Original Article

Features Of Patients Admitted With Heart Failure And Having Diuretic Resistance

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ABSTRACT

Objective: The current study aimed to identify the features of diuretic resistance (DR) in patients with heart failure who were hospitalized in a tertiary care hospital's cardiology department.

Materials & Methods: Between January 1, 2014, and December 31, 2014, retrospective observational research was carried out in the Khyber Teaching Hospital cardiology department in Peshawar. There were 560 adult patients diagnosed with heart failure who were hospitalized within a year. Excluded patients were 152 who were released in less than 24 hours and 113 whose full data was not accessible. Thus, the research comprised the remaining patients (560-152-113= 295) whose records were examined. A cutoff point of 160 mg of furosemide per day was established for patients I/V, who were classified as diuretic responders (using < 160 mg/day; group I) and diuretic resistant (using > 160 mg/day; group II).

Results: There were 295 patients, of whom 175 (59.32%) were male and 120 (40.67%) were female. The patients' average age was 65+7 years. Group I consisted of 190 patients (64.4%) who responded to diuretics, whereas group II consisted of 105 patients (35.9%) who were resistant to diuretics. In group I, there were 114 (60%) males and 76 (40%) females; in group II, there were 61 (58%) males and 44 (41%) females. Clinical and laboratory parameters, comorbidities, and the kind of therapy each group got were compared. Compared to group I, patients with DR (group II) had noticeably greater rates of CAD, diabetes, and asthma. DR patients (Group II) had lower heart rates and blood pressure systolic and diastolic than those in Group I. However, group I had a higher JVP and more noticeable edema in the foot. Compared to group I, patients with DR (group II) had higher rates of anemia, hypokalemic, and hyponatremic conditions. In addition, their creatinine, glucose, and cholesterol levels were higher than those of group I. Those with DR (Group II) used B Blockers, spironolactone, and inotropes at much greater rates than those in Group I. **Conclusion:** Patients with heart failure often struggle with diuretic resistance. Patients with DR have substantially distinct characteristics from those who react well to diuretics. When such patients are identified early on, doctors can adopt more aggressive treatment plans, which promotes quicker healing and shorter hospital stays.

Keywords: Diuretic Resistance, heart failure

INTRODUCTION

One prevalent cause of morbidity and death is heart failure [1]. Acutely decompensated heart failure is a potentially fatal condition that requires hospitalization right away [2, 3, 4]. Up to 90% of patients who are hospitalized are given loop diuretics, which are the most efficient and quick-acting medications for reducing acute heart failure symptoms and signs [4, 5, 6]. Even with increased dosages of diuretics, many individuals do not react right away. Poor clinical outcomes for these individuals include increased mortality and repeated hospitalisation [7] .Early identification may enable doctors to implement aggressive treatment plans from the outset, resulting in early symptom alleviation and a shorter hospital stay. Because different individuals have distinct pathophysiologic causes and various studies have employed different definitions of diuretic resistance, the precise prevalence of diuretic resistance is uncertain.It is still unclear exactly what pathophysiology underlies diuretic resistance. Due to the breaking phenomenon, the quantity of diuresis in normal persons decreases with time after a given diuretic dosage. The primary cause of this is neurohormonal activation, brought on by the first diuretic effect's lowering of the extracellular fluid amount. Delayed absorption of diuretics leads to lower peak drug levels in the ascending loop of Henle, which are inadequate to elicit maximal natriuresis and

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are another cause of diuretic resistance in heart failure. The renal response to endogenous natriuretic peptides decreases as heart failure worsens.

Laur O et al. have also shown that the main mechanism of DR is distal tubular compensation.8 Chronic diuretic usage increases the amount of solute delivered to the distal regions of the nephron, which results in hyperplasia and hypertrophy of the distal nephron's epithelial cells.

This counteracts diuretics' effects by increasing the kidney's solute resorption capacity by up to three times. A decrease in cardiac or renal function, noncompliance with diuretic dosages, and concomitant use of medications such as NSAIDs, COX inhibitors, and thiazolidinediones may also result in a reduced diuretic response in addition to these reasons. These may also lead to a decline in renal function and the emergence of cardiorenal syndrome [10, 11].

By identifying the clinical characteristics of DR patients, we can quickly identify these individuals after their hospital stay and implement aggressive treatment plans that may alleviate symptoms sooner and reduce hospital stays. Scientists have looked for biochemical and clinical indicators to forecast the diuretic response.

The poorer diuretic response has been linked to more advanced heart failure, renal impairment, metabolic disorders, and atherosclerotic disease, according to research by Valente MA [12] et al. Mortality and early rehospitalization have also been shown to be predicted with poor diuretic response [12, 13].

Additionally, Djenamba K et al. discovered a substantial difference between the features of individuals who responded to diuretics and those who did not [14]. However, Elizabeth J. et al. discovered that DR incidence cannot be predicted by baseline characteristics 15.

We were unable to locate any local research on this topic. The current study's objective was to identify the features of DR patients with heart failure who were hospitalized in a tertiary care hospital's cardiology department.

MATERIALS & METHODS

Reviewing the medical records of patients diagnosed with heart failure hospitalized in the cardiology department of Khyber Teaching Hospital in Peshawar between January 1 and December 31, 2014, was retrospective observational research.

There were 560 adult patients diagnosed with heart failure who were hospitalized within a year. Fifty-two patients were disqualified after being released in less than 24 hours. Eleven3 patients had their entire data unavailable, and they were therefore omitted. Thus, the research included the remaining patients (560-152-113= 295). Every patient's document was examined for clinical, laboratory, and demographic information in addition to the care they were getting.

The furosemide dosage administered to Patients I/V on Day 2 (after 48 hours of admission) was determined to be the cutoff point between diuretic responders (using < 160 mg/day; Group I) and diuretic resistive (using > 160 mg/day; Group II).

SPSS vs. 14 was used to input and analyze all of the data. The mean plus standard deviation was computed for continuous data, and the student's T-test was used for comparison. The chi-square test was used to compare categorical variables, which were reported as frequencies or percentages. A difference between the groups was deemed significant if the P value was less than 05.

RESULTS

There were 295 patients, of whom 175 (59.32%) were male and 120 (40.67%) were female. The patients' average age was 65+7 years.

Group I consisted of 190 patients (64.4%) who responded to diuretics, whereas group II consisted of 105 patients (35.9%) who were resistant to diuretics. In group I, there were 114 (60%) males and 76 (40%) females; in group II, there were 61 (58%) males and 44 (42%) females.

The two groups' various comorbidities are shown in Table I. Compared to group I, patients with DR (group II) had noticeably greater rates of CAD, diabetes, and asthma.

A variety of clinical signs in heart failure patients are shown in Table II. DR patients (Group II) had lower

heart rates and blood pressure systolic and diastolic than those in Group I. However, group I had a higher prevalence of edematous feet and elevated JVP.

Table III lists the results of many laboratory tests performed on heart failure patients. Compared to group I, patients with DR (group II) had higher rates of anemia, hypokalemic, and hyponatremic conditions. In addition, their creatinine, glucose, and cholesterol levels were higher than those of group I.

Patients with heart failure utilize several drugs, as shown in Table IV. those with DR (Group II) used B Blockers, spironolactone, and inotropes at much greater rates than those in Group I.

Table 1: Comorbidities in Patients with Heart Failure

	Group-I (n= 190)	Group-II (n = 105)	P Value
CAD n(%)	81 (43.15)	58 (55.23)	0.019
HTN n(%)	155 (81.57)	88 (83.80)	0.183
DM n(%)	76 (40)	51 (48.57)	0.027
Tobacco Smoking n(%)	21 (11.05)	12 (11.42)	0.793
Past Stroke n(%)	22 (11.57)	13 (12.38)	0.413
Asthma / COPD n(%)	22 (11.57)	16 (15.23)	0.017

Table 2: Clinical Findings in Patients with Heart Failure.

	Group-I (n= 190)	Group-II (n= 105)	P Value
Systolic Blood Pressure (mmhg)	148 ± 15	140.5 ± 14.9	0.006
Diastolic Blood Pressure (mmhg)	81.2 ± 13	75.9 ± 12.8	0.008
Heart Rate (beat/m)	82.6 ± 15	78.1 ± 13	0.009
Resp. Rate (breath/m)	20.8 ± 3.9	21.9 ± 4.8	0.072
JVP ≥ 10 cm n(%)	150 (78.9)	73 (69.52)	0.009
Edema ≥ + 2 n(%)	155 (81.57)	73 (69.52)	0.007
Rales ≥ 1/3 Lungs fields n(%)	68 (35.78)	39 (37.14)	0.065

Table 4: Medications used by Patients with Heart Failure.

	Group-I n=190	Group-II n=105	P Value
ACE n(%)	104 (54.73)	55 (52.38)	0.305
ARB n(%)	36 (18.94)	17 (16.19)	0.190
BB n(%)	115 (60.52)	74 (70.47)	0.018
Spironolactone n(%)	66 (34.73)	29 (27.61)	0.029
Loop Diuretic n(%)	190 (100)	105 (100)	NA
Digoxin n(%)	43 (22.63)	21 (20)	0.184
Nitrates n(%)	18 (9.4)	9 (8.5)	0.312
Inotropes n(%)	24 (12.63)	23 (21.90)	0.009

Table 3: Laboratory Investigations of Patients with Heart Failure.

	Group-I (n= 190)	Group-II (n = 105)	P Value
HB gm/dl	12.20 (± 1.4)	11.92 (± 1.5)	0.029
Sodium mmole/L	140 (± 3.5)	137.0 (± 3.9)	0.045
Potassium mmole/L	4.39 (± 0.69)	4.07 (± 0.53)	0.008
Chloride mmole/L	108 ± 7	105 ± 8	0.064
Urea mg/dl	51 ± 8	55 ± 9	0.040
Creatinine mg/dl	1.2 ± (0.3)	1.5 ± 0.4	0.000
Glucose mg/dl	138 ± 13	159 ± 21	0.009
Cholesterol mg/dl	168 ± 13	182 ± 17	0.012

DISCUSSION

Hospitalized acute heart failure patients get diuretics. An inadequate diuretic response increases morbidity and mortality. Identifying diuretic nonresponders' clinical and biochemical features and applying this knowledge in clinical practice may help predict DR shortly after hospitalization [16]. Once these persons are identified, more aggressive and other treatments may be tried. We found that diuretic responders had lower incidences of CAD, diabetes, asthma, and COPD than DR patients. Our DR patients showed lower

diastolic and systolic blood pressure. Our test findings showed that DR patients had lower hemoglobin, sodium, and potassium and higher glucose, creatinine, and urea.

Djenamba K et al. found hyponatremia, lower LVEF, higher inotrope use, and poorer renal function in DR patients. A severe heart failure profile and a poor prognosis were associated with higher diuretic dosages [14]. Our study outcomes were comparable, except for prognosis, which was not our purpose. Elizabeth J. et al. compared diuretic responders and DR by gender, blood pressure, renal function, diabetes, HTN, CAD, and ACE use. It's surprising that they found none and concluded these features cannot predict DR [15].

Our study found that DR patients utilized beta-blockers more, spironolactone, and inotropes. DR medicine use increased significantly, according to Voors AA et al. [17] Our findings are similar to an earlier study showing lower edema and JVP and increased CAD, DM, hyperlipidemia, and COPD/asthma in DR. The study's test results showed higher glucose, creatinine, and urea but neither hypernatremia nor hypokalemia [17].

With the same aims, Valente MAE et al. [12] showed that DR patients were more likely to have diabetes, CAD, and renal impairment. Multivariable regression analysis showed that systolic blood pressure and serum potassium were negatively linked with poor diuretic response. Beta-blockers, smoking, high cholesterol, and diabetes were also linked [12]. Olinger CC et al. found that IV loop diuretics' natriuretic response was unpredictable depending on the diuretic dose or creatinine level [18].

Oneyebeke C et al. found a minimal impact of renal impairment on DR. They advised more research to understand DR's core mechanism [19].

In addition, Aronson D et al. [20] examined the hemodynamic profile and clinical variables that affect loop diuretic response in abruptly decompensated heart failure. They found that loop diuretic dose, renal functioning, lowered systolic blood pressure, fluid intake, and male sex independently predicted urine output.

Ter Maaten JM et al. [21] examined 26 biochemical and clinical markers at baseline and throughout 24hour heart failure diuretic treatment. They found a strong link between renal and atherosclerosis biomarkers and poor diuretic responsiveness. In addition to creatinine and urea, they found that novel renal markers, including neutrophil gelatinize-associated lipocalin, correlated with disease-related kidney impairment. They also found that baseline and deteriorating renal function affect diuretic responsiveness. DR patients also showed much lower potassium, salt, and chloride levels.

Both high TG and low HB predicted DR. Finally, the clinical baseline model showed that high systolic blood pressure, increased weight and JVP, less frequent diabetes, PCI, COPD, BB, and metolazone use, and higher spironolactone use were associated with a positive response. They found that although the above markers may assist in identifying individuals at risk of diuretic response (DR) after 24 hours, their therapeutic value in predicting DR at the time of acute heart failure hospital admission is limited. Understanding pathophysiology We mentioned several diuretic resistance pathways in the beginning.

Diuretics reach a therapeutic concentration in the tubule by renal secretion and, to a lesser degree, glomerular filtration. Diabetes and atherosclerosis may cause glomerulus closis and reduce GFR. Both illnesses may reduce responsiveness due to inflammation and RAS activation [22, 23, 24]. Our investigation supported earlier findings that DR patients had a greater frequency of CAD and DM.

Hypotension in heart failure reduces renal perfusion and increases congestion, while the feedback loop to regulate renal blood flow, GFR, and salt level worsens renal function [22]. DR patients in our study showed greater hypotension than group I, which may have contributed to their illness.

Chronic diuretics may structurally modify the tubular epithelium, causing salt retention, congestion, and neurohormonal activation. Because diuretics temporarily reduce neurohormone levels [25] and alleviate congestion, greater dosages may be needed [26].

Similar to our results, most studies have demonstrated that DR patients have reduced renal function, but this does not mean this is the major cause.

DR is partially caused by renal impairment, according to Valente MA [12] et al. and Testani et al [13]. Many things might cause this. Ischemic heart failure and atherosclerosis-related symptoms such as dyslipidemia, DM, and prior MI were more common in DR patients, according to our and other research [12]. Diuretics may not work for some people due to atherosclerotic kidneys. Ischemic heart disease may also increase renal artery stenosis [27], lowering DR.

DR patients exhibited reduced congestion indications (JVP and edoema), as did our study [17]. Diuretics may not work since fluid redistribution may worsen their heart failure instead of fluid accumulation. Loop diuretics are not volume-overloaded and may cause dehydration and renal function loss. Therefore, they may not be the best treatment for these patients. Therefore, diuretics work better for people with greater peripheral edema and congestion.

Many treatments for DR have been suggested, including combining diuretic groups, continuously infused furosemide, ionotropic hypotension support, and ultra filtration22. To improve diuretic responsiveness in acute decompensated heart failure, Zachari LC et al. proposed resistance-based treatments [28]. Kissling KT et al. found that oral HCTZ and IV CTZ increased diuresis in hospitalized heart failure patients with loop DR. CTZ increased urine output but not length of stay or mortality [29].

CONCLUSION

Patients with heart failure often struggle with diuretic resistance. Patients with DR have substantially distinct characteristics from those who react well to diuretics. When such patients are identified early on, doctors may be able to adopt more aggressive treatment plans, which might promote quicker healing and shorter hospital stays.

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