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Original Research Article

Hypothermia with Neurogenic Disorders in Hypoglycemic Coma (Pavlov-Sokolova Syndrome): Relevance, Diagnosis, and Clinical Characteristics

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Name of Author:
Bogdan V. Pavlov[1], Alyona I. Sokolova[2], Ibrokhimdzhon D. Kuziev[1], Bogdan A. Sklyarov[3], Irina A. Kulikova[1], Vladimir A. Molchanov[1], Sabina S. kyzy. Akberova[1] and Artem S. Kazaryan[4]

Affiliation: *[1]Department of Propaedeutics of Internal Diseases and Faculty Therapy of the Institute of Medicine and Health Care named after G. R. Derzhavin, Tambov, Russian Federation*
[2]Department of Pathology, Federal State Budgetary Educational Institution of Higher Education "Tambov State University named after G.R. Derzhavin", Tambov, Russian Federation
[3]Federal State Autonomous Educational Institution of Higher Education «N.I. Pirogov Russian National Research Medical University» of the Ministry of Health of the Russian Federation, Moscow, Russian Federation
[4]Department of Hospital Therapy with a Course in Psychiatry of the Institute of Medicine and Health Care named after G. R. Derzhavin, Tambov, Russian Federation.
Corresponding Author:
Bogdan V. Pavlov

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Abstract: ***Introduction***. Hypoglycemia accompanied by hypothermia and neurogenic disorders (Pavlov-Sokolova syndrome) is a rare but severe complication of diabetes. Despite its clinical relevance, it remains poorly recognized due to the lack of standardized diagnostic and therapeutic approaches. This study aimed to analyze the clinical and pathogenetic features of Pavlov-Sokolova syndrome and identify diagnostic criteria to improve early detection and outcomes. ***Materials and methods.*** A retrospective analysis included 3,473 patients with type 1 and type 2 diabetes aged 21–35 years. Inclusion criteria were documented hypoglycemia (<2.2 mmol/L), hypothermia (<35°C), and neurological impairment. Patients were classified into neurogenic, thermoregulatory, mixed, and atypical forms based on clinical presentation. Student's t-test and χ^2 test have been used for statistical analysis. ***Results***. Pavlov-Sokolova syndrome was diagnosed in 427 patients (12.3%), predominantly in type 1 diabetes (85.9%). The mixed form prevailed (80.1%) among the other forms. The atypical one showed the highest mortality (33.3%). EEG revealed diffuse slowing in 89% of cases. Neuroimaging detected reversible cerebral edema in 4.7% and cortical atrophy in 1.6%. Thyroid hormone was most frequent in the mixed form. The "warm blanket" symptom proved to be a novel diagnostic marker, with high reliability of the Pavlov scale (Cronbach's $\alpha = 0.85$). A significant correlation was observed between the "crazy head" symptom and hypoglycemia severity. ***Conclusion***. Pavlov-Sokolova syndrome is a heterogeneous and life-threatening hypoglycemic complication. Early diagnosis by some neurogenic and thermoregulatory markers particularly the symptom of "warm blanket" makes possible timely, personalized treatment and assists in the elaboration of standardized diagnostic and therapeutic programs.

Keywords: hypoglycemia, hypothermia, diabetes mellitus, neurogenic disorders, hormonal imbalance, EEG, TSH, T3, T4, classification of coma, differential diagnosis.

INTRODUCTION

Hypoglycemic syndrome with neurogenic impairment, known as Pavlov-Sokolova syndrome, is a complex and poorly understood clinical entity that

complicates severe hypoglycemia and poses a significant clinical challenge, particularly for patients with diabetes mellitus (DM).[1] This syndrome is characterized by a combination of profound hypothermia (a core body temperature below 35°C) and signs of central nervous system (CNS) dysfunctions such as coma, seizures, and neurological deficits—within the context of critically low blood glucose levels.[2] Unlike conventional hypoglycemic coma, Pavlov-Sokolova syndrome presents with distinct clinical features that necessitate a distinct approach to diagnosis and management.[3]

The pathophysiological mechanisms underlying the development of this syndrome are not yet fully elucidated. It is hypothesized that both the direct neurotoxic effects of glucose deprivation on the central nervous system [4] and dysregulation of the autonomic nervous system, which plays a critical role in thermoregulation,[5] contribute to the onset of hypothermia. Clinical evidence also suggests a potential role for neuroendocrine factors, including hypothalamic dysfunction, in the pathogenesis of this condition.[6] Despite its relative rarity, Pavlov-Sokolova syndrome represents a serious clinical problem due to the associated risks of irreversible brain damage and high mortality.[3;7] Consequently, early diagnosis and prompt, adequate treatment are critical for improving patient outcomes and reducing the risk of long-term neurological complications.[8] The current lack of unified diagnostic and therapeutic guidelines, compounded by limited awareness of the syndrome among clinicians, often hinders the provision of timely and effective medical care.[3]

The body of literature specifically devoted to Pavlov-Sokolova syndrome remains limited, underscoring the need for further investigation. Some studies highlight the importance of rigorous body temperature monitoring in comatose patients with hypoglycemia.[5] Others focus on developing diagnostic and treatment algorithms aimed at the rapid normalization of glucose levels and the active correction of hypothermia.[2] In recent years, there has been growing interest in the application of novel technologies, such as continuous glucose monitoring [9] and advanced thermometry, for the early detection and prevention of this syndrome.[1] However, most available studies are descriptive in nature, and larger, controlled trials are required to establish the most effective strategies for treatment and prevention.

Furthermore, in certain forms of diabetes such as MODY (Maturity-Onset Diabetes of the Young), hypoglycemic episodes may present in a milder, often asymptomatic fashion, with HbA1c levels frequently remaining within the near-normal range. This clinical presentation may also be associated with Pavlov-Sokolova syndrome, warranting further investigation.[10] Therefore, there is a clear and pressing need to establish standardized approaches for the diagnosis and management of Pavlov-Sokolova syndrome, considering individual patient characteristics and disease severity.[5]

The development of personalized patient management strategies, grounded in a comprehensive assessment of neurological status, glycemic control,[11] and core body temperature (6), is of paramount importance. Equal attention must be paid to the prevention of hypoglycemia, especially in patients with labile diabetes,[12] and to educating both patients and their families on recognizing the symptoms of hypoglycemia and administering appropriate first aid.[2]

The aim of this study was to investigate the borderline state of transition from severe hypoglycemia to deep coma in patients with diabetes mellitus and Pavlov-Sokolova syndrome.

MATERIALS AND METHODS

The study included 3,473 patients diagnosed with type 1 (n = 2,967) and type 2 (n = 506) diabetes mellitus, aged 21 to 35 years. The inclusion criteria were a confirmed diagnosis of diabetes mellitus, a documented history of hypoglycemic coma with a blood glucose level below 2.2 mmol/L, the presence of hypothermia (body temperature below 35°C), and concurrent neurological disorders, including impaired consciousness, seizures, or focal neurological symptoms. The exclusion criteria were concurrent sepsis, traumatic brain injury, or acute cerebrovascular accident.

This was a retrospective study based on an analysis of electronic health records. The diagnosis of hypoglycemia was confirmed by documented laboratory data showing a decrease in blood glucose levels to below 2.2 mmol/L. Hypothermia was assessed by recording the minimum body temperature documented during the hypoglycemic episode. The neurological examination involved assessing the level of consciousness using the Glasgow Coma Scale (GCS), identifying focal neurological deficits, and recording the occurrence of seizures.

The form of Pavlov-Sokolova syndrome was classified according to the temporal sequence of hypothermia and neurological disorder onset, as well as the presence of any atypical clinical manifestations.

Statistical analysis was performed using the SPSS software package, version 13.0. Descriptive statistics were used to characterize the sample. For the analysis of differences between groups, the Student's t-test and the chi-square (χ^2) test were applied.

RESULTS

Of the 3,473 patients with diabetes mellitus examined,

427 (12.3%) were diagnosed with hypothermic syndrome accompanied by neurogenic disorders, consistent with Pavlov-Sokolova syndrome.

The distribution of patients by clinical syndrome type is presented in Table 1. As can be seen from the data presented in Table 1, the mixed form, in which hypothermia and neurological impairment are simultaneously observed, is the most common occurring in 80.1% of cases. This underscores the close relationship between metabolic and neurogenic mechanisms in the pathogenesis of the syndrome. The thermoregulatory form is detected less frequently, in 16.4% of cases, which is likely due to an isolated impairment of thermoregulatory mechanisms in the absence of pronounced neurological symptoms. The neurogenic and atypical forms are significantly less common, occurring in 3.5% and 0.7% of cases, respectively. Despite their low frequency, they are clinically significant due to the increased risk of complications.

Table 1

Form of the Syndrome	Number of Patients	Percent (%)
Mixed form	342	80.1%
Thermoregulatory form	70	16.4%
Neurogenic form	15	3.5%
Atypical form	3	0.7%
Total	427	100%

Distribution of patients by clinical forms of pavlov-sokolova syndrome

Table 2 presents the prevalence of the syndrome by diabetes type. As can be seen from the data presented in Table 2, most patients in the study 85.9%—were with type 1 diabetes. This confirms their increased vulnerability to hypoglycemia due to their dependence on exogenous insulin. In patients with type 2 diabetes, the syndrome was significantly less common—14.1% of cases—which is likely due to more stable glycemic control in this group.

Table 2.

Type of Diabetes	Number of Patients with the Syndrome	Percentage of Total Patients with the Syndrome
Type 1 diabetes	367	85.9%
Type 2 diabetes	60	14.1%
Total	427	100%

Prevalence of the syndrome in diabetes mellitus types 1 and 2

The clinical characteristics of patients with Pavlov-Sokolova syndrome are presented in Table 3. The average age of patients, 27.8 years, corresponds to the active working age group and reflects the long duration of the disease in individuals with type 1 diabetes. Severe hypoglycemia—an average of 1.8 mmol/L—combined with hypothermia (mean body temperature 33.2°C) indicate a severe energy deficit, which has a critical impact on brain function. All patients experienced severe depression of consciousness, assessed on the Glasgow Coma Scale (GCS) below 8 points, which allows this symptom to be considered a key diagnostic criterion for the syndrome. The presence of seizures in 15.9% of patients and focal neurological symptoms in 2.8% of patients indicates a high degree of damage to the central nervous system and emphasizes the severity of the clinical condition during the acute period.

Table 3.

Characteristic	Value
Average age, years	27.8 ± 3.5
Gender (male/female)	235 / 192
Average glucose level, mmol/L	1.8 ± 0.4
Average minimum temperature, °C	33.2 ± 1.2
Impaired consciousness (GCS < 8)	427 (100%)
Convulsions	68 (15.9%)
Focal neurological symptoms	12 (2.8%)

Clinical characteristics of patients with pavlov-sokolova syndrome

Table 4 presents the frequency of Pavlov-Sokolova syndrome by diabetes type. The results demonstrate that the mixed form of Pavlov-Sokolova syndrome is most common in patients with type 1 diabetes, occurring in 80.3% of cases. This is likely due to the lability of glycemic control and frequent episodes of hypoglycemia characteristic of this group, which contribute to both impaired thermoregulation and damage to the central nervous system. The neurogenic form was significantly less common, occurring in 3.8% of patients, but is characterized by a high risk of irreversible neurological sequelae, making it particularly clinically significant.

Table 4.

Form of the Syndrome	Type 1 Diabetes (n=367)		Type 2 Diabetes (n=60)	
	Number	Percent	Number	Percent
Mixed form	295	80.3%	47	78.3%
Thermoregulatory form	55	15.0%	15	25.0%
Neurogenic form	14	3.8%	1	1.7%
Atypical form	3	0.8%	0	0%

Prevalence of clinical forms of pavlov-sokolova syndrome by diabetes type

Among patients with type 2 diabetes, the thermoregulatory form was most frequently observed, accounting for 25% of the total number in this subgroup. Moderate hypoglycemia, combined with the presence of comorbidities such as chronic heart failure, can contribute to the development of severe hypothermia even with a relatively stable neurological picture. An atypical form of the syndrome was not recorded in this group of patients, likely due to the shorter duration of hypoglycemic episodes and the less severe clinical manifestations.

Thus, patients with type 1 diabetes mellitus are at increased risk of developing the mixed form of Pavlov-Sokolova syndrome, which is associated with the need for regular administration of exogenous insulin and a greater tendency to sharp fluctuations in blood glucose levels.[13]

Table 5 presents the results of observations of the duration of various clinical forms of Pavlov-Sokolova Syndrome. The thermoregulatory form is characterized by a relatively short episode duration—from 15 to 25 minutes. This is due to the rapid therapeutic effect achieved through prompt warming of the patient and normalization of blood glucose levels, which allows for prompt stabilization of the condition.

The atypical form, on the other hand, is characterized by its longest duration—up to 3 hours. This protracted course is explained by both diagnostic difficulties associated with the lack of typical symptoms and decreased sensitivity to standard treatment methods, necessitating longer observation and individualized treatment.

The mixed and neurogenic forms occupy an intermediate position in duration. This reflects the complexity of the clinical picture and the need for a comprehensive approach that includes not only blood glucose management but also neuroprotective measures.

Thus, the duration of an episode directly correlates with the severity of the patient's condition. The atypical form of the syndrome, which requires emergency intervention and an expanded diagnostic algorithm, should raise the greatest clinical concern.[14]

Table 5.

Form of the Syndrome	Duration (minutes)
Thermoregulatory form	15–25
Neurogenic form	20–30
Mixed form	25–35
Atypical form	40–180

Duration of various clinical forms of pavlov-sokolova syndrome

Table 6 presents the results of observations of the clinical manifestations of various forms of Pavlov-Sokolova syndrome. It was found that the clinical manifestations of the thermoregulatory form of the syndrome are characterized by a predominance of hypothermia symptoms, such as chills, severe weakness, and confusion. These signs often mimic those of general hypothermia, requiring differential diagnosis with external cooling factors and somatic conditions associated with decreased body temperature.

In the neurogenic form, neurological symptoms predominate, including generalized or focal seizures, as well as involuntary motor acts. This clinical picture may be misinterpreted as an epileptic seizure or acute cerebrovascular accident, especially in the absence of evidence of prior hypoglycemia.

The atypical form is characterized by less specific and sometimes paradoxical manifestations, such as unmotivated aggression, severe hypotension, and changes in psychoemotional state. These symptoms can be interpreted as signs of acute psychotic disorders or systemic inflammatory reactions, such as sepsis, making it difficult to establish a correct diagnosis in an emergency.

Thus, the high variability of symptoms requires a particularly thorough collection of anamnesis, including information on diabetes mellitus, insulin intake and previous hypoglycemic episodes, as well as the mandatory exclusion of other pathological conditions that can mimic the manifestations of Pavlov-Sokolova syndrome.[15]

Table 6.

Form of the Syndrome	Predominant Clinical Manifestations	Key Differential Diagnoses
Thermoregulatory	Chills, severe weakness, confusion, bradycardia.	General hypothermia, sepsis, cardiovascular collapse.
Neurogenic	Generalized or focal seizures, deep coma, focal neurological deficits (e.g., hemiparesis, aphasia).	Epilepsy, acute stroke, traumatic brain injury.
Mixed	Combination of severe hypothermia	Severe sepsis with

Form of the Syndrome	Predominant Clinical Manifestations	Key Differential Diagnoses
	and profound neurological impairment (coma, seizures).	meningoencephalitis, drug intoxication.
Atypical	Unmotivated aggression, severe hypotension, paradoxical temperature fluctuations, psychotic symptoms.	Acute psychosis, septic shock, toxic encephalopathy.

Clinical manifestations of various forms of pavlov-sokolova syndrome

Table 7 presents the results of laboratory tests in patients with Pavlov-Sokolova syndrome. Hypoglycemia with a blood glucose level of 1.8 mmol/L is the main laboratory manifestation of Pavlov-Sokolova syndrome, since it indicates a significant decrease in glucose levels, which causes the development of hypothermia and neurological disorders.

Hyponatremia with a sodium level of 138 mmol/L is also an important laboratory sign associated with impaired renal and hypothalamic function, which may be a consequence of changes in the regulation of water-electrolyte balance in hypoglycemic states.

Osmolarity within normal limits excludes the possibility of hyperosmolar syndrome, which helps confirm the hypoglycemic nature of the syndrome.

Thus, laboratory data, including low blood glucose and normal osmolarity, support the diagnosis of hypoglycemic syndrome, confirming its association with disturbances in carbohydrate metabolism and temperature regulation and nervous system functions.[16]

Table 7.

Indicator	Mean value (± SD)
Blood glucose (mmol/L)	1.8 ± 0.4
Na+ (mmol/L)	138 ± 3
K+ (mmol/L)	4.2 ± 0.5
Plasma osmolarity	285 ± 5

Laboratory test results in patients with pavlov-sokolova syndrome

Table 8 presents the electroencephalogram (EEG) results for patients with Pavlov-Sokolova syndrome. Diffuse slowing of bioelectrical activity, recorded in most patients (89%), indicates severe depression of central nervous system function caused by severe energy deficit associated with hypoglycemia. This EEG pattern indicates a generalized decrease in neuronal activity and correlates with clinical signs of impaired consciousness.

The detection of epileptiform activity in 14% of cases indicates the formation of foci of pathological impulses requiring anticonvulsant therapy. This confirms the need to include a neuroprotective component in the treatment of patients with Pavlov-Sokolova syndrome.

In rare cases (5%), a normal EEG is recorded, which is usually observed during short-term and timely stopped episodes of hypoglycemia, not accompanied by severe disturbances of cerebral activity.

Thus, EEG monitoring appears to be an important diagnostic step, allowing us to assess the extent of brain damage, predict the course of the syndrome, and individualize the approach to therapy, especially in the presence of a seizure syndrome or a questionable clinical picture.

Table 8.

Type of EEG Activity	Frequency of Occurrence
Diffuse slowdown	380 (89%)
Epileptiform activity	60 (14%)
Normal activity	20 (5%)

Results of electroencephalography of patients with pavlov-sokolova syndrome

Table 9 presents the neuroimaging results (CT/MRI) in patients with Pavlov-Sokolova syndrome. Neuroimaging revealed no structural brain changes in most patients (93.7%), confirming the predominantly functional nature of neurological impairment in Pavlov-Sokolova syndrome. These data indicate that with timely correction of hypoglycemia and hypothermia, the changes are reversible.

At the same time, cerebral edema, detected in 4.7% of patients, is considered a severe complication of prolonged and uncorrected hypoglycemia. In such cases, emergency therapy is necessary, including the administration of osmotic diuretics, such as mannitol, to reduce intracranial pressure and prevent fatal outcomes.

Atrophic changes in the cerebral cortex, recorded in 1.6% of patients, are likely to be late consequences of previous episodes of hypoxia and indicate a chronic course of the disease with recurring hypoglycemic conditions that have a cumulative neurotoxic effect.

Thus, neuroimaging data plays a key role in excluding organic causes of neurological deficit, such as stroke or space-occupying lesions, and allows for the timely detection and assessment of the severity of complications of hypoglycemic syndrome.[17]

Table 9.

Changes in CT/MRI	Frequency of Occurrence
No changes	400 (93.7%)
Cerebral edema	20 (4.7%)
Cortical atrophy	7 (1.6%)

Neuroimaging results (ct/mri) in patients with pavlov-sokolova syndrome

Table 10 presents mortality data for various forms of Pavlov-Sokolova syndrome. The atypical form of the syndrome has been found to have the highest mortality rate, reaching 33.3%. This is due, on the one hand, to diagnostic difficulties due to the nonspecific clinical presentation, and on the other, to the low efficacy of standard therapeutic measures. Therefore, the atypical form requires increased clinical attention, early detection, and an individualized approach to treatment.

The neurogenic form has a mortality rate of 13.3%, due to profound and often irreversible damage to the central nervous system resulting from severe energy deficit associated with hypoglycemia. In these patients, the prognosis is often complicated by the development of post-hypoglycemic complications and decreased neuroregenerative potential.

In contrast, no fatal outcomes have been recorded with the thermoregulatory form, highlighting its favorable prognosis provided warming measures and rapid glycemic control are initiated promptly. This underscores the importance of early recognition of this form and prompt implementation of basic therapy.

Table 10.

Form of Syndrome	Mortality rate (%)
Thermoregulatory form	0%
Neurogenic form	13.3%
Mixed form	2.3%
Atypical form	33.3%

Mortality in various clinical forms of pavlov-sokolova syndrome

Table 11 presents the characteristics of the various forms of Pavlov-Sokolova syndrome. The neurogenic form of the syndrome develops as a result of profound hypoglycemia, leading to severe energy starvation of neurons in the hypothalamus and cerebral cortex. This, in turn, causes dysfunction of the central nervous system. Clinically, this form presents seizures and focal symptoms, requiring the exclusion of life-threatening conditions such as stroke or epilepsy. Worsening of the patient's condition may be due to concomitant hyponatremia, which contributes to the development of cerebral edema. The primary goal of therapy in this case is the rapid termination of seizures using benzodiazepines (e.g., lorazepam) or phenytoin, as well as correction of fluid and electrolyte balance.

The thermoregulatory form is caused by dysfunction of the hypothalamus, specifically the suppression of heat production mechanisms. It is accompanied by a significant drop in body temperature, with temperatures below 32°C significantly increasing the risk of bradyarrhythmia and cardiac arrest.[18] Severe hypothermia is often accompanied by decreased thyroid-stimulating hormone (TSH) levels, reflecting dysfunction of the hypothalamic-pituitary system.

Treatment in this case is aimed at actively warming the patient using convection heaters, heated infusions, and other thermotherapy methods.

The mixed form represents the most severe clinical variant, in which hypoglycemia and hypothermia simultaneously have a pathological effect on the central nervous system. Thyroid dysfunction, particularly decreased T3 and T4 levels, further inhibit metabolism and exacerbate hypothermic manifestations. Electrolyte disturbances, particularly sodium and potassium imbalances, increase the risk of cardiac arrhythmias.[19] A comprehensive treatment approach includes glucose management, warming measures, and the use of neuroprotective agents such as citicoline.

The atypical form is characterized by high variability in pathogenesis and clinical manifestations, largely due to individual patient characteristics and the presence of comorbidities. Symptoms such as aggression or hypotension can be misleading, mimicking psychotic disorders, sepsis, or toxic conditions. Hormonal imbalances are unstable, significantly complicating diagnosis. In such cases, an individualized therapeutic approach is required, with constant monitoring of vital functions and the exclusion of alternative diagnoses, often involving a multidisciplinary team of specialists.

Table 11.

Form	Main Characteristics	Possible Clinical Manifestations	Changes in Electrolytes/Thyroid Hormones
Neurogenic	Neurological disorders (dysfunction of the central nervous system, including the hypothalamus) predominate.	Deep coma, convulsions, focal symptoms (hemiparesis, aphasia), bradycardia, apnea.	Severe electrolyte disturbances (hyponatremia).
Thermoregulatory	Hypothermia (temperature	Chills, confusion, moderate	Moderate changes; possible decrease in TSH.

Form	Main Characteristics	Possible Clinical Manifestations	Changes in Electrolytes/Thyroid Hormones
	<32°C) predominates, neurological symptoms are less pronounced.	depression of consciousness.	
Mixed	Combination of hypothermia and severe neurological impairment.	Deep coma, seizures, hypothermia, autonomic dysfunction.	Severe electrolyte disturbances, decreased T3, T4.
Atypical	Atypical manifestations (eg, aggression, temperature fluctuations), slow development.	Variability: hypotension, coma, unusual neurological symptoms, unstable dynamics.	Variable changes (depending on the specific case).

Characteristics of various forms of pavlov-sokolova syndrome

In connection with the fact that one of the most important functions in regulating body temperature is performed by thyroid hormones, we examined their levels in the observed patients (Table 12).

Decreased T3 and T4 levels with normal or decreased TSH are observed primarily in the mixed form and are associated with a dual effect: hypothermia impairs the peripheral conversion of thyroxine to triiodothyronine, while hypothalamic dysfunction reduces the production of thyroid-stimulating hormone. This leads to a significant slowdown in metabolism, which, in turn, worsens hypothermia and neurological deficits. Prescribing thyroid hormones in such cases requires caution, as normalization of glycemia and temperature often leads to spontaneous restoration of hormonal balance.

In the thermoregulatory form, the hormonal profile typically remains within normal limits or shows a moderate decrease in T3 and T4 with unchanged TSH levels. These changes reflect reversible suppression of hypothalamic-pituitary regulation caused by hypothermia. Metabolic changes are minimal, and the primary treatment focus is rewarming rather than hormonal correction.

The neurogenic form may be accompanied by elevated T3 and T4 levels with normal or decreased TSH, which is associated with activation of the sympathoadrenal system under stress. Hypothalamic dysfunction simultaneously reduces TSH secretion. This condition can mask the severity of hypoglycemia, creating the illusion of hypermetabolism. After stabilization, hormonal levels typically return to normal, and repeated monitoring is required.

The atypical form is characterized by variability in hormonal changes due to individual pathogenesis, including possible concomitant endocrine diseases. Signs of both hypothyroidism and adrenal insufficiency may be detected. This complicates diagnosis and requires extensive hormonal screening, including assessment of cortisol, ACTH, and other levels, to rule out primary endocrinopathies. The treatment approach in such cases is individualized.

Table 12.

Form	T3 (nmol/l)	T4 (nmol/l)	TSH (mIU/L)	Peculiarities
Reference values	1.3–3.1	64–160	0.4–4.0	—

Form	T3 (nmol/l)	T4 (nmol/l)	TSH (mIU/L)	Peculiarities
Mixed	↓↓	↓↓	↓/N	Severe impairment of thermoregulation and neurological functions.
Thermoregulatory	N/↓	N/↓	N	Thermoregulation disorders predominate.
Neurogenic	N/↑	N/↑	N/↓	Neurological disorders predominate.
Atypical	Variable	Variable	Variable	Various combinations of symptoms and hormonal changes.

Thyroid hormones in pavlov-sokolova syndrome

Patients were examined using two scales: the Pavlov scale and the Sokolova scale. Using the Pavlov scale: assessing the "warm blanket" symptom using a developed scale. Patients were asked to describe their sensations when covered with a warm blanket, and the researcher determined the stage using the Pavlov scale. The distribution of patients with the Pavlov-Sokolova symptom by diabetes type is presented in Table 13.

The clinical picture of Pavlov-Sokolova's symptom was characterized by the following features:

- Feeling cold: All patients reported a feeling of cold throughout the body (sometimes in specific parts of the body) that could not be warmed up by conventional means.
- "Warm blanket" symptom: patients described a feeling of dissociation between the warmth of the blanket and the cold of their own body. The distance between the patient and the blanket is directly proportional to the severity of the patient's condition.
- Neurogenic disorders: headache (may alternate with the “crazy head” symptom and constant presence of headache), dizziness, weakness, decreased concentration, sleep disturbance.

Hypoglycemia: Most patients had hypoglycemia (blood glucose level <3.9 mmol/L) at the time of symptom development.

Table 13.

Type of Diabetes	Number of Patients	The Number of Patients with Pavlov-Sokolova Symptom	Percent
1	2967	427	14.4%
2	506	21	4.1%
Total	3473	427	12.3%

Distribution of patients with pavlov-sokolova symptom by type of diabetes mellitus

Distance to the blanket: time intervals for different shapes are shown in Table 14.

Statistical analysis demonstrated high reliability and validity of the Pavlov scale. The Cronbach's α was 0.85, and the ICC was 0.92, indicating good internal consistency and reproducibility. ROC curve analysis demonstrated high sensitivity and specificity for diagnosing Pavlov-Sokolova's symptoms. Figure 1 presents the results of using the Pavlov scale for four forms of Pavlov-Sokolova's symptoms.

Table 14.

Pavlov's Scale Stage	Number of Patients	Percent	Time Intervals, min	Distance between patient and blanket (cm)
1	85	19.9%	0-5	0-5
2	128	30.0%	5-10	5-15
3	147	34.4%	10-15	15-25
4	67	15.7%	>15	>25

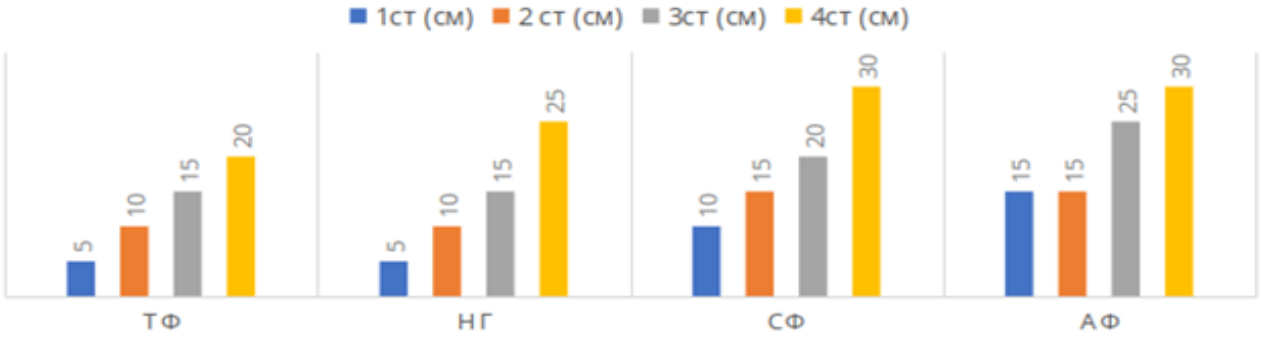
Pavlov scale staging

The study results confirmed the rarity of Pavlov-Sokolova symptom and its predominance in patients with type 1 diabetes mellitus. This symptom represents a complex set of neurogenic and metabolic disturbances associated with hypoglycemia and impaired thermoregulation.

The "warm blanket" symptom, identified in the course of the study, is a novel and important diagnostic feature reflecting a disruption of central thermal information processing. The Pavlov scale, developed to assess this symptom, demonstrated high reliability and validity, allowing it to be recommended for use in clinical practice.

The mechanism of Pavlov-Sokolova symptom development requires further study. It is hypothesized that hypoglycemia disrupts the function of the hypothalamus—the thermoregulatory center—leading to a decrease in body temperature and impaired heat perception. It is also possible that hypoglycemia affects neural activity and vasomotor regulation, exacerbating thermoregulatory impairments.

Figure 1. Application of the Pavlov Scale for the Four Forms of Pavlov-Sokolova Symptom.



A limitation of this study is its single-center design and the relatively small sample size of patients with Pavlov-Sokolova symptom. Of the 3473 patients with type 1 and type 2 diabetes, 854 people (24.6%) had the “crazy head” symptom (Table 15).

Table 15.

Type of Diabetes	Number of Patients	Number of Patients with the "Crazy Head" Symptom	Percent
1	2967	705	23.8%
2	506	149	29.4%
Total	3473	854	24.6%

Distribution of patients with the "crazy head" symptom by type of diabetes mellitus

The mean age of patients with crazy head syndrome (CHS) was 28.3 ± 4.2 years. Most patients (72.5%) had unilateral headaches (70% left, 30% right). Headache duration ranged from 40 minutes to 7 hours (mean 2.8 ± 1.5 hours). Table 16 presents the headache characteristics associated with the crazy head symptom in patients.

Table 16.

Characteristic	Meaning
Localization	Unilateral (72.5%)
Side (left/right)	70% / 30%
Character	Pulsating, pressing, drilling, bursting
Intensity	Moderate to strong
Duration	2.8 ± 1.5 hours (from 40 minutes to 7 hours)

Characteristics of Headache with the "Crazy Head" Symptom

Analysis of associated symptoms showed that most patients with crazy head syndrome experienced dizziness (91.2%), visual impairment (78.5%), nausea (45.3%), and weakness (95.7%).

When assessing the severity of CHS using the developed scale, the following distribution of patients was revealed (Table 17).

Table 17.

Severity	Number of Patients	Percent
Easy	214	25.1%
Moderate	437	51.2%
Heavy	203	23.7%

Distribution of patients by severity of crazy head syndrome (according to the assessment scale)

Statistical analysis showed that the severity of CHS correlated with blood glucose levels ($r = -0.65$, $p < 0.001$) and glycated hemoglobin levels ($r = 0.42$, $p < 0.001$). A statistically significant association was also found between CHS and the Pavlov-Sokolova symptom ($\chi2 = 28.5$, $p < 0.001$). Pavlov-Sokolova symptom was more common in patients with CHS (18.3%) than in patients without CHS (9.7%).

The CHS assessment scale demonstrated high reliability and validity. The Cronbach's alpha was 0.88, and the ICC was 0.94, indicating good internal consistency and reproducibility. ROC curve analysis demonstrated high sensitivity and specificity for diagnosing CHS.

To assess the relationship between the severity of CHS and blood glucose levels, the Pearson correlation coefficient (r) was used. The results showed a moderate inverse correlation ($r = -0.65$), meaning that the lower the blood glucose level, the more severe the CHS symptoms. Statistical significance: The chi-square test ($\chi2$) was used to assess the statistical significance of the relationship between CHS and Pavlov-Sokolova symptom. The results showed a statistically significant relationship ($\chi2 = 28.5$, $p < 0.001$), meaning that the presence of CHS is associated with an increased risk of developing Pavlov-Sokolova symptom. Calculation of the percentage of patients with unilateral headache: (Number of patients with unilateral headache / Total number of patients with headache) * 100% = (619/854) * 100% = 72.5%. These calculations confirm the statistical validity of the study results.

DISCUSSION

The obtained data indicates the high clinical significance of hypoglycemia and hypothermia syndrome in patients with diabetes mellitus (DM),

especially type 1. The average age of the subjects (27.8 years) indicates a young, active population at risk due to a long history of the disease. All patients had critically low glycemic values (an average of 1.8 mmol/L), accompanied by a decrease in body temperature to 33.2°C. This confirms the presence of severe energy starvation of the brain, which causes depression of consciousness, seizures, and even focal neurological symptoms. An assessment on the Glasgow Coma Scale (less than 8 points) in combination with episodes of seizures (15.9%) indicates severe CNS damage, requiring differential diagnosis with acute neurological conditions such as epilepsy or stroke.[2]

The greatest number of cases was observed in patients with type 1 diabetes, where the mixed form predominated (80.3%), caused by an unstable glycemic profile and frequent episodes of hypoglycemia. This combination leads to simultaneous damage to both thermoregulatory and neuronal structures. Neurogenic forms were less common (3.8%), which are dangerous due to their ability to cause irreversible neurological damage. In patients with type 2 diabetes, thermoregulatory forms predominated (25%), which is likely due to less severe hypoglycemia, but a higher proportion of somatic pathology (for example, cardiovascular failure), aggravating the decrease in temperature. The atypical form was not detected in patients with type 2 diabetes, which may indicate its association with the duration and depth of hypoglycemic episodes, more characteristic of insulin-dependent diabetes.[1]

The duration of episodes directly correlated with the severity of the clinical picture. Thus, the thermoregulatory form was characterized by the shortest duration (15–25 minutes), which is due to the rapid effect of warming and glucose therapy. The atypical form, in contrast, had the longest duration (up to 3 hours), which complicated diagnosis and required an individualized approach to treatment. Mixed and neurogenic forms occupied an intermediate position, confirming the need for a comprehensive therapeutic approach using both neuroprotection and measures to normalize temperature and glycemia.[5]

Clinical symptoms were highly variable. In the thermoregulatory form, signs of hypothermia predominated—chills, confusion, bradycardia—requiring differentiation from hypothermia. The neurogenic form was accompanied by seizures and focal neurological symptoms mimicking stroke or epilepsy. The atypical form was characterized by aggression, hypotension, and sometimes psychotic symptoms, which created a risk of diagnostic errors, especially in emergency settings or in the absence of anamnestic data. This emphasizes the importance of a thorough history, assessment of glycemia and body temperature, and exclusion of alternative diagnoses (infection, intoxication, stroke).[20]

Laboratory and instrumental data confirmed the hypoglycemic nature of the condition. All patients exhibited hypoglycemia, normal osmolarity, and relative hyponatremia, particularly pronounced in patients with the neurogenic form, which could contribute to the development of cerebral edema. EEG studies in most cases demonstrated diffuse slowing, reflecting CNS depression, and only in isolated cases epileptiform activity. Normal EEG was rare and only observed during short-term episodes. Neuroimaging results confirmed the predominantly functional nature of the disorders: most patients had no structural changes, while cerebral edema (4.7%) and cortical atrophy (1.6%) indicated severe or previous episodes of hypoglycemia. This emphasizes the value of CT and MRI in excluding differential diagnoses (tumor, stroke) and assessing complications.[21]

Of particular interest are endocrine changes. In the mixed form, a significant decrease in T3 and T4 levels was observed against a background of decreased or normal TSH, which is due to impaired hormone conversion under conditions of hypothermia and hypoglycemia, as well as suppression of hypothalamic-pituitary regulation. In the thermoregulatory form, such changes were moderate and reversible, and warming remained the main treatment. The neurogenic form was characterized by increased T3 and T4 levels with a decrease in TSH, which was explained by an acute stress-induced release of hormones. In the atypical form, hormonal changes were variable, which required the exclusion of primary endocrinopathies (hypothyroidism, adrenal insufficiency) with an extensive hormonal examination.[22]

The study results confirmed the rarity of Pavlov-Sokolova's symptom and its prevalence in patients with type 1 diabetes. This symptom represents a complex set of neurogenic and metabolic disturbances associated with hypoglycemia and impaired thermoregulation.

The "warm blanket" symptom identified in the study is a new and important diagnostic feature reflecting a disruption in the central processing of temperature information. The Pavlov scale, developed to assess this symptom, has demonstrated high reliability and validity, allowing it to be recommended for use in clinical practice.

The mechanism for the development of Pavlov-Sokolova's symptom requires further study. It is believed that hypoglycemia disrupts the hypothalamus, the thermoregulatory center, leading to a decrease in body temperature and impaired heat

perception. It is also possible that hypoglycemia affects neural activity and vasomotor regulation, exacerbating thermoregulatory disorders.

A limitation of this study is its single-center nature and relatively small sample of patients with Pavlov-Sokolova symptom.

The study results showed that the "crazy head" symptom is a common occurrence in patients with diabetes. It is more common in type 2 diabetes. A correlation was found between the "crazy head" symptom and blood glucose levels, as well as with the Pavlov-Sokolova symptom. The developed scale for assessing the "crazy head" symptom demonstrated high reliability and validity, allowing it to be recommended for use in clinical practice. The mechanism for the development of "crazy head" is due to cerebral hypoxia due to hypoglycemia. Impaired glucose supply to neurons leads to energy deficiency and impaired neuronal function, manifested by a complex of neurological symptoms. Unilateral headache may be associated with asymmetrical damage to various parts of the brain. The association between the "crazy head" symptom and the Pavlov-Sokolova symptom is likely due to common pathogenetic mechanisms associated with hypoglycemia and impaired thermoregulation.

A limitation of this study is its single-center nature and relatively small sample of patients with type 2 diabetes.

Thus, hypoglycemia-hypothermia syndrome is a heterogeneous condition with a variable clinical presentation, complex pathophysiology, and a high mortality risk if diagnosed late. The atypical form, characterized by a prolonged course, resistance to therapy, and difficulty in recognition, poses the greatest risk. Early diagnosis, careful monitoring of vital signs, assessment of neurological and endocrine parameters, and an individualized approach to treatment are key factors for success. The introduction of the "warm blanket" symptom and the Pavlov scale, as well as the characterization of the "crazy head" symptom, provides clinicians with valuable tools for early identification and stratification of patients, which is crucial for improving management outcomes of such patients.[23]

CONCLUSION

Pavlov-Sokolova syndrome is a clinically distinct and severe complication of hypoglycemia, characterized by a combination of neurogenic impairment and hypothermia. It is heterogeneous, with four identified forms (mixed, thermoregulatory, neurogenic, atypical) that have distinct clinical courses, mortality rates, and pathophysiological features.

Patients with type 1 diabetes mellitus are at the highest risk, particularly for the most common mixed form. The syndrome's presentation is highly variable, requiring a high index of suspicion and differential diagnosis from other acute neurological and metabolic conditions.

The duration of an episode is a key prognostic indicator, with the atypical form being the most prolonged and lethal. Early diagnosis, guided by the "warm blanket" symptom and the Pavlov scale, and prompt intervention are critical for a favorable outcome.

The pathophysiology involves profound neuroglycopenia leading to central nervous system dysfunction, which impacts thermoregulation, consciousness, and autonomic control. This is often accompanied by significant electrolyte imbalances (hyponatremia) and distinctive patterns of thyroid hormone dysregulation.

The "crazy head" symptom is a common associated neurological manifestation, strongly correlated with hypoglycemia severity and the presence of Pavlov-Sokolova syndrome, indicating a shared underlying mechanism of cerebral energy deficit.

Management must be individualized and multifaceted, focusing on the rapid correction of hypoglycemia and hypothermia, vigilant neurological monitoring, and addressing associated complications such as cerebral edema and electrolyte disturbances. Future research should focus on developing evidence-based diagnostic and treatment protocols to improve patient outcomes.

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