# Enterococcal bacteremia in a teaching hospital in the Central region of Saudi Arabia

*Fawzia E. Al-Otaibi,* MD, KSFPath (Micro), *Abdelmageed M. Kambal,* MBBS, FRCPath, *Rubana A. Baabbad,* MD, KSF.

## ABSTRACT

**Objective:** To study enterococcal blood stream infection including the different species isolated, their antibiotic resistance associated risk factors and outcome of treatment.

**Methods:** A retrospective and prospective study was carried out over a 12 month period between June 2001 and May 2002 in King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia. Sixty episodes of enterococcal bacteremia with clinical significance detected in adults and neonates were included. Statistical analysis of the epidemiological characteristic, etiologic risk factors and mortality were determined.

**Results:** Fifty-four (90%) of the episodes were hospital acquired. Fifty-five percent of patients were elderly males and 20% were neonates. Patients usually have severe underlying diseases (57%) and the mortality rate was 28%. The estimated duration of hospital stay after acquiring the Enterococcal bacteremia was 40 days. The source of bacteremia remained undetermined in 72% of the episodes. Gastrointestinal tract, urinary tract and intravascular catheter were the most frequently recognized associated sites of infection. Thirty-three patients (55%) had previously received antimicrobial agents (mainly cephalosporins). In this study, intravascular catheter ($p$=0.0002), urinary catheter ($p$=0.00001), mechanical ventilation ($p$=0.002), previous surgery (digestive tract surgery ($p$=0.01) and prior stay in an intensive care unit ($p$=0.03) were the factors associated with Enterococcal bacteremia and mortality.

**Conclusion:** Efforts to reduce the occurrence of enterococcal bacteremia should be focused on appropriate use of cephalosporins and external devices.

**Saudi Med J 2004; Vol. 25 (1): 21-25**

The incidence of enterococcal infection, mainly hospital-acquired, has increased over the past 2 decades.[1,2] They are anticipated to precipitate management problems in the near future as isolates with novel mechanism of acquired resistance to antimicrobials are more frequently seen.[3] They have greater capacity for transmitting these resistance to other species and even other genera.[4] One of the most clinically important manifestation of enterococcal infection is bacteremia.[2] *Enterococcus faecalis* and *Enterococcus faecium* account for most of the infections caused by the genus *Enterococcus*.[5] These infections including bacteremia, usually originate from the gut or the urinary tract. In a recent years, there has been a dramatic increase in *Vancomycin Resistant Enterococci* (VRE).[6,7] Strains with high level resistance to penicillin, ampicillin and aminoglycoside are also more commonly seen.[8] Due to its associated morbidity and mortality enterococcal infections now represent a major challenge to clinicians.

**Methods.** This study was carried out on patients with Enterococcal bacteremia admitted to the King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia, a tertiary teaching hospital with 850 beds that serves a population of ≤1.5 million inhabitants. Prospective investigations were carried out on some

From the Department of Pathology/Microbiology (Al-Otaibi, Kambal) and the Department of Pediatrics (Baabbad), College of Medicine, King Khalid University Hospital, Riyadh, *Kingdom of Saudi Arabia*.

Received 8th July 2003. Accepted for publication in final form 20th September 2003.

Address correspondence and reprint request to: Dr. Fawzia E. Al-Otaibi, Assistant Professor, Department of Pathology/Microbiology (32), College of Medicine, King Saud University, PO Box 2925, Riyadh 11461, *Kingdom of Saudi Arabia*. Tel. +966 (1) 4671088/4671010. Fax. +966 (1) 4672462.

patients while the other investigations were retrospective. Patients were followed until discharge or death. Epidemiological, microbiological and clinical informations were gathered including age, gender, hospitalization ward (medical wards, surgical wards, or intensive care units [ICUs]), community or nosocomial acquisition, source of the bacteremia, underlying diseases and their severity and exogenous risk factors for acquisition of bacteremia. The following exogenous risk factors were recorded: (i) intravascular catheter, urinary catheter, nasogastric tube, mechanical ventilation, parenteral nutrition and previous stay in an ICU, if present in 72 hours prior to or at the onset of the Enterococcal bacteremia; and (ii) previous administration of antimicrobial agents or surgical treatments, if present 14 days prior to or at the onset of Enterococcal bacteremia. All patients with clinically significant Enterococcal bacteremia were included as cases. Patients with more than one episode were excluded and only the first episode was included. Episodes considered to be transient were excluded. An episode of bacteremia was defined as the isolation of one or more organisms from one or more blood cultures from the same patient under circumstances in which clinical evidence suggested a common source and in which the time of isolation were not separated by an asymptomatic period when the patient was not receiving antibiotic treatment. When the common source was unknown or multiple sources were evident, all positive blood cultures detected within 48 hours of another positive blood culture was considered to represent the same bacteremic episode.[9] Clinically significant bacteremia was defined as an episode of bacteremia in a patient in whom the clinical evidence of infection existed for ≥ 8 hours.[9] If signs or symptoms lasted for <8 hours, the episode was considered to be transient and excluded. An episode of bacteremia was considered to be hospital-acquired when the onset occurred 48 hours after admission, with no evidence that the infection had been present previously.[10] In any other circumstances, the infection was considered to be community-acquired. The following 2 criteria, microbiological and clinical, were used to define the source or sources of enterococcal bacteremia: (i) isolation of the same species of *Enterococcus* from clinical samples and from blood cultures within the time corresponding to the episode of bacteremia; and (ii) presence of clinical symptoms and signs of infection (based on interview, physical examination and non-microbiological complementary tests performed within the time corresponding to the episode of bacteremia, in the absence of evidence of the contrary). When clinical and microbiological criteria did not allow for the determination of the enterococcal bacteremia source, bacteremia was considered to be of unknown origin.[10] The severity of the underlying diseases was classified according to the criteria of McCabe and Jackson.[11] A patient was considered to have diabetes mellitus when a concentration of glucose in plasma of >140 mg/dl on >1 occasion on an empty stomach. Chronic renal failure was defined as a creatinine level in plasma of more than 2 mg/dl accompanied by data suggesting it was a chronic disturbance (namely confirmation of its previous existence, normocytic normochromic anemia, renal atrophy and renal osteodystrophy). Patient was considered to have liver cirrhosis when they had a definitive diagnosis (namely diagnostic liver biopsy) or a probable diagnosis (based on clinical and analytical data suggesting chronic liver disease, hepatobiliary dysfunction and portal hypertension). Neutropenia was defined as a polymorphonuclear leukocyte count of <1000/μL. Severity of illness was classified according to the definitions recommended by the consensus conference of the American College of Chest Physicians and the Society of Critical Care Medicine (Sepsis, severe sepsis, and septic shock).[12] Patients with sepsis (not severely ill or without hemodynamic compromise) were compared with those with severe sepsis or septic shock (with hemodynamic compromise or severely ill). Antimicrobial treatment was considered to be appropriate when the patients received at least 48 hours of intravenous doses of an antimicrobial agent active in vitro against the organisms isolated in the blood culture. In the case of *Enterococcus species (Enterococcus spp)*, these included penicillins, ureidopenicillins, carbapenems, glycopeptides, and quinolones in monotherapy or associated with aminoglycosides. In the remaining circumstances, the antimicrobial therapy was considered to be inappropriated.[13]

***Culture and identification of isolates.*** The requested blood cultures was made by the physician in charge on each patient. Blood samples were inoculated in blood culture bottles for aerobic and anaerobic pathogens (5-10 ml/bottle), with 2 or 3 sets obtained from each patient (Bactec Alert). Bottles were incubated at 35°C for a maximum of 5 days. Blood isolates were identified to species level using API strep system (bio Merienx SA, France); susceptibility to ampicillin, piperacillin, vancomycin, imipenem and ciprofloxacin were determined by the E-test (ABBIODISK, Sweden). Susceptibility to teicoplanin and resistance to high concentration of aminoglycosides was not assessed.

**Results.** Included in the study were 60 consecutive patients who had episodes of clinically significant enterococcal bacteremia during a 12 month period (June 2001-May 2002). Two patients with transient episodes and one patient with enterococcal endocarditis were excluded. A total of 54 episodes (90%) were hospital acquired. Their epidemiological features, underlying diseases and the exogenous risk factors associated with enterococcal bacteremia are illustrated in **Table 1** and **Table 2**. Most patients with enterococcal bacteremia were males (55%). The median age was 60 years, and 70% were located in ICUs. Twenty percent of patients were neonate (<1 month). Patients usually have severe underlying

diseases (57%) and a relatively high percentage of them had ultimately fatal outcome (28%). The most frequent underlying diseases were diabetes mellitus (18%), chronic renal failure (17%), malignancies (16%), heart disease (13%), liver cirrhosis (5%), and neonates prematurity predominate in (75%). The most frequent exogenous risk factors were intravascular catheter (73%), mechanical ventilation (63%), urinary catheter (37%) and surgery (32%). Thirty-three (55%) of patients had previously received antimicrobial agents with no activity against *Enterococcus spp* (cephalosporins, mainly cefuroxime and ceftazidime). A total of 52 episodes (87%) of bacteremia were caused by *Enterococcus faecalis*, 5 (8%) by *Enterococcus faecium*, and 3 (5%) by *Enterococcus durans*. Seventeen (28%) were polymicrobial. In the polymicrobial group gram-negative rods were the most frequently associated organisms occurring in 13 of the episodes (76%). Whereas gram-positive cocci occurred in three of the episodes (18%). Gram-positive cocci and gram-negative rods occurred in one episode (6%). Antimicrobial susceptibility of the isolates was shown in **Table 3**.

***Clinical features.*** Sources of enterococcal bacteremia were intra-abdominal in 11 patients (18%), intravascular catheter in 5 patients (8%), urinary tract in 4 patients and central nervous system (CNS) in one patient. Three patients had multiple sources. The source of bacteremia was undetermined in 40 (72%) of patients. A total of 58 patients (97%) had fever, 43 (72%) had alteration of mental status, 6 (10%) oliguria, 5 (8%) hypotension and one (2%) disseminated intravascular coagulation. Twenty-four (40%) had sepsis and 7 (12%) had severe sepsis with septic shock (namely hemodynamic compromise was present). Appropriate antimicrobial therapy was given to 49 patients (82%). The frequently used antimicrobial agents were beta-lactam antibiotic, either alone (19 patients [32%]) or with an aminoglycoside (12 patients [20%]). Other antimicrobials used were glycopeptide alone (15%) or associated with an aminoglycoside (12%), quinolone alone (3%) or associated with an aminoglycoside (1%), and sequential treatments due to other bacterial isolates (18%) (beta-lactam antibiotics and Azactam, beta-lactam antibiotics and aminoglycosides, quinolones and glycopeptides). The mean duration of therapy was 10 days and the median duration of hospital stay after acquiring the enterococcal bacteremia was 40 days.

***Mortality rates.*** The in-hospital mortality rate was 28%. The crude mortality rate was higher among patients in the ICU (76%) than among those in surgical (6%) or medical wards (18%); $p$=0.03). The crude mortality rate was not related to age, gender, presence of sepsis or septic shock. Patients with fever and severe underlying diseases had a higher mortality rate (57%, $p$=0.0006), and those patients who had a long duration of hospital stay before the onset of bacteremia also had a higher crude mortality rate (50%, $p$=0.0004). Exogenous risk factors associated with a

**Table 1 -** Demographic and clinical characteristics of patients with enterococcal bacteremia.

| Demographic clinical characteristics | Patient N | (%) |
|---|---|---|
| ***Age*** | | |
| <1 month | 44 | (73) |
| 40 - 60 year | 25 | (42) |
| 60 - 80 year | 23 | (38) |
| ***Gender*** | | |
| Male | 33 | (55) |
| Female | 27 | (45) |
| ***Ward*** | | |
| Medical | 13 | (22) |
| Surgical | 5 | (8) |
| Intensive care unit | 42 | (70) |
| ***Underlying disease*** | | |
| Diabetes mellitus | 11 | (18) |
| Renal failure (hemodialysis) | 10 | (17) |
| Liver cirrhosis | 3 | (5) |
| Solid organ cancer | 8 | (13) |
| Hematologic malignancy | 2 | (3) |
| Neutropenia | 1 | (2) |
| Heart diseases | | |
| Valvular heart disease | 2 | (3) |
| Ischemic heart disease | 6 | (10) |
| Connective tissue disease | | |
| Systemic lupus erythematosis | 2 | (3) |

**Table 2 -** Exogenous risk factors of bacteremia.

| Characteristics | Patient N | (%) |
|---|---|---|
| Intravascular catheter | 44 | (73) |
| Mechanical ventilation | 38 | (63) |
| Prior use of antimicrobials | 33 | (55) |
| Urinary catheter | 24 | (37) |
| Surgery | 19 | (32) |
| Parenteral nutrition | 4 | (7) |
| Nasogastric tube | 2 | (3) |

**Table 3 -** Susceptibilities of 20 *Enterococcal strains* causing bacteremia in hospitalized patients.

| Antimicrobial, MIC(µg/mL) | E. faecalis (n=15) n (%) | E. faecium (n=3) n (%) | E. durans (n=2) |
|---|---|---|---|
| Ampicillin (resistant ≥16) | 0 | 1 (33) | 0 |
| Imipenem (intermediate, 8; resistant, ≥16) | 1 (7) | 2 (67) | 0 |
| Ciprofloxacin (intermediate, 2; resistant, ≥4) | 4 (27) | 2 (67) | 0 |
| Vancomycin (intermediate, 8-16; resistant, ≥ 32) | 0 | 1 (33) | 0 |
| Piperacillin (resistant, ≥ 16) | 0 | 2 (67) | 0 |

E. faecalis - *Enterococcal faecalis,* E. faecium - *Enterococcal* faecium, E. durans - *Enterococcal durans*

higher crude mortality rate were placement of a urinary catheter (94%, $p$=0.00001), central lines (88%, $p$=0.002) mechanical ventilation (88%, $p$=0.002), prior stay in an ICU (65%, p=0.030) and previous surgery (59%, $p$=0.01). Among the types of surgery, digestive tract surgery is associated with the highest mortality (35%, $p$=0.04). Parenteral nutrition, previous administration of antimicrobial agents, enterococcal species and polymicrobial etiology did not modify the crude mortality rate. Infection with an organism resistant to ampicillin was also not related to mortality.

**Discussion.** In previous studies, a number of poor prognostic factors related to enterococcal bacteremia have been described. Some of those are advanced age,[14,15] severe underlying disease and immunodeficiences,[14-17] nosocomial acquisition,[15,16] polymicrobial etiology,[15,18] multiple or intra-abdominal sources or surgical wound infection,[15] prior surgery,[15] hemodialysis,[17] prior use of antimicrobials,[14,15] severe infection,[13] and inappropriate antimicrobial therapy.[13-15,18] It is evident that all of these factors could be related to each other in hospitalized patients. Thus, a multivariate analysis is needed to clarify, which factors are really important for prognosis.

In this study, several underlying diseases and exogenous risk factors were related to enterococcal bacteremia. However, only urinary catheter, central lines, mechanical ventilation, previous surgeries, prior stay in an ICU and the presence of severe underlying disease has been associated with mortality. These findings are similar to other reports. In a retrospective analysis of 81 enterococcal bacteremias, 41 of them were clinically significant, independent risk factors associated with a fatal outcome of clinically significant bacteremias were inappropriate antimicrobial therapy (OR, 17), prior use of antimicrobials (OR, 14) and the presence of severe underlying diseases (OR, 10).[14] In another case control study, Caballero-Granado et al[19] found that the exogenous risk factors associated with 30-day crude mortality among patients with enterococcal bacteremia were placement of a urinary catheter (presence [32%] versus absence of risk factors [10%]; $p$=0.007; 95% CI), mechanical ventilation (56% versus 14%; $p$<0.001; 95% CI), prior stay in an ICU ($p$<0.002) and patients with hemodynamic compromise (50% versus 11%; $p$<0.01). The crude mortality rate among patients with enterococcal bacteremia is similar to the rate among patients with bacteremia caused by other gram-positive cocci (crude mortality, 14-24%) and lower than the rate among patients with bacteremia caused by gram-negative rods (crude mortality rate, 20-50%) and yeasts (crude mortality rate, 90%).[2,15] The in-hospital mortality rate was intermediate in the present study (28%) compared with that reported by other authors (13-68%),[14-19,21-24] and it is similar to the rate reported by Caballero-Granado et al[19] (29%). In their controlled study, they considered this rate to be insignificant in the group of patients with enterococcal bacteremia compared with the control group without enterococcal bacteremia. However, some groups of patients did have a significant attributable mortality rate (namely patients who did not receive appropriate antimicrobial therapy and those with a worse clinical status). The duration of hospital stay is an index of cost in resources, both in personnel and supplies. In a case control study, Caballero-Granada et al,[19] studies the duration of hospital stay of patients with enterococcal bacteremia and compared it with that of their matched control patients and concluded that enterococcal bacteremia without endocarditis does not increase mortality rate but extend the duration of hospital stay (>5 weeks) of the patients who contracted it. Similar to this finding in our study the mean duration of hospital stay after acquiring the enterococcal bacteremia was 40 days and this extended duration has been associated in this study with mortality ($p$=0.0004). Some series have reported a high frequency of previous administration of antimicrobial agents.[15,18,22,25] Leounge et al[26] compared the nosocomial infections caused by *Staphylococcus aureus* and *Enterococci* for 6 months in a general hospital in San Francisco, USA. These authors found a strong association between *Enterococci* and the development of superinfections (93%), mainly related to the administration of cephalosporins (73%) of all enterococcal infections). In contrast, Staphylococcus aureus infections were associated with previous administration of antimicrobial agents in 43% of the cases (associated with previous administration of cephalosporins in 23%).[26] In a case-control study, Pallares et al[27] found that the independent risk factors for the development of enterococcal bacteremia were the previous administration of cephalosporins and the presence of a urinary catheter. In this study 55% of patients had previously received antimicrobial agents (mainly cephalosporins) and intravascular catheter. Mechanical ventilation and urinary catheter were the most frequent exogenous risk factors related to enterococcal bacteremia and mortality. The mechanism by which the cephalosporins increase the incidence of enterococcal infections is not known. However, it is believed that cephalosporins (and other antimicrobial agents with low activity against enterococci) could facilitate bacterial overgrowth in the bowel and subsequent carriage to the lymphatic node and the blood stream.[4] The presence of other factors (nasogastric tube and surgery) and the capacity of enterococci for being carried by fomes (urinary catheter, intravascular catheter and hands)[1,28] would favor the spread of colonization and subsequent infection. The relationship between enterococcal bacteremia and urinary catheter is the consequence of a disruption of natural barriers by exogenous devices on surfaces colonized by saprophytic flora. In one study *Enterococcus spp*. cause up to 16% of all nosocomial urinary tract infections and 6% of the bacteremic ones.[29,30] The risk factors described for the development of these infections have been urinary

tract anomalies, prior antimicrobial therapy, and prior urinary tract instrumentation. In this study, the last 2 has been found to be a significant risk factors for the development of enterococcal bacteremia.

Surgical treatment has been associated with the development of enterococcal bacteremia in prior studies. In one study, 74 of 153 (48%) patients with enterococcal bacteremia had undergone recent major surgery or had sustained full-thickness burns or multiple traumatic injuries.[15] Carton et al[31] compared patients with nosocomial enterococcal infections and those with nosocomial infections caused by other organisms. They found a 2-4-fold higher frequency of enterococcal infections among patients with prior surgical operation of the gastrointestinal, genital or urinary tract. In this study surgical treatment of all these locations was found to be a risk factor for enterococcal bacteremia and only abdominal surgery was significantly associated with mortality.

In conclusion, enterococcal bacteremia represent an important nosocomial problem with increasing incidence in patients with serious underlying diseases, prolonged hospital stay and prior treatment with antibiotics. This trend reflects the increased frequency for invasive monitoring and therapeutic procedures in seriously ill patients, the use of extremely potent broad spectrum antibiotics, and the rising numbers of immunocompromised patients. Measures such as appropriate use of invasive devices, (for example urinary catheter, mechanical ventilation, central lines), the use of restricted antibiotics (especially cephalosporins) and improved compliance with hand washing, should be further investigated in clinical trials.

**Acknowledgment.** The authors would like to thank Mr. Syed Abdul Khader for typing the manuscript.

## References


1. Korten V, Murray BE. The nosocomial transmission of enterococci. ***Curr Opin Infect Dis*** 1993; 6: 498-505.
2. Pittet D. Nosocomial blood stream infections. In: Wenzel RP, editor. Prevention and control of nosocomial infections. 2nd ed. Baltimore (MD): William & Wilkins; 1993. p. 512-555.
3. Eliopoulos GM. Increasing problems in the therapy of enterococcal infections. ***Eur J Clin Microbiol Infect Dis*** 1993; 12: 409-412.
4. Jett BD, Huycke MM, Gilmore MS. Virulence of enterococci. ***Clin Microbiol Rev*** 1994; 7: 462-478.
5. Schaberg DR, Culver DH, Gayness RP. Major trends in the Microbial etiology of nosocomii infections. ***Am J Med*** 1991; 91: 725-755.
6. Centers for Disease Control and Prevention. Nosocomial enterococci resistant to vancomycin - United States, 1989-1993. ***JAMA*** 1993; 270: 1796.
7. Huycke MM, Sahm DF, Gilmore MS. Multiple-drug resistant enterococci: the nature of the problem and as agenda for the future. ***Emerg Infect Dis*** 1998; 4: 239-249.
8. Grayson ML, Elipoulos GM, Wennersten CB, Ruff KL, De Girolami PC, Ferraro MJ et al. Increasing resistant to beta-lactam antibiotics among clinical isolates of *Enterococcus faecium*: a 22 year review at one institution. ***Antimicrob Agents Chemother*** 1991; 35: 2180-2184.
9. Roberts FJ, Geere IW, Goldman A. A three year study of positive blood cultures, with emphasis on prognosis. ***Rev Infect Dis*** 1991; 13: 34-46.
10. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. ***Am J Infect Control*** 1988; 16: 128-140.
11. McCabe WR, Jackson GG. Gram-negative bacteremia. Etiology and ecology. ***Arch Intern Med*** 1962; 110: 847-855.
12. American College of Chest Physicians and Society of Critical Care Medicine Consensus Conference Committee. Definitions of sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. ***Chest*** 1992; 101: 1644-1655.
13. Caballero-Granado FJ, Cisneros JM, Luque R, Torres-Tortosa M, Gamboa F, Diez F, et al. Comparative study of bacteremias caused by *Enterococcus spp*. with and without high-level resistance to gentamicin. The Grupo Andaluz para el estudio de las Enfermedades Infecciosas. ***J Clin Microbiol*** 1998; 36: 520-525.
14. Hoge CW, Adams J, Buchanan B, Sears SD. *Enterococcal bacteremia*: to treat or not to treat, a reappraisal. ***Rev Infect Dis*** 1991; 13: 600-605.
15. Maki DG, Agger WA. *Enterococcal bacteremia*: clinical features, the risk of endocarditis and management. ***Medicine*** 1988; 67: 248-269.
16. Shlaes DM, Lery J, Wolinsky E. *Enterococcal bacteremia* without endocarditis. ***Arch Intern Med*** 1981; 141: 578-581.
17. Landry SL, Kaiser DL, Wenzel RP. Hospital stay and mortality attributed to nosocomial enterococcal bacteremia: a controlled study. ***Am J Infect Control*** 1989; 17: 323-329.
18. Graninger W, Ragette R. Nosocomial bacteremia due to *Enterococcus faecalis* without endocarditis. ***Clin Infect Dis*** 1992; 15: 49-57.
19. Caballero-Granado FJ, Becerril B, Cuberos L, Bernabeu M, Cisneros JM, Pachon J. Attributable mortality rate and duration of hospital stay associated with *Enterococcal bacteremia*. ***Clin Infect Dis*** 2001; 32: 587-594.
20. Dougherty SH, Flohr AB, Simmons RL. "Breakthrough" *Enterococcal septicemia* in surgical patients. 19 cases and a review of the literature. ***Arch Surg*** 1983; 118: 232-238.
21. Malone DA, Wagner A, Myers JP, Watana Kunakorn C. *Enterococcal bacteremia* in two large community teaching hospital. ***Am J Med*** 1986; 81: 601-606.
22. Gullberg RM, Homann SR, Phair JP. *Enterococcal bacteremia*: Analysis of 75 episodes. ***Rev Infect Dis*** 1989; 2: 74-85.
23. Garrison RN, Fry DE, Berberch S, Pol KHC Jr. *Enterococcal bacteremia*: clinical implications and determinants of death. ***Ann Surg*** 1982; 196: 43-47.
24. Barrall DT, Kenney PR, Slotman GJ, Burchard KW. *Enterococcal bacteremia* in surgical patients. ***Arch Surg*** 1985; 120: 57-63.
25. Venditti M, Tarasi A, Visco Comandini U, Gentile G, Girmenia C, Micozzi A, et al. *Enterococcal septicemia* in patients with hematological malignancies. ***Eur J Clin Microbiol Infect Dis*** 1993; 12: 241-247.
26. Leoung GS, Chaisson RE, Mills J. Comparison of nosocomial infections due to *Staphylococcus aureus* and *Enterococci* in a general hospital. ***Surg Gynecol Obstet*** 1987; 165: 339-342.
27. Pallares R, Pujol M, Pena C, Ariza J, Martin R, Gudiol F. Cephalosporins as risk factors for nosocomial *Enterococcus faecalis* bacteremia. A matched case-control study. ***Arch Intern Med*** 1993; 153: 1581-1586.
28. Uttley AH, George RC. Nosocomial Enterococcal infections. ***Curr Opin Infect Dis*** 1991; 4: 525-529.
29. Ackermann RJ, Monroe PW. Bacteremic urinary tract infection in older people. ***J Am Soc Geriatr Dent*** 1996; 44: 927-923.
30. Morrison AJ, Wenzel RR. Nosocomial urinary tract infections due to enterococcus. Ten years experience at a university hospital. ***Arch Intern Med*** 1986; 146: 1549-1551.
31. Carton JA, Maradona JA, Asensi V, Pierez Gonzalez F, Lopez Ponga B, de la lglesia P. Infection hospitalaia por *Enterococcus*. El uso previo de antibioticos como factor de resgo a travis de un estudio de casosy controles. ***Med Clin (Barc)*** 1993; 101: 769-773.