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MICROBIOLOGICAL AND CLINICAL PROFILE OF INFECTIVE ENDOCARDITIS PATIENTS OF LOCAL POPULATION OF PAKISTAN

Dr. Sonya Bashir[1], Dr. Sana Abid[1], Dr. Rabia Fawad
[1]Yusra Medical and Dental College, Islamabad.
[2]Demonstrator in Rai Medical College, Sargodha.
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Abstract:
Introduction: Infective endocarditis (IE) is an infection of the cardiac valves or mural endocardium caused by bacteRai and fungi producing a wide variety of systemic signs and symptoms through several mechanisms, including both sterile and infected emboli and various immunological phenomena. ***Objectives of the study:*** *The basic aim of the study is to find and analyze the Microbiological and clinical profile of infective endocarditis patients of local population of Pakistan.* ***Methodology of the study:*** *This study was conducted at Yusra medical college Islamabad and Rai medical college Sargodha during March 2018 to June 2018. This was a prospective cohort study performed at the Clinical Laboratory (microbiology section) and cardiothoracic surgery of the hospitals. We identified suspected IE patients from samples submitted at the clinical lab: all blood and relevant tissue samples (cardiac vegetation, cardiac valves, valvular abscess etc.) that were received with history suggestive of endocarditis were enrolled and verbal consent obtained for it.* ***Results****During the study period, 100 patients with clinical diagnosis of IE were prospectively enrolled (table 01). Mean age of patients was 34.84 years with 72.1% being males. Adult representation was 84.6% and 15.4% were below 16 years. Using the MoDC 65.4% (n = 50) were identified as "definite cases of infective endocarditis" rest fell in the "possible case".* ***Conclusion:*** *It is concluded that Infective endocarditis remains a constant source of menace in medical practice, with associated morbidity and mortality.*

Corresponding author:
Dr. Sonya Bashir,
Yusra Medical and Dental College,
Islamabad.
Pakistan.
E-mail: soniabashir626@gmail.com

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INTRODUCTION:

Infective endocarditis (IE) is an infection of the cardiac valves or mural endocardium caused by bacteRai and fungi producing a wide variety of systemic signs and symptoms through several mechanisms, including both sterile and infected emboli and various immunological phenomena. The modified Dukes' diagnostic critera i have been in use for case definition as definite or possible IE. Infective Endocarditis (IE) is associated with significant disease burden, globally [1]. In 2010, IE was associated with 1.58 million disability-adjusted life-years or years of healthy life lost as a result of death and nonfatal illness or impairment. In past few decades the epidemiology, microbiologic profile and treatment outcomes of patients with IE in developed countries have changed significantly [2]. Rheumatic heart disease (RHD) which was once considered the main risk factor for IE is now being superseded by other factors such as invasive vascular interventions (IVI), prosthetic cardiac devices, implants and correction procedures for congenital cardiac defects [3].

IE studies conducted in Pakistan mainly retrospectively designed; have highlighted younger population being affected more frequently than those reported in the western world. As regards etiologic agents, most published studies have limitations in terms of poor sensitivity of bacteRail culture methods utilized, such as conventional in-house blood culture methods. As a result up to 50% of IE cases are reported as culture negative [4]. Lack of authentic data of the common etiologic agents and their susceptibility pattern seriously hampers the choice of empirical antibiotic treatment. Moreover, there is a complete dearth of information that correlates use of vascular / cardiac procedure and implants with IE, disease severity and treatment outcomes in Pakistan [5].

IE patients with cardiac interventions / prosthetic valves have worse outcomes or complicated disease course compared to patients with native valves. A study in Cleveland compared long term post-surgery survival amongst patient with endocarditis having native valve endocarditis (NVE) and prosthetic valve disease (PVE) and reported improved survival in patients with NVE [6]. This may possibly be due to increased disease severity in patients with PVE. Brenan et al. in their study at 605 centers within the Society of Thoracic Surgeons Adult Cardiac Surgery Database showed an elevated 12-year risk of reoperation and endocarditis amongst bio prosthesis patients [7].

Objectives of the study

The basic aim of the study is to find and analyze the Microbiological and clinical profile of infective endocarditis patients of local population of Pakistan.

METHODOLOGY OF THE STUDY:

This study was conducted at Yusra medical college Islamabad and Rai medical college Sargodha during March 2018 to June 2018. This was a prospective cohort study performed at the Clinical Laboratory (microbiology section) and cardiothoracic surgery of the hospitals. We identified suspected IE patients from samples submitted at the clinical lab: all blood and relevant tissue samples (cardiac vegetation, cardiac valves, valvular abscess etc.) that were received with history suggestive of endocarditis were enrolled and verbal consent obtained for it. We followed blood / tissue culture to determine the microbiological and antimicrobial susceptibility profile of all recruited patients. The study was exempted from ethical approval by the research ethics committee of hospitals.

Inclusion CriteRai

All suspected patients admitted under the service of internal medicine and cardio thoracic surgery fulfilling the modified Duke's criteRai (MoDC) for IE were considered eligible and were enrolled.

Exclusion CriteRai

Eligible patients who could not be contacted for history were excluded. Any samples with damaged blood culture bottles or tissue in unsterile container were rejected and not included in the study. Details of patient's clinical and microbiological profile were collected prospectively and entered in the predefined data collection form.

Statistical analysis

The data of respiratory function were compared between the smoker and non-smoker groups using the independent t-test for normally distributed data or the Mann-Whitney U test for other distributions. Differences were considered statistically significant at $p<0.05$.

RESULTS:

During the study period, 100 patients with clinical diagnosis of IE were prospectively enrolled (table 01). Mean age of patients was 34.84 years with 72.1% being males. Adult representation was 84.6% and 15.4% were below 16 years. Using the MoDC 65.4% ($n=50$) were identified as "definite cases of infective endocarditis" rest fell in the "possible case". Cultures were sent on all 104 enrolled patients. Approximately 35% ($n=36$) of patients were

admitted at AKUH and were followed up for clinical outcomes. Blood culture samples for laboratory diagnosis only, were received for 82.7% of the enrolled cases. Of these, 47.6% cases had 3 sets, while 14.6% had 2 sets of blood culture samples.

Table 1: Microbiological profile and antibiotic resistance pattern of isolates from patient with infective endocarditis received at the AKUH clinical laboratory ($n = 100$)

Microorganism	Total number cases $n = 100$(%)	Percent resistance of antibiotic for the species									
		CN	CI	ER	PE	VA	CH	OX	CP	AM	CR
Gram positive organism	**68 (65.4)**										
Staphylococcus species	**24 (23.1)**										
•*S. aureus*	18 (17.3)	27.0	22.2	50.0	100	00	00	77.	44.4	–	–
MSSA	4 (3.8)										
MRSA	14 (13.5)										
•CONS	6 (5.8)	16.6	16.6	33.3	100	00	00	83.3	60.0	–	–
Streptococcus species	**36 (34.7)**	NP	20.0	40.0	14.2	00	–	–	–	–	02.8
•*S. pneumoniae*	2 (1.9)										
•*S. mitis*	8 (7.7)										
•*S. oralis*	5 (4.8)										
•*S. sanguis*	3 (2.9)										
•*S. viridans*	3 (2.9)										
•*S. milleri*	1 (1.0)										
•*S. bovis*	3 (2.9)										
•*Streptococcus species*	5 (4.8)										
•*Granulicatella adiacens*	1 (1.0)										
•*Aerococcus viridans*	2 (1.9)										
•*Gemella haemolysan*	1 (1.0)										
Enterococcus species	**4 (3.8)**	–	50.0	50.0	00	25.0	–		50.0	–	
*Corynebaterium*species	**4 (3.8)**	00	00	–	00	25.0	00			–	
Gram negative organism	3 (2.9)	–	–	–	–	–	33.3	–	00		
Fungus	3 (2.9)	No resistance to azoles and Amphotericin									
Candida albicans, Aspergillus niger, Fusarium species											
Culture negative cases	30 (28.8)	–									

DISCUSSION:

IE remains to be an uncommon disease with sporadic incidence, yet a serious entity in modern medicine, as its diagnosis requires a high degree of suspicion and treatment involves a holistic approach. Although there has been a notion that the incidence of IE has increased in recent years, contemporary population-based data have been lacking to support this opinion[8]. Guidelines from most professional societies, such as American Society for Microbiology (ASM) and Infectious Disease Society of America (IDSA), recommend that adult patient with suspected IE must be investigated by drawing at least 3 blood culture sets with appropRaite volume. In our study population only 47.3% of total patients recruited had 3 sets of blood culture. Inaccessibility to health facilities, increasing diagnostic cost and lack of awareness are factors that often contribute to poor compliance to these essential pre-analytical components of blood culture analysis in Pakistan. We found *Streptococcus* group of bacteRai to be the most frequently isolated organisms from blood and tissue cultures in both groups[9]. These findings are similar to those published by other groups nationally and from neighboring countries like China, India as well as internationally. Although *Streptococci* seem to predominate in developing regions, most western and developed parts of the world report *S. aureus* as the predominant causative agent of IE [10].

Human brucellosis is common in Pakistan in patients with risk factors such as animal exposure, use of unpasteurized milk etc. Blood cultures positive for patients suffering from Brucella infections are often reported from this lab, however none of the cultures in this study yielded Brucella sp., as a cause of endocarditis[11]. This could be because of selection bias of our patients as most of the samples recruited in the study were from patients under cardiac care. In addition, we had limitation of non-availability of methods such as PCR and serological analysis [12].

CONCLUSION:

It is concluded that Infective endocarditis remains a constant source of menace in medical practice, with associated morbidity and mortality. HRG can encounter a more complicated clinical course requiring further surgical interventions, readmissions or death as opposed to native valve endocarditis patients therefore we recommend close follow up of high risk population.

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