Some Microbial and Immunophysiological Parameter in Patients with Renal Failure

Abdalnabi J Abid  Rana Jalil
Biology Dept., Coll. Of Science For Women, Babylon Univ. – Iraq
Corresponding author e-mail: dr_almamory59@yahoo.com

Abstract
Background: Escherichia coli reported to be the most common bacteria isolate from patients with renal failure, while Klebsilla pneumoniae were found to be the second common isolated, followed by Staphlococcus aureus. Also study explained an increased in levels of IL-17, Fas L, creatinine, urea. Objectives: To isolate microorganisms from patients with renal failure, also to determined Immunophysiological parameter for patients. Methods: 102 blood sample (61 male (59.8%) and 41 female (40.1%)), 150 urine sample for patients undergoing hemodialysis at industrial kidney unit in Marjan Teaching Hospital from November 2013 to June 2014. All sample were cultured on different media for full bacteriological identification. In addition blood samples were taken from patients for immunophysiological tests. Results: The most common gram negative bacterial isolates were Escherichia coli (38.8%), followed Klebsilla pneumoniae (34.32%), Enterobacter spp (6.71%) and Pseudomonas aerogenosa (4.47%). The gram positive bacteria were Staphylococcus aureus (13.43%) and Staphylococcus epidermidis (2.24%). Also results explained an increased in levels of IL-17, Fas L, creatinine, urea.

Keywords: IL17, Fas-L, Bacteria, S. creatinine, B. urea

Introduction
Renal failure is a condition in which the kidneys fail to remove metabolic end-products from the blood and regulate the fluid, electrolyte, and pH balance of the extracellular fluids. The underlying cause may be renal disease, systemic disease, or urologic defects of no renal origin. Renal failure can occur as an acute or a chronic disorder. Acute renal failure is abrupt in onset and often is reversible if recognized early and treated appropriately. In contrast, chronic renal failure is the end result of irreparable damage to the kidneys, it develops slowly, usually over the course of a number of years (Chue et al., 2010).

The accumulation of nitrogenous wastes is an early sign of renal failure, usually occurring before other symptoms become evident. Urea is one of the first nitrogenous wastes to accumulate in the blood, and the blood urea level becomes increasingly elevated as renal failure progresses (Katzung and Bertram, 2007), raised levels of potassium, decreased levels of calcium, increased levels of phosphate, and in later stages anemia.

Chronic kidney failure (CKD) requires renal replacement therapy, which may involve a form of dialysis. Dialysis is the process of removing waste products and excess fluids from the body. There are two types of dialysis: hemodialysis and peritoneal dialysis. In hemodialysis (HD), blood is removed from the body and pumped by a machine outside the body into a dialyzer (artificial kidney) (Mark, et al., 2003). Although true and complete replacement of renal function is not provided by dialysis, this modality removes metabolic wastes and excess body water, and replenishes body buffers in order to sustain life (Rebecca et al., 2010).

Study found the most common causative organism is Escherichia coli, but, Pseudomonas, Staphylococcus aureus, and Staphylococcus epidermidis may also cause this infection, other gram-negative rods including Klebsilla Pneumoniae and Enterobacter spp, which also causes Kidney failure (Springhouse, 2005).

All aspects of inflammation and immune function may be affected adversely by the high levels of urea and metabolic wastes, including a decrease in granulocyte count, impaired humoral and cell-mediated immunity, and defective phagocyte function (Haroun et al., 2003). The acute inflammatory response and delayed-type hypersensitivity response are impaired, the serum levels of cytokines such as IL-17, Fas L are elevated due to general overproduction and inadequate clearance of these substances (Eleftheriadis et al., 2007).

Materials & Methods
Microbial samples were isolated from 150 patients with renal failure Specifically hemodialysis at industrial kidney unit in Marjan Teaching Hospital. Routine diagnostic test were used as a tool for microbial identification, starting by Macroscopical appearance, cultures on different media included (Nutreint agar, Blood agar, Macconky agar and Manitol agar), to more biochemical tests which included haemolysis on blood agar, Oxidase, Catalase, Coagulase, Indole, Monitol, Methyl red, Urase and Vogas proskauer tests (Collee et al., 1996).

Immunological finding included the evaluation of IL-17 and Fas L. Elisa techniques were used in the testing of sera samples, also these tests was conducted in accordance with the manufacturer's instructions.
BOSTER, while physiological tests included urea, creatinine, these tests was conducted in accordance with the manufacturer's instructions bioMerieux.

Statistical analysis included the use of the specialized statistical software SPSS to determine the values of Least significant differences (LSD) in t-test and data was subjected in Excel to draw the paragraphs (Nizi.,2000).

Results

From 150 isolate of UTI in patients about (134) 89.3% of Sample had positive bacterial culture and (16) 10.6% of them had negative culture as shown in table (1).

<table>
<thead>
<tr>
<th>Urine Culture</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture positive</td>
<td>134</td>
<td>89.3%</td>
</tr>
<tr>
<td>Culture negative</td>
<td>16</td>
<td>10.6%</td>
</tr>
<tr>
<td>Total</td>
<td>150</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Escherichia coli* is the most common bacteria 52 (38.3%), followed by *Klbsialla pneumoniae* 46 (34.32%), *Staphylococcus aureus* 18 (13.43%), *Enterobacter spp.* 9 (6.71%), *Pseudomonas aeruginosa* 6 (4.47%) and *Staphylococcus epidermidis* 3 (2.23%) as shown in figure (1).

![Figure (1) Types and percentage of bacterial isolates](image)

Immunological findings included the determination of serum levels of IL-17 and Fas L. The level of IL-17 was significantly raised in all age groups of patients suffering from chronic renal failure in comparison to the control group, especially age group (31-40) accounted (144.33±1.528) while the levels in control group about (49±6.506), (P<0.05) as in table (2).
Table (2) Level of IL-17 in all renal failure patients

<table>
<thead>
<tr>
<th>Classes</th>
<th>groups</th>
<th>IL-17 Level pg/ml M±SD</th>
<th>L.S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-20</td>
<td>Patients</td>
<td>123.3±28.34</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>58±6</td>
<td>45.4</td>
</tr>
<tr>
<td>21-30</td>
<td>Patients</td>
<td>133.3±22.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>55.2±0.251</td>
<td>36.07</td>
</tr>
<tr>
<td>31-40</td>
<td>Patients</td>
<td>144.33±1.528</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>49±6.506</td>
<td>2.44</td>
</tr>
<tr>
<td>41-50</td>
<td>Patients</td>
<td>126±5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>42.5±0.5</td>
<td>8.05</td>
</tr>
<tr>
<td>51-60</td>
<td>Patients</td>
<td>129.3±11.504</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>37±1</td>
<td>18.51</td>
</tr>
<tr>
<td>61-70</td>
<td>Patients</td>
<td>57±29.72</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>27.5±2.5</td>
<td>16.52</td>
</tr>
<tr>
<td>71-80</td>
<td>Patients</td>
<td>57.3±12.86</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>18.5±0.5</td>
<td>20.63</td>
</tr>
</tbody>
</table>

Fas L was significantly raised in the groups of patients suffering from renal failure in comparison to the control group, the age group (10-20) accounted (121.7±3.51) while the levels in control group was (34±2) (P<0.05) as in table (3).

Table (3) Level of FasL in all renal failure patients

<table>
<thead>
<tr>
<th>Classes</th>
<th>groups</th>
<th>FasL Level pg/ml M±SD</th>
<th>L.S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-20</td>
<td>Patients</td>
<td>121.7±3.51</td>
<td>6.28</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>34±2</td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>Patients</td>
<td>92.3±31.94</td>
<td>51.21</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>24.5±0.5</td>
<td></td>
</tr>
<tr>
<td>31-40</td>
<td>Patients</td>
<td>42.3±15.37</td>
<td>4.82</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>19.23±0.257</td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td>Patients</td>
<td>42.63±15.53</td>
<td>3.43</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>17.5±0.5</td>
<td></td>
</tr>
<tr>
<td>51-60</td>
<td>Patients</td>
<td>39.3±11.5</td>
<td>18.44</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>15.2±0.251</td>
<td></td>
</tr>
<tr>
<td>61-70</td>
<td>Patients</td>
<td>36.7±20.82</td>
<td>3.206</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>13±2</td>
<td></td>
</tr>
<tr>
<td>71-80</td>
<td>Patients</td>
<td>32.3±7.51</td>
<td>12.27</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>9.5±1.5</td>
<td></td>
</tr>
</tbody>
</table>

Urea level a highly significantly p<0.05 has been observed in all age groups and the highest concentration was showed in the age group (61-70) years and was (41.8mmol/L) compared with control group (2.3mmol/L), p<0.05 as in figure (2).
Figure (2): Level of Urea in all renal failure patients compared with control group. Creatinine were recorded as a higher in age group (21-30) years and range (1033 mmol/L) compared with control group (71.93 mmol/L) p<0.05 as in figure (3).

Figure (3): Level of Creatinine in all renal failure patients compared with control group.

Discussion
Patients with kidney failure are more prone to developing urinary tract infections, the mere act of passing urine tends to flush out the urinary tract of infectious agents so they cannot gain a foothold and cause problems (Rajiv Vij et al., 2009). Once the kidneys fail and the production of urine is decreased, this normal flushing action is gone. UTIs usually are caused by bacteria which normally inhabit the bowel and spread to the urinary tract by local extension may be explained by a greater incidence of urinary obstructions which in turn leads to infections (Ishani et al., 2005).

These results were agreed with other result obtained by (Leblebicioglu and Esen., 2003), had reported that 78.4% of patients with UTI had positive culture and those with negative culture may be associated with Mycoplasmal or Chlamydial infections. Approximately 20% of woman attending to S.T.D clinic have Mycoplasma in their urinary tract (Brook et al., 2007).
These results were agreed with other result obtained by (AL-Jammaly., 2005), when he studied genitourinary tract infections among Women in Mosul and showed that (33.6%) of UTI in woman were caused by Escherichia coli. As well, (Gordon and Jones., 2003), showed that 47% of UTI were caused by Escherichia coli,

Generally, Escherichia coli is the most common bacteria, because it has some virulence factors, which helps in pathogenesis, as pili, which are responsible for adherence in the urinary tract epithelium. With the intention of the adhesion has important role in the ascending to kidney, (Pallett and Hand.,2010). However, it appeared that K pneumoniae is the second causative agent in this study because it isolated from (34.32%) of all isolates. So that ,it was different from(AL-Jammaly., 2005), who showed that only (10.8%) of UTI among woman in Mosul were caused by K pneumoniae , (Jones et al., 2002), who showed that 11% of UTI were caused by K pneumoniae, the difference between recent study and (Jones et al., 2002) and (AL-Jammaly, 2005) may reflect the difference in population behavior or personal hygiene, because K pneumoniae is present in feces of about 5% of normal individuals (Brook et al., 2007), So that, bad hygiene may lead to UTI.

In addition to E coli and K pneumoniae, also staphylococcus aureus was important causative agent that cause in this study, because it represented in 13. 43% of all isolates So that these results were differ from the results obtained by Epidemiologic studies had reported that 40-60% of hemodialysis patients are carriers of Staphylococcus as a normal flora (Ena et al.,1994). One of the most cause of UTI in hospitalized patients is Pseudomonas aeruginosa due to its ability to resist different types of antibiotics and other chemicals which used in sterilization processes in hospitals(Dennis, et al.,2001; Cruze, et al.,2009).

The chronic inflammatory state is considered to be a driving force for Autoimmune Glomerulonephritis ( AGN). In recent years the IL-17RA/Th17 axis appears to contribute to the pathogenesis of human AGN ( Sinclair and Stevens .,2007). that IL-17 signaling is critical for the development of renal pathology and inflammatory changes in the kidney,Consequently IL-17 enhanced the production of proinflammatory cytokines and chemokines from tubular epithelial cells ( Steinman ,2007). which are implicated in the recruitment of innate effector cells in the kidney in addition to the rise in the thyroid gland, which is in the case of excessive increase in chronic renal failure patients as this height increases to stimulate Th cells and thus increase the production of IL -17( McLachlan and Rapoport.,2000).

The Fas L/Fas system regulates immune and inflammatory responses. FasL is expressed by renal cells and its expression increases during kidney damage (Andersen et al., 2006). Where the damage is happening in the kidney leads to apoptosis and thus stimulate the FasL. Who in turn stimulates Fas receptor which Interfere with FasL and consists FADD compound which passes several pathways to to arrived to target cells in kidney (Ghadimi et al.,2002).

Urea level a highly significantly p<0.05 has been observed in all age groups and the highest concentration was showed in the age group (61-70) years .The reason for the high concentration of urea in the blood serum of patients with chronic renal failure to the fact that urea basic nitrogen material from metabolic waste, which consists mainly in the liver and exclude from the blood by the urine, In the event of a malfunction, and a shortage of kidney function leads to few exclude of urea and accumulate and concentration its increases in the blood (Patel et al.,2007) . Blood urea were increased production due to either to a high protein diet or to excessive destruction of cellular proteins of the body as in ;fever, heavy infections .At nearly all types of kidney disease will scoring in urea retention (Harmon.,2009).

The concentration of creatinine were recorded as a higher in age group (21-30) years In contrast, there was significant highly in creatinine is a waste product of muscle breakdown. The same finding was observed many reviews (Allen,2012) Healthy kidneys were exclude creatinine from the blood by the urine whereas ,the kidney failure creatinine buls in blood until it is removed by dialysis.that the causes of creatinine levels elevation in serum of kidney failure as End Stage Renal Failure (ESRF) was relative independent of protein ingestion, water intake, and rate of urine production (Rebecca et al.,2003). Increased dietary intake of creatine or eating a lot of meat can increase daily creatinine excretion,( Faull., 2007).

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