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Hypoglycemia in Geriatric Patients with Diabetes: A Review

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A B S T R A C T

The prevalence of diabetes tends to be high, 42% of geriatric patients admitted have a diabetes diagnosis, and 33% of these patients experience hypoglycemia. Hospitalization is necessary for diabetic elderly individuals because their blood glucose levels make them more vulnerable to other complications. The research aims to examine the frequency of hypoglycemia in older individuals, including those with diabetes, which may be caused by the administration of antidiabetic that lower blood sugar levels. This study is a narrative review of publication that discussed hypoglycemic incidence among geriatrics in PubMed and Google Scholars databases. The type of study included the original article, not the abstract or thesis document from 2016–2021. Sulfonylurea and insulin groups are the most frequently prescribed, and they cause hypoglycemia in diabetic older people, with the rate of hypoglycemic incidence of more than 50%. Other groups of antidiabetes that geriatrics received were alpha-glucosidase inhibitors, dipeptyl peptidase-4, glucagon-like peptide-1, and biguanide, which has been prescribed as monotherapy and combined therapy. The prevalence of hypoglycemic in geriatrics is still present, along with their diabetes medication. For geriatric individuals with DM, routine blood glucose monitoring is advised to prevent diabetic complications.

Keywords: geriatric; hypoglycemia; insulin; adverse, diabetes mellitus

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1. Introduction

One of the chronic illnesses that poses a serious threat to the global health system is diabetes mellitus (1). The DM disease itself or complications in other related tissues can cause morbidity and mortality. These complications can also increase the disease's incidence, severity, and duration. As diabetes care and glycemic control improve in the general population, the prevalence of hypoglycemia as a consequence of diabetes treatment, is increasing (2).

Severe episodes of hypoglycemia greatly raise the chances of short-term and long-term death in those with diabetes. Additionally, the natural responses of body to hypoglycemia might increase the possibility of cardiovascular events such as coronary thrombosis and arrhythmia; moreover the hypoglycemia in elderly are the risk factors for dementia (3) (4). In patients with diabetes mellitus, hypoglycemia has been identified as a predictor of mortality, end-stage renal disease, cardiac injury, unprecipitated arrhythmia, and incident fall episodes. Disturbed consciousness may result from hypoglycemia, which accumulate and increase the risk of functional impairment. The situation of exercise intolerance with physical limitation among diabetic patients is also established by the cardiac influences of recurrent hypoglycemia. Additionally, the presence of medical morbidities such as chronic kidney disease, polypharmacy, and poor medication adherence frequently accompanies hypoglycemia, all of which may increase the risk of frailty to a particular degree (5).

Because of aging, diabetes tends to be more common among the senior population (6). Of the elderly admitted, 42% had been diagnosed with diabetes, and a third had hypoglycemia (7).
Due to lower blood glucose control and other difficulties affecting morbidity and mortality, elderly persons with diabetes are more likely to experience complications that require hospital treatment (8). Elderly people who use antidiabetics are susceptible to hypoglycemia 1-3 times over the course of the three months that they use the medication (9). In the elderly, hypoglycemia is characterized by a decrease in blood sugar to less than 70 mg/dL (3.9 mmol/L) (10).

Counterregulation is impacted by the process of aging. Aging diminishes the ability of healthy older individuals without diabetes to regulate glucose levels in response to hypoglycemia by impairing the counter-regulatory responses of glucagon, growth hormone, and adrenaline. This delays the autonomic process that would normally trigger symptoms. Low glucose levels hinder the proper secretion of the pancreas, kidneys, and liver, hence impairing their functioning. This contributes to dysfunction of the autonomic nervous system in all individuals with diabetes (11).

Imbalance in the control of glucose levels in the kidneys, liver, and endocrine system has detrimental effects on the brain. The brain has a decrease in quick reaction time, ability to perform many tasks, and sustained focus when it is deprived of glucose, its main source of energy. In patients with normal cognitive function, it may take up to an hour for hypoglycemia to be resolved before the brain regains full functionality (2) (12).

The incidence of hypoglycemia in geriatric patients may be caused by a variety of factors, including polypharmacy, pharmacokinetic and pharmacodynamic changes, hormonal regulation disorders, food and water intake disturbances, decreased intestinal absorption, and cognitive disorders, as well as other organ disorders that cause disruption of the ability to metabolize antihyperglycemia. A number of factors, including polypharmacy, alterations in pharmacokinetics and pharmacodynamics, poor hormonal regulation, reduced intestinal absorption, decreasing food and water consumption, and cognitive impairment, contribute to the increased prevalence of hypoglycemia in the elderly. Heart failure, renal failure, and liver problems that impair the body's capacity to efficiently metabolize antihyperglycemia are among the other conditions that might affect older adults with illness (1); (13); (9). When compared to heart issues, the presence of renal failure also raises the risk of hypoglycemia during treatment (14). The signs and symptoms of hypoglycemia are influenced by beta blockers, angiotensin Converting Enzyme inhibitors (ACE-i), corticosteroids, and other drug interactions that older people may experience (10). The purpose of this review is to address the prevalence of hypoglycemia in older adults, particularly those with diabetes, that can be brought on by the use of antidiabetic medications or other substances that drop blood sugar.

2. Material and Methods

This study employs a narrative study design to identify studies relating to hypoglycemia in geriatric patients with diabetes. We searched and identified various research articles via PubMed database and Google Scholar with the keywords "Diabetes Mellitus," "Geriatric", and "Hypoglicemia" as relevant references. The original article of research that found the incidence of hypoglycemia in diabetes geriatric patients was included to be discussed. We exclude the review article, thesis document, abstract, and article in proceeding for the selected process. A number of relevant articles of literature were gathered, selected, summarized, and discussed during the process. We obtained 10 relevant articles, which represented the primary source for this review article. We use the journal article related to hypoglycemia in geriatric patients that was published within 10 years.

3. Result and Discussion

Several studies discussing the incidence of hypoglycemia in geriatrics are summarized in the following table:

Table 1. Description of hypoglycemia experienced by geriatrics in several studies

Study	DM type	Glycemic check (average)	Average age (years)	Therapy	Drugs cause hypoglycemia
(15)	Type 2	Glucose level 164.7 mg/dL HbA1C 8.2%	74.1	DPP-4 inhibitor 42.4% Metformin 15.9% Alfa-GI 17.7% TZD 7.7% GLP-1 analog 3.5% SU 27.1% Glinide 3.5% Insulin 55.9%	Insulin (OR 2.17, 95% CI: 1.16–4.08)
(9)	Type 2	HbA1C 7.1%	73.3	Combination insulin + SU + others 4.6% Combination insulin + others Oral Hypoglycemia Drugs 5.1% SU or noninsulin 50.1% Biguanid 29.7% Alfa-GI 0.9% DPP-4 inhibitor 6.2% others 0.2%	SU or noninsulin
(14)	Type 2	Not mentioned	Not mentioned	Metformin 52.4% SU 26.4% Insulin 7.35 DPP-4 inhibitor 4.6% GLP-1 RA 3.4%	insulin and sulfonylurea (OR 1⁄4 4.74; 95% CI 3.67–6.06)
(16)	Type 1 and 2	Glucose level 37 mg/dL	60.3	Insulin Octreotide	Insulin (OR, 5.4; 95% CI, 2.8 –10)
(17)	Type 1 and 2	HbA1C 6.734%	70	SU 11% Metformin 16% Metformin+SU 21% Insulin 31% Insulin +SU 7% Insulin + Metformin 13% SU+Metformin+ Pioglitazon 1%	Not mentioned
(18)	Type 1 and 2	HbA1C 7% Glucose level 37.9%	69.5	SU 41.3% Insulin 29% SU or Insulin 65.3% SU+insulin 5% others 24.7%	SU+insulin: severe hypoglycemia; Glimepirid: frequent hypoglycemia
(19)	Type 1 and 2	HbA1C <7% : 9.8% (n=8)	75	Glibenclamid 36.5% Glimepirid 15.3% Glicazid 11% Metformin 9.4% Insulin 25% SU+metformin 7.05% Insulin+metformin 3.55%	Not mentioned
(20)	Type 1 and 2	HbA1C (2012) 7.2%	75.4%	Metformin 80% DPP-4 inhibitor 10.1% Gliburide 2.9% Glicazid 11.7% Insulin 7%	Not mentioned
(21)	Type 1 and 2	Not mentioned	65-75: 57.8%	Receive no drugs 21.9% Metformin 63.1% SU 47.6% Thiazolidinedione 4.8% Alfa-GI 9% Meglitinide 2%	SU+insulin: high hypoglycemia risk
(22)	Not mentioned	HbA1C in SU: 7.8% BG: 7.0% DPP-4 inhibitor: 7.4%	>65: 41.56%	SU 11.44% BG 35.67% DPP-4 inhibitor 52.89%	Not mentioned

Information:
Alfa-GI; alpha glucosidase inhibitors; DPP-4: dipeptidyl peptidase-4; GLP-1: glucagon-like peptide-1; HbA1C: glycosylated hemoglobin; SU: sulfonylurea; TZD: thiazolidinedione; Oral Hypoglicemia drugs: Oral Hyperglicemia drugs; BG: Biguanide

The percentage of elderly individuals receiving treatment for hypoglycemia varies by country; in Asia, it ranges between 3.7% and 9.3 per 1000 people; in Europe and the US, it is between 3.52-6.7 per 1000 persons (1). A study by Kim et al. (2016), which found that older participants made up over 50% of DM patients who had hypoglycemia and required hospitalization. Most elderly individuals with hypoglycemia are older than 70 years of age (table 1). According to research by Fu et al.(14) the rate of hospitalization for hypoglycemia was found to be correlated with age over 65. Age is one of the factors related to the incidence of geriatric care due to hypoglycemia.

Compared to blood glucose level measurements, HbA1C provides information on blood glucose levels over a longer period. High HbA1C readings (table 1) are linked to hospitalizations for hypoglycemia in the elderly (1). Patients with frequent and sustained hypoglycemia have a HbA1C of less than 7% (15). Laboratory evidence suggests a low transient glucose level in cases of abrupt or emergency hypoglycemia. When elderly patients with hypoglycemia are treated medically, their blood sugar levels are less than 50 mg/dL (16); (18). It is difficult to predict hypoglycemia in elderly patients due to their high variability in glucose levels, and variations in HbA1C levels among elderly subjects can signify various conditions. For this reason, it is advised that all elderly individuals have their average daily range (ADR) measured daily (23); (15). When determining a geriatrician's risk of hypoglycemia, this method can be helpful. In elderly patients, blood glucose management is crucial to preventing hypoglycemia-related death and morbidity (14). Behavioral habits, such irregular meals, and treatment strategies for diabetes also impact the possibility of developing hypoglycemia. Individuals who engage in strict glucose control, use insulin or sulfonylurea medications have a notably higher risk of experiencing hypoglycemia compared to those who follow a less restrictive approach to managing blood sugar levels or use non-insulin or non-sulfonylurea medications for diabetes (28).

Table 1 lists the medication classes that elderly patients with hypoglycemia are prescribed: biguanides, thiazolidinedione, alpha-GI, sulfonylureas, insulin, octreotide, GLP-1 receptor agonists, DPP-4 inhibitors, and their combinations. The majority of these medications are included in recommendations for the management of diabetes in the elderly (24). The drug metformin, a member of the biguanide class of antidiabetics, is most frequently prescribed to elderly patients with diabetes. Metformin can reduce mortality associated with cardiovascular disease, is highly successful in decreasing blood sugar levels, and does not result in weight gain. Compared to sulfonylureas, metformin has a lower incidence of hypoglycemia. If metformin alone is unable to meet glycemic control targets, it can be supplemented with other medications such as insulin or oral antihyperglycemics (24).

Even in quite substantial doses, sulfonylureas are still utilized to treat diabetes in the elderly (15); (18); (21). The sulfonylurea class of medications, which includes gliclazide, glyburide, and glimepiride, carries the risk of hypoglycemia and weight gain. In older patients, glyburide should be avoided as it can worsen hypoglycemia more than glimepiride and glipizide (24); (18). The study conducted by Kim Fu (14), revealed a correlation between the risk of hypoglycemia in elderly participants and the use of sulfonylureas, as indicated by the odds ratio value. Hypoglycemia risk may also rise when sulfonylureas and insulin are used together (9,14,18,21).

Pioglitazone and rosiglitazone are two thiazolidinediones that are frequently used in the treatment of diabetes mellitus; however, there is no conclusive evidence linking these two medications to hypoglycemia in older adults. Thiazolidinedione, however, should not be used in older adults due to the possibility of fluid retention, which exacerbates the condition of older adults with a history of heart failure. As a result, DM patients with grade III and IV heart failure should not take this medication. Osteoporosis and bone fractures are potential side effects of thiazolidinedione use that can pose a risk or cause morbidity in elderly persons. (24).

In older adults, alpha-GI, also known as alpha glucosidase inhibitor, is moderately effective in decreasing blood sugar levels. The reason for the high rate of non-compliance with this drug's administration is the existence of gastrointestinal diseases, including diarrhea and flatulence (19). Due to the milder consequences of hypoglycemia, the usage of Alfa-GI in senior patients varied from 0.9% to 17% in numerous studies (9); (15); (21). Dipeptyl peptidase-4 (DPP-4) inhibitors are generally well tolerated by older adults and seldom result in hypoglycemia, similar to Alfa-GI. DPP-4 use is not advised for elderly people with a history of cardiovascular problems and necessitates consideration of the existence or lack of pancreatitis symptoms(24).

GLP-1 RA (glucagon-like peptide 1 receptor agonist) is administered to elderly patients at a dose of 2%–3.5% (21); (14); (15). The GLP-1 RA drug category consists of semaglutide and liraglutide. GLP-1 is a receptor agonist that prevents hypoglycemia in older adults by increasing insulin release and decreasing glucagon secretion. GLP-1 RA is a medication that suppresses hunger and delays

stomach emptying; its most common side effect is nausea (24).

Percentage of elderly people (2%) utilize the meglitinide group to treat their diabetes (15). Meglitinides function by attaching to certain sulfonylurea receptors on pancreatic beta cells, hence boosting insulin production. The Cochrane literature indicates that meglitinide has a similar therapeutic efficacy to metformin and that substantial or severe hypoglycemia is not frequently experienced. If the patient is not a good candidate for metformin because of the metformin-induced diarrhea side effect, meglitinide is administered (26).

In Ishikawa's research (15) on geriatricians, the use of insulin was 55.9%, which is a relatively high rate. When glycemic control is not achievable for patients with type 2 diabetes mellitus, insulin is used. To evaluate the efficacy and safety of insulin, blood glucose levels must be checked regularly (24). Insulin is also used to lessen the negative effects of oral antidiabetics on the liver and kidneys, particularly in older adults whose organ function has declined (16). The risk of hypoglycemia in older adults can be raised by insulin use either alone or in conjunction with other antidiabetics, particularly sulfonylureas (21); (14). The benefits and hazards of sophisticated therapy regimens for the elderly must be considered. Thus, the combination of insulin and sulfonylurea is not recommended for use in geriatrics (24).

Octreotide (16) is another medication prescribed to elderly adults that results in hypoglycemia but is not part of the diabetes treatment plan. Octreotide inhibits insulin secretion as part of its endocrine impact. To prevent the decline in endogenous insulin, which serves as a buffer against hypoglycemia, exogenous insulin is administered to reduce the production of growth hormone, glucagon, and endogenous insulin. The inhibitory action of glucagon secretion by ocreotide to lower levels of hormone release upsets the feedback loop. Consequently, concurrent insulin and octreotide treatment increases the risk of hypoglycemia (16).

4. Conclusion

In older adults, hypoglycemia exacerbates previously mild physical and cognitive impairments. Malnutrition increases susceptibility and contributes to hypoglycemia (27). Both major and light hypoglycemia can happen to older adults. Major hypoglycemia is potentially fatal and calls for specialized care, such as the use of medications to raise blood sugar levels or address other side effects. Minor hypoglycemia can be treated in the interim by giving foods that raise blood sugar levels rapidly (16). The significance of a particular treatment in the elderly population to lessen the effects of hypoglycemia; this treatment ought to be administered utilizing an alternative method to that of treating hypoglycemia in adults or younger individuals (14). In elderly diabetic patients, routine blood glucose monitoring has been suggested as a means of preventing hyperglycemia complications. Complications from dysglycemia can be avoided with early diagnosis and treatment (1).

5. CONFLICT OF INTEREST

There is no conflict of interest before and after this study.

6. References

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