

## ORIGINAL ARTICLE

### HYPERGLYCEMIA IN GRADE III AND GRADE IV MALNUTRITION WITH DEHYDRATING GASTROENTERITIS

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**ABSTRACT: OBJECTIVE OF THE STUDY:** To study the incidence of hyperglycemia in grade III AND IV malnutrition with no signs and some signs of dehydration. **SETTING:** Tertiary care center located in north Karnataka. **DESIGN:** Prospective observational study involving 21 children. **METHODS:** All the children with grade III and grade IV malnutrition presenting with diarrhea of less than 14 days duration, having no signs to some signs of dehydration. **RESULTS:** Hyperglycemia was observed in three of 21 children hypoglycemia was observed in six children. **CONCLUSION:** Although hypoglycemia is common finding in moderate and severely malnourished children with dehydrating gastroenteritis, hyperglycemia should also be suspected and treated. Long term follow up of these children is needed involving larger number of people in multicenter studies.

**KEYWORDS:** Hyperglycemia, Malnutrition, Dehydrating Gastroenteritis.

**INTRODUCTION:** Protein energy malnutrition is defined as "A range of pathological condition arising from co incidental lack in varying proportions of proteins and carbohydrates, occurring most frequently in infants and young children and commonly associated with infections.<sup>[1]</sup> Malnutrition is mostly caused by combinations of inadequate dietary intake, lack of good care and adverse effects of infections. Fifty-60% of malnutrition cases are established by 2 years of age with severe malnutrition contributing for 2-5% of preschool children.<sup>[1]</sup> Malnutrition accounts for 46% all causes of deaths below five years of age and seven percent of all deaths.<sup>[1]</sup> Complications of malnutrition with acute diarrhea are many which may lead to death. They are; dehydration shock, hypoglycemia, hyperglycemia, hypothermia, dyselectrolytemia, septicemia, congestive cardiac failure, severe anemia, nutritional deficiencies.<sup>[2]</sup>

Malnutrition with acute diarrhea is usually associated with hypoglycemia. However, there are reports of hyperglycemia in patients with dehydrating gastro enteritis.<sup>[3,4,5,6,7]</sup> There is only one report of hyperglycemia with dehydrating malnutrition in malnutrition.<sup>[3]</sup> In other study, hyperglycemia was not significantly elevated in malnutrition compared to well-nourished children.<sup>[6]</sup> Not many Indian and Asian studies are available to correlate moderate and severe malnutrition. Hence, study was undertaken to know the incidence of hyperglycemia in dehydrating gastro enteritis in severely malnourished children and effect of rehydration on hyperglycemia.

**MATERIALS AND METHODS:** The children under study admitted to diarrhea treatment and training unit, Department of pediatrics, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India in year 2000 were included in the study. All cases were recorded and assessment of dehydration was done as per WHO guidelines.<sup>[8]</sup>

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All children under study were assessed for malnutrition as per Indian Academy of Pediatrics classification.<sup>[9]</sup> Weight/age 51-60% were considered grade III malnutrition and weight/age less than 50% considered grade IV malnutrition.

**INCLUSION CRITERIA:** Children less than 5 years of age with grade III and IV malnutrition presenting with diarrhea of less than 14 days and no signs or some signs of dehydration were included.

**EXCLUSION CRITERIA:** Children with acute diarrhea with severe dehydration, paralytic ileus, pneumonia, meningitis pre admission oral rehydration therapy (ORT) were excluded. All children meeting the inclusion criteria were subjected for sampling of blood sugar at the time of admission and after rehydration. Blood glucose estimation was done using standard method.

Acute diarrhea was defined as three or more watery or loose stool lasting less than 14 days. Recent change in consistency than mere frequency was considered.<sup>[10]</sup> Detailed history regarding duration, frequency, vomiting, frequency of urine in preceding eight hours, nature of fluid child was taking prior to admission, nature of feeds child was receiving both prior and during diarrheal episodes. Children were assessed for signs of dehydration, presence of pneumonia, otitis media, septicemia, meningitis and urinary tract infections.

Recent onset of sunken was taken in to consideration. Dryness of mouth and absence of tears were considered on back ground of other features as they were unreliable in severely malnourished children due to atrophy of lacrimal and salivary glands and more ever, dryness could not be expected when the child had taken drinks recently. Skin pinch was interpreted with caution in marasmus as there was loss of skin turgor and marasmic kwashiorkor and kwashiorkor as there was oedema. Documented weight loss if recent weight known and presence of thirst were taken as reliable signs of some dehydration and weak or absent radial pulse and decreased or absent urine output as signs of severe dehydration. Absence of thirst was against simple dehydration and considered septicemia.

Children with no signs and some dehydration was treated using WHO ORS containing sodium chloride 3.5gms, sodium bicarbonate 2.5gms or trisodium citrate 2.9gms, potassium chloride 1.5gms, anhydrous glucose 20gms giving 90meq/L of sodium, 80meq/L of chloride, 20 meq/L of potassium, 10meq/L of lactate or 30meq/L of bicarbonate and 111 meq/L of glucose when dissolved in one liter of water.

Children with no dehydration were treated as per plan a management i.e., 10-20ml/kg of ORS along breast feeding in less than 6 months of age, breast feeding and weaning food for patient aged 6 months to 12 months of age and family pot diet when age was more than 12 months of age to take care of daily fluid requirements. In children with some signs of dehydration, 75ml/kg of ORS was given though at lower rate i.e. over 6-8hrs instead of 4 hours ordinarily required for well-nourished patients to prevent fluid over load congestive cardiac failure in compromised heart. In addition, ongoing loss due to diarrhea was replaced with ORS at 5-10ml/kg/stool. Antibiotics were given for period of 5-7 days when stool microscopy showed more than 10-15 pus cells /high power field. Vitamin A and nutritional supplementation were initiated as per guidelines.

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Patients were discharged when diarrhoea was stopped, infection completely treated, immunization received, weight gain of >10gms/kg/day for at least three consecutive days, mother educated regarding hygienic preparation of food, recognition of diarrhoea, ORS preparation and administration during diarrhoeal episodes and recognition of danger signs.

**RESULTS:** Twenty one children aged less than 5 years with grade III and IV malnutrition presenting with diarrhoea of less than 14 days and no signs or some signs of dehydration were analysed.

Demographic profile revealed that most of the diarrhea occurred in age group of 7-12 months followed by 13-24 months age group. Majority of study group were males (57.15%). 3/5<sup>th</sup> were from rural areas (61.90%). Four had diarrhea in past (19.05%). Only five children were immunised. 14 patients were partially immunized and 2 were unimmunized, sub group mostly from rural areas. Fifteen children (71.5%) were exclusively breast fed in the first 6 months of life. Vomiting was also predominant symptom with 19 children having the same (90.4%) followed by fever (76%). Grade III malnutrition group were thirteen while grade IV malnutrition nine. Fifteen patients had some dehydration (8 in grade III malnutrition and 7 in grade IV malnutrition). All but one child with Grade IV malnutrition had some dehydration.

Only two children required intravenous fluids one each in grade III and grade IV malnutrition due to failure of ORT. Three patients had periorbital puffiness, but none had congestive cardiac failure. All were less than or equal to 12 months of age. Duration of ORT in these children was less than 8 hours.

Three children with diarrhea presented with hyperglycemia at admission. All were less than 2 years of age and in grade III malnutrition only. Mean blood sugar at admission of these patients was 160mg/dL and mean blood sugar after rehydration was 91mg/dL (table 3). Mean blood sugar before and after rehydration in grade IV malnutrition was respectively 53.8mg/dL and 75mg/dL. Mean blood sugar before and after rehydration in grade III malnutrition was respectively 92.5mg/dL and 81.6mg/dL

Six were hypoglycemic at admission (28.5%). All but one was below 2 years of age. Five out of these 6 hypoglycemic patients had some dehydration at admission, with equal distribution among both sexes. Mean blood sugar in those with hypoglycemia was 46.83mg/dL, of two received intravenous fluids.

**DISCUSSION:** Prospective observational study involving 21 patients presenting with acute diarrhea a grade III and grade IV malnutrition with no or some dehydration, admitted to tertiary care center of north Karnataka, India from April 1999 to March 2000.

Our observations showed incidence of hyperglycemia in dehydrating gastroenteritis is 14.2%. This incidence closely correlated with observations of Anju Seth et al who observed hyperglycemia at 10% in study population of 50.<sup>[3]</sup> Similarly, Glyn. Jones et al reported 10.2% in their large study group population of 868 patients.<sup>[11]</sup> However, Mandell et al reported high incidence of hyperglycemia with 40% of 50 patients.<sup>[5]</sup> reported highest incidence of hyperglycemia with 55% in 27 patients was reported by one study in 1984.<sup>[6]</sup> Likewise, there are case reports of hyperglycemia in dehydrating gastroenteritis.<sup>[7,12]</sup> All cases of hyperglycemia were

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below 18 months of age which is consistent with observations of different studies. H. Heggarty et al.<sup>[12]</sup> reported all 6 cases below 22 months of age. Mnadell et al.<sup>[5]</sup> below 36mo, Glyn-Jones et al below 22mo, Robinowitz et al.<sup>[6]</sup> 6mo-24mo, Anju Seth et al.<sup>[3]</sup> below 12mo, Roger E Stevenson et al below 18mo of age.<sup>[7]</sup> Over all, there was no sex predilection.

In our study, all children were belonging to grade III malnutrition. Anjuseth et al reported hyperglycemia in both grade III and grade IV malnutrition.<sup>[3]</sup> However, Robinowitz et al found no difference in the hyperglycemia in well-nourished and malnourished children. Other studies did not compare severe malnutrition.<sup>[6]</sup> Mean blood sugar in those with hyperglycemia in our study group was 160mg/dL whereas values were higher in other studies. Blood sugar values from the studies of western population were higher than Indian population according to one study.<sup>[3]</sup> None of our patient was positive for ketone bodies. Mean blood sugar level after rehydration was 91mg/dL compared to mean value of  $77.17 \pm 13.2$ mg/dL in those with hyperglycemia at admission. Mean blood sugar level both before and after rehydration was higher in grade III malnutrition than grade IV malnutrition (89.82mg/dL and 50.71mg/dL against 82.7mg/dL and 74.71mg/dL), but values were statistically insignificant. Ours is the only study to compare between grade III and grade IV malnutrition to the best of our knowledge.

**PATHOPHYSIOLOGY:** Although hypoglycemia is expected in severe malnutrition with gastro enteritis with or without dehydration, there are reports of hyperglycemia in these children. Multiple mechanisms could be involved in pathogenesis of hyperglycemia. Carbohydrate metabolism abnormality has been observed with I infections such as, herpes simplex and vesicular stomatitis virus.<sup>[13]</sup> On quantitative analysis, decrease in insulin receptor concentration at the time of insertion of viruses in to cells rather than altered synthesis of macromolecules. There was no increase in degradation of insulin in these children.<sup>[13]</sup>

Nor adrenaline could impair the removal of intravenously administered glucose through elevated fatty acids, which interfere with normal metabolism of glucose. This may be one of important reasons in stressful situations like gastroenteritis.<sup>[14]</sup> Fasting plasma insulin levels are generally low in severe protein energy malnutrition, raising during recovery and reaching peak during phase of rapid growth. During recovery glucagon follows the same pattern as insulin there is subnormal response of insulin to glucose load or to stimulation with glucagon, which may persist for many months after recovery from severe malnutrition. Insulin response was significantly higher in those who received supplementary potassium and in some cases glucose tolerance improved with administrations of small quantities of chromium. Plasma concentration of steroid hormones which function in opposite to that of insulin, functioning as catabolic hormones is increased in starvation and infection and there is good correlation between plasma concentration of steroid hormones and severity of weight deficit and infection. Glucocorticoids aid in mobilization of amino acids which act as substrate for gluconeogenesis. Metabolic effects are due to, in part, on the balance between two hormones, insulin and cortisol. Ratio of their levels could be useful index of metabolic state.

Jaun F, Soto M D et al in their study of experimental hyper tonicity concluded that movement of Na<sup>+</sup> in to cells and K<sup>+</sup> and H<sup>+</sup> out of cells during phase of hyper tonicity could alter metabolic functions of isolated tissues, sub cellular particle and purified enzymes.<sup>[15]</sup>

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Ulrich et al observed consumption of tissue slices varied with different levels of tonicity of bathing medium. Rate of glycolysis was found to be inhibited progressively in renal slices with increasing tonicity.<sup>[16]</sup> Severe degree of metabolic disturbance of cells leads to extracellular accumulation of other intracellular components namely, potassium, phosphates, glucose, other organic acids as demonstrated by Soto.<sup>[17]</sup>

Hypoglycemia was observed in six of 21 patients with blood sugar level less than 54mg/dl, incidence falling within the range of 10-50% mentioned in one study.<sup>[18]</sup> Five of six were below two years of age and four of six were having grade IV malnutrition and five of six had some dehydration indicates that multiple factors such decreased intake, depleted glycogen stores increased demand and decreased counter regulatory regulation of glucose homeostasis could play a role. Mean blood sugar levels in those with hypoglycemia was 46.83mg/dL comparable to reported level of 10-40mg/dL.<sup>[18]</sup> Blood sugar levels less than 20 mg /dL which suggest possible serious infection and is often fatal was observed in none of our study population. This could be explained by exclusion of severe dehydration, pneumonia, meningitis, urinary tract infection in our study population. None had hypothermia. However, two of six children had temperature of more than 38.3<sup>0</sup>c. Two of them received intravenous fluid.

**SUMMARY:** Three (14.2%) with III and IV malnutrition with no or some dehydration were hyperglycemic at admission. None of the children with hyperglycemia received intravenous fluids and insulin. Mean blood glucose levels in non-hyperglycemic children before and after rehydration were 64.05%±18.2mg/dL and 77.17±13.2mg/dL respectively. Mean blood glucose before and after rehydration in those presented with hyperglycemia were 160mg/dL and 91mg/dL respectively.

**Limitations of study:** This is the prospective observational study involving small sample, conducted at single center. Hormone assay was not done in this study. Long term follow up is required to know whether children presenting with hyperglycemia really develop diabetes at later age or not, and hyperglycemia indicates depleted pancreatic beta cell reserve or transient hypo function of pancreatic beta cells. Study strength lies in its number though small are larger than many studies. Multicentric randomised trials are needed in this direction.

**CONCLUSIONS:** Dehydrating gastro enteritis is both cause and result of malnutrition in India and developing countries. Commonly encountered metabolic abnormality in hypoglycemia. However hyperglycemia may also be present albeit lower frequency which should be recognized and treated accordingly. Multicentric studies involving different races are needed to establish finding unequivocally.

Character	No dehydration	Some dehydration	Severe dehydration
<b>Look at the condition*</b>	<b>alert</b>	<b>Restless, irritable</b>	<b>Lethargic, unconscious, floppy</b>
eyes	normal	sunken	Very sunken
tears	present	absent	Absent

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tongue	moist	dry	Very dry
Thirst*	Drinks normally	Thirsty, drinks eagerly	Drinks poorly, unable to drink
Feel skin pinch*	Goes back normally	Goes back slowly	Goes back very slowly
Decide	No signs of dehydration	Some signs of dehydration if patient has 2 or more signs including at least one* sign	Severe dehydration if patient has 2 or more signs including at least one* sign

Table 1: Showing Assessment of Dehydration as WHO Guidelines.

Age/sex	Gr. of Malnutrition	BS at admission	BS after rehydration
3.5months/M	III	142 mg/dL	94 mg/dL
10months/M	III	156mg/dL	98mg/dL
18months/M	III	182mg/dL	81mg/dL

Table 2: Showing Profile of Children with Hyperglycemia at Admission and After Rehydration

M-male, Gr-grade, BS-blood sugar

Age/sex	Gr* of malnutrition	Severity of dehydration	BS** at admission
9months/female	IV	Some	42 mg/dL
48months/male	III	No	53mg/dL
12months/male	IV	Some	42mg/dL
12 months/male	IV	Some	44 mg/dL
18months/male	IV	Some	52mg/dL
24months/male	III	Some	48mg/dL

Table 3: Showing Profile of Patients With Hypoglycemia at Admission

Gr-grade, BS-blood sugar

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