# ORIGINAL ARTICLE

# Hypoglycemia with Beta-Blocker in Patients with Type II Diabetes

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### ABSTRACT

Objective: To ascertain the frequency of hypoglycemia in diabetic patients using beta blockers.

# **Study Design:** A descriptive cross-sectional study.

**Place and Duration of Study:** The study was conducted in the Department of Nephrology and Medicine, Lady Reading Hospital Peshawar, Pakistan, from 10<sup>th</sup> October 2021 to 10<sup>th</sup> April 2022.

**Materials and Methods:** The total number of diabetic patients with hypoglycemia was 196, who were included in this study. The patients' medical record was assessed, and the use of beta-blocker was noted and recorded.

**Results:** This study included those patients whose ages ranged from 30 to 70 years, with a mean age of 51.964±6.38 years. The average duration of diabetes was 7.989±2.74 years, and an average weight of 87.178 kg. Male patients were 71.9%, and females were 28.1%, 43.9% of diabetic patients who had hypoglycemia used beta blockers.

**Conclusion:** According to this study, diabetic people who take oral beta-blockers have a higher risk of developing hypoglycemia. This research shows that Beta Blocker use causes increased chances of hypoglycemia in people with diabetes.

### Keywords: Beta Blocker, Hypoglycemia, Type II Diabetes.

*How to cite this:* Wali R, Mohammad N, Rehman N, Khan TU, Waqas M, Khan U. Use of Betablocker in Diabetic Patients Experiencing Hypoglycemia. 2023; 4(3): 253-257. doi: http://doi.org/10.37185/LnS.1.1.340

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# Introduction

Persistent hyperglycemia is a hallmark of diabetes mellitus (DM), a chronic metabolic condition.<sup>1</sup> It could be caused by poor insulin production, resistance to insulin's peripheral effects, or a combination of the two. In 2015, the international diabetes federation (IDF) estimated that 415 million adults had diabetes, between the ages of 20 and 79.<sup>2</sup> Given that this number is predicted to increase by

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Funding Source: NIL; Conflict of Interest: NIL Received: Jan 13, 2023; Revised: Jun 05, 2023 Accepted: Jun 08, 2023 another 1.2 billion by 2040, it has been proven that DM is a burden on public health globally<sup>1</sup> DM is broadly divided into type1, type 2 and gestational diabetes. Monogenic diabetes and secondary diabetes are two other, less prevalent kinds of diabetes.<sup>3</sup>

According to estimates, 3.5% of patients among noncritically sick hospitalized patients are characterized by hypoglycemia (blood glucose <70 mg/dL or 3.9 mmol/L). Patients in hospitals receiving insulin had a higher prevalence of hypoglycemia.<sup>4</sup> BB are often used in the treatment of hypertension and are part of therapy for heart failure and coronary artery disease.<sup>5</sup> By reducing the initial adrenergic manifestations of imminent hypoglycemia, BB treatment is thought to raise the chance of severe or sustained hypoglycemia.<sup>5</sup> According to a study by Dungan K. et al., 50% of diabetes patients were often using beta blockers who experienced hypoglycemia.<sup>°</sup> It is unknown whether hypoglycemia plays a role; however, BBs have been linked to a greater odd for cardiovascular incidents in diabetics with heart disease.<sup>7</sup> This study was conducted to know the association of beta blockers with hypoglycemia in diabetic patients. The result of this study will be helpful in adding of local knowledge about usage of BB in diabetics.

The objective of this research was to ascertain how frequently patients with diabetes used beta blockers who suffered hypoglycemia.

## **Materials and Methods**

The descriptive cross-sectional study was carried out at department of Medicine and Nephrology from 10<sup>th</sup> October 2021 to 10<sup>th</sup> April 2022. This study consisted of 196 individuals. Patients with diabetes who experience hypoglycemia have been found to use beta blockers, tab Atenolol 50mg once a day for more than 6 months.<sup>6</sup> After receiving approval from the ethical committee (ref# 210/LRH/MTI), the nonprobability consecutive sampling technique was applied. Age, gender, diabetes duration, and weight on the scale were taken as the patient's baseline demographic data. Patients and families gave their informed consent after being assured of the study's confidentiality and that there was no risk to them in participating. The patient's medical record was, evaluated betablockers was noted on a specifically created proforma.

Patients with diabetes for more than 1 year of both

genders of Age 30-70 years, were included. The admitted patients in ICU, who were on insulin infusion, had chronic kidney disease, conception on ultrasound, were taking atenolol more than 50 mg, and refused consent were excluded from study. The data was entered and analyzed using (IBM-SPSS-V-22). For qualitative characteristics like gender and beta-blocker use, frequency and percentage were computed. For quantitative characteristics, including age, diabetes duration, and weight, the mean ±SD were reported.

Age, gender, diabetes duration, and weight were all considered when stratifying beta-blocker use. A chi-square test after stratification was conducted and a *p*-value of  $\leq 0.05$  was determined to be statistically significant.

# Results

The study's sample population ranged in age from 30 to 70 years, with a mean age of 51.964 years, a mean duration of diabetes of 7.989 years, and a mean weight of 87.178 kg, as indicated in Table 1. According to Table 2, there were 72% male patients and 28% female patients. According to Table 3, betablockers were used by 43.9% of diabetic patients who had hypoglycemia. Tables 4, 5, 6, and 7 stratify beta-blocker usage by age, gender, diabetes duration, and weight.

Demographics	Mean	±SD	
Age (years)	51.964	±6.38	
Duration of diabetes (years)	7.989±2	7.989±2.74	
Weight (Kg)	87.178:	±7.49	
Table 2: Frequency and percentage of patier	ts in accordance to sex (n=196)		
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Table 3: Frequency and percentage of participants according to use of beta-blockers (n=196)			
Use of beta-blockers	Frequency	%age	
Yes	86	43.9%	
No	110	56.1%	
Total	196	100%	

Age (years)	Use of b	Use of beta-blockers	
	Yes	No	<i>p</i> -value
30-50	39(45.9%)	46(54.1%)	
51-70	47(42.3%)	64(57.7%)	0.621
Total	86(43.9%)	110(56.1%)	

Conden	Use of be	Use of beta-blockers	
Gender	Yes	No	<i>p</i> -value
Male	60(42.6%)	81(57.4%)	
Female	26(47.3%)	29(52.7%)	0.550
Total	86(43.9%)	110(56.1%)	

Duration of diskates (users)	Use of Beta-Blockers		
Duration of diabetes (years)	Yes	Νο	<i>p</i> -value
1-10	39(26.2%)	110(73.8%)	0.000
>10	47(100%)	0(0%)	
Total	86(43.9%)	110(56.1%)	

Table 7: Stratification of use of beta-blockers with respect to weight			
) A ( - : - h + () ( - )	Use of be	Use of beta-blockers	
Weight (Kg)	Yes	Νο	<i>p</i> -value
≤90	55(42%)	76(58%)	
>90	31(47.7%)	34(52.3%)	0.448
Total	86(43.9%)	110(56.1%)	

### Discussion

There is little data reporting the odds of hypoglycemia in people taking insulin and Beta Blockers (BB). BB usage was not mentioned in a large current hospitalized investigation that detected risk factors for hypoglycemia.<sup>8</sup> Cardona and associates failed to find a difference in risk based on BB use.<sup>9</sup> In a recent study, nonselective BB did not result in higher rehospitalization for older nursing home patients with acute myocardial infarction relative to SBB.<sup>10</sup> Similar to the previous study, 43.9% of diabetes individuals who had hypoglycemia used beta blockers. According to a study by Dungan K. et al. 50% of diabetes of the study of the study by Dungan K. et al. 50% of diabetes often.<sup>6</sup>

According to reports, using insulin for a longer period and developing more complicated insulin regimens are linked to a high odd of hypoglycemia and unawareness of hypoglycemia.<sup>11</sup> Beta-blocker use might not be significant in patients who have been on insulin for a long time, some of whom may already have lost.

Their early counter-regulatory responses or are blatantly uninformed of their hypoglycemia.<sup>12</sup> Also, whereas Beta Blocker treatment could lessen the loss of counter regulatory responses brought on by preceding hypoglycemia, the everlasting consequences are not certain, therefore, only long term BB treatment was included in this investigation.<sup>13</sup> In order to better understand the consequences of prolonged BB treatment and how it interacts with usage of insulin, more research is required.

In this trial, the risk of hypoglycemia was somewhat higher with SBB than with carvedilol. This discovery has not been explained, however, it may be connected to variations in beta and alpha receptor activation and resulting autonomic reactions to hypoglycemia.<sup>14</sup> It is the justification for rejecting those BB, which are rare and have more distinct features. Beta-blockers are therefore typically advised for people who also need concurrent insulin. The recent findings, however, imply that this advice might not be applicable to entire nonselective beta blockers. The  $\alpha$ -1 receptor blocking effects of Carvedilol and its action, it is capable of reducing the side effects of propranolol. While earlier research has shown that the beta-receptors mediated adrenergic effects to practically created hypoglycemia, reaction to practically acquired hypoglycemia shall not accurately represent counter-regulatory effects in long term treatment or in critical sickness.<sup>15</sup> Repeated stresses, for instance, may activate opioid receptors, in part through the adrenal glands -1 receptors, which may impede the counter-regulation of hypoglycemia.<sup>16</sup>

In the current trial, participants with no cardiac failure but not those having cardiac failure had an increased risk of hypoglycemia when using carvedilol plus SBB. A putative explanation is a decrease in hypoglycemia-related autonomic dysfunction brought on by BB usage.<sup>17</sup> The classes of beta blocker usage by research members were not identified in a subsequent inspection of the ACCORD research, which indicated higher deaths in people with coronary vascular disease and diabetes medicated with BB.<sup>18</sup> People having concomitant diabetes and HF, more studies need to be required to determine the link between beta-blocking and hypoglycemia.

Although it wasn't seen in earlier research, using BB in the ambulatory setting is linked to deaths and cardiovascular incidents in people with diabetes, probably because other risk factors are better controlled.<sup>16,19</sup> Although beta-blocker class and insulin usage were not specifically examined in these investigations, BBs did appear to prevent the rise in all-cause and coronary vascular deaths by having stringent blood glucose control in ACCORD research. The current results are in accordance with the latest empirical trial of OPD patients, which discovered nonselective BB was related to a potential decrease in deaths in individuals who experienced attacks of hypoglycemia.<sup>20</sup> No difference was found in deaths among the individuals treated with carvedilol and metoprolol in a different research of elderly homebased nursing patients who went home post cardiac infarction.  $^{\mbox{\tiny 10}}$ 

#### Conclusion

According to this study, diabetic people who use beta blockers have a high odds who developed hypoglycemia. Those individuals on Beta blockers increased hypoglycemic incidence within basal insulin non-recipients. SBB and carvedilol were linked to a higher hypoglycemic incidence in people without cardiac failure.

#### REFERENCES

- Zheng Y, Ley SH, Hu FB. Global etiology and epidemiology of type 2 diabetes mellitus and its complications. Nature reviews endocrinology. 2018; 14: 88-98. doi: 10.1038/nrendo.2017.151
- Malek R, Hannat S, Nechadi A, Mekideche FZ, Kaabeche M. Diabetes and Ramadan: a multicenter study in Algerian population. Diabetes research and clinical practice. 2019; 150: 322-30. doi: 10.1016/j.diabres.2019.02.008
- Picke AK, Campbell G, Napoli N, Hofbauer LC, Rauner M. Update on the impact of type 2 diabetes mellitus on bone metabolism and material properties. Endocrine connections. 2019; 8: R55-R70. doi: 10.1530/EC-18-0456
- Balijepalli C, Druyts E, Siliman G, Joffres M, Thorlund K, Mills EJ. Hypoglycemia: A review of definitions used in clinical trials evaluating antihyperglycemic drugs for diabetes. Clinical epidemiology 2017; 9: 291-6. doi: 10.2147/CLEP.S129268
- Tsujimoto T, Sugiyama T, Shapiro MF, Noda M, Kajio H. Risk of cardiovascular events in patients with diabetes mellitus on β-blockers. Hypertension. 2017; 70: 103–10. 10.1161/HYPERTENSIONAHA.117.09259
- Dungan K, Merrill J, Long C, Binkley P. Effect of beta blocker use and type on hypoglycemia risk among hospitalized insulin requiring patients. Cardiovascular diabetology. 2019; 18: 163. doi: 10.1186/s12933-019-0967-1
- Tsujimoto T, Kajio H, Shapiro MF, Sugiyama T. Risk of allcause mortality in diabetic patients taking beta-blockers. In Mayo Clinic Proceedings. 2018; 93: 409–18. doi: 10.1016/j.mayocp.2017.11.019
- Mathioudakis NN, Everett E, Routh S, Pronovost PJ, Yeh HC, Golden SH, et al. Development and validation of a prediction model for insulin-associated hypoglycemia in non-critically ill hospitalized adults. BMJ Open Diabetes Research and Care. 2018; 6: e000499. doi: 10.1136/bmjdrc-2017-000499

- Cardona S, Gomez PC, Vellanki P, Anzola I, Ramos C, Urrutia MA, et al. Clinical characteristics and outcomes of symptomatic and asymptomatic hypoglycemia in hospitalized patients with diabetes. BMJ Open Diabetes Research and Care. 2018; 6: e000607. doi: 10.1136/bmjdrc-2018-000607
- Zullo AR, Hersey M, Lee Y, Sharmin S, Bosco E, Daiello LA, et al. Outcomes of diabetes-friendly vs diabetes-unfriendly beta-blockers in older nursing home residents with diabetes after acute myocardial infarction. Diabetes, Obesity and Metabolism. 2018; 20: 2724–32. doi: 10.1111/dom.13451
- Giugliano D, Maiorino MI, Bellastella G, Chiodini P, Ceriello A, Esposito K. Efficacy of insulin analogs in achieving the hemoglobin A1c target of < 7% in type 2 diabetes: metaanalysis of randomized controlled trials. Diabetes Care. 2011; 34: 510–7. doi: 10.2337/dc10-1710
- 12. Segel SA, Paramore DS, Cryer PE. Hypoglycemia-associated autonomic failure in advanced type 2 diabetes. Diabetes. 2002; 51: 724–33. doi: 10.2337/diabetes.51.3.724
- Ramanathan R, Cryer PE. Adrenergic mediation of hypoglycemia-associated autonomic failure. Diabetes. 2011; 60: 602–6. doi: 10.2337/db10-1374.
- Mann SJ. Redefining beta-blocker use in hypertension: selecting the right beta-blocker and the right patient. Journal of the American Society of Hypertension. 2017; 11: 54–65. doi: 10.1016/j.jash.2016.11.007
- 15. Bolli G, de Feo P, Compagnucci P, Cartechini MG, Angeletti G, Santeusanio F, et al. Important role of adrenergic

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mechanisms in acute glucose counterregulation following insulin-induced hypoglycemia in type I diabetes. Evidence for an effect mediated by beta-adrenoreceptors. Diabetes. 1982; 31: 641–7. doi: 10.2337/diab.31.7.641

- Carey M, Gospin R, Goyal A, Tomuta N, Sandu O, Mbanya A, et al. Opioid receptor activation impairs hypoglycemic counterregulation in humans. Diabetes. 2017; 66: 2764–73. doi: 10.2337/db16-1478
- Farhat R, Su G, Sejling AS, Knight N, Fisher SJ, Chan O. Carvedilol prevents counterregulatory failure and impaired hypoglycaemia awareness in non-diabetic recurrently hypoglycaemic rats. Diabetologia. 2019; 62: 676–86. doi: 10.1007/s00125-018-4802-0
- Tsujimoto T, Sugiyama T, Shapiro MF, Noda M, Kajio H. Risk of cardiovascular events in patients with diabetes mellitus on β-blockers. Hypertension. 2017; 70: 103–10. doi: 10.1161/HYPERTENSIONAHA.117.09259
- Tsujimoto T, Kajio H, Shapiro MF, Sugiyama T. Risk of allcause mortality in diabetic patients taking beta-blockers. InMayo Clinic Proceedings. 2018; 93: 409–18. doi: 10.1016/j.mayocp.2017.11.019.
- Zaccardi F, Nystrup Husemoen LL, Thorsted BL, Webb DR, Paul SK, Davies MJ, et al. Selectivity of beta-blockers, cardiovascular and all-cause mortality in people with hypoglycaemia: an observational study. Nutrition, Metabolism and Cardiovascular Diseases. 2019; 29: 481–8. doi: 10.1016/j.numecd.2019.01.006