INTRODUCTION

Hypoglycemia can be due to different causes, and can lead to long-term consequences like epilepsy, moderate and severe psychomotor retardation, cerebral palsy and damage to the occipital cortex resulting in blindness. Risk factors, such as hypoxia, neonatal seizures and pathological jaundice would exacerbate hypoglycemic brain injury.1-5

Hyperglycemia may remain without any manifestations or it can cause glycosuria, osmotic diuresis, impaired immunologic function and intracranial haemorrhage. Similarly, hypoglycemia may be asymptomatic, or can lead to altered level of consciousness manifesting as irritability, lethargy or stupor. It may also present as apnoea, cyanotic spells, inability to take feed, jitteriness, seizures, hypotonia, shrill cry, instability of temperature regulation and rotating eye movements.6-8

Neonatal sepsis can disturb the glucose level. A neonate having sepsis develops reluctance to take feed and this can lead to hypoglycemia. Similarly increased metabolic demand and hypothermia caused by sepsis can bring down the glucose level. Sepsis has been known to be the cause of 9.6% cases of neonatal hypoglycemia.9 Increase in the production of stress hormones like adrenaline, cortisol and glucagons, in the patients of neonatal sepsis, can lead to high glucose level. Sepsis is a common cause of critical illness hyperglycemia in the paediatric age group.10

Glucose is a critical nutrient for the brain. A high or low blood glucose level may have a significant affect on the outcomes in patients of culture proven and probable neonatal sepsis. The objective of this study was to determine the blood glucose levels among patients with neonatal sepsis and probable sepsis and evaluate their association with the mortality rate.

METHODOLOGY

It was an analytical study conducted at the Neonatal Intensive Care Unit of Fazle Omar Hospital Rabwah, Pakistan from July 2007 to December 2008.

Neonatal sepsis was defined as the case presenting with clinical signs and symptoms of neonatal sepsis with isolation of pathogens from blood, CSF, or urine. Probable sepsis was defined as the case with clinical signs and symptoms of sepsis with one or both of these criteria; presence of a total leukocytes count of over 30000/cu mm³ or under 5000/mm³; CRP level > 6 ug /ml; existence of predisposing factors i.e. maternal fever or foul smelling liquor or prolonged rupture of membranes (> 12 hours) or presence of gastric polymorphonuclear leukocytes (5 or more polymorphonuclear cells/ high power field).
All neonates admitted at the study place during the study period with culture proven and probable neonatal sepsis were included in this study. Infants of diabetic mothers, those neonates who received intravenous glucose within 6 hours before admission, or after admission and before checking of glucose level, those cases who were initially suspected of sepsis or probable sepsis but the investigations did not support the initial diagnosis and those cases of neonatal sepsis whose glucose level was checked more than 1 hour after admission were excluded.

Glucose levels of all the studied neonates were checked and recorded, within 1 hour of admission, through glucometer (Glucometer ED 4207) using glucose oxidase strips,\textsuperscript{11,12} by trained staff nurses who were briefed about the standard procedure. Blood samples of all the patients were obtained for full blood counts, CRP levels and blood cultures and urine samples of all the patients were sent for routine examination and culture. Stomach aspirate was sent for microscopic examination, if the patient was received within 24 hours of birth.

Weight, age and outcome were recorded on a data form. Value below which glucose level should be labelled hypoglycemia have not been defined yet.\textsuperscript{13,14} For this study glucose levels were divided into four groups i.e. < 40 mg/dl, 40-100 mg/dl, 101-200 mg/dl and > 200 mg/dl. Patients were divided in two groups according to weight i.e. < 2.5 kg and ≥ 2.5 kg.

All patients included in this study were given appropriate antibiotics. The patients with glucose levels below 40 mg/dl, were given 2 cc/kg of 10% Dextrose water and if the patient was not able to take oral feed, it was followed by glucose infusion 8-10 mg/kg/minute. In those patients with glucose levels above 180 mg/dl, who required intravenous fluids, glucose infusion was restricted to 4-5 mg/kg/min. Patients whose glucose level did not come below 180 mg/dl for 12-24 hours, received insulin infusion. Ethical committee of Fazle Omar Hospital, approved the study.

Double entry of the data was done by doctors incharge of the study and the nursing staff. Statistical Package for Social Sciences (SPSS) 10.0 was used. Glucose levels were cross-tabulated with mortality outcomes and weight categories. Chi-square test was applied to study differences in the various categories and groups. A p-value of 0.05 or less was taken as showing significant association among variables and categories.

### RESULTS

A total of 502 patients were included in this study. Of these 87 died (17.3%). The glucose levels of 50 patients (9.9%) were below 40 mg/dl, these levels were between 40 mg/dl and 100 mg/dl for 322 patients (64.1%), for 95 patients (18.9%) the level was between 101 mg/dl and 200 mg/dl, and 35 patients (6.9%) had glucose level above 200 mg/dl.

As shown in Table I, most patients belonged to the group with glucose levels between 40 mg/dl to 100 mg/dl and this was the group that suffered the lowest mortality. The mortality increased sharply with glucose levels either above or below the 40-100 mg/dl range. In the group with the glucose levels above 200 mg/dl, 48.6% patients died. In the group with glucose levels below 40 mg/dl, 32% suffered mortality which was statistically significant (p < 0.001).

Table II shows glucose levels in the different groups according to the weight of the patients. Glucose levels below 40 mg/dl were more prevalent in patients with weight below 2.5 kg. Glucose levels above 200 mg/dl were more prevalent in the group weighing 2.5 kg or more which was significant (p=0.002).

### DISCUSSION

During the past few years many studies have been conducted to ascertain importance and consequences of hyperglycemia and hypoglycemia in both paediatric and adult patients. Several studies have shown that hyperglycemia is associated with adverse outcomes in the paediatric age group. Different reasons for this association have been proposed e.g. enhanced apoptosis, increased production of cytokine, hyper-coagulation, acute dyslipidemia, endothelial dysfunction etc. A study by Wintergerst et al. has shown that hyperglycemia, hypoglycemia and glucose variability are associated with increased mortality rates and increased length of stay in PICU.\textsuperscript{15}

Another study conducted by Hays et al. showed that in extremely low birth weight infants, high blood glucose
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concentrations increased the risk of death, intraventricular haemorrhage, as well as the increased length of stay in the hospital.16

The present study showed that among the neonates admitted with culture proven and probable sepsis in NICU, the risk of mortality rises with increasing levels of glucose above 100 mg/dl. In the cases with glucose levels between 40 mg/dl and 100 mg/dl, 9.9% patients died. This percentage increased to 23.2% in those with glucose levels between 101 mg/dl and 200 mg/dl and in the group with glucose levels above 200 mg/dl the mortality rate rose to 48.6%

In this study, 50 cases (9.9%) had blood glucose levels below 40 mg/dl. Among these patients, 16 (32%) suffered mortality. Mortality rate in this group was second only to the group with glucose levels above 200 mg/dl.

Hypoglycemia is one of the commonest metabolic derangements encountered in the neonatal age group. The new technique of continuous glucose monitoring detects many more episodes of low glucose concentration.17 Low blood glucose concentrations do not necessarily depict any serious problem and may be just a manifestation of metabolic adaptation to extrauterine life. A study conducted by Tanzer et al. showed that the glucose levels of one-third of healthy full term newborns dropped below 30 mg/dl, in the first 3 hours of life. Only 9% required treatment.18 However, when hypoglycemia is recurrent or is prolonged it can result in systemic and neurological consequences. This study shows that those cases of culture proven sepsis or probable sepsis who were admitted with blood glucose level below 40 mg/dl, had a significantly higher mortality rate. Studies have shown that 20-86% of low birth weight babies, who received glucose infusions showed increased prevalence of hyperglycemia, due to inefficient system of glucose metabolism.19-22 A study conducted by Kathy et al. showed that in the first week of life 80% of very low birth weight babies had episodes of glucose levels above 8 mmol/L (146 mg/dl), and 32% had glucose levels above 10 mmol/L (180 mg/dl). Risk factors for hyperglycemia included prematurity, small size at birth, use of inotropes, lipid infusions and sepsis.23

In a study conducted by Pati et al. the prevalence of hyperglycemia among NICU admissions and low birth weight patients was found to be lower as compared to studies quoted previously. It showed that among the term newborns admitted in NICU, 0.94% had hyperglycemia, while among very low birth weight babies the prevalence of hyperglycemia was 2.9%. In this study by Pati et al. neonatal hyperglycemia was defined as whole blood sugar levels of 150 mg/dl or more in preterms and 125 mg/dl or more in term babies.24

A study conducted by Kayiran et al. showed that among term and near term infants, glucose levels were not significantly different in different birth weight groups, during the first hour of life.25 Patients of neonatal sepsis and probable sepsis, with high glucose levels or with hypoglycemia, are at increased risk of death, and should be treated as high risk patients. Patients of neonatal sepsis and probable sepsis, should be detected early and should receive early treatment, before hyperglycemia and hypoglycemia set in. Studies are needed to ascertain whether or not more stringent control of glucose levels in patients of neonatal sepsis can improve outcomes.

CONCLUSION

Majority of patients with neonatal sepsis and probable sepsis had glucose levels between 40 and 100 mg/dl at admission. Those with the levels below 40 mg/dl and above 200 mg/dl had higher mortality rates.

REFERENCES


