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Risk Factor for Cardiac Permanent Pacemaker Infection

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ABSTRACT

Background: Cardiac pacemaker infections have increased globally due to increase in demand and lack of adequate knowledge about its significantly contributing risk factors. This study was therefore aimed to determine the prevailing causative microbes and risk factors of both single and dual chamber permanent pacemaker infections.

Methods: This was a retrospective case control study. Cases were selected as culture positive swab, Temporary pacemaker wire or catheter were matched with three controls for each variable using chi square test. Multivariate regression analysis was done to determine risk factors.

Results: Among 47 cases, 23.4% cases were infected by methicillin resistant staph aureus, 14.9% by methicilin susceptible Staphylococcus aureus, 10.6% by pseudomonas, 8.5% by escherichia coli and 6.4% by klebsiella. Temporary pacemaker/Central line placed >24 hours ago before permanent pacemaker implantation, remnant pacemaker leads, corticosteroid use, no antibiotic prophylaxis, diabetes, smoking and non-absorbable stitches had statistically significant association with permanent pacemaker infection using multivariate regression model analysis. Chronic obstructive pulmonary disease and non-absorbable stitches had a non-significant association.

Conclusions: Temporary pacemaker/Central line placed >24hours before permanent pacemaker implantation, remnant pacemaker leads, corticosteroid use, no antibiotic prophylaxis, diabetes, smoking and use of non-absorbable stitches are risk factors for permanent pacemaker infection. Staph aureus is the most prevalent microorganism causing infection.

Keywords: Causes; dual chamber; Infectison; permanent pacemaker; risk factor; single chamber.

INTRODUCTION

Infection is defined as invasion of body tissues by disease causing agents. It is a catastrophic complication related with permanent pacemaker(PPM). It might occur as a surgical site infection or late onset lead endocarditis.[1] There are different causes which predisposes patients to permanent pacemaker infection including repeated manipulation, prior temporary pacemaker usage, use of corticosteroids, malignancy and renal failure.[2-4] PPM infection can be caused by both typical[5,6] and atypical organisms[7] increasing cardiovascular morbidity, mortality and cost of treatment.[8,9] Different studies have highlighted the increase in infection rates of implantable cardiac devices[3,4,10,11] which is due to lack of adequate risk factor analysis and increase in the scope and demand of implantable devices. PPM infections are on the rise globally, which shows that either we have insufficient evidence or our evidence is not focusing with prevailing microbes which are leading to increase in the disease burden globally.

This study was therefore aimed to identify causes and risk factors of PPM infections. Identification of causative organisms will provide data about prevailing microbes responsible for PPM infections and give evidence for empiric treatment before culture results are available. Targeting the modifiable risk factors will curb down global disease burden of cardiovascular morbidity, mortality and financial budget of treating PPM infection.

METHODS

It was a retrospective case control study carried out at cardiology department of Rehman Medical Institute on all those patients who were hospitalized with PPM from 1st Jan,2015 to 31st Dec,2017. Patients were followed up for a period of upto one year from date of PPM implantation.

PPM infection is defined as invasion of body tissue by disease forming pathogen. It can manifest as surgical site infection with involvement of superficial skin and subcutaneous tissue with either purulent discharge

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or signs of infection like pain, tenderness, swelling, redness or it may herald as late onset endocarditis.[1] Cases with PPM infection were selected from hospital computer database record with positive swab, temporary pacemaker (TPM) wire or catheter tip culture when done after 48 hours incubation under aerobic and anaerobic conditions at 37°C from both genders with age more than 18 years and less than 90 years. Control group included three subjects for each case which were matched by age, gender, height, type of pacemaker, obesity, site of PPM implantation, time of PPM placement and follow up period. All those patients who had prior rheumatic heart disease vulvular lesions, suffered from infective endocarditis, were using immunosuppressive therapy for inflammatory bowel disease, post renal transplant patients, post liver transplant patients, post bone marrow transplant or had secondary focal source of bacteremia were excluded from the study population.

Sterile blood sampling technique was adopted (i.e hand hygiene, sterile dressing pack, sterile gloves and clean skin with chlorhexidine).Blood cultures were obtained by collecting 10ml blood from fresh venipuncture site in specialized culture and sensitivity bottles having 200ml nutrient broth and reducing substance added for growth of anaerobic microorganism. Ratio of blood to nutrient broth was maintained at 10ml to 200ml. After dust cap removal bottle top was swabbed with alcohol and were filled first before other blood samples. It was ensured that bottle is not over filled or under filled and 9ml of sterile blood is collected in each bottle.

The study abided by declaration of Helsinski and was approved by research and evaluation unit of Rehman Medical Institute after scrutiny of synopsis by research evaluation committee.

Data was analyzed by SPSS-20. Continuous variables were assessed as mean ± standard deviation. Categorical variables were assessed using chi square tests. Risk factors analysis was done using multivariate logistic regression model with permanent pacemaker infection status as dependent variable. P-value of <0.05 was considered statistically significant.

RESULTS

A total of 47 culture positive cases with PPM implantation both single and double chamber on either left or right side of the chest were selected as cases. Matching of cases with 3 controls was done in relation to age, gender, height, weight, type of pacemaker, site of implantation, follow up period and presence of hypertension using chi square test making it a total of 141 patients in control group. Basic characteristics and demographic data of cases and controls are described in table 1 below.

Table 1. Basic characteristics of cases and control group.

Index	Cases	Controls	p-value
Age(Years)	69± 12	68± 13	Matched
Gender: Male	27(57.4%)	77(54.6%)	Matched
Female	20(42.6%)	64(45.4%)	Matched
Height(cm)	156 ± 6	159 ± 8	Matched
Weight(kg)	62 ± 11	64 ± 10	Matched
Type of Pacemaker			
Single Chamber	38(80.9%)	114(80.9%)	Matched
Dual Chamber	9(19.1%)	27(19.1%)	Matched
Site of Implantation:			
Left Side of Chest	30(63.8%)	90(63.8%)	Matched
Right Side of Chest	17(36.2%)	51(36.2%)	Matched
Follow Up Time	365±18 days	360 ±20 days	Matched
Hypertension	19(40.4%)	52(36.9%)	Matched

p-values calculated by chi square test comparison Matched means that cases and controls were matched with that variable

Among 47 patients with PPM infection 38(80.9%) were having single chamber PPM and 9(19.1%) were having dual chamber pacemaker. Pus swab from infected pocket, catheter tip and infected wire tip of TPM were cultured for presence of microbiological organisms after 48 hours incubation under aerobic and anaerobic conditions at 37°C. The results of all the 47 infected positive culture PPM yielding different microbiological organisms are described in table 2 below.

Table 2. Pocket Swab/Catheter Tip/Temporary pacemaker wire Microbiological Culture causes of Permanent pacemaker infection.

Microorganism	Frequency
Proteus Mirabilis	2(4.3%)
E Coli	4(8.5%)
Acinetobacter Baumani	8(17%)
Mucor	1(2.1%)
Methicillin Resistant (CONS)	1(2.1%)
Klebsiella Pneumonia	3(6.4%)
Citrobacter	2(4.2%)
Pseudomonas	5(10.6%)
Methicillin Resistant Staph Aureus	11(23.4%)
Methicillin Susceptible Staph Aureus	7(14.9%)
Alpha Hemolytic Streptococcus	2(4.2%)
Morganella Morganii	1(2.1%)

Out of 47 culture positive patients with PPM infection, pulse generator was removed from all patients percutaneously. Pacing lead was removed from 43(91.4%) patients using either manual traction or locking stylet method and remnant leads remained in 4(8.6%) patients who had difficulty in removing the pacing lead. We therefore analyzed different risk factors contributing to PPM infection by multiple logistic regression analysis model using PPM infection as dependent variable. The results of multivariate regression model showed that TPM/central line, when present at the time of PPM implantation and administered more than 24 hours ago, presence of remnant pacemaker leads, corticosteroid use for any primary or secondary cause, no antibiotic prophylaxis before administration of PPM, presence of diabetes, smoking and closure of pocket with non-absorbable sutures were independent predictors of PPM infection. Chronic obstructive pulmonary disease(COPD) and absorbable sutures were not statistically significant predictors of increased risk of PPM infection. The results are shown in table 3 below.

Table 3. Multivariate logistic regression analysis for permanent pacemaker(PPM) Infection.

Variable	OR(95%CI)	P value
Central Line/TPM >24Hour before PPM	2.1(1.03-3.49)	0.035
Remnant Pacemaker Leads	1.89(0.79-6.48)	0,028
Corticosteroid Use	6.4(3.8 – 11.4)	0.031
No Antibiotic Prophylaxis	8.7(6.8-10.9)	0.005
Diabetes	3.2(1.1-6.4)	0.018
Smoking	0.7(0.2-1.8)	0.048
Stitches:		
Absorbable	0.4(0.2-0.98)	0.97
Non Absorbable	1.8(1.2-2.91)	0.023
COPD	0.93(0.6-3.8)	0.69

DISCUSSION

Implantable cardiac device infections are on the rise globally. Which suggest that either we don't have sufficient evidence of prevailing microbes or we are not targeting them appropriately. Despite the alarming rise in infection rates of implantable cardiac device infections, until recently, no authentic risk factor analysis using statistic models have been explained which is contributing to failure in curbing down the rise in disease burden. We therefore investigated and analyzed a number of devices and procedure related risk factors for both single and dual chamber permanent pacemaker(PPM) infections using multivariate regression model and provided evidence about prevailing microbes contributing for PPM infections in Asian population. Klug D et al[6] tried to determine potential risk factors of implantable cardiac devices but they included all devices including intracardiac defibrillator(ICD) which has more infection chances then PPM. Secondly it did not determine focused difference between single and dual chamber PPM. Moreover it failed to curb down infection rates since its publication in circulation in 2007 which implies that either it insufficiently identifies risk factors or they are inappropriately interpreted. We included all the potential risk factors with evidence of increasing the infection rates and included cases and control groups with only single and dual chamber PPM devices hereby eliminating any bias caused by other more infection prone implantable cardiac devices. A case control study done on implantable devices found that device infection rate is high in ICD placed than those of PPM and different risk factors are recognized as contributing to disease burden.[12] ICD devices are more prone to infection because they require repeated manipulations, Electrophsiological(EP) studies and our results also show that any form of manipulation like previous central line, presence of prior temporary pacemaker or remnant leads and removal of non-absorbable stitches increases the risk of permanent pacemaker infection. Similar observation are observed in another study in which CRT-D (Cardiac Resynchronization Therapy-Defibrillator) increases the risk of infection explaining that multiple leads placement is risk factor for device infection.[13] Glucocorticoids have pleiotropic immunomodulatory effect[14] and it increases the risk of infection. In population based cohort study use of glucocorticoids had a 2-6 fold increase risk of infections.[15] It supports our results in which use of glucocorticoids increases the risk of both single and dual chamber pacemaker infection. A recent data published in JAMA showed that smoking makes the patient prone and vulnerable surgical site infection.[16] Similar results are obtained in our study in which smoking was an independent risk factor for PPM infection. Chronic Obstructive Pulmonary Disease (COPD) had no significant association with PPM infection which is explainable because COPD patients take long term antibiotic prophylaxis.[17] It also explains that no antibiotic prophylaxis increases the risk of PPM infection, as been evident from our results and shown by Costa et al[18] from meta-analysis of 7 randomized control trials. Diabetes Mellitus is established risk factor for infection because the hyperglycemic environment causes immune dysfunction by damaging the neutrophils function, damage the intrinsic antibiotic system, innate immunity, neuropathy, micro and macro-angiopathies.[19] Our results

also confirmed diabetes mellitus as a risk factor for PPM infection by multivariate regression analysis. Although infection rate is higher in dual chamber pacemaker[20] but in our results, 80.9% of cases with infection had single chamber PPM. This is explainable because dual chamber pacemakers are expensive[21] and most patients of our locality prefer single chamber pacemaker over it due to financial restraints and lack of free health insurance policy. Increase in placement of single chamber pacemaker as compared to dual chamber is important factor contributing to increase prevalence of infection in our study. Lead placement either single or dual is not a recognized and well established cause of permanent pacemaker and some studies have compared both dual and single chamber permanent pacemaker infections with no significant difference between both.[22] Due to conflicting evidence a more powered study is required which compare equal number of both single and dual chamber pacemaker infection rates which was beyond the scope of our study.

Our study has few limitations. First been a retrospective cohort study there is inherent tendency of selection and recall bias. We tried to minimize the selection bias by selecting all culture positive cases from computer database and then matching the controls from official file record using chi square test analysis for each variable. Second we only selected culture positive cases which mean that culture negative cases of PPM infection due to any cause are not reflected by our data. Majority of our cases were single chamber pacemaker as compared to dual chamber pacemaker limiting our results to be generalized for dual chamber pacemaker.

CONCLUSIONS

The results of our study provide subjective and statistical evidence of potential risk factors responsible for permanent pacemaker infection. Further research is required to evaluate that minimizing the modifiable risk factors influence decrease in future permanent pacemaker device infection rates.

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