Epidemiology and etiology of catheter-related nosocomial infections in a Turkish hospital

Epidemiologia ed eziologia delle infezioni nosocomiali correlate a un catetere in un ospedale turco

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INTRODUCTION

Nosocomial infections are an important public health problem in many developing countries, particularly in intensive care units (ICUs) [1]. Device utilization in critically ill patients is responsible for a high risk of complications such as catheter-related bloodstream infections (CRBSI), Ventilator-Associated Pneumonia (VAP) and Urinary Tract Infections (UTI) [2]. In general, each unit may have in se a risk environment for development of infections, simultaneously containing many diverse factors that favour the spread of clinically evident and generally serious infections: the constant presence of serious concomitant diseases, the frequent use of invasive diagnostic methods procedures, the elevated selective pressure caused by multiple prolonged antibiotic treatment on endogenous and environmental flora [3]. As a result, the resistant rates of bacteria are high, the change over years is not predictable and continuous surveillance is necessary to monitor antimicrobial resistance and to guide antibacterial therapy for each hospital [4]. The aim of our study was to assess the causative agents of catheter-related nosocomial infections, the distribution rate of causative agents due to hospital units, infection sites and catheter types and determine the risk factors which facilitate these nosocomial infections.

PATIENTS AND METHODS

In this study a total of 219 patients who developed nosocomial infections and were treated in Sisli Etfal Training and Research Hospital between January 2001 and March 2003 were evaluated retrospectively. In all 337 bacterial strains were isolated. Nosocomial infection was defined as an infection developing 48 hours after admission and up to ten days after discharge from hospital. Nosocomial infections were defined according to Standards of Centers for Disease Control and Prevention (CDC) criteria [5]. “Symptomatic urinary tract infection” was defined using two criteria [5].

Criterion 1: the patient has one or more of the following signs or symptoms with no other recognized cause of fever (>38°C): urgency, frequency, dysuria or suprapubic tenderness, and a urine culture positive for $10^5$ or more microorganisms per millilitre with no more than two micro-organisms.

Criterion 2: the patient has at least two of the following signs or symptoms with no other recognized cause of fever (>38°C), urgency, frequency, dysuria or suprapubic tenderness and pyuria ($\geq$10 white blood cells per millilitre); organisms seen on Gram stain, diagnosed as urinary tract infection by a physician; or instituted treatment for a urinary tract infection by a physician [5].

For “ventilator-associated pneumonia” crite-
rion 1 was as follows: the patient has rales or dullness to percussion on physical examination of the chest and at least one of the following: new onset of purulent sputum or change in character of sputum; organism cultured from blood; or isolation of an etiologic agent from a specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy.

Criterion 2: the patient has a new or progressive infiltrate, consolidation, cavitation, or pleural effusion on chest radiography and at least one of the following: new onset of the purulent sputum or change in character of sputum; organism cultured from blood; or isolation of an etiologic agent from a specimen obtained by transtracheal aspirate, bronchial brushing or biopsy. Expectorated sputum cultures were not used for diagnosis of pneumonia [5].

Catheter Related Bloodstream Infection (CRBSI) is defined as bacteremia/fungemia in a patient with an intravascular catheter with at least one positive blood culture obtained from a peripheral vein, clinical manifestation of infection (fever, chills, and/or hypotension) and no apparent source for BSI except the catheter. One of the following should be present: a positive semiquantitative (>15 CFU/catheter segment) culture whereby the same organism (specimen and antibiogram) is isolated from the catheter segment and peripheral blood; simultaneous quantitative blood cultures with differential period of the CVC culture versus peripheral blood culture positivity of >2 hours [5].

Infections of central nervous system shunts were diagnosed with aspiration of the shunt reservoir to obtain cerebrospinal fluid (CSF) for examination and culture [6].

Data were recorded as overall patient day stay according to the total number of hospitalized patients for one year. Nosocomial infection rate was calculated as an infection count developed in 100 patients per 1000 hospital-day stay [7]. The urine samples from patients with urinary catheters were obtained with sterile procedure from the tips of the catheters. The micro-organisms isolated from the materials of the endotracheal aspiration tubes obtained by transtracheal aspiration (TTA) were accepted as pathogens. TTA samples were obtained from patients intubated with endotracheal tube and samples were obtained from catheter tips and subcutaneous tissues simultaneously from patients with intravascular catheters, ventriculoperitoneal shunts and drainage catheters, and cultivated on blood agar Eosin Methylene Blue (EMB) agar. The semi-quantitative method (Maki) was used for catheter cultures and conventional methods were used for the other culture types [8]. The isolated bacteria were identified with standard methods and their antibiotic susceptibility was determined according to the National Committee for Clinical Laboratory Standards (NCCLS) by the Bauer-Kirby Disc Diffusion Method [9].

 RESULTS

In our study the total number of patients hospitalized between January 2001 and March 2003 was 53,841. The number of patients who developed nosocomial infection during this period was 870. The total hospital stay was found to be 424,902 patient days. The nosocomial infection rate was 1.62%; infection rate per 1000 hospital stay was 2.05%. In our study, of 219 cases 90 (41%) were female, 129 (59%) male. It was observed that catheter infections were most frequent in 131 cases (60%) who were 45 years and older.

The most frequently isolated micro-organisms from catheter infections were *Pseudomonas spp* (17%), *Klebsiella spp* (16%), *Escherichia coli* (13%), *Acinetobacter spp*. (12%), Coagulase Negative Staphylococci (CNS) (11%) and methicillin-resistant *Staphylococcus aureus* (MRSA) (9%) (Table 1). Of the catheter infections, according to frequency 136 (59%) of them were due to urinary indwelling catheters, and 52 (23%) due to endotracheal tube usage (Table 2). The most frequently isolated causative agent in urinary catheter infections was *E. coli* (25%) followed by *Klebsiella spp*. (17%), *Pseudomonas spp*. (15%), *Enterobacter spp*. (8%), CNS and *Candida spp*. (8%), *Acinetobacter spp*. and *Proteus spp*. (5%) (Table 1). The number of the causative agents isolated from 52 (23%) cases who developed an infection due to tracheal intubation was found to be 116 (34%) and 72% of these micro-organisms were Gram-negative bacteria. The most frequently isolated causative agents were *Pseudomonas spp*. in 29 (25%) cases, *Acinetobacter spp*. in 24 (21%), *Klebsiella spp*. in 20 (17%), MRSA in 20 (17%), CNS in 9 (8%), Methicillin-sensitive *S. aureus* (MSSA) in 2 (2%) and 55 (24%) had polymicrobial infection (Table 2). Moreover, of the 229 catheters applied 55 (24%) had polymicrobial causative agents and, in all, 337 micro-organisms totally isolated (Table 2).

In our study the appearance rate of microorganisms quickly acquiring multiple drug resistance such as *Acinetobacter spp.*, MRSA, *Pseudomonas spp.*, CNS, Klebsiella spp. and Enterobacter spp. in intensive care units (ICUs) were found to be 88%, 84%, 63%, 58%, 56% and 45% respectively. Units where catheter infections were found to be most frequent were ICU

Table 1 - Distribution rate of causative agents by catheter type.

<table>
<thead>
<tr>
<th>Micro-organisms</th>
<th>Urinary catheter</th>
<th>Endotracheal tube</th>
<th>IV catheter</th>
<th>VP shunt</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>MRSA*</td>
<td>0</td>
<td>0</td>
<td>20</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>CNS**</td>
<td>13</td>
<td>8</td>
<td>9</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>MSSA***</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>29</td>
<td>17</td>
<td>20</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>Pseudomonas sp</td>
<td>26</td>
<td>15</td>
<td>29</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>42</td>
<td>25</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Acinetobacter spp</td>
<td>10</td>
<td>5</td>
<td>24</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>14</td>
<td>9</td>
<td>5</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Proteus spp</td>
<td>9</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Candida spp</td>
<td>14</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>12</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>171</td>
<td>51</td>
<td>116</td>
<td>34</td>
<td>29</td>
</tr>
</tbody>
</table>

* methicillin-resistant Staphylococcus aureus; **coagulase-negative staphylococci; ***methicillin-susceptible Staphylococcus aureus

Table 2 - Polymicrobial (≥ two causative agents) infection rate due to catheter types.

<table>
<thead>
<tr>
<th>Micro-organisms</th>
<th>Urinary catheter</th>
<th>Endotracheal tube</th>
<th>IV catheter</th>
<th>VP shunt</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Number of catheters with single causative agent</td>
<td>106</td>
<td>78</td>
<td>33</td>
<td>63</td>
<td>22</td>
</tr>
<tr>
<td>Number of catheters with polymicrobial causative agents</td>
<td>30</td>
<td>22</td>
<td>19</td>
<td>37</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total catheter numbers</strong></td>
<td>136</td>
<td>59</td>
<td>52</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td><strong>Total causative agents</strong></td>
<td>171</td>
<td>51</td>
<td>116</td>
<td>34</td>
<td>29</td>
</tr>
</tbody>
</table>

Table 3 - Distribution rates of cases by unit and catheter type.

<table>
<thead>
<tr>
<th>Units</th>
<th>Urinary catheter</th>
<th>Endotracheal tube</th>
<th>IV catheter</th>
<th>VP shunt</th>
<th>Total catheter</th>
<th>Total cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>ICU</td>
<td>42</td>
<td>31</td>
<td>52</td>
<td>100</td>
<td>8</td>
<td>32</td>
</tr>
<tr>
<td>Surgery</td>
<td>35</td>
<td>26</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Internal</td>
<td>59</td>
<td>43</td>
<td>0</td>
<td>0</td>
<td>12</td>
<td>48</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>136</td>
<td>60</td>
<td>52</td>
<td>23</td>
<td>25</td>
<td>11</td>
</tr>
</tbody>
</table>
and in the surgery units, Acinetobacter (8%), CNS (16%), and MRSA (12%) in de-
wellingly urethral catheters had been previously used prior to about 80% of nosocomial UTI [14, 16]. In a study 97.3% of UTI were associated with urinary catheters [18]. In another study this rate was estimated at 65.3% [17]. Franchi et al. found a UTI rate of 2.9/1000, *P. aeruginosa* being the most common pathogen (70.0%) in devices associated with UTI [12]. Of those patients having instrumentation, 10% to 30% will ultimately develop significant bacteriuria. It is estimated that 1% to 4% of bacteriuric patients will ultimately develop clinically significant bacteremia, with a case fatality rate of 13% to 30% [19]. In our study the most frequently isolated causative agent in urinary catheter infections was *E. coli* (25%) followed by *Klebsiella spp.* (17%), *Pseudomonas spp.* (15%), *Enterobacter spp.* (8%), CNS and *Candida spp.* (8%), *Acinetobacter spp.* and *Proteus spp.* (5%) (Table 1). In one study over 60% (65.3%) of urinary tract infections were associated with urinary catheters. *E. coli* (32.4%) was the most common pathogen reported, followed by *Klebsiella spp.* (17.0%), *Candida spp.* (12.8%), *Pseudomonas aeruginosa* (11.7%) and *Enterococcus* (8.5%) [17]. Black et al. and Warren reported that in UTIs with bacteremia the most frequently isolated causative agent was *E. coli* [20, 21]. Generally, nosocomial respiratory tract infections are the second most frequently seen after urinary tract infections, but take first place in ICU (18). In a study of cases of nosocomial pneumoniae and lower respiratory tract infections, 81.9% were associated with mechanical ventilation [18]. In another study the ventilator-associated pneumonia rate was found to be 20.4/1000 and the most common pathogens isolated were *P. aeruginosa* (38.3%) and MRSA (18.1%) [12]. In our study the number of the causative agents isolated from 52 (23%) cases which developed infection due to tracheal intubation was found to be 116 (34%) and 72% of these micro-organisms were Gram negative bacteria. The most frequently isolated causative agents were *Pseudomonas spp.* in 29 (25%) cases, *Acinetobacter spp.* in 24 (21%), *Klebsiella spp.* in 20 (17%), MRSA in 20 (17%), CNS in 9 (8%), *Methicillin-Sensitive S. aureus* (MSSA) in 2 (2%) and 55 (24%) had polymicrobial infection (Table 2). In a study by Kanafani et al. it was found that the
VAP rate was 47% in 70 cases which had mechanical ventilation for more than 48 hours, out of the isolated micro-organisms 83% were Gram-negative rods and the most frequently isolated bacteria were *A. anittratus* and *P. aeruginosa* [22]. In another study it was reported that of the 175 patients who had mechanical ventilation for more than 24 hours, 56 (32%) developed VAP [23]. Noor et al. reported that seventy (28%) out of 250 mechanically ventilation patients developed VAP (the VAP rate was 26 cases per 1000 ventilator days) [24]. Additionally, Gram negative organisms and *S. aureus* were responsible for over 90% of cases. In studies by Petdachai it was reported that in VAP the first three most frequently isolated Gram negative causative agents were *P. aeruginosa*, *K. pneumoniae* and *Acinetobacter spp.* [25] Polymicrobial infection was found in 11 specimens (12.9%) from enteral aspirate culture. In a study from India it was reported that the most frequently isolated micro-organisms from VAP in intensive care units were Gram negative bacteria, with *Pseudomonas spp.* in first place, and besides this 16.3% of the cases had polymicrobial infection [26]. In our study it was observed that especially in cases where urinary catheterization or endotracheal intubation had been performed, infections were often polymicrobial (Table 2).

The contamination of intravascular devices may lead to cellulites, abscess, septic trombophlebitis, bacteraemia, endocarditis and especially in patients where CVC have been applied sepsis may develop [27]. In a study from Brazil it was reported that the risk factors associated with contaminated catheter tips were ≥14 days hospital stay, ≥7 days catheterization and antibiotic therapy. CNS and *S. aureus* were the most common micro-organisms at the insertion site (78%) and in the catheter type (94%) [28].

The high counts of staphylococci, at the insertion site, and the significant association of this colonization with catheter tip contamination, indicate that the skin is an important reservoir of micro-organisms associated with catheter-related bloodstream infections. Recently the importance of CNS and especially that of *S. epidermidis* has increased worldwide as a nosocomial pathogen [27]. In a study performed by Pawar et al., pathogens isolated as CRBSI agents were *E. coli* (47%), *Acinetobacter spp.* (11.7%), *Enterobacter spp.* (5.8%), *Proteus spp.* (5.8%), methicillin-resistant Staphylococcus species (5.8%), and *Candida spp.* (11.7%) [29]. Franchi et al. found that the vascular catheter associated BSI rate was 19.1/1000; methicillin-resistant CNS 21.9% and *P. aeruginosa* 17.2% were isolated [12]. In another study per 1000 days of catheterization were 17.2 and 3.93, respectively for CNS and *P. aeruginosa* [30].

In our study the rate of staphylococci among the agents causing IV catheter infections and drainage site of infection was found to be 69% and 62%, respectively (Table 1). The frequency of micro-organisms as causative agents in IV catheter infections were CNS 35%, MRSA 17%, MSSA 17% and *Acinetobacter spp.* 14%, *Klebsiella spp.* 10%, *Candida spp.* 7%; the frequency in VP shunt and drainage site infections were CNS 29%, MRSA 19%, *Klebsiella spp.*, *Pseudomonas spp.*, MSSA 14%, *Acinetobacter spp.* 10% (Table 1).

In a study by Lyytikainen et al. it was reported that the frequency of the micro-organisms causing blood-borne infections due to IV catheter usage was CNS 31%, *S. aureus* 11%, *E. coli* 11%, enterococci 6%, *P. aeruginosa* 5%, *Candida spp.* 4% [31].

In our study out of 219 catheters applied to 229 cases, 55 (24%) had polymicrobial causative agents (Table 2). Urinary catheters and endotracheal tubes applied were 136 (59%) and 52 (23%) respectively (Table 2); the number of causative agents isolated from materials of these cases were found to be 171 (51%) and 116 (34%), respectively (Table 1).

Compared with other units in the hospital, the nosocomial infection rate of the intensive care units is known to be 5-10 times higher. In our study involving the 27-month period from January 2001 to March 2003 the nosocomial infection rate was 1.62%; the infection rate per 1000 hospital stay was found to be 2.05%. Among cases of nosocomial pneumonia and lower respiratory tract infections (LRTI), 81.9% were associated with mechanical ventilation, and 97.3% of urinary tract infections were associated with urinary catheter. According to the results of nosocomial infection studies in Turkey, the incidence of hospital infections varies between 1.0% and 8.6% [18]. In our study the nosocomial infection rate was found to be lower. This may be due to insufficient clinical specimens and/or the data obtained by the laboratory surveillance system.

Nosocomial infections become especially prominent in the intensive care unit where the rate is from two to five times that of the general inpatient population [32]. In the EPIC Study in
1992, pneumonia (47%) and lower respiratory tract infections were the most common nosocomial infections, followed by urinary infections and bloodstream infections. In National Nosocomial Infections Surveillance (NNIS) reports the most frequent infections were UTI. The results show that there may be variations in the rates and distributions of infections among multicentric studies [18].

In a study performed by Misset et al. prospective surveillance showed the following rates per 1000 procedure days: VAP 8.7, UTI 17.2, CVC colonization 6.1, and CVC-related bacteremia 2.0 [33]. In our study the catheter infection rates of hospitalized patients in different hospital units may be viewed in Table 3. All of the endotracheal tube infections were isolated from patients hospitalized in the ICU; infections due to usage of urinary catheters and iv catheters occurred most frequently (43 and 48% respectively) in internal units; the second highest frequency with the rate of 31 and 32%, respectively, was observed in the intensive care unit.

Ten cases hospitalized in the ICU had more than one catheter infection (Table 3). In our study the appearance rate of micro-organisms rapidly acquiring multiple drug resistance, namely Acinetobacter spp., MRSA, Pseudomonas spp., CNS, Klebsiella spp. and Enterobacter spp. in the ICU were found to be 88%, 84%, 63%, 58%, 56% and 45%, respectively.

In a study from India the rate of nosocomial pneumonia in cases monitored in the ICU was found to be 53.9% and mortality 47.3%. VAP rate was found to be 81.7% and mortality risk associated with ventilator applied 72.3% [26]. In our study 52 (23%) cases had mechanical ventilation, 45 (21%) were unconscious due to CNS pathologies. In addition, cases with tracheostomy and indwelling urinary catheters were 20 (9%) and 136 (59%) respectively. Besides, 83 (38%) of the cases had chronic illness, 27 of which (33%) diabetes mellitus, 16 (19%) malign diseases, 13 (16%) cardiovascular disease, and 27 (33%) renal system disease.

Erbay et al. reported that high prevalence of risk factors such as mechanical ventilation, coma, trauma and invasive procedures, such as nasogastric intubation and tracheotomy, are strongly associated with nosocomial infections in ICU [32].

According to the findings of Esen et al., univariate analysis of risk factors for the likelihood of the presence of infection showed that endotracheal tube, urinary catheter, multi-trauma on admission, stress ulcer prophylaxis, nasogastric feeding, mechanical ventilation and underlying cancer were risk factors [18]. The predisposing factor in 80% or more of nosocomial UTIs are related to the use of urethral catheters [21]. Catheter use is also a risk factor for sepsis: bacteraemic UTIs occurred in 4.9% of cases in our study, higher than previously reported [17]. It was reported that risk factors for UTI due to urinary catheters are prolonged usage of catheters, female sex, absence of antibiotic usage, abnormal creatine level, insufficient catheter care, diabetes mellitus, microbial colonization of the drainage bag and periurethral colonization [21].

The risk factors for the development of VAP are age (>60 years), chronic obstructive pulmonary disease, coma, unconsciousness, gastric aspiration, antibiotic usage, antiacid usage, autumn-winter periods, reintubation, self extubation, mechanic ventilation lasting more than 2 days, tracheostomy, diabetes mellitus, renal failure and blood transfusions. Cases where mechanical ventilation has been applied have 6-20 fold higher nosocomial pneumonia rates [34].

It was reported that risk factors for bacteraemia were jugular insertion side, catheterization longer than 10 days, catheter hub colonization, and catheter colonization by Gram negative bacilli, fungi and S. aureus [28]. Risk factors for catheter colonization vary according to the micro-organism which colonizes the catheter [28]. A high incidence was shown of infections associated to invasive procedures and the presence of multiresistant bacteria [12].

Hence it should be emphasized that as ICUs are important risk factors for the development of catheter infections, the resistance patterns of the isolated micro-organisms from the unit should be taken into consideration in selecting appropriate antibiotics. It is also important to avoid unnecessary catheterization and ensure that preventive measures be properly applied.

**Key Words:** catheter infections, ventilator associated pneumonia, risk factors

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In this study a total of 219 patients who developed nosocomial infections and were treated in Sisli Etfal Training and Research Hospital between January 2001 and March 2003 were evaluated retrospectively. In all, 337 bacterial strains were isolated in these patients. The aim of our study was to assess the causative agents of catheter-related nosocomial infections, the distribution rate of causative agents due to hospital units, infection sites and catheter types, and determine the risk factors which facilitate such nosocomial infections. The most frequently isolated causative agents in catheter infections were Pseudomonas spp. (17%), Klebsiella spp. (16%), E. coli (13%), Acinetobacter spp. (12%), Coagulase Negative Staphylococci (CNS) (11%) and Methicillin-Resistant S. aureus (MRSA) (9%). In 136 (59%) patients infections were due to urinary catheterization and in 52 patients (23%) due to tracheal aspiration catheters. Of the 229 catheters applied, the polymicrobial infection rate was found to be 24% (55 patients). Multiple drug resistant strains were more frequently isolated in Intensive Care Units (ICU).

It was emphasized that as ICUs are important risk factors for the development of catheter infections, the resistance patterns of the isolated microorganisms from the unit should be taken into consideration for the selection of appropriate antibiotics. We also conclude that it is important to avoid unnecessary catheterization and that preventive measures should be properly applied.

REFERENCES


[9] National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial disc


