A Clinical Study of Heart Failure with Preserved Ejection Fraction in Patients at College of Medical Sciences, Teaching Hospital: A Tertiary centre from Central Nepal


* Department of Cardiology, College of Medical Sciences, Teaching Hospital Bharatpur, Nepal
** Respiratory Medicine, Sandwell and West Birmingham Hospitals, NHS Trust, Birmingham, United Kingdom

Abstract- Heart failure is growing epidemic condition and nearly half of the patients have preserved ejection (EF>50%). We aim to observe the baseline clinical characteristics and factors affecting hospital stay and outcomes after 28 days of follow up. An observational study was conducted among 200 patients who presented clinical features of heart failure according to Framingham Criteria, with Left ventricular EF ≥ 50%, in College of Medical Sciences in the Department of Cardiology over a period of June 2015 to January 2017. Data were analyzed using IBM-SPSS 20.0 and descriptive and inferential analysis was performed.

Of 200 patients, 114(57%) were females and 86(43%) were males. The mean age of patient was 51.57(±16.81) years with range of 20 to 89 years. The most common risk factors were Hypertension (78%) followed by obesity (55.5%), smoking (50%), dyslipidemia (48%), and Diabetes mellitus (48%). The most common presenting symptom was dyspnea (96%) followed by fatigue (51%) and cough. Most of the patients had Grade I Left ventricular diastolic dysfunction 84%. Associated regional wall abnormalities were found in 11%, pulmonary arterial hypertension in 57.5% and pericardial effusion in 10%. Total mortality in this study was (n=7)3.5% of them 2% within 24 hours of hospitalization and 1.5% during subsequent hospitalization within 30 days of discharge. We concluded the incidence of heart failure with preserved ejection fraction (HFPEF) was more in female. Hypertension was the most common risk and worse NYHA functional class was associated with prolonged hospital stay and mortality, both significant statistically.

Index Terms- Ejection fraction, Heart failure, Risk, outcomes

I. INTRODUCTION

Heart failure (HF) is an epidemic affecting 5.1 million American adults based on 2013 estimates, and this epidemic will grow 25% by 2030 as the United States population continues to age.[1] HF is one of the leading causes of death, approximately 30,000 deaths per year. Recent studies have indicated that more than half patients diagnosed with HF even though ejection fraction (EF) is normal or near normal.[2] Heart failure is a clinical diagnosis.[3] An ejection fraction (EF) of <50% in a patient with heart failure symptoms is termed heart failure with reduced ejection fraction (HFREF), and an EF of ≥50% in a patient with heart failure symptoms is termed heart failure with preserved EF (HFPEF). Heart failure can occur in patients in whom left ventricular systolic contractile function appears to be normal when measured by the ejection fraction. Since systolic function was presumed to be normal in these patients, this form of heart failure was thought to be due to diastolic dysfunction or abnormal filling.[4] Studies have demonstrated that HFPEF is as prevalent as HFREF.[5] It is important to note that the above terms are not mutually exclusive as nearly all patients with systolic dysfunction have some degree of concomitant diastolic dysfunction.[6]

There has been an apparently steady rise in the prevalence of HFPEF over the past decade.[7] Despite this, there has been considerable controversy with regards to the existence of the condition, its terminology, the characteristics of the condition and the diagnostic criteria for HFPEF. The confusion has arisen as some authors suggested that systolic function is normal in HFPEF patients,[8] while others questioned if the two entities exist as a continuum of heart failure or whether they are distinct entities.[9] There are differences in microscopic and neuroendocrine features which consequently lead to differences in left ventricular structure and echocardiographic characteristics between HFPEF and HFREF. These differences are attributed by underlying or contributing factors such as aging, hypertension, diabetes, female gender, dyslipidemia and obesity.[10] Diastolic dysfunction is categorized by Doppler echocardiographic findings into the following progression.[11] Mild (Grade I), defined as impaired relaxation without or with mild evidence of increased filling pressures respectively; Moderate (Grade II), defined as impaired relaxation associated with moderate elevation of filling pressures or pseudonormal filling, and Severe, defined as advanced reduction in compliance or reversible (Grade III) or fixed (Grade IV) restrictive filling.

The common risk factors associated with HFPEF i.e. hypertension, diabetes and coronary artery diseases are more prevalent in India.[12] The exact prevalence and incidence of HFPEF are not known, it indicates a need to carry out the study which gives us an idea regarding the prevalence, etiology, morbidity and mortality pattern of this study. So, we have carried out the study to obtain the clinical profile of the patients experiencing HFPEF along with etiology, pharmacological treatments and short-term outcomes.
II. METHODS

This was a tertiary care centre hospital based cross sectional observational study conducted at the cardiology unit of college of medical sciences Bharatpur, Nepal. Ethical approval of this study was obtained from the same hospital with written informed consent from each patients or relatives wherever necessary. We observed 200 newly admitted patients in coronary care unit and cardiology ward who fulfilled the Framingham’s criteria of heart failure [13] for clinical diagnosis and LV ejection fraction more than or equal to 50%. A Performa was used for collecting information at admission on demographics and co morbidities including history of hypertension, diabetes mellitus and others. Physical assessment was done on all patients, and patients classified according to NYHA classification. For the study, ECHO either done during in-patient stay or done in past two months was accepted for the study.

The investigator administered structured questionnaires to obtain information on outcomes at discharge, and on drug prescriptions related to heart failure at discharge. Patients were then given follow-up visit date. The investigator administered structured questionnaires and collected information on common symptoms of heart failure, NYHA classification, and QOL at one month. Data were analyzed using IBM-SPSS 20.0 (IBM Corporation, Armonk, NY, USA). The t- test and Chi-square test were used for statistical analysis. A p-value < 0.05 was considered statistically significant for all statistical tests unless otherwise stated.

III. RESULT

Out of 200 cases, 114(57%) were females and 86(43%) were males. The mean age of patient was 51.57(±16.81) years with range of 20 to 89 years. 2/3rd of cases were in the age group of 40 to 80 years. (Table 1)

Table 1: Clinico-epidemiological profile of patients (n=200)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Age (in years)</td>
<td></td>
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<tr>
<td>&lt;20</td>
<td>1</td>
<td>0.5</td>
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<tr>
<td>21-40</td>
<td>58</td>
<td>29</td>
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<tr>
<td>41-60</td>
<td>75</td>
<td>37.5</td>
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<tr>
<td>61-80</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>&gt;80</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Mean age ± SD (years)</td>
<td>51.57±16.81</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>86</td>
<td>43</td>
</tr>
<tr>
<td>Female</td>
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<tr>
<td>Chhetri</td>
<td>26</td>
<td>13</td>
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<tr>
<td>Newar</td>
<td>33</td>
<td>16.5</td>
</tr>
<tr>
<td>Magar</td>
<td>17</td>
<td>8.5</td>
</tr>
<tr>
<td>Tharu</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Gurung</td>
<td>9</td>
<td>4.5</td>
</tr>
<tr>
<td>Others</td>
<td>27</td>
<td>13.5</td>
</tr>
</tbody>
</table>

The most common risk factors in our patients were Hypertension (78%) followed by obesity 55.5%, smoking (50%), dyslipidemia (48%), and Diabetes mellitus (48%), shown in figure 1. The most common presenting symptom was dyspnea (96%) followed by PND (55%), fatigue (51%) and cough (26%). Two patients presented with syncope as a presenting complaint. Figure 2.
et al. (2014),[14] the prevalence of HFPEF was 4.8% in participants over 65 years old, which was consistent with the result of a study conducted in central Italy that found a 4.9% HFPEF prevalence in 65–84 year-olds.[16] Hedberg et al. (2001),[17] reported that the prevalence of HFPEF in a population-based sample of 75-year-old participants was 6.8%. In the present study, majority of the patients, 2/3rd belong to age group 40-80 years. The mean age being 51.57±16.81 years, this is slightly lower than other studies.

The present study shows dyspnea (96%) and fatigue (51%) as commonest symptoms. 56% of the patients having dyspnea were in NYHA functional class III-IV. In a study done in India by Devasia et al. [18] Tachycardia was the commonest clinical sign (96%). Others were pedal edema (86%), raised JVP (63%) and pulmonary edema (46%). In present study commonest risk factor was HTN (78%), followed by obesity (overweight and class I & II obesity) 55.5%, smoking 50%, DM (48%), hyperlipidemia (48%) and AF(35%). In a study done in UK by Sosin et al.[19] obesity was found in, 36.3% with BMI>30 kg/m2, 29.2% had diabetes,50.0% had hypertension, 5.7% had a history of myocardial infarction, and 1.9% had history of arrhythmia. In a study by Liang Guo et al.,[15] risk factors of HFPEF were hypertension 44.9%, dyslipidemia 38.4%, history of heart disease 16.6%, abdominal obesity 15.7%,diabetes in 11.3% and BMI>30 was seen 5.9% patients.

In a study done in 2014 by Burke et al. [20] in USA, risk factors of HFPEF were hypertension 77%, dyslipidemia 38.4%, history of heart disease (CAD) 48%, chronic kidney disease in 33%, diabetes in 33% and mean BMI of patients in study was 30±9. Similarly, a study done in patient with HFPEF in USA by Devasia et al. [18] Tachycardia was the commonest clinical sign (96%). Others were pedal edema (86%), raised JVP (63%) and pulmonary edema (46%). In present study commonest risk factor was HTN (78%), followed by obesity (overweight and class I & II obesity) 55.5%, smoking 50%, DM (48%), hyperlipidemia (48%) and AF(35%). In a study done in UK by Sosin et al.[19] obesity was found in, 36.3% with BMI>30 kg/m2, 29.2% had diabetes,50.0% had hypertension, 5.7% had a history of myocardial infarction, and 1.9% had history of arrhythmia. In a study by Liang Guo et al.,[15] risk factors of HFPEF were hypertension 44.9%, dyslipidemia 38.4%, history of heart disease 16.6%, abdominal obesity 15.7%,diabetes in 11.3% and BMI>30 was seen 5.9% patients.

In this study, 92.5% patients received diuretics (loop diuretics, potassium sparing diuretics or combination),65% received Antiplatelets, 53% were prescribed Statins. Similarly, Amlodipine (CCB), Angiotensin receptor blockers, Angiotensin converting enzymes inhibitors, Beta blockers, Nitrates and Digoxin in 39%, 22%, 17.5%, 14%, 9% and 8% respectively. Out of 200 patients, 4 patients died within 24 hours of hospitalization, all of them presented in NYHA class III-IV. 196 patients were discharged; only 117 patients were able to follow up either by telephone contact or during OPD visit or re-hospitalization within 30 days. 12.5% patients were re-hospitalized within 30days, among them 3 patients died and cause of death being refractory cardiogenic shock in 2 patients and the other died of sudden cardiac death.

IV. DISCUSSION

Heart failure is growing burden around the world. In the current study, 10.5% of the patient admitted in the cardiology unit had HFPEF which was 48.6% of the total heart failure cases over the study period. In epidemiological cohort studies done in USA in 2014 by Charlotte Andersson et al. (2014),[14] the prevalence of HFPEF approaches 10% for people >80 years of age; and incidence rates seem stable in the face of a growing prevalence. In a study done in Northeast China in 2012 by Liang Guo et al. [15] the prevalence of HFPEF was 4.8% in participants over 65 years old, which was consistent with the
Lam et al.[21] Hypertension was present in 96% patients with mean SBP(132±23 mmHg) and mean DBP(67±14 mmHg).

In current study, Echocardiographic study showed mean LA 41.4±8.4mm, MR was seen in 48.5% and TR was seen in 49.5% cases. Most of the patients had Grade I LVDD 84%. PAH was seen in 57.5% and Regional wall motion abnormalities were seen in 11%. 10% patients had pericardial effusion among them 3 had moderate to large pericardial effusion and LA thrombus was seen in 1 patient. In a study done by Kaneko et al.[22] mean LA size was 4.13±1.0cm. In a study done by Yamamoto et al.[23] was 4.4±0.8cm. Similarly in a study done by Rossi et al.[24] mean LA size was 41±1.0cm. LA size is determined mainly by LV diastolic dysfunction. The relatively load-independency of a dilated LA provides an important advantage over Doppler parameters that are related to filling pressures. This is crucial as patients with HFPEF may have normal filling pressure at rest with disproportionate increase during effort. Thus, LA imaging may provide important clue for HFpEF diagnosis.[25]

In this study most of the patients 92.5%, were under diuretics which is the mainstay of treatment in heart failure. Other medication includes Antiplatelets, (65%), Statins (53%), CCB (39%), ARB (22%), ACEI (17.5%), B-blockers (14%), Nitrates (9%) and Digoxin (8%). In a study done in India by Devasia et al.[18] drugs prescribed to the patients with HFPEF were Diuretics (92%), Antiplatelets (68%), Statins (63%), ACEI (58%), Amlodipine (34%), Nitrates (12%), B-blockers (8%) and Digoxin in 6% patients. There are several clinical trials in the HFPEF population targeting on clinical symptoms, exercise capacity, diastolic dysfunction, and quality of life (QoL). Although there are tested treatments improving these outcomes, no confirmed positive outcomes in regard to mortality were obtained from all pharmacological therapies including diuretics, beta-blockers, RAAS antagonists, digitalis, HMG-CoA-reductase inhibitors (statins), non-dihydropyridine calcium channel blockers, and phosphodiesterase-5 inhibition (PDE-5 inhibition) so far.[25]

In this study QOL score at 30days was significantly associated with NYHA class on Admission (p<0.05), similarly QOL score at discharge was also significant with outcomes at 30days follow up (p=0.012), anemia at the time of admission as well as AF as risk of HFPEF were significant with outcomes at 30 days, (p=0.014) & (p<0.05). Out of 200 patients, 4 patients died within 24 hours of hospitalization, all of them presented in 30 days, (p=0.014) & (p<0.05). Out of 200 patients, 4 patients died within 24 hours of hospitalization, all of them presented in NYHA class III-IV at the time of hospitalization. A recent meta-analysis of 7688 patients with HFPEF followed for about 4 years found an overall mortality of 32% (about an 8% annual mortality rate).[27] In a study by Henkel et al.[28] annual mortality rates ranged from about 3.5 to 6% in 3 of the large randomized clinical trial to about 15% in the observational community-based Framingham Study.

V. LIMITATIONS

This was a hospital based study at a single site so the results may not be generalized to the community, however they could potentially be reference for further study at secondary and tertiary level hospitals. All the echocardiographic assessment parameters for left ventricular diastolic function could not be done in all the patients (eg.pulmonary S/D ratio, atrial reversal velocity was done in selected cases whenever required). However, E/A ratio, reversal with valsalva (whenever indicated) and E/e’ was done in all the studied patients. Proper and timely follow-up of the all patients could not be done.

VI. CONCLUSION

In conclusion, the incidence of heart failure with preserved ejection fraction (HFpEF) was more in female. Hypertension was the most common risk and worse NYHA functional class was associated with prolonged hospital stay and mortality. Although this study was done on single hospital and in a small population size, it revealed baseline information on heart failure with preserved ejection fraction which can be used as reference for further studies.

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AUTHORS

First Author: Dr. Rajesh Kumar Panjyiar, MD Internal Medicine, DM Cardiology Consultant Physician and Cardiologist, College of Medical Sciences, Bharatpur, Nepal Email: panjyiar.rajesh@gmail.com

Second Author: Dr. Ram Sundar Twayana, MD Internal Medicine Specialty Registrar, Respiratory Medicine, Sandwell and West Birmingham Hospitals, NHS Trust, Birmingham, United Kingdom Email:ram.twayana@nhs.net

Third Author: Dr. Shankar Laudari MD Internal Medicine, DM Cardiology Lecturer and Cardiologist, College of Medical Sciences, Bharatpur, Nepal Email:lshankar2@hotmail.com

Fourth Author: Dr. Sachin Dhungel MD Internal Medicine, DM Cardiology Lecturer and Cardiologist, College of Medical Sciences, Bharatpur, Nepal Email:sachindhungle@hotmail.com

Fifth Author: Dr. Madhu Gupta MD Internal Medicine, DM Resident College of Medical Sciences, Bharatpur, Nepal Email: madhugupta.md@gmail.com

Sixth Author: Dr. Laxman Dubey MD Internal Medicine, DM Cardiology Associate Professor, College of Medical Sciences, Bharatpur, Nepal Email: dubeylax@yahoo.com

Seventh Author: Dr. Gagnapatnam Subramanyam, DM Cardiology Professor and Head of Department, College of Medical Sciences, Bharatpur, Nepal Email: info@cmsnepal.edu.np

Corresponding Author: Dr. Ram Sundar Twayana, MD Internal Medicine Specialty Registrar, Respiratory Medicine, Sandwell and West Birmingham Hospitals, NHS Trust, Birmingham, United Kingdom Email:ram.twayana@nhs.net

Contact: +44 07533651659, +44 0121 553 1831

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