



## **Frequency of Hypoglycemia in Severe Acute Malnutrition**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

Malnutrition is a major health problem throughout the world and contributes to at least one third of all children deaths worldwide. Hypoglycemia is a basic metabolic complication in pediatric patients which can be easily prevented by proper care and management. Objective of this study was to determine the frequency of hypoglycemia in severe acute Malnourished children (SAM). The study was conducted in nutritional division of Nangarhar University Teaching Hospital pediatric department. For 8 months, all the patients were subjected for measurement of blood glucose level by glucose oxidase method. Hypoglycemia was labeled according to value mentioned in operational definition. The study included a total of 252 patients with SAM. 137 (54.4%) were Males and 115 (45.6%) females with no significant difference in the number of gender and with an average age of (Mean± SD) 16.20±11.74 (6 months to 60 months). Out of 252 patients 54.80% (138) were hypoglycemic, and 85.70%(216) suffering from Marasmus. 38.9% of children's caregivers were illiterate and 86.5% poor and middle-level of socioeconomic status. 12.7%(32) of the SAM children with hypoglycemia were dying, most of the patient from Nangarhar province. Sever acute malnutrition (SAM) constitutes a significant health problem and important cause of mortality and morbidity in children, in marasmus patients the hypoglycemia is more common than kwashiorkor children; early diagnosis and treatment can prevent and decrease the morbidity and

mortality of Sever acute malnutrition (SAM) in children significantly, education, socioeconomic status of caregivers are important in prevention of sever acute malnutrition (SAM) and their complications.

**Keywords:** Hypoglycemia; severe acute malnutrition; kwashiorkor; Marasmus.

## 1. INTRODUCTION

Malnutrition is a major health problem throughout the world and contributes to at least one third of all child deaths worldwide [1] in 2018, over 49 million children under 5 years of age were wasted, and of whom 70 million were severely wasted [2].

Malnutrition is defined as an imbalance between consumption and consumption either energy, protein or any other nutrient that damages body function [3]. Several suggestions for classification of malnutrition were suggested over the years, mostly in infants and children in developing countries. In 1955, Gomez et al. [4]. Suggested a classification of malnutrition in infancy and childhood based on child's weight compared to that of a child in the 50th percentile of the same age. A later classification by Waterlow et al. [2]. was based on z- Scores Standard Deviation (SD) which took into account both weight and height of the child. The World Health Organization (WHO) classification is based on Waterlow's system with some modifications [5].

Malnutrition is a nutritional deficiency resulting from either inadequate protein or energy intake. In 1959, Jelliffe introduced the term "protein calorie malnutrition", which has been replaced by "acute malnutrition". Olsen et al. [6]. Explained protein energy malnutrition as nutritional deficiency children in developing countries. All terms, though, refer to pediatric under nutrition as a state of nutrition in which deficiency of energy, protein and other nutrients leads to measurable adverse effects on tissue and body functions, and a clinical outcome of growth deviation [7,8].

Adequate and balanced nutrients are essential in diet, and provide normal and healthy physiological, physical and mental growth and development [9,10]. Malnutrition includes both under- nutrition and over nutrition. In children the cause of malnutrition includes both inaccessibility to sufficient nutrients resource due to poverty, low socioeconomic status and also due to misconception and myths related to foods, frequent infections and lack of breast feeding

[11,12]. Treatment of malnutrition specially SAM should include and identify both medical and social problems and providing solution to both issues [2] of under developed and third world countries are facing the major burden of malnutrition in children. Rapid rise in population and low socioeconomic status results in insufficient food intake and low nutritional value of food, thus further contributing to SAM [13,14,12]. Hypoglycemia is a common problem in SAM children and can cause drastic effects and brain damage. Glucose is the key energy component for brain function. During the initial stabilization phase of treatment of SAM in hospital, it is essential to manage the hypoglycemia and remember the complication due to hypoglycemia (morbidity and mortality) [15,16]. It is well known that glucose homeostasis is regulated by various gluco regulatory hormones which affect multiple target tissues, such as muscle, brain, liver, and adipocytes. Hypoglycemia is explained by WHO as glucose level is below or equal to 70mg/dl or 3milimoles/Lt in severe malnourished children [15,10]. In sever malnourished children (low blood glucose level) Hypoglycemia occurs due to many factors. Important cause of low blood glucose level in Malnourished children due to muscle wasting (in muscles glucose is stored as glycogen, muscle glycogen is used by muscles during exercise as energy source and can affect blood glucose indirectly by gluconeogenesis, muscle glycogen can provide precursors for gluconeogenesis). The second mechanism for low blood glucose level is impairment of protein and fat stores which provide precursors for gluconeogenesis (gluconeogenic amino acid form protein and glycerol from triglycerides degradation), the third one is frequent infection in SAM children that utilize large amount of glucose by body as energy source, and the last one absorption glucose is impaired [17,18,16].

However, if the patient is lethargic, unconscious or convulsing, then he or she should be given intravenous 5ml/kg of body weight of sterile 10% glucose, by nasogastric tube. If there is unavailability of intravenous glucose, then the nasogastric dose must be provided immediately. When the patient is conscious F-75 therapeutic

diet is advised, and fed at small intervals to avoid another episode of hypoglycemia [19]. Majority of hypoglycemia incidents happen at night time, because the patient and the caregiver are sleeping and feeds are missed resulting in low blood glucose level [20].

WHO has specially developed therapeutic diets of F-75, F100 and RUTF for the treatment of SAM children. These diets should be fed to children at regular intervals according to protocol [21]. Personal care and attention to every patient and management of low blood glucose level (hypoglycemia) remarkably increase SAM outcomes thus reducing the mortality rate in SAM patients [20,22,23].

The reason of the study was that hypoglycemia is one of the most important factors resulting in morbidity and mortality in children with SAM, with prevention and early intervention valuable for lives of many children can be saved in stabilization centers. The objective of this study was to determine the frequency of hypoglycemia in children less than five years of age suffering from severe acute malnutrition.

Among patients with Diabetes Mellitus, and in accordance with the International Hypoglycemia Study guidelines, serum glucose level under 54mg/dL is sufficiently low to suggest serious, clinically important hypoglycemia and thus should be routinely reported in clinical trials dealing with glucose-lowering agents and severe acute malnutrition was defined as very low weight for height ( $< - 3$  z score of the median of WHO growth Standards) [24]. For decades, it was assumed that serum glucose level is mostly regulated by two hormones-insulin and glucagon (pancreatic hormone which secretes respectively beta and alfa cells of islets of Langerhans). It is well known that glucose homeostasis is regulated by various glucose regulatory hormones which affect many target organs, such as muscle, brain, liver, and adipocyte [2,25].

There are some Biochemical markers for Nutritional status assessment that can be measured in the blood circulation, serum albumin being the most frequently used. Albumin level is affected by nutritional status [26]. However, there is still a controversy whether albumin level is a marker of nutrition status [27], because it plays a major role in various medical conditions [28].

Other biomarker suggested as an indicator of malnutrition is serum pre-albumin (transthyretin),

major site for synthesis of this protein is liver, and it has a half-life of about 2 days [29,30]. Furthermore, serum level of pre-albumin is not altered by hydration status [31]. A reverse correlation was found between pre-albumin level and mortality among hospitalized elderly patients with a decreased nutrient intake [32], and patients treated with hemodialysis and peritoneal dialysis [33]. On the other hand, among critically ill patients with inflammation, serum pre-albumin level was not a sensitive marker for evaluating the adequacy of nutrition support. It was found that only change in (CRP) C - reactive protein level was able to significantly predict changes in level of pre-albumin, indicating that increase in pre-albumin was as a result of improvement in inflammation, rather than nutrient intake [33,34,10].

## 1.1 Terms Definition

According to the report of the workgroup of the American Diabetes Association and the endocrine society, hypoglycemia can be classified as follows [35]:

**Severe hypoglycemia:** Severe hypoglycemia is a condition requiring assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions. Plasma glucose concentrations may not be available during an event, but neurological recovery following the return of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration.

**Documented symptomatic hypoglycemia:** Documented symptomatic hypoglycemia is an event during which typical symptoms of hypoglycemia are accompanied by a measured plasma glucose concentration  $\leq 70$ mg/dL ( $\leq 3.9$ mmol/L).

**Asymptomatic hypoglycemia:** Asymptomatic hypoglycemia is an event not accompanied by typical symptoms of hypoglycemia but with a measured plasma glucose concentration  $\leq 70$ mg/dL ( $\leq 3.9$ mmol/L).

**Probable symptomatic hypoglycemia:** Probable symptomatic hypoglycemia is an event during which symptoms typical of hypoglycemia are not accompanied by a plasma glucose determination, but that was presumably caused by a plasma glucose concentration  $\leq 70$ mg/dL ( $\leq 3.9$ mmol/L) [35].

**Pseudo-hypoglycemia:** Pseudo-hypoglycemia is an event during which the person with diabetes reports any of the typical symptoms of hypoglycemia with a measured plasma glucose concentration >70mg/ dL (>3.9mmol/L) but approaching that level [35].

**2. MATERIALS AND METHODS**

The study was conducted on 252 children of severe acute malnutrition in Nangarhar University Teaching hospital children Department Malnutrition division, Jalalabad, Afghanistan, from 2020/12/21 to 8/8/2021. Permission was taken from the Children Department, and patients with severe acute malnutrition were included from Medical outpatient department, with special emphasis on anthropometric measurements (Z-score and MAUC) and signs of malnutrition. The value was compared to standard growth charts the benefits and risks of study were explained to caregiver and written informed consent taken. All selected patients underwent measurement of blood glucose level by the laboratory of the Hospital by glucose oxidase method; for the blood sampling sterile 3ml disposable syringe was used to take blood from the cubital veins of patient and hypoglycemia was labeled according to value mentioned in operational definition.

Data was entered in computer and analyzed by SPSS-version.16.statiscs were applied to analyze the data .the quantities variables, weight for height, Z-score and age was calculated as Mean and Standard Deviation. The patients having hypoglycemia; outcome variables gender and edema was analyzed in patients with severe acute malnutrition detailed history was taken from caregiver and it included nutritional history. Through examination and collected data from individual health histories, demographic characteristics (age, sex, body weight, height, place of residence) on Socioencomic status and risk factors. The sampling technique was Non probability consecutive sampling method.

A physical examination was performed, along with laboratory tests (blood chemistry) to

measure Blood glucose, the history of certain diseases. Patients were included in the study according to the following criteria:

**Inclusion criteria:**

- patients 6-60 months of age
- having weight for height <-3 z scores of the median of WHO growth standards (SAM as defined in Operational definition).

**Exclusion criteria:**

- patients less than 6 and over 60 months of age
- patients with systemic diseases such as:
  - Congenital heart disease
  - Renal failure
  - cerebral palsy, and
  - Hemolytic disorders.

Descriptive statistics such as mean, frequency, compute variable, percentage, SD statistical tests have been used.

**3. RESULTS**

The study was conducted on 252 patients of severe acute malnutrition. All of the children were between 6 months to 60 months of age. Mean age of the children was (Mean ±SD) 16.20±11.74months (Table 1).

Among 252 children, 137 were male (54.4%) and 115 female(45.6%). Among all 216(85.7%) marasmus and 36(14.3%) were kawshierkor.115 (45.6%) <-4sd, 110(43.7%) patients z-score<-3sd, 9(3.6%) z-score <-2, 11(4.4%) z-score <-1 and 7(2.8%) z-score were <0.

Out of the 252 patients (138) 54.8% were found to be hypoglycemic and (114)45.9% were in Normoglycemic, out of 216 marasmus patients 121(56%) were hypoglycemic, and out of 36 kwashiorkor 17(47.2%) were hypoglycemic as shown in Tables 2 and 3.

**Table 1. Different descriptive statistics of study cases. (n=252)**

Variables	Mean & standard Deviation
Age (per months)	16.20±11.74
Weight (kg)	5.64±1.90
Height /length(cm)	66.50±8.88

**Table 2. Show distribution of malnutrition (Marasmus & Kwashiorkor) according to in Different age groups**

Age group(per months)	Frequency marasmus	Percentage%	Frequency of Kwashiorkor	Percentage%
6-16	155	71.8	22	61.1
17-27	34	15.7	9	25.0
28-38	12	5.6	3	8.3
39-49	11	5.1	1	2.8
50-60	4	1.9	1	2.8
Total	216	100.0	36	100.0

In Table 2, most of patients were in young age (6-16 months).

**Table 3. Distribution of hypoglycemia in Marasmus and Kwashiorkor patients**

Blood glucose	Frequency of hypoglycemia in Marasmus patients	Percentage%	Frequency of hypoglycemia in kwashiorkor	Percentage %
Hypoglycemia	121	56	17	47.2
Normal level of Glucose	95	44	19	52.8
Total	252	100	36	100

Table 3 shows that the frequency of hypoglycemia is more common in marasmus than kwashiorkor.

**Table 4. Shows the mother education, economic status of family and mortality**

		Frequency n =252	Percentage%
Mother education	Literates	154	61.10
	Illiterates	98	38.90
Economic status	Good	16	6.30
	Middle	18	7.10
	Bad	218	86.50
Mortality	Live	220	87.3
	Death	32	12.70
Location	Nangarhar	173	68.70
	Laghman	39	15.5
	Kunar	23	9.10
	Kabul	17	6.80

Table 4 shows 39.90% mother are uneducated, 86.50% of families are has low income, mortality (12.70%) died and most of the patients were from Nangarhar province.

#### 4. DISCUSSION

More than 20 million children under five years of age are affected by SAM, which is a curicial factor contributing to under five years children mortality [36,18].

According to Heikens, SAM patients are always at a high risk of facing morbidities and mortalities due to low immunity and complications even during hospital stay [37]. Hypoglycemia of SAM

which can cause brain damage because glucose is the key energy source for brain function [36]. A research by chist et.all in Bangladesh in November 2010 also concluded that hypoglycemia is vitally linked with morbidity and mortality in children with diarrhea and SAM [38].

A study done in India, more than 14% of SAM patients had hypoglycemia on admission to the hospital [39].

A similar study done in Pakistan in 2007, where 10% SAM children were suffering from hypoglycemia [40], these findings were also supported by another research in Karachi,

Pakistan in 2014, where 10% children suffering from SAM also had hypoglycemia [41].

The study was conducted in Bangladesh, in it was found that sever SAM children are highly susceptible to depressed cell mediated, humoral immune responses, impairment of IgA antibody production and compromised phagocytic activity (resulting in infectious disease, prolonged diarrhea, anorexia, vomiting and possible occurrence for fatal hypoglycemia) [42].

In our study the majority of the patients were male and residents of Nangarhar province with an average age of  $16.20 \pm 11.74$  (6 months to 60 months). Out of 252 patients 54.80%(138) were suffering from hypoglycemia, 85.70%(216) were Marasmic, 38.9% of children's caregivers were illiterate and 86.5% poor and middle-level of socioeconomic status. 12.7%(32) of the SAM children with hypoglycemia were die, the hypoglycemia is more common in marasmus patients then kwashiorkor children.

## 5. CONCLUSION

Like many other factors, SAM can increase the morbidity and mortality, in marasmus patients the hypoglycemia is more common than kwashiorkor children; early diagnosis and treatment can prevent and decrease the morbidity and mortality of SAM in children significantly, education, socioeconomic status of caregivers are important in prevention of SAM and their complications.

## DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## CONSENT

Written informed consent taken from patients.

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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