.</th>
<th>Mean age ± SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1DM</td>
<td>84</td>
<td>10±4</td>
<td>4</td>
<td>18</td>
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<tr>
<td>T2DM</td>
<td>63</td>
<td>54±6</td>
<td>42</td>
<td>67</td>
</tr>
<tr>
<td>DKA</td>
<td>57</td>
<td>37±17</td>
<td>11</td>
<td>62</td>
</tr>
</tbody>
</table>

Urine analysis result

Table 2. Distribution of UTI cases in diabetic patients.

<table>
<thead>
<tr>
<th>Number of samples/ percentage</th>
<th>T1DM</th>
<th>T2DM</th>
<th>DKA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of samples collected</td>
<td>84</td>
<td>63</td>
<td>57</td>
</tr>
<tr>
<td>Number of male/female of samples collected</td>
<td>48/36</td>
<td>34/29</td>
<td>36/21</td>
</tr>
<tr>
<td>Total number of infected samples/ percentage</td>
<td>54/ 64.28%</td>
<td>49/ 77.77%</td>
<td>42/ 73.68%</td>
</tr>
<tr>
<td>Number of male infected samples/ percentage</td>
<td>24/ 44.4%</td>
<td>27/ 55.1%</td>
<td>26/ 61.9%</td>
</tr>
<tr>
<td>Number of female infected samples/ percentage</td>
<td>30/ 55.5%</td>
<td>22/ 44.8%</td>
<td>16/ 38%</td>
</tr>
</tbody>
</table>

RESULTS

Bacteriological assay

Sampling design

During the study period, clean-catch urine samples were obtained by mid-stream method from T1DM patients, T2DM patients and from ketoacidotic patients. Table 1 shows the number of submitted UTI cases from each diabetes type with their age mean, SD, minimum and maximum age.

Total aerobic microbial count and pyuria results

As shown in table 2, out of 84 T1DM patients, 54 patients (64.28%) showed positive urine culture with bacteriuria and pyuria. Out of 63 T2DM patients, 49 patients (77.77%) showed positive urine culture and pyuria. Out of the 57 ketoacidotic patients, 42 patients (73.68%) showed positive urine culture and pyuria. The prevalence of UTI in female (30%) was higher than male (24%).

Identification of bacterial isolates

Isolated bacterial strains from urine samples were examined phenotypically for gram reaction, cell shape, culture description, and biochemical tests according to Bergey's manual (1994) and Koneman's Color Atlas and Textbook of Diagnostic Microbiology (2006). Finally, API was used for confirmation if needed. Out of 145 isolated strains, 68 were gram positive bacteria, 71 strains were gram negative and yeast strains represented in Candida albicans were detected in 6 samples. Figure 1 shows that the most frequently isolated uropathogens were Escherichia coli, followed by Enterococcus faecalis, Staphylococcus saprophyticus, Pseudomonas aeruginosa and Staphylococcus aureus.

Antibiotic susceptibility testing

Susceptibility of gram negative isolates As shown in figure 2, Escherichia coli showed 100% sensitivity to cephalothin (first generation cephalosporin) and imipenem, while its least sensitivity was to norfloxacin. Klebsiella pneumoniae exhibited the highest sensitivity to...
imipenem with percentage 100%, however, all strains were resistant to cefalexin, ofloxacin and norfloxacin. 

*Salmonella* was unique in being sensitive to all tested antibiotics except norfloxacin. As for *Morganella* its
highest sensitivity was to cephalothin with a percentage of 100%, while all strains were resistant to cefalexin, norfloxacin, and ampicillin / sulbactam with a percentage of 100%.

Proteus vulgaris was 100% sensitive to cephalothin, cefalexin, imipenem, and cefadroxil, meanwhile it was 100% resistant to the other antibiotics. Proteus mirabilis showed 100% resistance to cephalothin, while it showed full resistance to cefalexin, norfloxacin and ampicillin + sulbactam.

Pseudomonas aeruginosa exhibited 100% sensitivity to piperacillin-tazobactam and imipenem while it showed 100% resistance to piperacillin. The least sensitivity was exhibited to gentamycin and cefepime (fourth generation cephalosporin) with a percentage of 36.8% and 26.3%, respectively.

Susceptibility of gram positive isolates

Data presented in figures 6 and 7 illustrate that Staphylococcus aureus showed 100% sensitivity to ceftobiprole (fifth generation cephalosporin). As for linezolid, cefaclor (second generation cephalosporin), and cefotaxime (third generation cephalosporin) it showed the same sensitivity to them with a percentage of 89.4%. However, all Staphylococcus aureus strains were 100% resistant to methicillin, oxacillin, cloxacillin, and cefepime (fourth generation cephalosporin).

Staphylococcus saprophyticus showed 100% sensitivity to ceftobiprole and linezolid but 100% resistance to methicillin, oxacillin, cloxacillin, and cefepime.

All Staphylococcus epidermidis strains were sensitive
to imipenem, meropenem, linezolid, cefaclor, cloxacillin, cefotaxime, and ceftriaxone. Its sensitivity to oxacillin and cefipime was 50%, while it was 100% resistant to methicillin Enterococcus faecalis was 100% sensitive to teicoplanin and linezolid followed by vancomycin with a percentage of 86.9%. It showed very low sensitivity to penicillin and amoxicillin (8.7 and 13%, respectively).

Streptococcus pyogenes showed 100% sensitivity to linezolid and cephalothin while it showed 100% resistance to ampicillin, penicillin, erythromycin and clindamycin.

In conclusion, among the gram negative isolates Salmonella typhimurium showed the highest sensitivity to the tested antibiotics, while among the gram positive, Staphylococcus epidermidis was the most sensitive. On the other hand, Proteus vulgaris was the most resistant gram negative isolate while the gram positive isolates Staphylococcus aureus, Staphylococcus saprophyticus and Enterococcus faecalis had in parallel the same resistance level to tested antibiotics.

Yeast isolates

As shown in figure 7, Candida albicans sensitivity to voriconazole was greater than for both fluconazole and nystatin with a percentage of 83.4%.

Cytokines immunological assay

The same letter means that there is no significant difference between the two groups by using Duncan multiple comparison test at p<0.05. The different letters mean that there is a significant difference between the two groups by using Duncan multiple comparison test at p<0.05.

A significant difference was observed by using One Way Anova at P<0.05 between the five groups in IL-1β, IL-6 and SOD analysis as shown in table 3. By using Duncan multiple comparison test at P<0.05 in the analysis of each of IL-1β, IL-6 and SOD, there is a significant difference between normal control I and Type I diabetes, normal control I and DKA, DKA and Type I diabetes, as well as between normal control II and Type II diabetes.

Table 4 was constructed to identify that the value of 5.19 was the best cut-off point to predict response of IL-1β, 5.8 for IL-6 and 0.16 for SOD. IL-1β of 5.19 or more provided a sensitivity of 98%, and a specificity of 100%. IL-6 of 5.8 or more provided a sensitivity of 100% and a
Table 3. Study population of diabetic patients compared to controls.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>N</th>
<th>Minimum</th>
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<th>Mean</th>
<th>S.D</th>
<th>F-value</th>
<th>p-value</th>
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<td>10</td>
<td>27</td>
<td>58</td>
<td>42.50b</td>
<td>10.61</td>
<td>12.93</td>
<td>0.000*</td>
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<tr>
<td></td>
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<td>58</td>
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<td>9.07</td>
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<tr>
<td></td>
<td>DKA</td>
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<td>14</td>
<td>8.45a</td>
<td>3.02</td>
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<tr>
<td></td>
<td>Normal control group I</td>
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<td>5</td>
<td>19</td>
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<td>4.85</td>
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<tr>
<td></td>
<td>Normal control group II</td>
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<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
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<td>7.58</td>
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<td>7</td>
<td>3.20a</td>
<td>1.85</td>
<td>8.60</td>
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<td>Type 1</td>
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<td>8</td>
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<tr>
<td></td>
<td>Normal control group I</td>
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<td>-</td>
<td>-</td>
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<td>IL-1 B</td>
<td>DKA</td>
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<td>16.8</td>
<td>24.1</td>
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<td>20.13</td>
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<td>4.3</td>
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<td>DKA</td>
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<td>17.9</td>
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<tr>
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<td>0.19</td>
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<tr>
<td>SOD</td>
<td>DKA</td>
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<td>0.01</td>
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<td>0.17</td>
<td>0.23</td>
<td>0.20d</td>
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</table>

S.D = Standard Deviation

*= There is a significant difference by using One Way ANOVA at p< 0.05

Table 4. The best cut-off point, sensitivity and specificity of IL-1β, IL-6 and SOD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cut-off point</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>A.U.C</th>
<th>p-value</th>
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<tbody>
<tr>
<td>IL-1B</td>
<td>&gt;5.19</td>
<td>98.33</td>
<td>100</td>
<td>1</td>
<td>0.0001*</td>
</tr>
<tr>
<td>IL-6</td>
<td>&gt; 5.8</td>
<td>100</td>
<td>100</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>SOD</td>
<td>&gt;0.16</td>
<td>81.67</td>
<td>95</td>
<td>0.95</td>
<td>0.0001*</td>
</tr>
</tbody>
</table>

*= Significant at p<0.001.

specificity of 100%. SOD of 0.16 or more provided a sensitivity of 81.67% and a specificity of 95%.

**DISCUSSION**

Urinary tract infection is a common medical problem; sometimes, leading to deaths either from acute infection or from chronic renal failure (Khadka et al., 2012). Risk of UTI is higher with increasing duration of diabetes (Boyko et al., 2005). High urine glucose content and defective host immune factors predispose to infection. Hyperglycemia causes neutrophil dysfunction by increasing intracellular calcium levels and interfering...
with act in and, thus, diapedesis and phagocytosis. Also this may contribute to malfunctioning in the local urinary cytokine secretion and an increased adherence of bacteria to the cells of the uroepithelial cells (Saleem and Daniel, 2011). Vaginal candidiasis and vascular disease also play a role in recurrent infections (Brusch and Bronze, 2013).

A high prevalence of ASB (71 %) was recorded in this study. This value is higher than that reported in other studies ranging from 19 to 47.2 % (Baqai et al., 2008; Longdoh et al., 2013; Simkhada, 2013).

The study showed that males are more vulnerable to pathogenic attack than females throughout a wide age distribution. In terms of pathogenic distribution, E. coli was the most commonly recovered uropathogen with a percentage of 17.2 % which is the least recorded prevalence among other studies ranging from 30.8 to 83.7 % (Hryniewicz et al., 2001; Bonadio et al., 2006; Simkhada, 2013).

Enterococcus faecalis was the second most isolated uropathogen with a percentage of 15.8% which is obviously higher than other studies ranging from 1.7 to 9.52 % (Hryniewicz et al., 2001; Longdoh et al., 2013; Simkhada, 2013).

Staphylococcus saprophyticus had a prevalence of 15.1 % being less than that reported by Baskar et al. (2009) (55%). Pseudomonas aeruginosa and Staphylococcus aureus had the same prevalence with a percentage of 13.1 % which was higher than that obtained in other studies where Pseudomonas aeruginosa prevalence was found to range from 2.5 to 9.52 % (Hryniewicz et al., 2001; Ramana and Chaudhury, 2012; Longdoh et al., 2013; Simkhada, 2013).

Staphylococcus aureus prevalence was higher than that reported by Ramana and Chaudhury (2012) and lower than that found by Longdoh et al., (2013).

The least prevalence among G+ve bacteria was for Staphylococcus epidermidis (1.3%) as well as Streptococcus pyogenes which is lower than that reported by Longdoh et al. (2013). Among G−ve bacteria both Proteus vulgaris and Salmonella enterica had the least prevalence with percentage 0.68%.

These high percentages refer to the fact of being commensal bacteria colonizing the gastrointestinal tract (Franz and Horl, 1999) as well as referring to virulence factors related to these uropathogens. One of the most important virulence mechanisms in urinary tract infections is adherence which is an initial step in the infectious process for successful establishment of infection by bacterial pathogens which requires adhesion to host cells, this is done by adherence factor. Its importance also refer to its role in adhering to urinary catheter or other implants especially in case of hospitalized patients (nosocomial pathogens). Cell adhesion molecules includes pili as possessed by E.coli (Nagamatsu et al., 2015) and Klebsiella pneumoniae (Murphy et al., 2013), adhesins as used by Staphylococcus saprophyticus (Kline et al., 2010), Enterococcus faecalis (Nielsen et al., 2013) and Proteus mirabilis (Armbuster and Mobile, 2015), MSCRAMMs of staphylococcus aureus (Costa et al., 2013), Extracellular DNA Exopolysaccharides in Pseudomonas aeruginosa (Cole et al., 2014).

Urease is also a well-known virulence factor for a number of bacterial pathogens including, Proteus spp. (Armbuster, and Mobile, 2015), staphylococcus saprophyticus (Kline et al., 2010), Klebsiella spp. (Brisse S et al., 2006). It is essential for pathogenic bacteria to colonize in host and in maintenance of bacterial cells in tissues, having for toxic effect due to its enzymatic activity. Antimicrobial resistance among uropathogens causing community- and hospital-acquired UTIs is increasing (Bonadio et al., 2001). Upon investigating the susceptibility pattern of enterobacterial isolates with different antibiotics they showed high sensitivity rate with a percentage of 100% with cephalothin unlike data obtained by Sahm et al. (2001) who found 86.6% resistance. For Pseudomonas aeruginosa, its highest sensitivity was shown to piperacillin/ tazobactam with percentage 100 % which is in contrast to data obtained by Mokaddas and Sanyal, (1999) (14%).

On the other hand, Staphylococcus isolates showed highest sensitivity rate with percentage 100% to ceftobiprole which is similar to the observations of Bogdanovich et al., (2005). Enterococcus faecalis showed 100 % sensitivity to teicoplanin which is the same as found by Rudy et al., (2004). Streptococcus pyogenes exhibited 100% sensitivity to linezolid in accordance with that found by Cercenado et al. (2001). All isolates were also sensitive to cephalothin unlike the data of Longdoh et al. (2013) who reported a sensitivity percentage of 55% to similar cephalosporins. Candida albicans showed high sensitivity to voriconazole with a percentage of 83.4% followed by fluconazole and nystatin with a percentage of 66.6%. This sensitivity to azaoles was higher than that reported by longdoh et al. (2013) which was 28%, while sensitivity to nystatin was lower than that reported by the same authors (72.3%). In conclusion, the high ASB percentage observed in this study is of major public health importance since it is a leading cause to diabetic ketoacidosis which is together with hyperglycemic coma the most severe acute metabolic complication of diabetes mellitus (Umpierrez et al., 1996).

Circulating IL-6, TNF-α, and CRP have been determined as markers of the inflammatory response (Davi et al., 2003). Chemokines play a central role in inflammatory processes by regulating leukocyte migration into sites of tissue damage (Erbaigli et al., 2001). The proinflammatory cytokines, IL-1β, IL-6, and TNF-α have cytotoxic, cytostatic (inhibits insulin synthesis and secretion) or cytokidial actions to pancreatic islets by inducing nitric oxide (NO) production (Tchorzewski et al., 2001). IL-1beta is a regulator of the body's inflammatory response and is produced after infection, injury and antigenic challenge (Maedler et al., 2009). In this study,
IL-1β was examined randomly among Type 1 diabetes mellitus, Type 2 diabetes mellitus and ketoacidotic patients. Plasma levels of IL-1β in patients admitted were higher than control group which is a similar finding to that reported by Javed and Ahmed (2013). In the present study, the mean plasma level of IL-1β was nearly three, seven and five times the control group value in Type 1 diabetes mellitus, ketoacidotic and Type 2 diabetes mellitus patients, respectively.

IL-6 is reported to have multiple effects ranging from inflammation to host and tissue injury (Santhanam et al., 2003). It is known to increase inflammation and the development of vascular disease and atherosclerosis (Jain et al., 2003). IL-6 plasma levels were examined in Type 1 diabetes mellitus, Type 2 diabetes mellitus, and ketoacidotic patients blood, and the obtained values were significantly higher than control group plasma levels. These data were in accordance with other study by Wegner et al. (2013). In contrary Dogan et al. (2006) found that IL-6 was lower in diabetic patients. Several complications of diabetes mellitus are associated with increased activity of free radicals and accumulation of lipid peroxidation products (Prakash and Sudha, 2012). Numerous reports indicate variations in the levels of antioxidants in diabetic patients (Lee et al., 1995). This is due to decreased activity of antioxidant enzymes which increase the susceptibility of diabetic patients to oxidative injury. In this study, the level of SOD in the three groups of patients was lower than that of control group. This observation is in line with other study by Prakash and Sudha (2012), however, Moussa (2012) observed a significant increase in SOD levels in another study. Based on the above data as well as the ROC curve in this study, we can conclude that IL-1β, IL-6 and SOD are sensitive markers for diabetes complication.

REFERENCES


