Original Article

Co-morbidities as Determinant of Heart Failure: A Hospital Based Matched Case-Control Study

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ABSTRACT

To evaluate the one most common combination of co-morbidities that can lead to heart failure.

Methods: Total 374 participants (case=187 & control=187 with 1:1) of age ≥ 20 included in this case control study through non probability convenient sampling from hospitals of Tehsil Wazirabad and District Gujrat. 187 participants having heart failure were included in case group and 187 not having heart failure included in control group. A semi structure questionnaire was used to collect data and results were compiled through SPSS software. There was no gender specification in this study. **Results:** Results showed that frequency of single disease was 55 in case group and 88 in control group. Participants having >1 disease were 51 in cases and 55 in control. Frequency of >2 diseases was 44 and 41 in case and control group respectively and in >3 diseases 17 participants were in case group and 2 were in control group. As number of diseases increases in combination, frequency of participants increased in case group as compared to control group. This study was significant with P value less than 0.05 and odds ratio of combination of comorbidities was 1.213. **Conclusions:** The observed association indicated that combined effect of comorbidities is higher in case group to cause heart failure than one disease at a time. Hence, we concluded that combined effect of comorbidities is higher in case group to cause heart failure than one disease at a time.

INTRODUCTION

Heart failure is a serious medical emergency and a pandemic worldwide. In America 5.7 million people above the age of 20 years' experience heart failure and its prevalence and incidence is increasing day by day [1]. Heart failure is complex syndrome characterized by set of clinical symptoms including breathlessness, general fatigue, chest pain and lower limb edema. Heart failure occurs when heart could not properly pump blood as a consequence of impaired contraction and relaxation of heart chambers [2]. Heart failure syndrome includes coronary artery disease, myocardial infarction, hypertension and valvular heart diseases [3]. Despite the fact that science and technology have made much advancement; the morbidity and mortality of patients suffering from chronic heart failure is

still high. The reason is probably the presence of several co-morbid conditions that complicates the disease and also interferes in its management [4]. Comorbidities are the conditions or disorders that occur along with primary disease [5]. Both cardiovascular and non-cardiovascular co morbidities can lead to heart failure. Non cardiovascular co-morbidities includes Chronic Obstructive pulmonary disease (COPD), Chronic kidney disease (CKD), obesity, anemia, gout, thyroid dysfunction, sleep breathing disorders, hypercholesterolemia, diabetes, hypertension, hepatitis and depression [6]. According to the report release by the Network for Consumer Protection in a press on October, 1st 2017, Heart disease become more prevalent in Pakistan as every hour 12 patients die due to heart

attack. A study conducted in Baltimore, Maryland reported that Heart failure mortality increased due to non cardiovascular comorbidities [7]. In 2018 A study by Xin Zhao et al. proved that non cardiovascular comorbidities play equal part as cardiovascular comorbidities in increasing incidence, prevalence and mortality of heart failure [8]. Diabetes type 1 and type 2 are most common co morbidity that leads to cardiovascular disease and death [9]. Diabetes Mellitus is metabolic disease characterized by hyperglycemia. Type 1 diabetes is insulin dependent diabetes mellitus while type 2 in non- insulin dependent diabetes mellitus. Diabetes is present in half of patients suffering from heart failure. Diabetes and heart failure shares a bidirectional association that is if diabetes can cause heart failure; cardiovascular disease can also lead to diabetes mellitus. Possible mechanism is oxidative stress. Long standing hypertension and chronic diabetes damage the liver, kidney and lungs which are also a risk factor for heart failure [10].

Methods:

After approval from ethical committee a Hospital based matched case control study was conducted in a period of 4 months. Data was collected from hospitals (both government and private sector) of Tehsil Wazirabad and District Gujrat using semi structure questionnaire. A sample of 374 participants (case = 187, control = 187 with 1:1) was calculated at 95% confidence level. Participants of age ≥ 20 years were included in the study through Non Probability convenient sampling technique. An informed consent was taken from participants before filling of questionnaires. Patients having heart failure were included in case group and without heart failure were in control group as per inclusion criteria. Participants not exposed to risk factor were excluded from control group and participants who were diagnosed with HIV, Cancer and having age < 20 years were excluded from both case and control group. There was no gender specification in this study. Chi square test, binary logistic regression and odds ratio were calculated to analyze the data through SPSS software version 20.

Results:

According to study design case and control groups are dependent variables and comorbidities such as diabetes, anemia, Sleep apnea, hypercholesterolemia, gout, hypothyroidism, rheumatoid arthritis, COPD, CKD and hepatitis C were independent variables.

Figure 1: Demographic characteristic of participants

Figure 1 shows the demographic characteristic of participants. This indicates that 50-60 years old people are more prone to heart failure. Mean and standard deviation of age in case group was 55.58 ± 13.55 while in control group was 50.19 ± 13.51 .

Risk Factors		Groups		Total
		Control	Case	
Family history of heart disease	No	101	60	161
	Yes	86	127	213
Hypertensive patients	No	102	69	171
	Yes	85	118	203
Total		187	187	374

Table 1: Frequency of family history and hypertensive patients in both group (case and control)

Table 1 show frequencies of family history and hypertensive patients of both case and control group. This table indicated that 118 and 85 persons were hypertensive in case and control group respectively. While family history of 127 and 86 was positive in case and group respectively. So it is obvious that heart disease runs in families due to highest number of positive family history in case group.

Number of Disease with Heart failure	Groups		Total
	Control	Case	
Only one Disease	88(47.02%)	72(38.50%)	160(42.8%)
Two Disease at a time	55(29.41%)	51(27.27%)	106(28.34%)
Three Disease at a time	41(21.92%)	44(23.52%)	85(22.72%)
Four Disease at a time	2(1.06%)	17(9.09%)	19(4.9%)
Five Disease at a time	1(0.53%)	2(1.06%)	3(0.80%)
More Than Five Disease at a Time	0	1(0.53%)	1(0.26%)
Total	187	187	374

Table 2: Frequency of combination of comorbidities among both groups

Table 2 shows that total 160 subjects (case=72, Control=88) were those who had only one disease. There were 106 (case group=51 and control group=55) patients who had two disease at a time. 41 cases and 44 controls out of total 85 patients were having three diseases at a time. Total 19 patients (17 cases and 2 controls) had four diseases at a time. Combinations of five diseases were 3 in total number out of them 2 in case group and 1 in control group. 1 patient in case group had more than 5 diseases at a time.

	B	Chi-Square Wald	P-Value	Odds ratio	C.I at 95%	
					Lower	Upper
One disease with Heart failure	0			1		
More than 1 Disease with Heart Failure	.193	6.803	.009	1.213	1.049	1.403

Table 3: Adjusted Odds Ratio of Combined effect of comorbidities

Table 3 shows that odds ratio is 1.213 which means participants with more than two comorbidities have two times increased risk of developing heart failure as compared to participants with one disease.

DISCUSSION :

This study observed the relationship between comorbidities and heart failure and documented the one most common co-morbidity which leads to heart failure. Most of the participants in both groups were diabetic patients similar to result of another study [11]. Second most common disease that associated with heart failure was anemia. A study conducted in America also reported that anemia is a stronger risk factor to cause heart failure [12]. Third most common disease was Hypercholesterolemia in case group. A study conducted by Brian A. Ference et al. also measured the effect of cholesterol levels on

Myocardial Infarction and Heart Failure and proved that persistent increase in LDL and decrease in HDL is a major contributing factor towards Coronary artery disease (CAD) and heart failure [13]. Age and sex adjustment attenuated regional differences in IHD-as-risk factor but IHD remained rare in Sub-Saharan Africa. Hypertension prevalence was high in heart failure patients of all regions but the highest in Eastern and Central Europe and Sub-Saharan Africa [14]. Shannon M Danley et al. reported the prevalence of hypertension, obesity, and smoking increased over time. The risk of heart failure was particularly high for [coronary disease](#) and diabetes with odds ratios (95% confidence intervals) of 3.05 (2.36-3.95) and 2.65 (1.98-3.54), respectively [15]. [Christophe Bauters](#) et al. reported in his study increased risk of heart failure in diabetics; moreover, in diabetic populations, poor glycemic control has been associated with an increased risk of heart failure. Various mechanisms may link diabetes mellitus to heart failure: firstly, associated comorbidities such as hypertension may play a role; secondly, diabetes accelerates the development of coronary atherosclerosis; thirdly, experimental and clinical studies support the existence of a specific diabetic cardiomyopathy related to microangiopathy, metabolic factors or myocardial fibrosis [16]. Erik Ingelsson et al. reported variables reflecting glucose and lipid metabolism and variables involved in oxidative processes were compared with established risk factors for HF (prior myocardial infarction, hypertension, diabetes, electrocardiographic left ventricular hypertrophy, smoking, obesity, and serum cholesterol). Novel variables reflecting insulin resistance and dyslipidemia, together with a low beta-carotene level, were found to predict HF independently of established risk factors [17]. Kamyar Kalantaret al. stated that Traditional risk factors of a poor clinical outcome and mortality in the general population, including body mass index (BMI), serum cholesterol, and blood pressure (BP), are also found to relate to outcome in patients with chronic heart failure (CHF), but in an opposite direction. Obesity, hypercholesterolemia, and high values of BP have been demonstrated to be associated with greater survival among CHF patients. These findings are in contrast to the well-known associations of over-nutrition, hypercholesterolemia, and hypertension with a poor outcome in the general population [18, 19]. In diabetic subjects, age, diabetes duration, insulin use, ischemic heart disease, and elevated serum creatinine were independent risk factors for both prevalent and incident heart failure [20]. In this study two most common two diseases combinations observed in participants were diabetes plus anemia and diabetes plus hypercholesterolemia. Sleep apnea, hypercholesterolemia

and diabetes were most common three diseases combination observed in study. Sleep apnea, diabetes, anemia and COPD were a combination of 4 diseases which was observed in heart failure patients. There is no evidence supporting our study because no work has been done to evaluate the combined effect of comorbidities in past. Several studies conducted to evaluate the individual effect of comorbidity on heart failure and many of them include two or more diseases but investigate their effect individually.

CONCLUSIONS :

An increase in number of comorbidities among participants has more impact on morbidity and mortality of heart failure than single co-morbidity. In this study the main focus was to determine the combined effect of comorbidities on heart failure.

REFERENCES :

- [1] Savarese G, Lund LH. Global public health burden of heart failure. *Cardiac failure review*. 2017;3(1):7. <https://doi.org/10.15420/cfr.2016:25:2>
- [2] Brake R, Jones ID. Chronic heart failure part 1: pathophysiology, signs and symptoms. *Nursing Standard* (2014+). 2017;31(19):54. <https://doi.org/10.7748/ns.2017.e10349>
- [3] Angermann C. Comorbidities in heart failure: a key issue. *European Journal of Heart Failure Supplements*. 2009;8:i5-i10. <https://doi.org/10.1093/eurjhf/hfp009>
- [4] Wong CY, Chaudhry SI, Desai MM, Krumholz HM. Trends in comorbidity, disability, and polypharmacy in heart failure. *The American journal of medicine*. 2011;124(2):136-43. <https://doi.org/10.1016/j.amjmed.2010.08.017>
- [5] Kessler RC. The National Comorbidity Survey: preliminary results and future directions. *International Journal of Methods in Psychiatric Research*. 1995.
- [6] Van der Wal HH, van Deursen VM, van der Meer P, Voors AA. Comorbidities in heart failure. *Heart Failure: Springer*; 2017. p. 35-66. https://doi.org/10.1007/164_2017_27
- [7] Braunstein JB, Anderson GF, Gerstenblith G, Weller W, Niefeld M, Herbert R, et al. Noncardiac comorbidity increases preventable hospitalizations and mortality among Medicare beneficiaries with chronic heart failure. *Journal of the American College of Cardiology*. 2003;42(7):1226-33. [https://doi.org/10.1016/S0735-1097\(03\)00947-1](https://doi.org/10.1016/S0735-1097(03)00947-1)
- [8] Sharma A, Zhao X, Hammill BG, Hernandez AF, Fonarow GC, Felker GM, et al. Trends in Noncardiovascular Comorbidities Among Patients Hospitalized for Heart Failure: Insights From the Get With The Guidelines-Heart Failure Registry. *Circulation: Heart Failure*. 2018;11(6):e004646. <https://doi.org/10.1161/CIRCHEARTFAILURE.117.004646>
- [9] Rawshani A, Rawshani A, Franzén S, Eliasson B, Svensson A-M, Miftaraj M, et al. Mortality and cardiovascular disease in type 1 and type 2 diabetes. *New England Journal of Medicine*. 2017;376(15):1407-18. <https://doi.org/10.1056/NEJMoa1608664>
- [10] de Groote P, Lamblin N, Mouquet F, Plichon D, McFadden E, Van Belle E, et al. Impact of diabetes mellitus on long-term survival in patients with congestive heart failure. *European heart journal*. 2004;25(8):656-62. <https://doi.org/10.1016/j.ehj.2004.01.010>
- [11] Aune D, Schlesinger S, Neuenschwander M, Feng T, Janszky I, Norat T, et al. Diabetes mellitus, blood glucose and the risk of heart failure: A systematic review and meta-analysis of prospective studies. *Nutrition, Metabolism and Cardiovascular Diseases*. 2018;28(11):1081-91. <https://doi.org/10.1016/j.numecd.2018.07.005>
- [12] Horwich TB, Fonarow GC, Hamilton MA, MacLellan WR, Borenstein J. Anemia is associated with worse symptoms, greater impairment in functional capacity and a significant increase in mortality in patients with advanced heart failure. *Journal of the American College of Cardiology*. 2002;39(11):1780-6. [https://doi.org/10.1016/S0735-1097\(02\)01854-5](https://doi.org/10.1016/S0735-1097(02)01854-5)
- [13] Ference BA, Yoo W, Alesh I, Mahajan N, Mirowska KK, Mewada A, et al. Effect of long-term exposure to lower low-density lipoprotein cholesterol beginning early in life on the risk of coronary heart disease: a Mendelian randomization analysis. *Journal of the American College of Cardiology*. 2012;60(25):2631-9. <https://doi.org/10.1016/j.jacc.2012.09.017>
- [14] Khatibzadeh, S., Farzadfar, F., Oliver, J., Ezzati, M. and Moran, A., 2013. Worldwide risk factors for heart failure: a systematic review and pooled analysis. *International journal of cardiology*, 168(2), pp.1186-1194. <https://doi.org/10.1016/j.ijcard.2012.11.065>
- [15] Dunlay, S.M., Weston, S.A., Jacobsen, S.J. and Roger, V.L., 2009. Risk factors for heart failure: a population-based case-control study. *The American journal of medicine*, 122(11), pp.1023-1028. <https://doi.org/10.1016/j.amjmed.2009.04.022>
- [16] Bauters, C., Lamblin, N., Mc Fadden, E.P., Van Belle, E., Millaire, A. and De Groote, P., 2003. Influence of

- diabetes mellitus on heart failure risk and outcome. *Cardiovascular diabetology*, 2(1), pp.1-16.
<https://doi.org/10.1186/1475-2840-2-1>
- [17] Ingelsson, E., Ärnlöv, J., Sundström, J., Zethelius, B., Vessby, B. and Lind, L., 2005. Novel metabolic risk factors for heart failure. *Journal of the American College of Cardiology*, 46(11), pp.2054-2060.
<https://doi.org/10.1016/j.jacc.2005.07.059>
- [18] Kalantar-Zadeh, K., Block, G., Horwich, T. and Fonarow, G.C., 2004. Reverse epidemiology of conventional cardiovascular risk factors in patients with chronic heart failure. *Journal of the American College of Cardiology*, 43(8), pp.1439-1444.
<https://doi.org/10.1016/j.jacc.2003.11.039>
- [19] Wilhelmsen, L., Rosengren, A., Eriksson, H. and Lappas, G., 2001. Heart failure in the general population of men-morbidity, risk factors and prognosis. *Journal of internal medicine*, 249(3), pp.253-261.
<https://doi.org/10.1046/j.1365-2796.2001.00801.x>
- [20] Nichols, G.A., Hillier, T.A., Erbey, J.R. and Brown, J.B., 2001. Congestive heart failure in type 2 diabetes: prevalence, incidence, and risk factors. *Diabetes care*, 24(9), 1614-1619.
doi.org/10.2337/diacare.24.9.1614