

Original Article

## A STUDY OF VARIATION IN HYPOGLYCAEMIC SYMPTOMS RELATED TO PREPRANDIAL BLOOD GLUCOSE LEVELS IN YOUNG HEALTHY MEDICAL STUDENTS

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### ABSTRACT:

Glucose is an obligate metabolic fuel for the brain under physiologic conditions. If glucose levels decreases to a certain limit, can lead to neuroglycopenic symptoms(due to deprivation of glucose to CNS) and those attributable to the autonomic nervous system activation triggered by hypoglycemia (neurogenic or autonomic symptoms) .Students often complain about inability to concentrate and other symptoms of hypoglycemia in lectures which immediately precedes the lunch hour. This study investigates whether hypoglycemic symptoms are associated with decrease blood glucose levels in young healthy medical students.

A cross sectional study was conducted in 100 medical students between the age group 18-24 years of either gender. On the day of examination, subjects were instructed to have breakfast at 8:00am.At 1:00pm blood glucose levels were measured and a questionnaire prepared on likert scale was given to assess hypoglycemic symptoms. The subjects were divided in to two groups depending on blood glucose levels:Group I : < 80 mg/dl Group II : > 80 mg/dl.

Analysis of data have shown that Group I subjects had significant hypoglycemic symptoms like hungerpangs, lack of concentration, headache as compared to Group II.

The study concluded that Variations in hypoglycaemic symptoms during the pre prandial period are present and do not require exponentially low blood glucose levels. Non-specific hypoglycaemic symptoms tend to occur and should not be attributed to low blood glucose levels.

Keywords: Nondiabetic subjects, Hypoglycemia, Hypoglycemic symptoms

#### Introduction:

The human body for its normal functioning maintains itself in homeostasis through different mechanisms. One such mechanism involves the homeostatic regulation of certain metabolic components, the most important is Blood Glucose Level. Decrease in Blood Glucose levels causes a disruption to the homeostasis ranging across all systems but concentrating more on the Central Nervous System precisely the Autonomic Nervous System.

Manifestations of Hypoglycaemia can affect the Autonomic Nervous System, either Adrenergic or Cholinergic divisions-Adrenergic symptoms being Tremors, Anxiety and Tachycardia. Cholinergic Symptoms being Sweating, Hunger and Weakness. Counter Regulatory mechanisms in the body are in place to rectify these disruptions but may sometimes lead to development of symptoms.

Early manifestations include palpitations, headache, anxiety, blurred vision, dizziness, confusion, hunger, and nausea. For prolonged or severe hypoglycaemia, manifestations include unusual behaviour, hallucinations, seizures, hypothermia, focal neurologic deficits, and coma<sup>1</sup>. Conventionally, symptoms of hypoglycemia are divided into those directly attributable to glucose deprivation from the CNS (neuroglycopenic symptoms) and those attributable to the autonomic nervous system activation triggered by hypoglycemia (neurogenic or autonomic symptoms).

Hypoglycaemia quickly causes energy failure in cerebral neurons and deprivation of glucose to the Central Nervous System and this is manifested by the onset of neuroglycopenic symptoms. The neuroglycopenic symptoms studied in this study are confusion/inability to concentrate, dizziness, drowsiness and visual changes like blurred vision<sup>2,3</sup>.

The normal fasting level of plasma glucose in peripheral venous blood is 70–110 mg/dL (3.9–6.1 mmol/L). In arterial blood, the plasma glucose level is 15–30 mg/dL higher than in venous blood.

All the previous studies done were on diabetic subjects and limited data is available about non-diabetic subjects<sup>4</sup>.

The present study was undertaken to know whether decreased blood glucose levels are necessary for the development of hypoglycaemia symptoms in non-diabetic subjects.

**MATERIALS AND METHODS:**

**STUDY DESIGN :** Cross sectional study

**DURATION OF STUDY:** 2 years

**SAMPLE SIZE:** 100

**STUDY GROUP:** young healthy individuals of Osmania medical college

**AGE GROUP :** 18-24 years

**INCLUSION CRITERIA :**

- Healthy students of either gender, between 18-24 years

**EXCLUSION CRITERIA :**

- Individuals below 18 and above 24 years
- Individuals who do not eat breakfast and chronically starve.
- Individuals with known Thyroid Disorders and Diabetes Mellitus.
- Individuals who are on any medications.
- Individuals with BMI>25
- Individuals with addictions

The equipment used was:

1. Dr. Trust blood pressure monitor to measure Blood pressure
2. Digital weighing machine
3. Height measuring stand
4. One touch Glucometer

The subjects were examined for:

1. Weight in kilograms
2. Height in meters
3. Blood pressure ( Systolic, Diastolic & Mean Arterial Blood pressures) in mm of Hg
4. Heart Rate in beats per minute
5. BMI was calculated using Quetelet formula

$$\text{BMI} = \text{weight in kg} / \text{height in m}^2$$

6. Blood glucose levels were measured using one touch glucometer and strips.

**PROCEDURE**

1. The study was done in Osmania Medical College, Hyderabad, Telangana .
2. Institutional ethics committee approval was obtained.
3. Weight was measured using digital weighing machine.

4. Height was measured using height measuring stand.
5. The subjects on the previous day were given instructions.
  - On the day of examination, Subjects were instructed to have their breakfast at 8:00am.
  - At 1:00pm they were given a questionnaire with their personal details
  - Blood glucose levels were measured
6. The questionnaire included the hypoglycemia symptoms and the symptoms were:
  - a. hunger pangs-hunger contractions
  - b. confusion-inability to concentrate
  - c. headache,
  - d. sleepiness,
  - e. dizziness-blackening in front of eye
  - f. anxiety/sweating,
  - g. palpitations-feeling of one's own heartbeat
  - h. blurred vision.
7. The objective symptoms were
  - a. Pulse rate,
  - b. Systolic blood pressure and
  - c. Diastolic pressure.
8. Pulse rate was recorded manually and the systolic and diastolic blood pressure was recorded using the Dr. Trust blood pressure monitor.
9. Each symptom was graded using the Likert's scale from 1 to 5 where
  - 1 NOT AT ALL AWARE**
  - 2 SLIGHTLY AWARE**
  - 3 MODERATELY AWARE**
  - 4 VERY MUCH AWARE**
  - 5 EXTREMELY AWARE.**
10. Headache, sleepiness, blurred vision and anxiety or sweating whenever experienced by the subjects were marked by them ranging from not at all aware to extreme awareness.
11. Blood glucose levels were measured using the one touch glucometer under aseptic conditions. Based on the recorded blood glucose levels the subjects were divided into two groups

Group I <80mg/dl

Group II >80mg/dl

#### STATISTICAL ANALYSIS:

The data was entered in Microsoft excel 2007 and was analysed by SPSS for Windows, Version 16.0. Chicago, SPSS Inc (Statistical Package of Social Sciences). Unpaired t test was used to find the significance between mean values of hunger pangs, confusion/inability to concentrate, headache, sleepiness, dizziness, anxiety/sweating, palpitations, blurred vision, pulse rate, systolic blood pressure, diastolic blood pressure in between the two groups. Data has been presented as mean, standard deviation or 95% confidence intervals. P value <0.05 was considered as statistically significant (\*)

#### RESULTS:

In the present study, out of 100 subjects (50 in Group I and 50 in Group II), the mean age of Group I is  $19.24 \pm 0.87$  and of Group II is  $19.16 \pm 0.82$ . The mean BMI of group I is  $21.32 \pm 4.34$  and that of Group II is  $22.62 \pm 5.07$ .

TABLE 1: Analysis of subjective Hypoglycemic Symptoms among Group I and Group II

PARAMETER	GROUP I <80mg/dl n=50	GROUP II >80mg/dl n=50	P VALUE
Hunger Pangs	$3.86 \pm 0.91$	$3.24 \pm 1.07$	0.0057*
Confusion/Inability to concentrate	$3.09 \pm 0.85$	$2.42 \pm 0.79$	0.0003*
Headache	$3.11 \pm 0.76$	$2.51 \pm 0.92$	0.0016*
Sleepiness	$3.31 \pm 1.05$	$3.53 \pm 1.12$	0.3702
Dizziness/Light headedness	$2.83 \pm 0.86$	$2.92 \pm 0.86$	0.5396

Anxiety/sweating	2.74±0.92	2.78±0.94	0.8468
Palpitations	2.34±0.76	2.56±0.86	0.2173
Blurred vision	2.69±1.32	2.58±1.05	0.6804

Table 2: Analysis of Objective Hypoglycemic Symptoms among Group I and Group II

PARAMETER	GROUP I <80mg/dl n=50	GROUP II >80mg/dl n=50	P VALUE
PR	101.97±10.69	96.95±11.11	0.0366*
SBP	128.57±15.65	127.95±14.52	0.8470
DBP	82.00±9.41	78.80±10.85	0.1551

TABLE 3: PARAMETERS WITH SIGNIFICANT P VALUES (P&lt;0.05)

PARAMETER	GROUP I <80mg/dl n=50	GROUP II >80mg/dl n=50	P VALUE
HUNGER PANGS	3.86±0.91	3.24±1.07	0.0057*

CONFUSION	3.09±0.85	2.42±0.79	0.0003*
HEADACHE	3.11±0.76	2.51±0.92	0.0016*
PR	101.97±10.69	96.95±11.11	0.0366*

There is a significant awareness of Hunger Pangs, Confusion, Headache and Pulse Rate in Group I compared to Group II with significant P values. The mean values for the awareness of Blurred Vision, Systolic Blood Pressure and Diastolic Blood Pressure was increased in Group I compared to Group II but with no statistical significance.

#### DISCUSSION:

In the present study, out of 100 subjects (50 in Group I and 50 in Group II), the mean age of Group I is 19.24±0.87 and of Group II is 19.16±0.82. The mean BMI of group I is 21.32±4.34 and that of Group II is 22.62±5.07.

The data presented in Table 3 shows rise in the awareness of Hunger Pangs, Confusion, Headache and Pulse Rate with significant p values in Group I compared to Group II.

In the present study, awareness of hunger pangs(p value is 0.0057) in the Group I with lower blood glucose levels when compared to Group II is significant<sup>3,5</sup>.

In the present study, confusion / inability to concentrate (p value is 0.0003) in Group I had a higher mean value compared to Group II and shows statistical significance<sup>5,6</sup>.

In this study, headache(p value is 0.0016) was experienced more by the subjects in Group I compared to Group II<sup>2,4</sup>.

In the present study the mean values for sleepiness in Group II was slightly more than Group I with no statistical significance (p value is 0.3702)<sup>4</sup>

In this study the mean values of light headedness/dizziness in Group II was slightly more than Group I with no statistical significance(p value is 0.5396)<sup>4</sup>.

The present study showed similar mean values with regard to anxiety/sweating with no statistical significance (p value is 0.8468)<sup>7</sup>

The present study showed almost equal mean values but with a slight decrease in mean values of palpitations in Group I with no statistical significance (p value is 0.2173)<sup>3</sup>.

The present study showed a very slight increase in the mean values of blurred vision with Group I being more aware when compared to Group II but with no statistical significance (p value is 0.6804).<sup>7</sup>

This study shows an increase in the mean pulse rate in Group I when compared to Group II with statistical significance (p value is 0.0366)<sup>7,8</sup>

The present study shows no significant changes in the mean values of the systolic blood pressure with no statistical significance (p value is 0.8470)<sup>9</sup>.

This study shows a fall in the mean diastolic blood pressure in Group II i.e., blood glucose levels >80mg/dl with no statistical significance (p value is 0.1551)<sup>9</sup>

Group I in this study recorded lesser mean values of BMI when compared to group II but there is no statistical significance. (p value is 0.1729). Previous studies done show lower BMI levels cause an increase in the appearance of hypoglycaemia symptoms.<sup>10,11</sup>

Pilot Study conducted by Morgana Mongraw-Chaffin et al<sup>12</sup> in female nurses to test the concordance of hypoglycemic symptoms with low glucose values in young non-diabetic individuals showed lower glucose values significantly associated with higher odds of experiencing hypoglycemic symptoms.

Study conducted by Elizabeth J. Simpson et al<sup>10</sup> in female population of the UK investigated the prevalence of hypoglycaemia and concluded that more than a third of women in the UK reported symptoms attributing to hypoglycaemia with a relation to body mass index.

Glucose concentrations within the peripheral venous blood are maintained within the range of 70-100mg/dl throughout the day. The data on pre prandial concentration of venous blood glucose levels in non-diabetic individuals is not clearly available to our knowledge. Hence the subjects were divided into two groups. Group I < 80mg/dl and Group II > 80mg/dl. This was done as the data collected followed normal distribution and to carry out statistical analysis.

During hypoglycemia intracellular glucose concentration falls causing a subsequent reduction in glycolysis-generated adenosine triphosphate (ATP) in the mitochondria of the cell. This closes ATP-sensitive potassium ( $K^+$ ) channels causing the intracellular  $K^+$  concentration to rise and this depolarizes the cell membrane. There is opening of voltage-dependent  $Ca^{2+}$  channels allowing influx of  $Ca^{2+}$ . Increase in intracellular  $Ca^{2+}$  concentration causes secretion of glucagon through exocytosis. There is a change in membrane potential (i.e. depolarization of the cell membrane).<sup>13</sup>

Cortisol, epinephrine, glucagon and insulin form the counter regulatory hormones.

The target organs for these counter regulatory hormones are muscle fat and liver. There is a decrease in the glucose utilisation through muscle fat and increase in glucose output from liver through glycogenolysis.



Counterregulatory hormones antagonize insulin action and suppress its endogenous secretion through  $\alpha$ -adrenergic mechanism, thus promoting an increase in plasma glucose.

Development of the hypoglycaemia symptoms in the study group are as follows.

### **Hunger pangs**

The physical sensation of hunger is related to contractions of the stomach muscles. These contractions are called hunger pangs. Their severity is believed to be triggered by high concentrations of the ghrelin hormone. Ghrelin is released from the oxyntic glands of the stomach when blood sugar levels get low.

When mealtime approaches, the body takes steps to soften the impact of the homeostasis-disturbing influx of fuels by releasing insulin into the blood, and lowering the blood glucose levels. Lowering of blood glucose levels causes preprandial hunger<sup>14</sup>.

### **Confusion-inability to concentrate**

Confusion is characterised by impaired orientation, diminished attention and aberrant perception. It is due to the inability of the brain neurons to function properly as there is deficiency of glucose supply to the brain.

### **Headache**

Headache results from signals interacting within the brain, blood vessels and surrounding nerves. During a headache, multiple mechanisms activate specific nerves that affect muscles and blood vessels. These nerves send pain signals to the brain, causing a headache.

Hypoglycemia induced headache is usually felt as a dull throbbing pain in the temples. Changes in water tension of the tissues possibly the brain, induced by low plasma glucose can likely be the cause.<sup>15</sup> Small fluctuation in blood glucose levels may induce alterations in the nociceptive system of the brain<sup>16</sup>

### **Pulse Rate**

Cardiac output increases during hypoglycaemia owing to an initial increase in heart rate and then in stroke volume. Moderate hypoglycaemia results in a fall in diastolic blood pressure and a rise in systolic blood pressure. Increase in cardiac output during hypoglycaemia is due to increased sympatho-adrenal activity, resulting in increased heart rate and contractility<sup>9</sup>

### **CONCLUSION**

The present study shows that decreased blood glucose levels have given rise to hypoglycemic symptoms but the plasma glucose levels haven't reached the hypoglycemic levels. As the blood glucose levels are within normal range the subjects can be encouraged to refrain from obesogenic behaviour in the anticipation of development of hypoglycaemic symptoms. The human body is equipped to maintain itself in homeostasis during 4-5hrs starvation.

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