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Comparative Evaluation of Cases with Community-Acquired Infective Endocarditis and Health Care-Associated Infective Endocarditis

Toplumdan Edinilmiş ve Sağlık Hizmeti İlişkili İnfektif Endokardit Olgularının Karşılaştırmalı Değerlendirilmesi

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ABSTRACT

Purpose: The present study aimed to comparatively evaluate the cases with health care-associated infective endocarditis and the cases with community-acquired infective endocarditis.

Material and Methods: Of the cases followed for infective endocarditis (IE), 21 (40 %) had health care-associated infective endocarditis and 31 (60 %) community-acquired infective endocarditis.

Results: Comparing the cases with community acquired infective endocarditis and the cases with health care-associated infective endocarditis, it was determined that advanced age (58.0 ± 15.1 years vs. 41.3 ± 14.4 years, $P=0.000$), presence of chronic renal insufficiency ($P=0.001$) and diabetes mellitus ($P=0.016$) as concomitant diseases, being previously hospitalized ($P=0.0001$), hemodialysis in terms of diagnostic and therapeutic interventions ($P=0.022$), presence of central venous catheter ($P=0.022$), and undergone intervention for gastrointestinal system ($P=0.060$), as well as laboratory results including positive blood culture growth for *S. aureus* and Enterococcus ($P=0.037$), and complications such as development of embolic event ($P=0.008$), spondylodiscitis ($P=0.034$) and stroke ($P=0.007$) were statistically significantly more common in health care-associated infective endocarditis cases. Whilst mortality was higher in health care-associated infective endocarditis cases (28.6 %), it was determined that there was no statistically significant difference between the groups.

Conclusion: Health care-associated infective endocarditis is a disease that is more common in the patients at advanced age, with concomitant disease and the history of exposing invasive procedures in the past for diagnostic and therapeutic purpose, and it is a disease with high morbidity and mortality that courses with serious complications.

Key words: Infective endocarditis, health care-associated infective endocarditis, community-acquired infective endocarditis

ÖZET

Amaç: Çalışmamızda sağlık bakımı ilişkili infektif endokardit ile toplumdan edinilmiş infektif endokardit olgularımızın karşılaştırılması olarak değerlendirilmesi amaçlanmıştır.

Materyal ve Metod: Olgularımızın 21 (% 40)'inin sağlık bakımı ilişkili infektif endokardit ve 31 (% 60)'inin de toplumdan edinilmiş infektif endokardit olduğu belirlendi

Bulgular: Çalışmamızda sağlık bakımı ilişkili infektif endokardit ile toplumdan edinilmiş infektif endokardit olgularımızın karşılaştırılması olarak değerlendirilmesi amaçlanmıştır. Toplumdan edinilmiş infektif endokardit ile sağlık bakımı ilişkili infektif endokardit olguları karşılaştırıldığında; ileri yaşın (58.0 ± 15.1 yıl ve 41.3 ± 14.4 yıl, $P= 0.000$), eşlik eden hastalıklar açısından kronik böbrek yetmezliğinin ($P= 0.001$), ve diyabetes mellitus varlığının ($P= 0.016$), önceden hastanede yatmış olmanın ($P= 0.0001$), tanı ve tedavi amaçlı uygulanan girişimler açısından özellikle hemodiyaliz uygulamalarının ($P= 0.022$), santral kateter varlığı ($P= 0.022$), ile gastrointestinal sisteme girişim yapılmasının ($P= 0.060$), laboratuvar bulguları açısından kan kültüründe *S.aureus* ve *Enterokok* üremesinin ($P= 0.037$), ve son olarak komplikasyonlar açısından ise embolik olay ($P= 0.008$), spondilodiskit ($P= 0.034$) ve stroke gelişiminin ($P= 0.007$) sağlık bakımı ilişkili infektif endokardit olgularında istatistiksel olarak da anlamlı olacak şekilde daha yüksek olduğu saptandı.

Sonuç: Mortalite sağlık bakımı ilişkili infektif endokardit olgularında (% 28.6) daha yüksek bulunurken iki grup arasında bu yönde istatistiksel olarak fark olmadığı tespit edildi. Sonuç olarak, sağlık bakımı ilişkili infektif endokardit, ileri yaşta ve eşlik eden hastalığa sahip, öykülerinde tanı ve tedavi amaçlı invaziv girişim uygulanan ciddi komplikasyonlar ile seyreden ve yüksek mortalite oranına sahip bir hastalıktır.

Anahtar kelimeler: İnfektif endokardit, sağlık bakımı ilişkili infektif endokardit, toplumdan edinilmiş infektif endokardit.

INTRODUCTION

Infective endocarditis (IE) is the infectious diseases of heart valves, endocardium, prosthetic valve or any other prosthetic material often caused by the bacteria. It has been determined that epidemiological profile of IE has significantly changed in the last few years particularly in the industrialized countries¹. Today, IE, which in the previous years has involved young adults having well-defined heart valve diseases (mostly rheumatoid disease), has been reported to result from health care-associated interventions and influence old patients without known heart valve disease² or with prosthetic valves³. Health care-associated infective endocarditis (HAIE), which occurs as a complication of health care-associated bacteremia, accounts for nearly 30% of IE cases with an incidence reported to become higher than three times in the recent years⁴. Knowing characteristics of this disease, which has high morbidity and mortality, and early diagnosis and treatment are life-saving. The present study, which is the first study conducted on this subject until today in Turkey, aimed to compare characteristics of patients with HAIE followed at our hospital with the characteristics of patients with community-acquired IE (CAIE), as well as to discuss the results with literature.

MATERIAL and METHOD

Patient selection

The present study comprised a total of 52 cases with definite IE, who had been followed according to the modified Duke criteria between January 2005 and January 2014 at our hospital⁵. The cases were retrospectively evaluated. Information on epidemiological characteristics of the cases, as well as clinical features, concomitant diseases and the diseases that made the patients susceptible to IE, previous hospitalizations, invasive procedures, laboratory results, culture results, antibiotherapies, in-hospital complications, and information on mortality were obtained from patient files. Information on patients was recorded in the patient follow-up forms. Patient files were grouped according to the definition of HAIE and CAIE. Grading of comorbidities was done using Charlson comorbidity index⁶.

Definitions

Health care-associated IE (HAIE); is defined as the occurrence of IE signs/symptoms 48 hours after hospitalization; or history of hospitalization within the last 6 months; or occurrence of IE signs/symptoms during hospital stay in the last 6 months after one of tooth extraction, urogenital intervention (cystoscopy, bladder catheterization), interventions to gastrointestinal system (endoscopy, esophageal dilatation), cardiac surgery, intravascular catheterization, and surgical intervention to mucous membrane or infected skin, which are known to be associated with bacteremia that poses risk for IE and with blood circulation

infection; or occurrence of IE signs/symptoms in the subjects that involved in extra-hospital health service practices (any of the following criteria: living in nursing homes, intravenous therapy at home, receiving wound care or nursing, attendance to hospital or hemodialysis unit in the last 30 days or receiving intravenous chemotherapy, and history of hospitalization for two or more days in the last 90 days)^{7,8}.

Community-acquired IE (CAIE); is defined as observing IE signs/symptoms 48 hours before hospitalization in the patients without history of hospitalization in the last 6 months and without contact with health care services^{7,8}.

Statistical analysis: Statistical analysis of data was done using SPSS 17.0 package program. Categorical measurements were summarized as number and percentage, whereas continuous measurements were summarized as mean and standard deviation (median and minimum – maximum, when necessary). Categorical variables were compared by Pearson chi-square test or Fisher's test statistics. Comparison of continuous variables between groups was done by assessing the distribution, and Student's t-test was used for the parameters that distributed normally according to the number of variables, whereas Mann Whitney-U test was used for the parameters that distributed not normally. The level of statistical significance was considered to be $P < 0.05$ for all tests.

RESULTS

Of the 52 cases with definite IE followed between January 2005 and January 2014 according to the modified Duke criteria, 34 (67%) were male and the mean age was 48.08 ± 16.74 years (19-81 years). It was determined that 21

(40%) cases had HAIE and 31 (60%) cases had CAIE. Demographic, clinical and laboratory characteristics of the cases are demonstrated in Table 1.

Comparing the cases with community-acquired infective endocarditis and HAIE, statistically significant correlation was found between advanced age and HAIE (58.0 ± 15.1 year vs. 41.3 ± 14.4 years, $P = 0.0001$). The most common accompanying disease was diabetes mellitus (DM) and chronic renal insufficiency (CRI) in the cases with health care-associated infective endocarditis, whereas it was prosthetic valve disease in the cases with CAIE. Statistically significant correlation was determined between health care-associated infective endocarditis and CRI ($P = 0.001$), DM ($P = 0.016$) and high Charlson comorbidity index ($P = 0.0001$).

With regard to the risk factors, statistically significant relation was determined between previous hospitalization ($P = 0.0001$), receiving hemodialysis ($P = 0.022$), central venous catheterization ($P = 0.022$), intervene in gastrointestinal system ($P = 0.060$) and HAIE.

Gram positive bacteria were isolated from 81% of the cases with positive growth in blood culture. Statistically significant difference was determined between HAIE and growth of *S. aureus* and enterococcus in blood culture ($P = 0.037$).

With regard to the complications, statistically significant relation was observed between embolic event ($P = 0.008$), spondylodiscitis ($P = 0.034$), stroke ($P = 0.007$) and HAIE. Although there was no statistically significant difference between two groups in terms of mortality, mortality rate was higher in HAIE (28.6%) group.

Table 1. Demographic, clinical and laboratory characteristics of HAIE and CAIE cases

	HAIE (n=21)	CAIE (n=31)	P
Age	58±15.1	41.35±14.4	0.0001
Male gender	15 (71.4%)	19 (61.3%)	0.558
Underlying disease			
DM	9 (42.9%)	3 (9.7%)	0.016
CRI	9 (42.9%)	1 (3.2%)	0.001
Cardiac diseases			
Rheumatic valve disease	1 (4.8%)	3 (9.7%)	0.465
Congenital heart disease	-	2 (6.5%)	0.351
Prosthetic valve disease	4 (14.3%)	11 (35.5%)	0.116
Charlson comorbidity index	4 (0-7)	0 (0-3)	0.0001
Natural valve involvement	17 (81%)	20 (64.5%)	0.166
Involved valve			
Aortic valve	3(14.3%)	7 (22.6%)	0.500
Mitral valve	12 (57.1%)	16 (51.6%)	
Tricuspid valve	4 (19%)	3 (9.7%)	
Other*	2 (9.6%)	5 (16.1%)	
Presenting complaints			
High fever	15 (71.4%)	23 (74.2%)	1.000
Shortness of breath	8 (38.1%)	11 (35.5%)	1.000
Weakness	17 (81%)	23 (74.2%)	0.741
Physical examination findings			
Fever	6 (28.6%)	14 (45.2%)	0.260
Murmur	19 (42.9%)	18 (58.1%)	0.397
Confusion	2 (9.5%)	3 (9.7%)	0.707
Splenomegaly	-	3 (9.7%)	0.264
Risk Factor			
Previous hospitalization	7 (33.3%)	-	0.0001
HD	4 (7.7%)	-	0.022
Central catheterization	4 (7.7%)	-	0.022
Angiography	1 (4.9%)	-	0.404
Cardiac valve surgery	1 (4.9%)	-	0.404
Intervention to genitourinary system	1 (4.9%)	-	0.404
Intervention to gastrointestinal system	3 (14.3%)	-	0.060
Growth in blood culture			
No growth	8 (25.8%)	2 (9.5%)	0.037
<i>S. aureus</i>	5 (23.8%)	5 (16.1%)	
CNS	3 (14.3%)	4 (12.9%)	
Viridans streptococci	1 (4.8%)	8 (25.8%)	
Enterococci	7 (33.3%)	1 (4.8%)	
-			
Complications			
Embolic event	14 (67.7%)	9 (29%)	0.008
Stroke	8 (38.1%)	2 (6.5%)	0.007
Spondylodiscitis	5 (23.8%)	1 (3.2%)	0.034
Heart failure	4 (19%)	5 (16.1%)	1.000
Surgery	10 (47.6%)	24 (77.4%)	0.028
Mortality	6 (28.6%)	3 (9.7%)	0.083

*Involvement of more than one valve

DISCUSSION

Today, prolonged lifetime in line with the developments in field of medicine, with gradually increasing invasive procedures in diagnosis and treatment, and the patients' close contact with health care implementations because of their concomitant diseases enhances the risk of health care-associated bacteremia and IE⁹. HAIE, which accounts for 7-34% of infective endocarditis cases, appears today as a growing problem because of high mortality rate changing between 25% and 45%¹⁰. Patients under HD account for the substantial proportion of the patients with health care-associated infective endocarditis^{11,12}. Studies demonstrated that receiving HD is an independent risk factor for HAIE^{4,11}. Nevertheless, DM, cancer, and diseases that require immunosuppressive treatment were determined as the comorbidities in the patients with HAIE¹. Raymond et al. reported that patients with HAIE are characteristically at advanced age and have comorbidities such as DM and CRI. Consistent with the literature, the present study determined statistically significant relation between advanced age, high Charlson comorbidity index, CRI, DM and HAIE.

It was determined that mitral valve is the most frequently involved valve in the patients with CAIE and HAIE. In the literature, any specific valve involvement has not been reported for HAIE. The present study found no statistically significant relation between HAIE and valve involvement.

In the literature about HAIE, invasive procedures, primarily hospitalization and vascular interventions (central venous catheter, peripheral venous route), and presence of pacemaker were determined as the risk factors^{7,8,13}. Consistent with the literature, the present study determined statistically significant relation between previous hospitalizations, contact with health care service (receiving HD), invasive interventions (HD, central venous catheterization, intervene in gastrointestinal system) and HAIE.

When all IE cases were evaluated in terms of causal agents, it was determined that the distribution of agents (Streptococcus spp, Staphylococcus spp. and Enterococcus spp. accounted for 81% of all cases with growth in blood culture) was consistent with the literature. Whilst viridans group streptococci were the most common agents in CAIE cases, staphylococci and enterococci were the most common agents in HAIE cases. Staphylococci and enterococci are the bacteria most frequently lead to HAIE, and these bacteria come via vascular route or originate from skin or urinary system, where invasive procedure is performed and has the potential for bacteremia⁴. In the present study, when both groups were compared in terms of agents isolated from blood culture, statistically significant relation was determined between the growth of staphylococci and enterococci in blood culture and HAIE.

HAIE's being a disease with high mortality and complications is attributed to the presence of comorbidities concurrent with overall weakness in the patients of advanced age and to the fact that it is caused by more virulent bacteria⁷. Neurological events occur in 20-40% of IE cases and may result from vegetation embolus. Stroke is not only a serious neurological complication, but also enhances mortality and morbidity¹⁴. In the present cases, the most frequent complication was embolic event with stroke was the most frequently determined embolic event.

When the cases were evaluated in terms of mortality rate, it was found higher in HAIE cases (28.6% vs. 9.7%). This was attributed to the fact that bacteria in HAIE are more virulent and they cause embolic complications more frequently, as well as to the fact that advanced age patients have more than one comorbidity.

In Turkey, there are many studies conducted on IE and these studies demonstrated only the prevalence of nosocomial IE. We think that the

present study will contribute to the literature since it is the first study on HAIE from Turkey.

In conclusion, HAIE with gradually increasing incidence is a serious clinical disease, which is more prevalent in the patients of advanced age and courses with mortality and complications. Therefore, the patients that are considered to have IE should be precisely evaluated for the route of contamination, treated as soon as possible, and closely followed for potential complications.

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