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A Comparative Study of Clinical Profile and Outcomes of Patients with Ischemic and Non-Ischemic Complete Heart Block

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Abstract: ***Background: Complete heart block (CHB) is a medical emergency and usually requires immediate intervention. Either cardiac ischemia or non-ischemic conditions can cause CHB. Aim: To compare baseline clinical characteristics associated with ischemic versus non-ischemic causes of CHB and their outcomes. Materials and Methods: This was a single centre retrospective, observational study. Consecutive 250 patients with CHB from January-December 2016 were included. Patients were characterized into non-ischemic and ischemic groups based on cardiac marker elevation, electrocardiogram changes and/or cardiac catheterization findings. In all patients, demographics, pre-existing comorbidities, prior use of nodal blocking agents and ejection fraction (EF) were recorded. The primary outcome was all-cause mortality and secondary outcome was pacemaker implantation. Statistics Analysis: Mean and standard deviation were calculated for all continuous variables. Percentages were calculated for all categorical variables. Unpaired student's 't' test was utilized to find out the difference between means and to calculate the significance level and p-value. RESULTS: Out of 250 patients, 137 had ischemic and 113 had non-ischemic CHB. The mean age was 60.54 years in ischemic group and 61.32 years in the non-ischemic group (p=0.58). Patients with ischemic CHB had a lower mean EF [44.2%v/s 55.2% (p<0.01)]. In the ischemic group 55 patients (40%) presented with cardiogenic shock compared to 6 (0.07%) in the non-ischemic group (p<0.001). There was no statistically significant difference in terms of gender, hypertension, thyroid dysfunction, prior usage of nodal blocking agents and electrolytes and statistically significant difference was present between ischemic and non ischemic groups in diabetes mellitus (DM) (56.9% vs 45%p=0.006), dyslipidaemia (13.1%vs0.5%p=0.001) and smoking (31.3%v/s14.1%p<0.001). In the ischemic group 112 patients had inferior wall myocardial infarction (IWMI) (81.7%) and 21 had anterior wall myocardial infarction (AWMI) (15.3%). RCA was the most common culprit vessel (73%). Seventy patients underwent percutaneous coronary intervention and 10 were referred for CABG. For outcomes,8 out of 113 (0.07%) patients with non-ischemic CHB died compared to 33 out of 137 (24.1%) ischemic CHB (p<0.001). Permanent pacemaker (PPI) was implanted in 76 out of 113 patients (67.2%) in the non-ischemic group compared to 14 out of 137 (10.2%) in the ischemic group (p<0.001). Out of the patients who underwent PPI, 9 had AWMI and 5 had IWMI. Conclusion: Patients with ischemic CHB have lower mean EF with majority having IWMI and had higher mortality. Risk factors like DM, dyslipidaemia and smoking are more frequent in the ischemic group and they are less likely to get a permanent pacemaker compared to non-ischemic CHB. In the ischemic group patients with AWMI got more PPI than IWMI.***

Keywords: Complete Heart Block (CHB), Coronary Artery Disease (CAD), Inferior Wall Myocardial Infarction (IWMI), Anterior Wall Myocardial Infarction (AWMI), Ejection Fraction (EF) & Permanent pacemaker (PPI), Diabetes mellitus (DM).

1. Introduction

Complete heart block or third-degree AV block occurs when no atrial activity is conducted to the ventricles because of interruption in the transmission of the impulse that originated from SA node in the atria to the ventricles, either due to an anatomical or functional impairment in the AV conduction system and therefore the atria and ventricles are controlled by independent pacemakers.[1]The global prevalence of CHB has been reported to be 0.04%.[2]The atrial pacemaker can be sinus or ectopic (tachycardia, flutter, or fibrillation) and the ventricular focus is usually located just below the region of the block, which can be above or below the His bundle bifurcation. The causes of the third degree heart block in children could be congenital [3] or familial [4] and in adults is related to ischemia (of atrioventricular node) or could be non-ischemic including increasedvagal tone, fibrosis (Lenegre's disease in patients with age <60) [5],sclerosis (Lev's disease inpatients with age >70) of the conduction system,[6] electrolyte abnormalities, infiltrative diseases or iatrogenic including nodal blocking medication, cardiac surgery, catheter ablations and transcatheter aortic valve implantation. The ventricular rate in acquired complete heart block is less than 40 beats/min but can be faster in congenital complete AV block.The clinical presentation depends on the level of the block and the escape rhythm that develops.[7] Junctional or atrioventricular (AV) nodal escape rhythm develops, which is a narrow complex, when the block is within the atrioventricular node or at the level of His bundle. The escape rhythm is a wide QRS complex when the block is below the His bundle (infraHisian). In 85 to 90 percent of human hearts, the arterial supply to the AV node is a branch from the right coronary artery that originates at the posterior intersection of the AV and interventricular grooves (crux). A branch of the circumflex coronary artery provides the AV nodal artery in the remaining hearts. Moreover, usually the damage in AV node or his bundle is not due to the abnormality in proper AV node, but more probably due to obstruction in arteries that supply blood to AV node. Atrioventricular block occurs without associated intraventricular conduction system abnormalities in 12% to 25% of patients with acute myocardial infarction.[8]First-degree AV block occurs in 2% to 12% of patients, second-degree AV block in 3% to 10% of patients, and third-degree AV block in 3% to 7% of patients. Approximately 70%of patients with abnormalities of atrioventricular conduction without bundle branch block have evidence of an infero-posterior infarction. The reasons for the increased incidence of AV conduction abnormalities are related to the coronary blood supply to the AV node and activation of cardiac reflexes with augmentation of parasympathetic tone during inferior ischemia (infarction) may also be responsible. In addition, in some cases, adenosine released during inferior infarction may cause AV block.[9]The risk of progression from first-degree AV block to high-grade AV block (during

inferior infarction) varies from 10% to 30%, and that of second-degree AV block to complete heart block is approximately 35%.CHB had been independently related with an escalated risk of in-hospital mortality for acute MI and also with the occurrence of heart failure, cardiogenic shock and atrial fibrillation. Although the incidence of complete AV block in acute myocardial infarctions has decreased following thrombolytic therapy, the mortality still remains high.[10] The determination of the actual cause of CHB and the underlying culprit artery would lead to improved prognosis of such patients.

In this study, we analyzed the clinical characteristics pertaining to new onset CHB and the outcomes in ischemic and non-ischemic CHB patients. Thus, our aim was to study the clinical profile, risk factors, angiographic distribution and in-hospital outcomes of patients with complete heart block.

2. Materials and Methods

This was a single centre retrospective, observational study conducted in a tertiary care teaching hospital. Consecutive 250 patients with CHB from January-December 2016 were included. The diagnosis was confirmed by an electrocardiogram by a cardiologist. Patients were characterized into non-ischemic and ischemic groups based on cardiac marker elevation, electrocardiogram changes and/or cardiac catheterization findings. Temporary pacemaker was implanted followed by permanent pacemakers in patients who required its implantation and occurrence of any type of complications was noted down.

Inclusion criteria:
Patients with the age >18 years and a new diagnosis of the complete heart block were included in the study.

Exclusion criteria:
1) Patients with a pre-existing /known history of CHB and
2) Patients with congenital heart disease.

Data collection
From all the patients included in the study demographic data including age, gender, body mass index; pre-existing comorbidities including diabetes mellitus, hypertension, previous coronary artery disease, history of cardiac surgery, acute kidney injury on admission, chronic kidney disease, thyroid disease, history of cancer; use of nodal blocking agents, electrolyte abnormalities on admission and echocardiographic findings including ejection fraction, regional wall motion abnormalities were recorded. The primary outcome was all-cause mortality while the secondary outcome was permanent pacemaker placement.

Statistical analysis
All the statistical analysis were performed on Microsoft-excel spread sheets and Statistical Package for Social Science Software (SPSS) for Microsoft Windows, version 20.0, (IBM Corp., Armonk, NY;USA) MedCalc V.12.7.1.0. [MedCalc Software, Mariakerke, Belgium. Mean and standard deviation were calculated for all continuous variables. Percentages were calculated for all categorical variables. Unpaired student's 't' test was utilized to find out the difference between means and to calculate the significance level and p-value. A p value of< 0.05 was considered statistically significant.

3. Results

A total of 250 patients were included in the study out of which 137 had ischemic CHB and 113 had non-ischemic CHB. Of all the patients, 59% (147/62) were males,49% (123/250) had diabetes mellitus,1.6% (4/250) had hypothyroidism, 48% (120/250) had hypertension, 19% (48/250) had chronic kidney disease, 15% (37/250) had a history of coronary artery disease,19% (48/250) were on nodal blocking agents, 23% (58/250) were smokers, 15% (37/250) were alcoholics (Table 1).

There was a male preponderance (69%) in the ischemic group whereas in the non-ischemic group females constituted 53%.The mean age was 60.54 years in ischemic CHB group and 61.32 years in the non-ischemic group (p=0.58).Patients with ischemic CHB had a lower mean EF as compared to non-ischemic group [44.2% v/s 55.2% (p<0.01)].In the ischemic CHB group 55 patients (40%) presented with cardiogenic shock compared to 6 (5.6%) in the non-ischemic group (p<0.001). There was a statistically significant difference between ischemic and non ischemic groups in diabetes mellitus (DM) (56.9 % vs 45 % p=0.008), dyslipidemia (13.1% vs 6% p=0.01) and smoking (31.3% v/s14.% p<0.001). In the ischemic group 112 patients had IWMI (81.7%) and 21 had AWMI (15.3%).

On angiography, 35 patients had multivessel disease and 55 had single vessel disease. RCA was the most common culprit vessel (73%). In the study group a total of seventy patients underwent percutaneous coronary intervention and 10 underwent coronary artery bypass grafting (CABG).For outcomes,8 out of 113 (7%)patients with non-ischemic CHB had in-hospital death compared to 33 out of 137 (24.1%)ischemic CHB (p<0.001) (Figure 1). Permanent pacemaker was implanted in 76 out of 113 patients (67.2%)in the non-ischemic group compared to 14 out of 137 (10.2%) in the ischemic group (p<0.001) (Figure 2) (Table-2). Out of the patients who underwent PPI ,9 had AWMI and 5 had IWMI .

4. Discussion

In this study of 250 patients, clinical profile, risk factors, angiographic distribution and in-hospital outcomes of patients with complete heart block were analysed and a head to head comparison between ischemic and non ischemic CHB was done. The majority of patients were males and the common symptoms were chest pain, dyspnoea, giddiness. In our study there is no statistically significant difference between the mean age of presentation between the two groups. There was a statistically significant difference in the mean EF and patients presenting with complete heart block which can be accredited to ischemia resulting in reduced myocardial function. There was no statistically significant difference in terms of gender, hypertension, prior usage of nodal blocking agents and electrolytes disturbances between the two groups. Non-ischemic third degree heart block is hypothesized to be more frequent in patients with thyroid

disease. In our study, as suggested previously there was no difference between the ischemic and non-ischemic complete heart block with regards to thyroid disease. Diabetes mellitus, dyslipidaemia and smoking which are known to be the risk factors for development of coronary artery disease are higher in ischemic group. Majority of the patients in the ischemic group had IWMI and the most common culprit artery on angiographic examination was RCA in agreement with previous studies. In a study by, Jim MH et al it has been observed that complete AV block occurred exclusively due to dominant RCA obstruction (95%) in the patients and 56% patients had multivessel disease. Moreover, they also found that complete AV block complicated acute inferior wall MI in 12.7% of the patients.[11].On contrary, Bassan et al have reported that involvement of LAD disease was more prevalent in patients who developed AV block.[12] CHB patients with anterior wall acute MI have a poorer prognosis than those with inferior wall acute MI.[13]

In the present study, there is a significant difference in the number of patients presenting with cardiogenic shock between the two groups. The prognosis of complete heart block (CHB) complicating acute myocardial infarction is poor and in-hospital death rates are significantly higher compared to patients with myocardial infarctions not associated with CHB. There was a statistically significant difference between the two groups in terms of permanent pacemaker implantation and the patients with ischemic CHB are less likely to get a permanent pacemaker. This is because CHB in ischemic group is temporary and conduction recovers once revascularization is done. For primary outcomes, patients with ischemic CHB died more frequently compared to patients with non-ischemic CHB, and this difference was statistically significant. This suggests that the patients with ischemic CHB do worse than the CHB patients without ischemia. In a study by Murtaza Sundhu et.al.., they found no significant difference in terms of moratlity in between ischemic and non ischemic groups even though the patients in ischemic group died more frequently.[14] However, the prognosis of patients following pacemaker implantation for isolated CHB is excellent.

5. Limitations

1) This was a retrospective cross-sectional study design where follow-up of patients was not observed.
2) Single centred study which could have the chances of bias.
3) This study has small sample size.

6. Conclusion

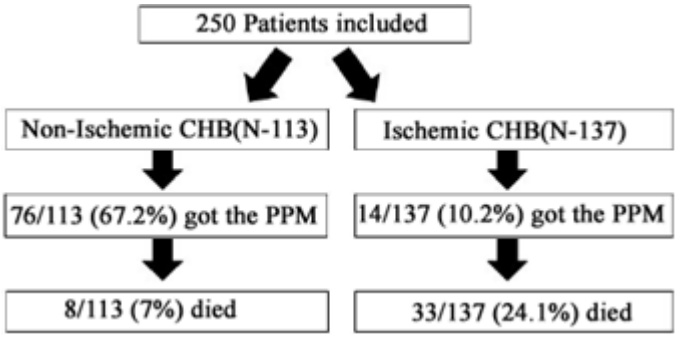
Patients with ischemic complete heart block have a more frequent history of coronary artery disease and risk factors for CAD like smoking, diabetes mellitus and dyslipidaemia are also significantly higher in this group. Patients with ischemic CHB have lower mean EF with majority having IWMI and RCA being the most common culprit vessel. They have higher in-hospital mortality and are less likely to get a permanent pacemaker compared to non-ischemic CHB. In the ischemic group when compared with IWMI, patients with AWMI had more permanent pacemaker implanted.

Table 1: Baseline Characteristics

Variables	Ischemic (N=137)	Non-ischemic (N=113)	p – Value
Age	60.54±11.5	61.32±11.3	0.58
Male	94	53	0.07
Female	43	60	0.02
Diabetes mellitus	78	45	0.008
Hypertension	60	60	1
History of thyroid disease	1	3	0.4
History of Coronary Artery disease	27	10	0.01
History of chronic kidney disease	18	30	0.03
Dyslipidemia	18	7	0.01
Smoking	43	15	0.001
Alcohol addiction	25	12	0.08
Nodal blocking agent prescribed	21	16	0.8
Ejection Fraction (EF)	44.2±8.0%	55.2±8.6%	<0.001

Table 2: Outcomes

Variables	Total (N=250)	Ischemic (N=137)	Non-ischemic (N=113)	p – Value
Primary Outcome				
Alive	209	104	105	p<0.001
Dead	41	33	8	
Secondary Outcome				
Permanent pacemaker placed	90	14	76	p<0.001
Permanent pacemaker Not Placed	160	123	37	



Flow chart showing the overview of the study
CHB-complete heart block ; PPM- permanent pacemaker management

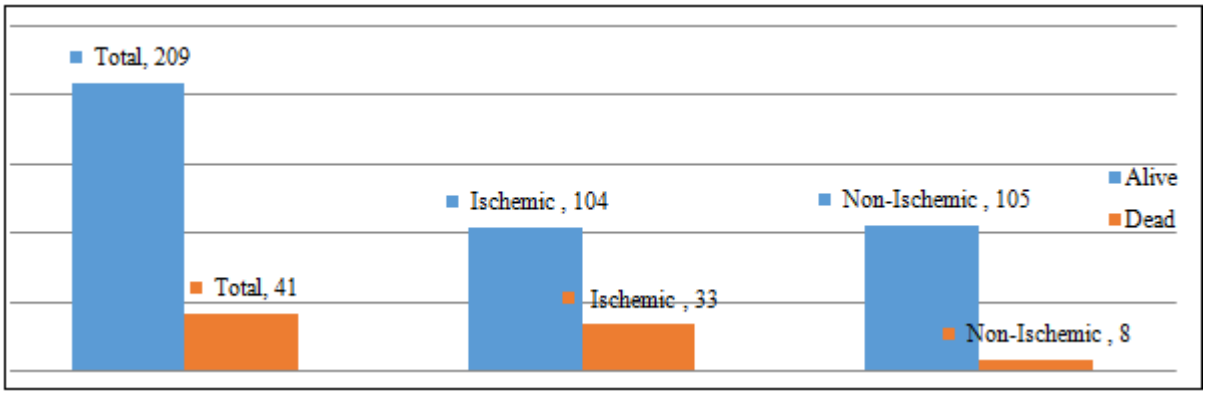


Figure 1: Primary outcomes graph

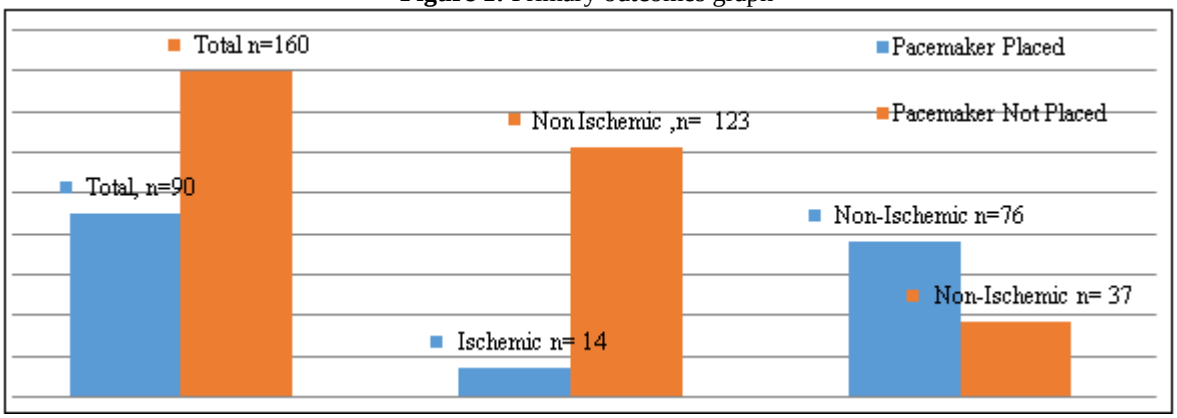


Figure 2: Secondary outcomes graph

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