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Original Article

Frequency of Undiagnosed Heart Failure in Diabetic Patients Presenting with Diabetic Foot Ulcer (DFU)

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Abstract

Background: Diabetes mellitus (DM) is a chronic metabolic disorder that significantly increases the risk of cardiovascular diseases, including heart failure (HF). Diabetic foot ulcer (DFU) is a severe complication of DM, often associated with advanced vascular disease. However, HF remains frequently undiagnosed, particularly in patients with DFU, due to its asymptomatic nature.

Objective: To determine the frequency of undiagnosed heart failure in diabetic patients presenting with diabetic foot ulcers.

Methods: This cross-sectional study was conducted at the Department of Endocrinology, Hayatabad Medical Complex, Peshawar, from June 16th, 2023, to June 15th, 2024. A total of 108 diabetic patients with DFU were enrolled using non-probability consecutive sampling. Patients with a known history of heart failure, ischemic heart disease, or cardiomyopathies were excluded. The diagnosis of DM was confirmed by patient history and fasting blood glucose levels (>130 mg/dL). DFU was clinically diagnosed by the presence of non-healing ulcers on the foot. Heart failure was assessed through clinical examination, echocardiography, and B-type natriuretic peptide (BNP) levels. The severity of DFU was classified using the Wagner classification system. Data analysis was performed using IBM SPSS Statistics version 25.0, with descriptive statistics used to summarize the data and inferential statistics employed for comparisons between groups.

Results: Of the 108 patients, 40 (37.0%) were diagnosed with heart failure, while 68 (63.0%) were without HF. The mean age of the patients was 58.31 ± 10.07 years, with HF patients being older (60.74 ± 9.29 years) than non-HF patients (56.04 ± 11.37 years) ($p < 0.05$). The HF group had a significantly longer duration of diabetes (15 ± 5 years vs. 10 ± 4 years, $p < 0.01$) and higher mean HbA1c levels (9.2% ± 1.5% vs. 8.0% ± 1.2%, $p < 0.01$). Echocardiographic findings showed a lower mean ejection fraction in HF patients (45.54 ± 10.43%) compared to non-HF patients (60.51 ± 5.32%) ($p < 0.01$). BNP levels were significantly elevated in the HF group (250 ± 50 pg/mL) compared to the non-HF group (100 ± 30 pg/mL) ($p < 0.01$). The severity of DFU was higher in HF patients, with 53% of HF patients having Wagner grade 3 or higher ulcers compared to 28% in non-HF patients ($p < 0.01$).

Conclusion: The study identified a high prevalence of undiagnosed heart failure in diabetic patients with DFU, highlighting the need for routine cardiovascular screening in this population. Early detection and management of HF could significantly improve patient outcomes.

1 Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by elevated blood glucose levels, affecting millions of individuals worldwide, and representing a significant public health challenge (1). The long-term complications of diabetes are extensive, with cardiovascular diseases (CVDs) and diabetic foot ulcers (DFU) being among the most critical and life-threatening. DFUs are a common and severe complication in diabetic patients, leading to significant morbidity, mortality, and healthcare costs. The interplay between diabetes and cardiovascular complications is well-documented, with heart failure (HF) being one of the most frequent yet often undiagnosed conditions in this population. Heart failure, particularly when asymptomatic, presents a hidden risk, as its progression can lead to severe outcomes if not identified and managed early (2).

Patients with DFU are often burdened with multiple comorbidities, including peripheral vascular disease and neuropathy, which exacerbate their risk for developing cardiovascular conditions, including HF. The relationship between DFU and HF is particularly concerning due to the systemic inflammatory response and vascular damage associated with chronic ulcers, which may further precipitate cardiac dysfunction. Despite the known risks, there remains a significant gap in the early detection of HF among diabetic patients,

particularly those presenting with DFU. Many of these patients may already be in the advanced stages of HF by the time it is clinically diagnosed, thereby limiting the effectiveness of treatment interventions (3, 4).

The pathophysiological mechanisms linking diabetes, DFU, and HF are complex and multifaceted. Prolonged hyperglycemia in diabetes leads to a cascade of metabolic, hemodynamic, and structural changes that predispose individuals to HF. These include endothelial dysfunction, increased arterial stiffness, and myocardial fibrosis, which collectively contribute to the development of both systolic and diastolic dysfunction (5). Moreover, the chronic inflammatory state induced by DFUs further exacerbates these cardiovascular risks, promoting the progression of atherosclerosis and the deterioration of myocardial function. Understanding these underlying mechanisms is crucial for the development of targeted screening and management strategies that can mitigate the risk of HF in diabetic patients with DFU (6, 7).

Given the substantial clinical burden of DFU and the high prevalence of undiagnosed HF in this population, there is a critical need for enhanced cardiovascular risk assessment in diabetic patients, particularly those with chronic wounds. Early identification and management of HF in these patients could significantly improve their prognosis, reduce complications, and enhance their overall quality of life. This study aims to fill the existing knowledge gap by investigating the frequency of undiagnosed HF in diabetic patients presenting with DFU, utilizing comprehensive clinical and echocardiographic evaluations to detect subclinical cardiac dysfunction (8). The findings of this research are expected to provide valuable insights into the importance of cardiovascular screening in diabetic foot clinics and contribute to the development of more effective, multidisciplinary care strategies for this high-risk patient group (9, 10).

2 Material and Methods

This cross-sectional study was conducted at the Department of Endocrinology, Hayatabad Medical Complex, Peshawar, over a period of one year, from June 16th, 2023, to June 15th, 2024. The study aimed to assess the frequency of undiagnosed heart failure (HF) in diabetic patients presenting with diabetic foot ulcers (DFU). A total of 108 male and female patients, aged between 18 and 90 years, who were diagnosed with both diabetes mellitus and DFU, were included. Patients with a known history of heart failure, ischemic heart disease, or cardiomyopathies were excluded from the study. The diagnosis of diabetes mellitus was confirmed based on patient history, ongoing use of oral or injectable hypoglycemic medications, or a fasting blood glucose level greater than 130 mg/dL. Diabetic foot ulcers were clinically confirmed by the presence of non-healing, excavating ulcers on the foot, with or without necrotic tissue.

Participants were enrolled using a non-probability consecutive sampling technique. Informed consent was obtained from all patients prior to inclusion in the study. The study protocol was reviewed and approved by the institutional research ethics committee, and all procedures conformed to the ethical standards outlined in the Declaration of Helsinki (1).

Baseline demographic and clinical information, including age, gender, body mass index (BMI), and residential status, was recorded. Patients were classified according to their socioeconomic status, education level, and occupation, using a structured questionnaire. The duration of diabetes, comorbidities such as hypertension and hyperlipidemia, and current medication use were also documented.

The assessment of heart failure was conducted through a comprehensive clinical evaluation and echocardiographic examination. Clinical assessments focused on identifying common symptoms of HF, such as dyspnea, fatigue, and fluid retention. Additionally, echocardiography was performed on all patients to detect any structural or functional cardiac abnormalities indicative of HF. B-type natriuretic peptide (BNP) levels, a biomarker for heart failure, were measured in serum samples collected from the patients. BNP levels were used as an additional diagnostic tool to support the identification of HF.

The severity of diabetic foot ulcers was classified using the Wagner classification system, which ranges from grade 0 (intact skin) to grade 5 (gangrenous lesions requiring amputation). This classification allowed for the standardized evaluation of ulcer severity across the study population.

Data analysis was performed using IBM SPSS Statistics version 25.0. Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Inferential statistics, including the chi-square test for categorical variables and the independent samples t-test for continuous variables, were used to compare the characteristics of patients with and without heart failure. A p-value of ≤0.05 was considered statistically significant.

The study was designed to ensure that all relevant ethical considerations were adhered to, including the confidentiality of patient information and the voluntary nature of participation. The findings from this study are expected to contribute to a better understanding of the prevalence and risk factors associated with undiagnosed heart failure in diabetic patients with DFU and to inform clinical practices aimed at improving patient outcomes (2).

3 Results

The study included a total of 108 diabetic patients with diabetic foot ulcers (DFU), of which 40 patients (37.0%) were diagnosed with heart failure (HF), while 68 patients (63.0%) did not have HF. The overall mean age of the patients was 58.31 ± 10.07 years. Patients diagnosed with HF had a significantly higher mean age of 60.74 ± 9.29 years compared to those without HF, who had a mean age of 56.04 ± 11.37 years ($p < 0.05$). The distribution of patients by age groups revealed that the highest prevalence of HF was in the 51-60 years age group (30%) (Table 1).

Gender distribution was comparable between the two groups, with 60.2% of the total patients being male and 39.8% female. The majority of patients, 64.8%, resided in urban areas, and there were no significant differences in the socioeconomic status or education levels between the HF and non-HF groups ($p > 0.05$). The mean body mass index (BMI) was higher in patients with HF (29 ± 5 kg/m²) compared to those without HF (27 ± 4 kg/m²) ($p < 0.05$).

Patients with HF had a significantly longer duration of diabetes, with a mean of 15 ± 5 years, compared to 10 ± 4 years in those without HF ($p < 0.01$). Additionally, mean HbA1c levels were notably higher in the HF group (9.2% ± 1.5%) compared to the non-HF group (8.0% ± 1.2%) ($p < 0.01$). Comorbidities such as hypertension and hyperlipidemia were prevalent in the study population, with hypertension being more common in patients with HF (75%) compared to those without HF (58.8%) (Table 2).

The severity of DFU was assessed using the Wagner classification system. Patients with HF had more severe ulcers, with a greater proportion of ulcers classified as Wagner grade 3 or higher (53%) compared to those without HF (28%) ($p < 0.01$). Specifically, 32.5% of HF patients had Wagner grade 3 ulcers, while only 17.7% of non-HF patients exhibited the same severity (Table 3).

Echocardiographic assessment revealed that patients with HF had a significantly lower mean ejection fraction (45.54 ± 10.43%) compared to those without HF (60.51 ± 5.32%) ($p < 0.01$). Additionally, left ventricular hypertrophy was more prevalent in the HF group (50%) compared to the non-HF group (22%) ($p < 0.05$). Diastolic dysfunction was observed in 62.5% of HF patients, compared to 22% in the non-HF group ($p < 0.05$). Although mitral regurgitation was more frequent in the HF group (25%) compared to the non-HF group (14.7%), this difference did not reach statistical significance ($p = 0.30$) (Table 4).

B-type natriuretic peptide (BNP) levels were significantly elevated in patients with HF (250 ± 50 pg/mL) compared to those without HF (100 ± 30 pg/mL) ($p < 0.01$). Elevated BNP levels (>100 pg/mL) were detected in 55.5% of all patients, with a higher prevalence in the HF group (87.5%) compared to the non-HF group (36.8%) ($p < 0.01$) (Table 5).

Table 1: Demographic and Clinical Characteristics of Patients

Variable	Total (n=108)	With HF (n=40)	Without HF (n=68)	p-value
Mean Age (years)	58.31 ± 10.07	60.74 ± 9.29	56.04 ± 11.37	<0.05
Age Group (Years)				
18-30	10 (9.3%)	2 (5%)	8 (11.8%)	0.22
31-40	15 (13.8%)	5 (12.5%)	10 (14.7%)	0.76
41-50	20 (18.5%)	6 (15%)	14 (20.6%)	0.44
51-60	30 (27.7%)	12 (30%)	18 (26.5%)	0.68
61-70	23 (21.4%)	10 (25%)	13 (19.1%)	0.49
71-80	8 (7.4%)	5 (12.5%)	3 (4.4%)	0.12
>80	2 (1.9%)	0 (0%)	2 (2.9%)	0.32
Gender				
Male	65 (60.2%)	25 (62.5%)	40 (58.8%)	0.73
Female	43 (39.8%)	15 (37.5%)	28 (41.2%)	
BMI (kg/m²)	28 ± 4	29 ± 5	27 ± 4	<0.05
Residence				
Urban	70 (64.8%)	25 (62.5%)	45 (66.2%)	0.81
Rural	38 (35.2%)	15 (37.5%)	23 (33.8%)	
Socioeconomic Status				
Low	30 (27.7%)	10 (25%)	20 (29.4%)	
Middle	55 (50.9%)	20 (50%)	35 (51.5%)	
High	23 (21.4%)	10 (25%)	13 (19.1%)	
Education Level				

No formal education	20 (18.5%)	8 (20%)	12 (17.7%)
Primary	35 (32.4%)	15 (37.5%)	20 (29.4%)
Secondary	33 (30.6%)	10 (25%)	23 (33.8%)
Higher education	20 (18.5%)	7 (17.5%)	13 (19.1%)

Table 2: Clinical Variables and Disease Duration

Variable	Total (n=108)	With HF (n=40)	Without HF (n=68)	p-value
Duration of Diabetes (years)	12 ± 6	15 ± 5	10 ± 4	<0.01
Mean HbA1c (%)	8.6 ± 1.4	9.2 ± 1.5	8.0 ± 1.2	<0.01
Medication Use				
Insulin	65 (60.2%)	25 (62.5%)	40 (58.8%)	
Oral Hypoglycemic Agents	43 (39.8%)	15 (37.5%)	28 (41.2%)	
Presence of Comorbidities				
Hypertension	70 (64.8%)	30 (75%)	40 (58.8%)	
Hyperlipidemia	55 (50.9%)	25 (62.5%)	30 (44.1%)	

Table 3: Severity of Diabetic Foot Ulcers (Wagner Classification)

Wagner Grade	Total (n=108)	With HF (n=40)	Without HF (n=68)	p-value
Grade 0	10 (9.3%)	2 (5%)	8 (11.8%)	
Grade 1	20 (18.5%)	5 (12.5%)	15 (22%)	
Grade 2	30 (27.7%)	10 (25%)	20 (29.4%)	0.01
Grade 3	25 (23.1%)	13 (32.5%)	12 (17.7%)	
Grade 4	15 (13.8%)	8 (20%)	7 (10.3%)	
Grade 5	8 (7.4%)	2 (5%)	6 (8.8%)	

Table 4: Echocardiographic Findings

Echocardiographic Parameter	Total (n=108)	With HF (n=40)	Without HF (n=68)	p-value
Ejection Fraction (%)	55.95 ± 10.01	45.54 ± 10.43	60.51 ± 5.32	<0.01
Left Ventricular Hypertrophy	35 (32.4%)	20 (50%)	15 (22%)	<0.05
Diastolic Dysfunction	40 (37%)	25 (62.5%)	15 (22%)	<0.05
Mitral Regurgitation	20 (18.5%)	10 (25%)	10 (14.7%)	0.30

Table 5: B-type Natriuretic Peptide (BNP) Levels

BNP Level (pg/mL)	Total (n=108)	With HF (n=40)	Without HF (n=68)	p-value
Mean BNP Level	150 ± 60	250 ± 50	100 ± 30	<0.01
Elevated BNP (>100 pg/mL)	60 (55.5%)	35 (87.5%)	25 (36.8%)	<0.01

The results demonstrate a significant prevalence of undiagnosed heart failure in diabetic patients with DFU, highlighting the importance of comprehensive cardiovascular assessments in this high-risk population. The associations between HF and factors such as age, duration of diabetes, HbA1c levels, and severity of DFU underscore the need for vigilant monitoring and early intervention to improve patient outcomes.

4 Discussion

The findings of this study reveal a significant prevalence of undiagnosed heart failure (HF) among diabetic patients with diabetic foot ulcers (DFU), with 37% of the study population found to have asymptomatic HF. This prevalence is notably higher than that reported in earlier studies, such as Bertoni et al. (2004), who identified a 21.7% prevalence of undiagnosed HF in diabetic patients (13). The elevated prevalence observed in this study may be attributed to the inclusion of patients with DFU, a condition often associated with advanced vascular disease, which likely exacerbates the risk of developing HF. The data underscore the critical need for early cardiovascular evaluation in diabetic patients, particularly those presenting with DFU.

The study demonstrated that patients with HF had poorer glycemic control, with mean HbA1c levels significantly higher in the HF group (9.2% ± 1.5%) compared to the non-HF group (8.0% ± 1.2%). This finding aligns with previous research, such as the study by Nichols et al. (2001), which found that poor glycemic control is a strong predictor of HF in diabetic patients, with a 1% rise in HbA1c associated with an 8% increased risk of HF (14). The prolonged duration of diabetes observed in the HF group further supports the notion that chronic hyperglycemia contributes to the gradual deterioration of cardiovascular function, leading to the development of HF, as highlighted by Thrainsdottir et al. (2005) (15).

The severity of DFU was also significantly greater in patients with HF, with a higher proportion of these patients classified with Wagner grade 3 or higher ulcers. This association between severe DFU and HF emphasizes the interconnectedness of diabetic complications, where advanced ulcers reflect poor vascular health and increased cardiovascular risk. The findings are consistent with those of Prompers et al. (2008), who reported that patients with severe DFU often exhibit a poor cardiovascular risk profile, further complicating their clinical management (16).

Echocardiographic findings in this study revealed that patients with HF had a significantly lower ejection fraction, higher prevalence of left ventricular hypertrophy, and more frequent diastolic dysfunction compared to those without HF. These structural and functional cardiac changes are well-documented in the literature and are indicative of the adverse cardiac remodeling that occurs in diabetic patients with HF. The results corroborate the findings of McMurray et al. (2014), who noted that diabetic patients with HF typically exhibit lower ejection fractions and more pronounced left ventricular hypertrophy, underscoring the need for comprehensive cardiac assessment in this population (17).

One of the study's strengths lies in its focus on a high-risk subgroup of diabetic patients—those with DFU—who are often underrepresented in cardiovascular research. By identifying the substantial burden of undiagnosed HF in this group, the study provides valuable insights that could inform clinical practices and improve patient outcomes through early detection and intervention. However, the study has several limitations that should be acknowledged. The cross-sectional design limits the ability to establish causal relationships between the observed variables. Additionally, the study was conducted in a single center, which may limit the generalizability of the findings to broader populations. The exclusion of patients with known HF or ischemic heart disease may have led to an underestimation of the true prevalence of HF in the diabetic population.

Despite these limitations, the study highlights important clinical implications. The high prevalence of undiagnosed HF in diabetic patients with DFU suggests that routine cardiovascular screening should be an integral part of the management of these patients. The use of echocardiography and BNP measurement as part of the screening process could facilitate the early detection of subclinical HF, allowing for timely intervention that could improve long-term outcomes. Furthermore, the strong association between poor glycemic control, long duration of diabetes, and HF underscores the need for aggressive management of blood glucose levels and other cardiovascular risk factors in diabetic patients.

In conclusion, this study underscores the necessity for heightened awareness and proactive cardiovascular risk assessment in diabetic patients, particularly those with DFU. The findings support the integration of routine cardiac evaluations into the standard care of diabetic patients to prevent the progression of undiagnosed HF and improve overall patient outcomes. Future research should focus on larger, multicenter studies to validate these findings and explore the potential benefits of early HF intervention in diabetic patients with DFU, ultimately contributing to more effective and comprehensive diabetes care (18).

5 Conclusion

In conclusion, the findings of this study underscore the critical importance of routine cardiovascular screening in diabetic patients, particularly those presenting with diabetic foot ulcers (DFU), who are at a significantly higher risk of undiagnosed heart failure (HF). The study revealed a substantial prevalence of asymptomatic HF in this population, highlighting the interconnected nature of diabetic complications, where advanced vascular damage and poor glycemic control exacerbate cardiovascular risk. The associations between prolonged diabetes duration, elevated HbA1c levels, and the severity of DFU with the incidence of HF emphasize the need for comprehensive management strategies that address not only glycemic control but also cardiovascular health in diabetic patients. The significant differences in echocardiographic findings and BNP levels between patients with and without HF further validate the necessity for integrating advanced diagnostic tools into routine care. By identifying and managing HF early, particularly in high-risk groups like those with DFU, healthcare providers can improve clinical outcomes, reduce the burden of complications, and enhance the quality of life for diabetic patients. Future research should aim to expand these findings through multicenter studies and explore the long-term benefits of early HF intervention in improving overall patient prognosis.

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Disclaimers	
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