GLYCAEMIC CONTROL IN THE CRITICALLY ILL PATIENTS AT THE CRITICAL CARE UNIT, KENYATTA NATIONAL HOSPITAL

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GLYCAEMIC CONTROL IN THE CRITICALLY ILL PATIENTS AT THE CRITICAL CARE UNIT, KENYATTA NATIONAL HOSPITAL

A dissertation submitted in part fulfillment of the requirement for the degree of Masters in Medicine in Anaesthesia, University of Nairobi.

Ng'ang'a W. Kuria

2009.

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DECLARATION

This research proposal is my original work and has not been presented for any award in any university.

Date 24/9/09

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DEDICATION

To Beatrice M. Kabera and Wesley K. Ng'ang'a for giving me enough reasons to wake up every morning and face the challenges of the day.

ABSTRACT

Objective-To study the patterns of glycaemic control in the critically ill patients admitted at the critical care unit, Kenyatta National Hospital, (CCU-KNH).

Design-A prospective cross-sectional study.

Setting-Critical Care Unit, Kenyatta National Hospital.

Subjects-critically ill patients admitted at the CCU-KNH.

Methods- Over three months, data on blood sugar determinations as done on patients on admission to the CCU-KNH and subsequently the determinations done routinely on the patients for twenty four hours follow up period while still admitted in the unit. Other data collected included diabetes mellitus status, treatment with steroids and modes of feeding.

Results-A total of a hundred and ninety six patients were recruited. The mean random blood glucose on admission was 8.1mmol/l, while the mean random blood glucose at 0-6 hours post admission was 7.7mmol/l, 6-12 hours was 8.4mmol/l, 12-18hours was 7.4mmol/l and at 18-24hours was 7.3mmol/l. The commonest corrective measure for hyperglycaemia increasing the dose of insulin infusion whereas for hypoglycaemia, it was infusion with 50% dextrose solution. Only 7% of the patients had diabetes mellitus. 21% of the patients were on treatment with steroids and there was mostly no statistically significant difference between the glucose profiles of those on steroids and those without except at between 6-12 hours post admission. The commonest mode of feeding was enteral and there were no significant differences in glucose profiles among the various modes of feeding.

Conclusion- Majority of the patients admitted at the CCU-KNH have random blood glucose values that are well with the normal range. More focused corrective measures need to be adopted for the few patients who have deranged blood glucose values. A chart to record details regarding blood glucose management needs to be availed.

LIST OF ABBREVIATIONS

CCU..... Critical care unit.

KNH.....Kenyatta National Hospital.

FBS..... Fasting blood sugar.

RBS.....Random blood sugar.

OHS.....Oral hypoglycemic agents.

NPO.....Nil per oral.

SPSS.....Statistical package for social scientists.

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INTRODUCTION AND LITERATURE REVIEW

Common problems in the critically ill patients.

The critical care unit at KNH is a 21-bed open unit. Patients in need of critical care are admitted from the various hospital departments such as accidents and emergency, both medical and surgical wards, and also from the operating theatres.
Patients are also admitted as referrals from other public and private health facilities all over the country. As a result, the unit has a heterogeneous patient composition consisting of adult and pediatric surgical and medical patients.
The unit admits an average of 100 patients in a month, with an average mortality rate of 38% as per the annual data of 2005[1].

A team comprising of intensivists, post graduate doctors pursuing career in anesthesia and nursing staff does the day to day running of the unit. Specialists in other areas of medicine are consulted routinely, as per patients' needs.
In a study of 188 CCU-KNH subjects involving follow up for outcome three months post CCU discharge, it was found out that the mean length of CCU stay was 5.78 days, with a median of three days and a range of between one and eighty one days. Majority of the patients (27.7%) stayed in the CCU for two days but overall, 87% of the patients spent between one and nine days in the CCU. There were various reasons for CCU admission, with most subjects having been admitted to CCU for cardiovascular monitoring and inotropic support (24.5). The other indications included ventilatory support (20.2), hyperventilation (18.6%), post operative monitoring (12.2%), airway protection (11.7%), multiple organ support (8.5%) and electrolyte imbalances (4.3%)[2].

Critical illness is defined as any clinical situation in which there is failure of one or more organ or organ system to the extent of requiring external intervention to sustain the function of the affected organ or organ system. Patients with critical illness fall loosely into two groups: those with conditions that are unstable and have potential to deteriorate rapidly e.g. acute coronary syndrome, subarachnoid hemorrhage, acute pancreatitis); and those with overt physiological deterioration and a form of shock that need treatment in CCU (e.g. hypovolaemic, cardiogenic, spinal, septic, anaphylactic

shock)[3]. Certain clinical problems are commonly and recurrently encountered in the critically ill patients. Wholistic management of all these problems is paramount to the survival of these patients.

Cardiovascular failure is a frequent finding in the critically ill patients. It may be acute or chronic and when associated with pulmonary problems, effects of cardiovascular insufficiency may be exacerbated because of reduced oxygenation of blood. Cardiovascular monitoring and support in the CCU aim to pre-empt the development, or provide early recognition, of circulatory shock followed by rapid and effective support of the circulation to prevent the downward spiral in to multiple organ failure. Alteration of preload, cardiac function and afterload may occur very quickly and unpredictably, so that real time measurement of the changes is vital to ensure early intervention and assessment of the effects of therapeutic intervention[4].

Another common indication for patients' admission into the CCU is the need for artificial ventilation of the patients' lungs. The main indication for artificial ventilation of a patient's lung in the CCU is inability to maintain a satisfactory arterial partial pressure of oxygen. There are many pathological conditions, which produce hypoxaemia, but all have the same basic problem-an area of lung with greater pulmonary blood flow than alveolar ventilation leading to shunting. Artificial ventilation is aimed at overcoming this ventilation-perfusion mismatch. The other common indication for artificial ventilation is inability to protect the airway, which is usually due to a low Glasgow coma scale score resulting for instance from severe head injury and acute poisoning affecting the central nervous system.

Patients with cervical spinal cord injuries above the third cervical vertebra, muscular dystrophy or neurological disorders such as acute flaccid paralysis will require assisted ventilation in the CCU at some point in the course of the illness.

The effect of artificial ventilation and oxygen therapy should be assessed continuously by pulse oximetry and regular blood gas analysis. This gives a more reliable measure of oxygenation as well as providing information regarding the arterial partial pressure of carbon dioxide and acid base status.

Infections in the CCU are a common cause of mortality and morbidity. Such infections especially in their severe forms may be the reason for admission into CCU or may be acquired as nosocomial infections in the CCU. It has been observed that mortality among patients with prolonged critical illness exceeds 20% with most of deaths being attributable to sepsis and multiple organ failure. Each year, these conditions affect more than half a million patients in the USA alone. An increased susceptibility to severe infections during critical illness as well as adverse effects of an excessive systemic inflammatory response on organ function may be operative[5].

Severe stress associated with critical illness, invasive procedures such as insertion of central venous catheters, pressure ulcers, endotracheal intubation or tracheostomy are some of the factors that predispose CCU patients to infections. Studies have demonstrated impairment of host defenses, including decreased polymorphonuclear leukocyte mobilization, chemotaxis, and phagocytic activity related to hyperglycemia.
In a study to investigate the effects of normoglycemia on the endothelium, it has been observed that maintaining normoglycemia with intensive insulin therapy during critical illness protects the endothelium, likely in part via inhibition of excessive iNOS-induced nitric oxide release, and thereby contributes to the prevention of organ failure and death. iNOS is an isoform of nitric oxide synthase, associated with generation of high concentrations of nitric oxide that are proinflammatory and may evoke organ damage in conditions of ischaemia and reperfusion[6].

In a randomized control study of patients who needed intensive care for more than five days, 451 patients were analyzed. The control group received conventional insulin therapy whereas the intervention group received intensive insulin therapy. They observed that more than two thirds of patients admitted in intensive care units develop signs of severe inflammatory response syndrome caused by either infection or tissue damage, and a substantial number of these patients progress to shock and multiple organ failure. They also noted that severe hyperglycemia is prominent feature in critically ill patients. Maintaining normoglycemia with insulin significantly prevented multiple organ failure and bloodstream infections, and shortened the duration of antibiotic treatment, the number of days with leucopenia/leucocytosis, and the duration of hyperthermia/hypothermia; together these resulted in less lethality.

Whether these beneficial effects are attributable to the prevention of hyperglycemia, the increased availability of insulin or both remains speculative. Multivariate regression analysis revealed that the anti-inflammatory effect of intensive insulin therapy as indicated by the lowering of circulating C-reactive protein; to a large extent explained the prevention of acute renal failure and mortality in the intensive insulin therapy group. They therefore concluded that intensive insulin therapy suppresses the hepatic acute phase response, as indicated by circulating C-reactive protein levels and that this anti-inflammatory property at least partially explains the beneficial effect on organ failure and mortality in surgical critically ill patients[7].

Early and prompt diagnosis of infections and institution of the correct antibiotic therapy is vital in curtailing progression of these infections to full-blown sepsis. This calls for baseline and serial chest x-rays, full blood counts, cultures and sensitivity pattern for blood, tracheal aspirate, and urine among other potential sites of infection. Nosocomial pneumonia is a leading cause of death from hospital acquired infections, with an associated crude mortality rate of approximately 30% in Britain.

A common type of nosocomial infection is ventilator-associated pneumonia, which refers specifically to nosocomial bacterial pneumonia that has developed in patients who are receiving mechanical ventilation by endotracheal tube or tracheostomy[8].

Numerous other medical conditions may require admission and management in the CCU. These include:

- Acute renal failure.
- Electrolytes and acid-base derangements.
- Hypoxic brain damage.
- Permanent cerebral dysfunction from e.g. prolonged hypoglycemia.
- Adult respiratory distress syndrome.
- Deep venous thromboembolism.
- Gastric ulceration with significant hemorrhage
- Pressure sores (ulcers) with significant systemic effects.

Metabolic derangements pose a serious challenge in the day to day management of the CCU patients. These derangements include alterations in acid base balance that may

result for instance from shock due to cardiac failure. Varying degrees of renal insufficiency are also relatively more prevalent in CCU patients with the resultant alteration of electrolytes and acid-base status of the patients

Deranged blood sugar control is common in the critically ill patients. As a result, they are frequently hyperglycemic and are also prone to episodes of hypoglycemia. Hypoglycemia in the critically ill patients is usually difficult to note clinically since sedation and/or muscular paralysis in these patients normally suppress the sympathetic nervous system. Hypoglycemia also occurs in patients who present to CCU with poisoning.

Such hypoglycemia is normally due to lack of adequate nutritional intake. Another common cause of hypoglycemia is medication. Such medications include surreptitious insulin injection or oral hypoglycemic agents especially the long acting ones such as chlorpropamide, ethanol, salicylates, quinine, pentamidine and beta-blockers. Tumours associated with hypoglycemia include insulinomas and retroperitoneal sarcomas. Liver dysfunction, hypopituitarism and myxoedema can also cause hypoglycemia[9].

Nutritional mismanagement of critically ill patients is also associated with either hypoglycemia or hyperglycemia. An example is failure to reduce the sugars in the diet of a diabetic patient or a patient whose blood sugars are already elevated from treatment with steroids or due to the critical illness itself. Having CCU patients due for surgery on nil by mouth status for longer than necessary predisposes them to hypoglycemia. Failure to start feeding the patients as soon as is practically possible upon admission to CCU puts them also at the risk of developing hypoglycemia. Two types of nutritional protocols have been evaluated; simple and complex. The simple nutritional protocol resulted in more efficacious glucose control compared to that obtained with the complex ones. They therefore concluded that nutritional protocol should be kept simple to facilitate efficacious glucose control with an adaptive model predictive controller[10].

Hyperglycemia is prevalent in critical care, as patient experience stress induced hyperglycemia even with no history of diabetes mellitus. Hyperglycemia in critical care is not largely benign, as was once thought and it has a deleterious effect on outcome. However, clinical results are highly variable and there is little agreement on what levels of performance can be achieved and how to achieve them[11].

Hyperglycemia can be aggravated by infusions of fluids containing dextrose such as 50% dextrose, treatment with steroids and other medications that cause hyperglycemia such as thiazide diuretics. Hyperglycemia is also commonly due to undiagnosed diabetes mellitus or wrong or missed medication in patients whom it has been diagnosed. A significant amount of the dextrose in peritoneal dialysis solutions is absorbed. Renal failure induces insulin resistance, so hyperglycemia may occur.

The metabolic response to critical illness includes stimulation of the hypothalamic-pituitary-adrenal axis, resulting in increased growth hormone and prolactin levels. Growth hormone levels are high early in the course of critical illness and then typically become quite low.

Cortisol levels are usually increased, and these endocrine changes result in hyperglycemia. Catecholamines, both endogenous and exogenous, also contribute to the hyperglycemia of critical illness.

Why endeavor to achieve strict blood sugar control in the critically ill patient? Hypoglycemia, defined as a blood glucose concentration of less than 2.5mmol/l, if prolonged for more than four hours is a recognized cause of permanent cerebral dysfunction. Hypoglycemia can also lead to brain death especially in the presence of hypotension and/or hypoxia. Hypoglycemia can also cause or aggravate coma, convulsions, impaired cognitive function, and intellectual decline.

Whereas previous practice was to treat only marked hyperglycemia (e.g.>200mg/dl), more recent evidence suggests that control should be more rigorous[12].

A prospective, randomized, controlled trial of intensive insulin therapy in 1548 critically ill patients, most of who had undergone cardiac surgery was conducted. The investigating team hypothesized that hyperglycemia or relative insulin deficiency (or both) during critical illness may confer a predisposition to complications such as severe infections, polyneuropathy, multiple organ failure, and death. The intervention group received an insulin infusion to maintain serum glucose concentration between 80 and 110mg/dl, whereas the control group blood glucose was maintained between 180 and 200mg/dl. ICU mortality was decreased in the treatment group form 8% to 4.6 %(P <0.04).

In addition to mortality reduction, the patients with insulin infusion had fewer infections, decreased transfusion requirements, and a shorter duration of mechanical ventilation, reduced cases of acute renal failure requiring dialysis or hemofiltration and reduced critical-illness polyneuropathy. Intensive insulin therapy reduced the number of deaths from multiple-organ failure with sepsis, regardless of whether there was history of diabetes mellitus or hyperglycemia. Intensive insulin therapy reduced the use of CCU resources and the risk of complications that are common in among patients requiring intensive care, including episodes of septicemia and a corresponding need for prolonged antibiotic therapy[13].Multivariate logistic regression analysis of the data from the Van den Barghe study indicates that the blood glucose control rather than insulin dose was related to reduced mortality, critical illness polyneuropathy and bacteraemia[14].

In a related study, a team of researchers looked at the benefits of intensive insulin therapy in post cardiac surgery patients admitted in the intensive care unit, and found out that short-term glycemic control with insulin during intensive care clearly evoked sustained positive outcome benefits. This was particularly so for prolonged critically ill cardiac surgery patients and without inducing a substantial burden for the patient, his/her relatives or society [15].

It has also been found out that those diabetic patients who underwent coronary artery surgery developed short term infectious complications at post-operative blood sugar more than 11.5 mmol/l [16]. These findings also concur with results from the study by McAlister where 27% of patients who had undergone coronary artery bypass grafting, and had mean blood glucose greater than or equal to 12.5 mmol/l suffered adverse outcomes postoperatively including non-fatal stroke, septic complications and death [17].

In another study looking at the glycemic control during surgery in diabetic patients, 113 diabetic patients undergoing emergency and elective surgery in the KNH operation theatres were recruited. The results showed that, among other findings, good glycemic control, (mean blood sugar less than 10 mmol/l) was not associated with immediate postoperative complications. However patients with mean blood glucose of more than 10.1 mmol/l were likely to experience immediate post operative complications that included poor reversal from anesthesia, respiratory distress, hypotension and admission to the intensive care unit[18].

In other research works at the Mayo Clinic Proceedings, the potential benefits of glycemic control during acute illness included;

- Elimination of glucose-induced osmotic diuresis.
- Maintenance of macrophage and neutrophil function.
- Insulin-induced beneficial trophic changes on mucosal and skin barriers.
- Insulin-induced beneficial modulation of inflammatory mediators.
- Decreased free radical production and enhanced nitric oxide formation.
- Enhanced erythropoiesis and reduced hemolysis.
- Reduced cholestasis.
- Improved liberation from mechanical ventilation secondary to a direct anabolic effect of insulin on respiratory muscle function and less hyperglycemic injury of neuronal axons.
- Less axonal dysfunction and degeneration [19].

Methods of blood sugar control

Various methods are employed to maintain blood sugar within an acceptable range. The method chosen depends on the patient at hand and the blood sugar levels. These methods are as follows;

Diet

Diet plays a significant role in determining the blood sugar levels. Therefore when prescribing a nutritional plan for a critically ill patient, the pattern of blood sugar levels should be borne in mind. Patients' clinical condition will also influence the nutritional plan e.g. diabetic patients will require feeds that are lower in refined carbohydrates to avoid sudden upsurge in post prandial blood glucose. This applies to patients whether they are on total parenteral nutrition, enteral or oral nutrition.

The fluids administered in a patient also influence the blood sugars. Administration of fluids such as 5 to 25% dextrose as part of the fluid regimen will result in hyperglycemia. On the other hand, continuous administration of non-dextrose containing fluids such as normal saline without concomitant attention to proper nutrition will result in hypoglycemia.

Therefore a middle ground is reached by alternating dextrose and non-dextrose containing fluids accompanied by regular blood sugar measurements.

Pharmacological methods

Pharmacological agents are also used in blood sugar control.

Agents commonly in use to manage hyperglycemia can be classified as follows:

- Insulin.
- Oral hypoglycemic agents-insulin secretagogues such as sulfonylureas e.g.tolbutamide, meglitinides e.g. repaglinide.

  -Biguanides e.g. metformin.

  -Thiazolidinediones e.g. rosiglitazone.

  -Alpha-glucosidase inhibitors e.g.acarbose.

Insulin is a small protein with a molecular weight in humans of 5808. It's produced in the pancreatic beta cells. It contains 51 amino acids arranged in two chains (alpha and beta) linked by disulfide bridges. Proinsulin, a long single-chain protein molecule, is processed within the golgi apparatus and packaged into granules, where it is hydrolyzed into insulin and a residual connecting segment called C-peptide by removal of four amino acids. Insulin and C-peptide are secreted in equimolar amounts in response to all insulin secretagogues. Granules within the beta cells store the insulin in the form of crystals consisting of two atoms of zinc and six molecules of insulin.

Insulin is released from the beta cells at a low basal rate and at a much higher stimulated rate in response to a variety of stimuli, especially glucose. Other stimulants such as other sugars (mannose), certain amino acids (e.g., leucine, arginine), hormones

such as glucagon-like polypeptide-1 and vagal activity are recognized. Basal insulin values of 5-15 microU/ml (30-90pmol/L) are found in normal humans with a peak rise to 60-90 microU/ml (360-540pmol/L) during meals.

The insulin receptor consists of two covalently linked heterodimers, each containing an alpha subunit, which is entirely extracellular and constitutes the recognition site and beta subunit that spans the membrane. The beta subunit contains a tyrosine kinase. The binding of an insulin molecule to the alpha subunit at the outside surface of the cell activates the receptor and through a conformational change brings the catalytic loop of the opposing cytoplasmic beta subunits into close proximity. This facilitates mutual phosphorylation of tyrosine residues on the beta subunits and tyrosine kinase activity directed at cytoplasmic proteins.

Insulin also influences cell growth and the metabolic functions of a wide variety of tissues and the cells depend on insulin to facilitate glucose entry into their cytoplasm for metabolism. This is carried out via a network of phosphorylations within the cell that represent insulin's second message. Consequently, this results in multiple effects, including translocation of glucose transporters (especially GLUT 4) to the cell membrane with a resultant increase in glucose uptake; increased glycogen synthase activity and increased glycogen formation; multiple effects on protein synthesis, lipolysis, lipogenesis; and activation of transcription factors that enhance DNA synthesis and cell growth and division. Various hormonal agents (e.g. glucocorticoids) lower the affinity of the receptors for insulin. As such, lack of insulin, whether relative or absolute, is detrimental to tissues such as the brain which fully depend on glucose, as the sole energy source for their metabolism since glucose can not be transported into the cell.

Insulin forms the cornerstone, as a hypoglycemic agent, in the management of hyperglycemia. It's used alone or in combination with the other oral hypoglycemic agents and diet modification. It's effective in both insulin and non-non insulin dependent diabetes mellitus[20].

Tight glycemic control in critically ill patients can best be achieved using protocol involving continuous insulin infusion combined with frequent blood glucose determinations (hourly to 4 hourly) and the use of the last two blood glucose values to determine the insulin infusion rate. It has also been suggested that the blood glucose

target to aim for must be between 4 and 8 mmol/l and depends on local possibilities (personnel, fast and accurate point of care blood glucose determination, among other factors) and the prevailing blood glucose levels before starting a protocol[21].

Four principle types of injected insulins are available: (1) rapid-acting,with very fast onset of action and short duration of action;(2)short-acting, with rapid onset of action;(3)intermediate-acting; and (4)long-acting, with slow onset of action.

Inhaled rapid-acting human insulin is available as a powder for alveolar absorption. Premixed preparations of insulin with various percentages of short- and long-action insulin are also available for clinical use. Administration of insulin can be done through several doses in a day (pulses) or via continuous intravenous infusion. The standard mode of insulin therapy is subcutaneous injection using conventional disposable needles and syringes.Continuous subcutaneous insulin infusion devices are also available. The major shortcoming with subcutaneous insulin administration include;

- Poor absorption in patients wih hypovolaemia e.g. in shock. Correction of the hypovolaemia may result in sudden absorption of the insulin with resultant hypoglycemia.
- Reduced,absent or infected subcutaneous tissue e.g. in severe burns.
- Itching or infection at the injection sites.

In a randomized multicenter study (VICEP), it was observed that complications of insulin therapy include hypoglycemia. This is especially so where intensive insulin therapy is applied in blood sugar control[22].

This is the most common and deleterious complication of insulin therapy. It may result from a delay in taking a meal,inadequate carbohydrate consumed, unusual physical exertion or a dose of insulin that is too large for immediate needs. Insulin allergy, immune insulin resistance and lipodystrophy at the injection sites are other recognized complications of insulin therapy[20].

Thiazolidinediones act to decrease insulin resistance. Their primary action is the regulation of the genes involved in glucose and lipid metabolism and adipocyte differentiation. As such, they have a slow onset and offset of activity over weeks or even months. Combination therapy with sulfonylureas and insulin can lead to hypoglycemia.

The major action of sulfonylureas is to increase insulin release from the pancreas. Two additional mechanisms of action have been proposed-a reduction of serum glucagon levels and closure of potassium channels in the extrapancreatic tissues. Agents with long half-lives such as chlorpropamide with a half-life of 32 hours have a tendancy to cause prolonged hypoglycemic reactions especially in the elderly patients.

Biguanides' blood glucose-lowering action does not depend on functioning pancreatic beta cells. Currently proposed mechanisms of action include reduced hepatic and renal gluconeogenesis,slowing of glucose absorption from the gastrointestinal tract,with increased glucose to lactate conversion by enterocytes,direct stimulation of glycolysis in tissues,with increased glucose removal from the blood and reduction of plasma glucagon levels.

Biguanides are most often prescribed for patients whose hyperglycemia is due to ineffective insulin action, ie, insulin resistance syndrome. They are contraindicated in patients with renal disease, alcoholism, hepatic disease, or conditions predisposing to tissue anoxia (eg. Chronic cardiopulmonary dysfunction), because of an increased risk lactic acidosis induced by biguanides in the presence of these diseases.

Alpha glucosidase inhibitors include acarbose and miglitol. They act as competitive

inhibitors of intestinal alpha glucosidases and reduce the post prandial digestion and absorption of starch and disaccharides. The consequence of enzyme inhibition is to minimize upper intestinal digestion and differ digestion (and thus absorption) of the digested starch and disaccharides to the distal small intestine, thereby lowering postmeal glycemic excursions as much as 45-60mg/dl and creating an insulin-sparing effect. Monotherapy with these drugs is associated a modest drop (0.5-1%) in glycohemoglobin levels and a 20-25mg/dl fall in fasting glucose levels.

A major shortcoming of the oral hypoglycemic agents is the limited use in the critically ill patients because of;

- Patients may be on nil by mouth status and on total parenteral nutrition.
- Erratic or unpredictable absorption from the gasrointestinal tract eg.due to impaired circulation caused by shock, renal failure etc.

- Inability to monitor their effects closely eg. hourly compared to insulin as they take time to cause effects.
- They are contraindicated (relatively or absolutely) in patients with other conditions eg. renal desease, alcoholism ,hepatic disease, as stipulated above.

Management of hypoglycemia entails review of possible causes or predisposing factors eg. feeding scedules,oral hypoglycemic agents or insulin dosages and then adjusting accordingly. Specific treatment then involves infusion with a dextrose containing fluid eg. 25mls of 50% dextrose i.v. stat, followed by an i.v. infusion of 10% dextrose adjusted as per the blood sugar levels done regularly eg. 2hourly or as deemed fit for each particular patient.

Glucagon is also used to treat hypoglycemia, a major indication being in emergency treatment of severe hypoglycemic reactions in patients with type 1 diabetes mellitus when unconsciousness precludes oral feedings and intravenous glucose is not possible.

The immediate pharmacologic result of glucagon infusion is to raise blood glucose at the expense of stored hepatic glycogen. There is no effect on skeletal muscle glycogen, presumably because of lack of glucagon receptors on skeletal muscle[20].

Monitoring of blood sugar levels

Various techniques are used to measure the blood glucose levels. Almost all the techniques commonly used currently are enzymatic reactions-based (e.g. hexokinase or glucose oxidase methods) and other methods such as photometric or oxidation-reduction techniques are rarely used. Semi-quantitative preprandial urine testing is the time honoured method of assessing blood sugar control, but its limitations in this role have become increasingly apparent, not only in patients with insulin dependent diabetes mellitus(IDDM) but also in non-insulin dependent diabetes mellitus(NIDDM) patients where a raised renal threshold for glucose may mask persistent hyperglycemia. In addition, negative urine tests fail to distinguish between a normal and low blood sugar levels which is a particular disadvantage since the aim of treatment is a normal blood glucose level while avoiding hypoglycemia

Portable blood glucose monitors use reflectance photometry to measure the amount of light reflected from a test pad containing reagent. A sample of blood (from a finger prick) is placed on the test pad, which is attached to a plastic support. The test strip is then inserted into the meter. After a fixed time period, the results appears on a digital display screen.

A few devices use electrochemistry; the enzymatic reaction in an electrode incorporated on the test strip produces a flow of electrons. The current, which is directly proportional to the amount of glucose in the sample is converted into a digital readout. Large variability exists among meters as to the test time (15-120 seconds) and reading range(40–400mg/dl to 0-600mg/dl). Calibration is automatic on some devices, whereas others use lot-specific code strips. All manufacturers supply control solutions. Strict adherence to the user-instructions is necessary to obtain accurate results.

Additional innovations include systems that abort testing if the sample volume is inadequate and built-in programs that simplify quality control[23].

In a systematic review of the literature ,it was found out that in most of the studies,hand held meters with strips were used. The literature on point-of-care testing suggests that accuracy varies with the different hand held meters. They also found out that an ICU-based blood glucose analyzer had the best correlation coeficient with their gold standard (central clinical laboratory measurement),they preffered using this device to hand held meters. Furthermore, the studies evaluated used capillary, venous, or arterial blood gas for glucose measurement. Its known that full blood glucose and plasma glucose values differ, and the same is true for arterial and venous blood samples[21].

Several factors such as user variability and patient's hematocrit affect the accuracy and reproducibility of these devices. These assays are unreliable at very high and very low glucose concentrations(<60 and >500mg/dl). Because intramuscular volume depletion,a common feature of diabetic ketoacidosis, markedly increases the blood viscosity, inaccurately low blood glucose results may be obtained.

Test strips using whole blood results in glucose concentration approximately 10%-15% lower than plasma or serum glucose concentration.

Visual test strips whose colour change depends on the blood glucose levels are available whereas other test strips have a meter[23].

Point-of-care glucose meter values of both capillary (fingerprick) and arterial or central venous catheter blood samples have been compared with laboratory glucose values in critically ill patients. The difference between the point-of-care values and the laboratory values was not statistically significant. The lack of difference between glucose values obtained with the point-of-care device whether capillary or catheter blood was used and the laboratory glucose analyser, supports the common practise in critical care units of using catheter rather than fingerprick blood for point-of-care testing. With the advent of aggressive glucose management protocols to decrease infection risks in critically ill patients,blood samples are needed frequently and use of catheter blood samples avoids the painful needle sticks to obtain capillary blood [24].

The most common errors in use of handheld glucose meters such as proper application, timing and removal of excess blood, have been eliminated by advances in technology. Additional innovations that reduce operator errors include systems that abort testing if the sample volume is inadequate, built-in programs that simplify quality control and memory that allows the instrument to store upto several hundred glucose readings that can be downloaded into a computer.[23]

Glycated adult hemoglobin (HbA1c) levels are asessed to determine blood glucose control over a period of the preceeding 6-8 weeks. The rate of synthesis of glycated hemoglobin is a function of the exposure of the red blood cells (rbc) to glucose. The very close relationship obtained between total HbA1c and the mean blood glucose concentration supports the expectation that such measurements taken during a normal working day are more representative of the usual prevailing blood glucose levels than those obtained in hospital or in day-patients.

The aim of blood glucose control is to maintain HbA1c levels at between the normal of 4-6% of total hemoglobin. Levels greater than 8% indicate poor glycemic control over the previous 6-8 weeks. Glycated serum proteins ('fructosamine') are also measured and , because of their shorter half-life, give an indication of glycemic control over the preceeding two weeks. Glycated albumin can too be used to assess levels of glycemic control[25].

RATIONALE

The myriad benefits of maintaining euglycemia in the critically ill patients have been confirmed again and again in a number of randomised controlled trials. At the same time, the effects of both hyperglycemia and/or hypoglycemia on both mortality and morbidity in the critically ill patients are well known.

Most of these trials have been carried out in the critical care facilities in the developed countries especially in Europe and North America. Similar trials need to be carried out in the critical care facilities in the developing world because the patient population in the critical care facilities is slightly different in both set ups.

In the developed countries,critical illness is mainly comprised of complications arising from diseases such as diabetes mellitus and hypertension whereas in the developing countries a significant percentage of critical illness is related directly or indirectly to trauma.

In the critical care unit at KNH, no study had been done to determine how well or how poor the blood sugar control is with reference to internationally recommended values. Its also not possible to tell how the blood sugar control is in the different subgroups of the CCU patients and whether our daily endeavours that aim to achieve euglycemia in the critically ill patients are effective.

This study therefore had the aims of investigating how blood glucose control is in the critically ill patients at CCU- KNH with the hope that the information obtained would act as a foundation upon which to build up our efforts in as far as wholistic management of the critically ill patients is concerned.

RESEARCH QUESTION

Is the glycemic control optimal in the critically ill patients at the critical care unit in Kenyatta National Hospital?

GOAL

Improve glycaemic control in the critically ill patients at the critical care unit in Kenyatta National Hospital .

BROAD OBJECTIVE

To study patterns of glycemic control in the critically ill patients at CCU-KNH.

SPECIFIC OBJECTIVES

1. Study the general levels of glycaemia in the critically ill patients in the critical care unit at Kenayatta National Hospital, with respect to hypoglycemia, euglycemia and hyperglycemia.
2. Determine the common factors that contribute to glycaemic derangements in the critically ill patients at the critical care unit at Kenayatta National Hospital.
3. Determine the measures taken and their effectiveness in patients whose glycaemic levels are out of range in the critical care unit at Kenyatta National Hospital.
4. Make recommendations on how to achieve and/or maintain euglycemia in the critically ill patients at the critical care unit at Kenyatta National Hospital.

METHODOLOGY

Study design

This was a prospective cross-sectional study.

Study population and site

This was comprised of the critically ill patients admitted at the CCU-KNH.

Sample size

In this study, sample size was calculated as follows;

$$n=\frac{z^2pq}{d^2}$$ (Fischer et al 1998)[26]

Whereby;

n is the sample size (if the target population is more than 10,000).

z is the standard normal deviation at the required confidence level, in this case its 1.96.

p is the proportion in the target population estimated to have characteristics being measured, which is the proportion of the patients in the CCU with normal blood sugars (euglycemia). Since the proportion was unknown, 50% or 0.5 was made use of.

q is 1-p which is equal to 1-0.5=0.5.

d is the level of statistical significance set which is 0.05.

Therefore;

$$n=\frac{(1.96)^2 \text{ X } 0.5\text{X}0.5}{(0.05)^2}$$

$=384.16$

Since the population in this study is less than 10,000, further calculation of the sample size done as follows;

$$nf = \frac{n}{1+n/N}$$

Whereby;

nf is the desired sample size (when the population is less than 10,000).

n is the desired sample size (when the population is more than 10,000) which in this case is 384.16 from the above calculation.

N is the estimate of the population size, which in this case is the number of patients that will have been in the CCU during the four months of the study period. From the literature[1,2], this was noted to be approximately 400 patients.

Therefore;

$$nf = \frac{384.16}{1+(384.16/400)}$$

=195.960008 and this is rounded to 196 patients.

Pilot study

A pilot study was carried out two weeks before the actual data collection was done. This was aimed at testing the data collection and storage tools. All the short comings noted were duly corrected and the relevant changes incorporated to come up with fine tuned study tools.

Study Procedure

Sequential sampling was employed to select the patients. This was through selecting all patients who were newly admitted to the critical care unit at Kenyatta National Hospital during the study period.

Informed consent to include a patient into the study was obtained from the respective patients if they were fit enough to consent. If unfit to consent, the consent was obtained from their relatives or guardians.

An interviewer-administered data capture instrument was used to collect data. The demographic details of the patient were obtained from the patient, patient's guardian or patient's file. These included the name, sex, age, primary diagnosis and /or other diagnoses, medications and type of feeds the patient was on at the time of data collection.

The 24-hour profile of blood glucose measurements done (in mmol/l) was obtained from the CCU laboratory records for patients admitted in the CCU for at least 24 hours. The patients' baseline blood sugar values, i.e. the values as at the time of admission were also be obtained. Blood sugars levels done after remedial measures to correct a deranged blood sugar level were also included in the data collected, besides noting the remedial measure taken. An average value was subsequently calculated. Since one of the objectives of the study was to look at general levels of glycaemic control, all the values of blood glucose obtained were considered during the data analysis. All these values were obtained from the CCU laboratory records since these are measured routinely at least once every morning between 6am and 7am daily.

Quality Assurance

In the critical care unit-KNH, a hand held glucose meter is routinely used by the laboratory staff to measure the blood sugar levels. The glucometer in use is branded Glucosure Plus® and is manufactured by the Apex Biotechnology Corporation of Taiwan. It has a capability of measuring blood sugar levels between 1.7mmol/l to 30.6mmol/l. The recommended sample is capillary whole blood. Only one brand of glucometer is used on all the CCU patients to avoid inter-glucometer variations of results.

The measurements are usually done by different laboratory technologists in the CCU laboratory. To avoid inter-user variability among the CCU laboratory staff, the type of blood sample, (i.e. fresh capillary whole blood) and the procedure for taking the blood sample, (finger prick) and for putting the sample on the test strip's reaction zone are standardized. A set of instructions to this effect is displayed on the CCU laboratory bench where the testing is done to act as a reminder to all the CCU laboratory technologists.

The manufacturer recommends that to perform a measurement, a sample of fresh capillary whole blood taken from a fingertip is put on the designated test area on the test strip which has already been inserted in the glucometer. It is ascertained that the blood drop completely fills the reaction zone. Testing must be performed immediately (within 15 minutes) after the sample is obtained from the patient. Results appear on the digital screen after 10 seconds.

The glucometer is calibrated regularly and every time a new batch of test strips are used. The manufacturer supplies the glucose control solutions and guidelines for performing the quality control testing. Quality control testing of the glucometer is done at least once every five days or after testing a hundred samples, whichever comes first. It aims to test the performance of the glucometer and the testing technique. Each package of the test strips comes with a coding card. The code number on the code card must match the code number on the test strip package. Coding of the glucometer is also done every time a new batch of test strips is used. Coding ensures that the glucometer and the test strips are harmonized. It must be confirmed that the test strips are within the expiration date every time a new batch of test strips is opened.

To further improve the on the quality assurance, blood sugars values obtained with the CCU glucometer were compared with blood sugars values from the same blood samples obtained by use of the spectrophotometric biochemistry analyzer in the main hospital laboratory which is the standard method for measuring blood sugars. This comparison was done at least once after every fifty samples had been tested as is routinely done. The blood samples for comparison from the CCU patients were chosen randomly. Any significant variation i.e. greater than 5%, between the values obtained with glucometer and the spectrophotometric analyzer called for the calibration of the

CCU glucometer, quality control testing and retesting of the patients so affected. These operating standards were strictly adhered to in the execution of this study.

The average of serial blood glucose levels taken in 24 hours, six hourly for the purpose of this study, for patients on continuous insulin infusion were obtained for such patients were enrolled in the study. In case the blood sugar values for a particular patient enrolled in the study were not available for whatever reason, then the researcher liaised with CCU laboratory staff to ensure that, at least, the routine blood sugar measurements were done.

Inclusion Criteria

Subjects included in this study were;

1. Those admitted in CCU-KNH for at least 24 hours and whose consent to be recruited into the study had been obtained.
2. Those newly admitted to the CCU-KNH during the execution of this study.

Exclusion Criteria

Subjects excluded from this study were;

1. Any patient who/whose relatives declined to consent to be recruited into the study.
2. Patients admitted in the CCU-KNH for less than 24 hours before discharge or death.
3. Patients admitted into the CCU-KNH prior to the commencement of this study.

Operational definitions [27,29,34]

- Hypoglycemia- plasma glucose levels $\leq$ 2.5mmol/l (45mg/dl) in venous blood provided the associated typical symptoms are evident and the symptoms are relieved by administration of glucose.
- Hyperglycemia- fasting (overnight) venous plasma glucose concentration $\geq$ 7.8mmol/l (140mg/dl) or, non-fasting/following ingestion of 75g of glucose, a venous plasma glucose concentration $\geq$ 11.1mmol/l (200mg/dl) at 2-hour interval.

Ethical considerations

1. The study formed part of the routine CCU care protocol and did not involve any extra expense or invasive procedure on the subjects recruited.
2. The nature of the study was explained to the respective patients if they were in a position to understand. Otherwise their guardians were informed and a written consent obtained.
3. Failure to consent did not alter in any way the subject's CCU quality of care delivered.
4. During the execution of the study, for all the deranged blood glucose encountered, the doctor on duty, if not already aware, was informed immediately to consider instituting remedial measures.
5. Permission to carry out the study was duly sought and obtained from the KNH research and ethics committee.

Data collection, processing and presentation tools

Information collected on the study questionnaire was collated, cleaned and verified. It was then entered into an MS- Excel database and stored in both soft and hard copies. The Stata version 10, (Stata corp. Texas) data processing software was used to analyze the data. Subsequently the processed data was presented in the form of charts, tables and graphs.

DATA ANALYSIS RESULTS

The study was carried out during the months of February, March and April 2009.Data was captured using questionnaires and entered into an MS-Excel database. A total of one hundred and ninety six patients admitted in the Critical Care Unit-Kenyatta National Hospital, (CCU-KNH) were recruited into the study. Subsequently, the data was analyzed using Stata version 10, (StataCorp, Texas). A p-value of less than 0.05 was considered to be statistically significant.

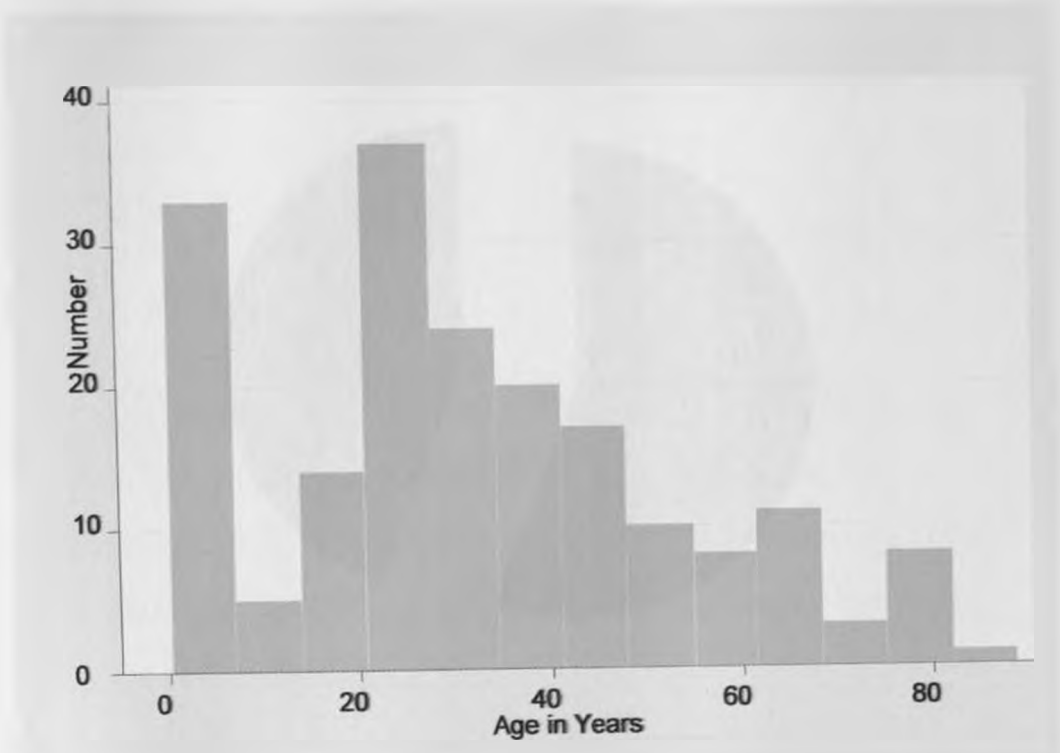

Figure 1, showing the age distribution in the study participants.

The mean age of the study sample was 32.2 years (95% C.I. 29 – 35.3 years).

Median age was 30 years, mode of 30 years and the range was from the age of 4 months to 89 years.

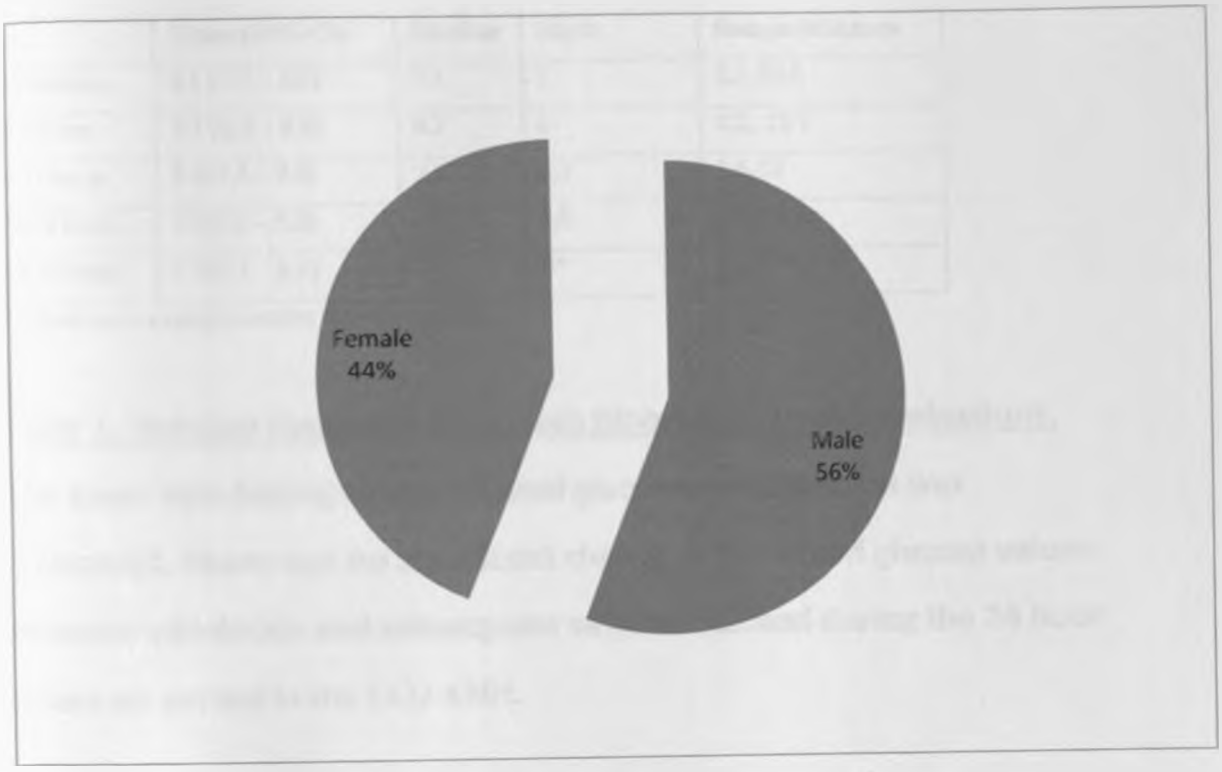

Figure 2, showing gender distribution in the study participants.

There were more males than females recruited into the study with males totaling 110 and females 86.

	Mean (95% CI)	Median	Mode	Range (min,max
Admission	8.1 (7.5 – 8.6)	7.3	5	2.1,30.6
0-6 hours	7.7 (6.5 – 8.8)	6.7	6	2.2, 25.7
6-12 hours	8.4(7.4 – 9.4)	7.5	6.3	1.6,33
12-18 hours	7.4(6.6 – 8.2)	6.5	4.8	2.7,24.9
18-24 hours	7.3(6.4 – 8.1)	7	0*	2.4,17.1

*=There were multiple modes for this variable.

Table 1, showing measures of random blood glucose determinations.

The mean non-fasting random blood glucose on admission was 8.1mmol/l. There was no significant change in the blood glucose values between admission and subsequent values obtained during the 24 hour follow-up period in the CCU-KNH.

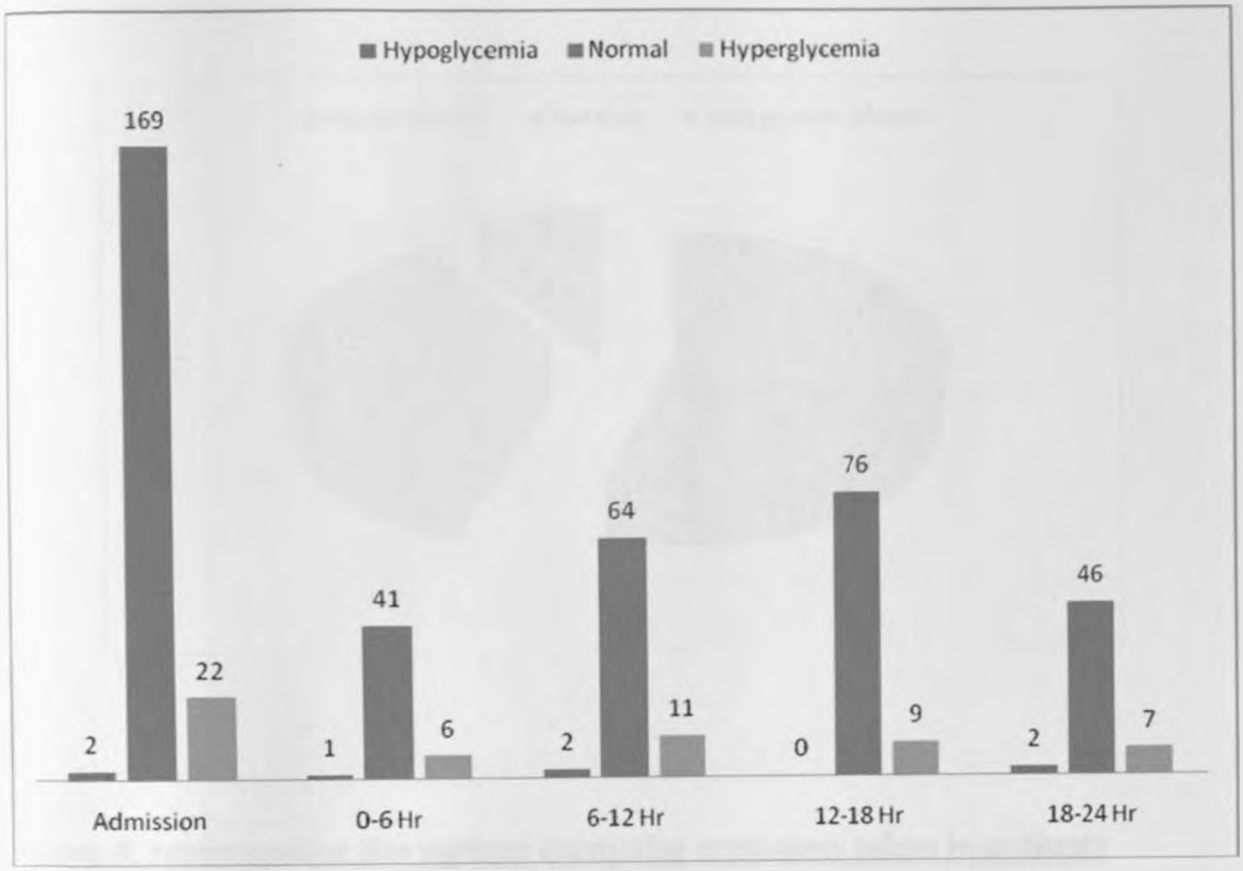

Figure 3. demonstrating non-fasting blood glucose levels at admission and in the subsequent 24 hours of follow up.

Majority of the patients had blood glucose levels that were within normal range on admission and also during the 24 hour follow-up in the CCU-KNH. Hypoglycaemia was less prevalent than hyperglycaemia in those that had deranged blood glucose levels. None of the blood glucose measurements was a fasting value.

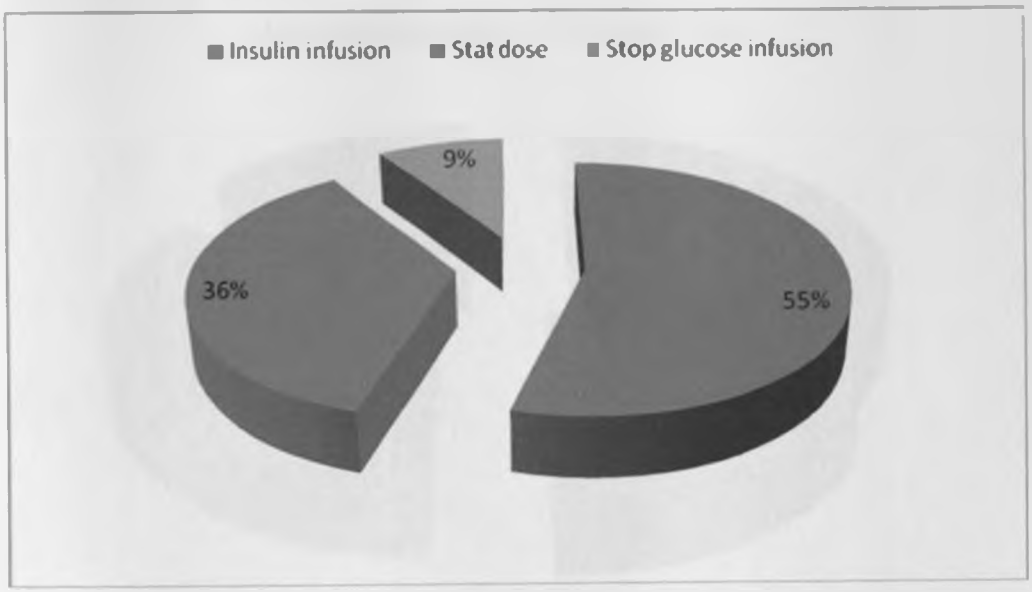

Figure 4. representing the various corrective measures taken in patients with hyperglycaemia.

The most commonly instituted corrective measure in patients with hyperglycaemia was infusion with soluble insulin undertaken in 55% of the patients, followed by giving a stat dose of soluble insulin, taken in 36% of the patients. In the remaining 9% of the patients, stoppage of infusion with glucose containing solutions was undertaken.

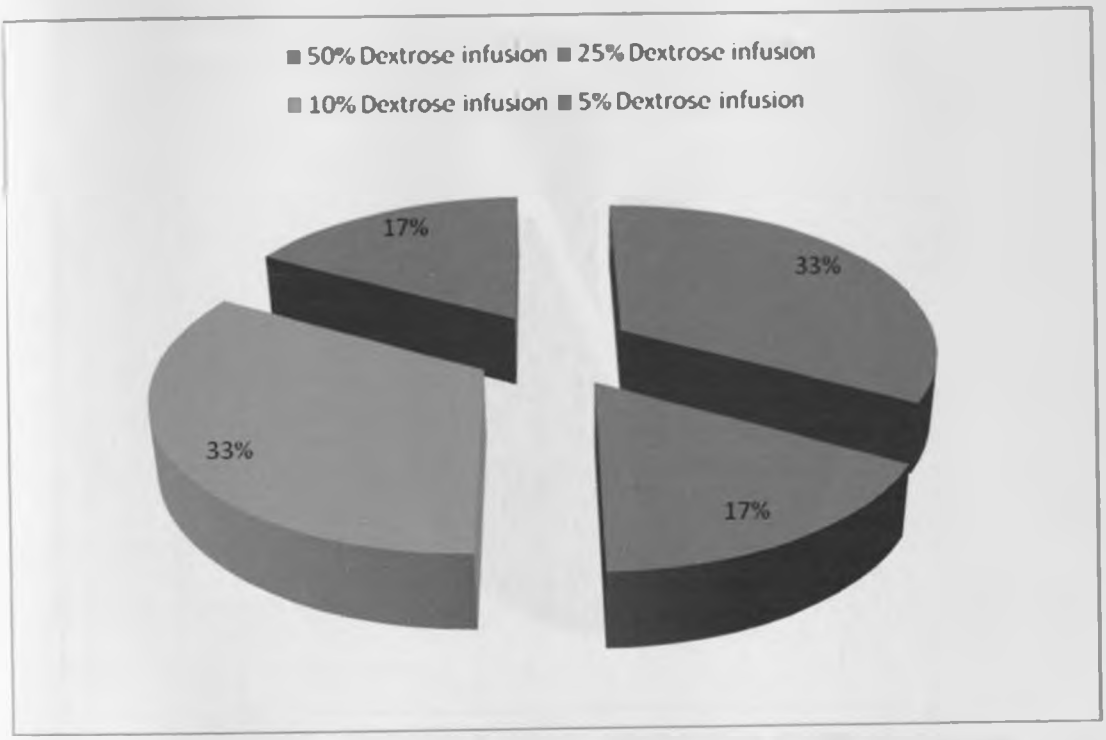

Figure 4. showing the corrective measures undertaken in patients with hypoglycemia.

The commonest corrective measure taken in patients with hypoglycaemia was infusion with dextrose containing solutions, with the 50% and 25% dextrose infusions comprising 50%. Infusion with 10% and 5% dextrose solutions was instituted in the rest of the patients with hypoglycaemia.

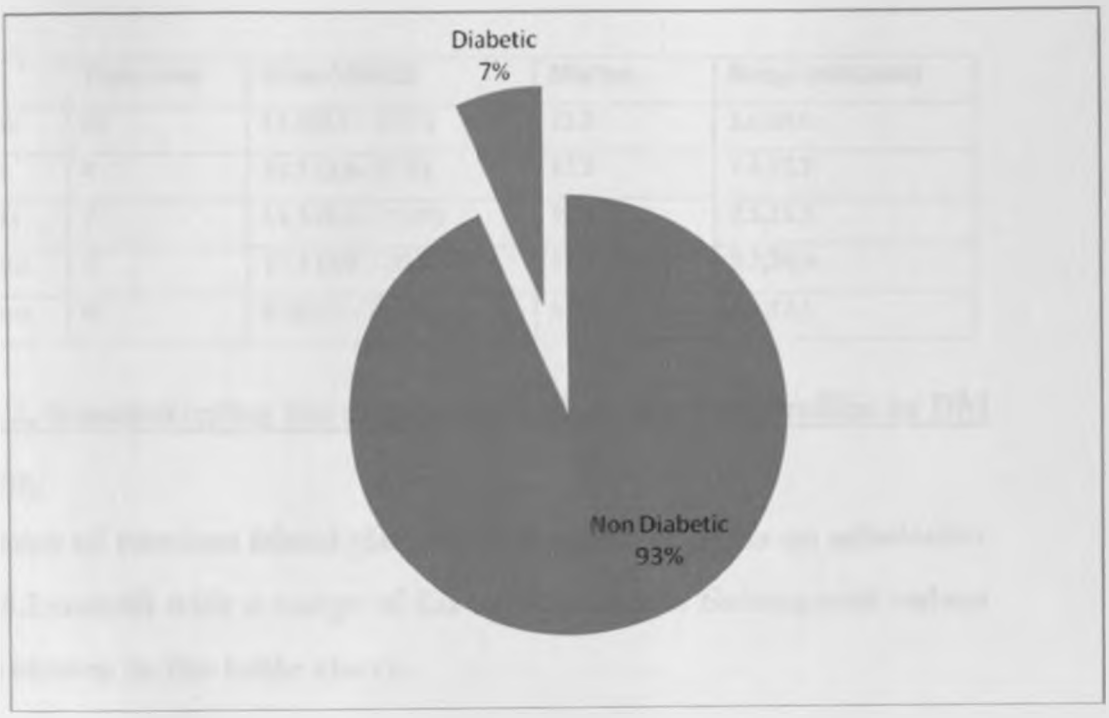

Figure 6. showing the distribution of Diabetes Mellitus among patients in the study population.

From the study population, only 13(7%) patients had diabetes mellitus diagnosed and/or confirmed elsewhere prior to admission into the CCU-KNH.

	Tests done	Mean 95%CI	Median	Range (min,max)
Admission	12	13.1(8.5 – 17.7)	13.8	3.6,30.6
0-6 hours	4	14.7 (2.0- 27.4)	12.8	7.4,25.7
6-12 hours	7	11.5 (8.1 – 15.0)	12.2	7.5,15.5
12-18 hours	7	13.1 (5.9 – 20.3)	11.2	3.7,24.9
18-24 hours	6	8.7(3.7 – 13.6)	6.5	5.1,17.1

Table 2. demonstrating the measures of blood glucose profiles in DM patients.

The mean of random blood glucose in diabetic patients on admission was 13.1mmol/l with a range of 3.6 to 30.6mmol/l. Subsequent values are as shown in the table above.

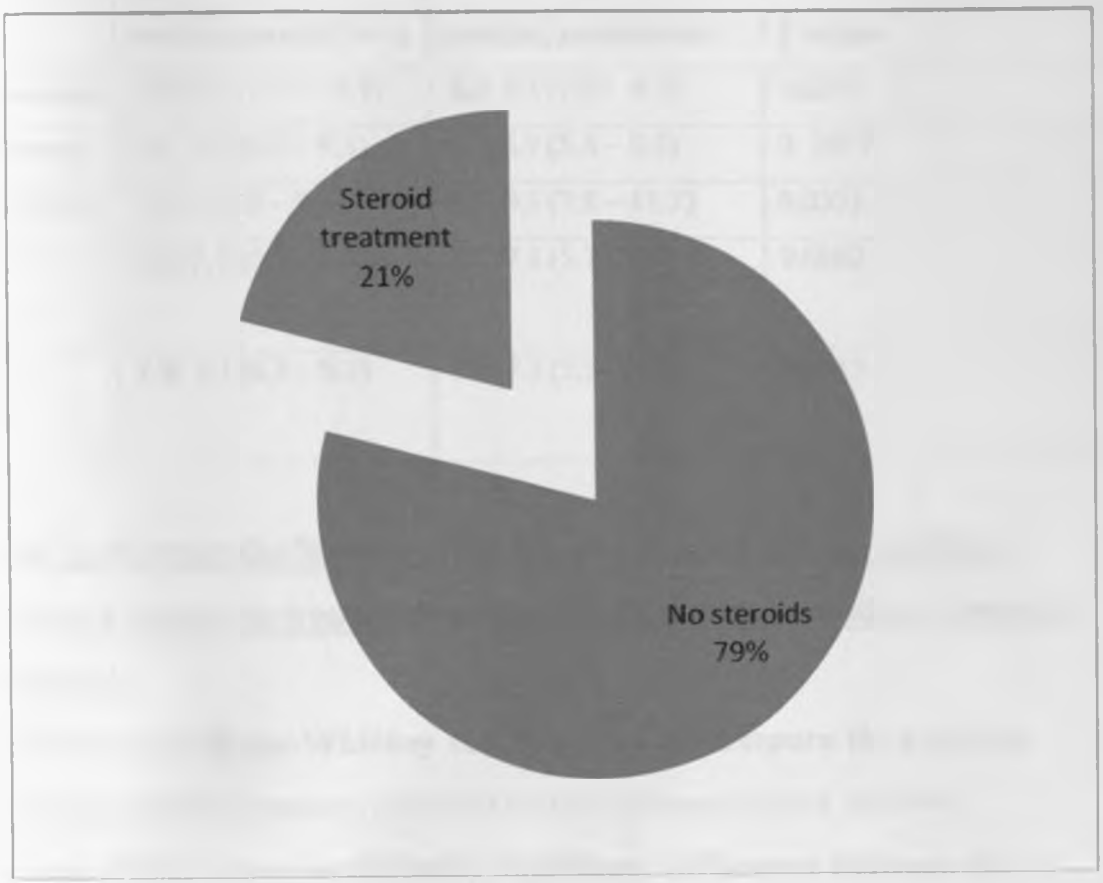

Figure 5. showing the distribution of patients with respect to treatment with steroids in study population.

A total of 41 patients out of the total 196 patients were on treatment with steroids for one reason or another. These steroids were started at the time of admission of the patients into the CCU-KNH.

	No steroids Rx	Steroid Rx	
	median,mean(95%CI)	median, mean(95%CI)	P value
Admission	7.25, 8.1 (7.3 – 8.7)	7.5, 8.2 (7.0 – 9.3)	0.6241
0-6 hours	6.8, 7.9 (6.5 – 9.5)	6.7, 6.9 (5.4 – 8.4)	0. 7017
6-12 hours	7.3, 8 (6.8 – 9.2)	8.8, 9.5 (7.8 – 11.2)	0.0351
12-18 hours	6.3, 7.4 (6.5 – 8.3)	7.1, 7.3 (5.7 – 8.8)	0.6862
18-24 hours	7.0, 7.2 (6.3 – 8.2)	7.0, 7.3 (5.3 – 9.3)	0.9615

Table 3, showing the Medians and Means of blood glucose profiles between patients on treatment with steroids and those without steroids treatment.

The Wilcoxon-Mann-Whitney test was used to compare the random blood sugar levels among patients on steroids and those without steroids. There was a statistically significant difference between the blood sugar levels of those on steroid treatment and those without at 6-12 hours as illustrated above.

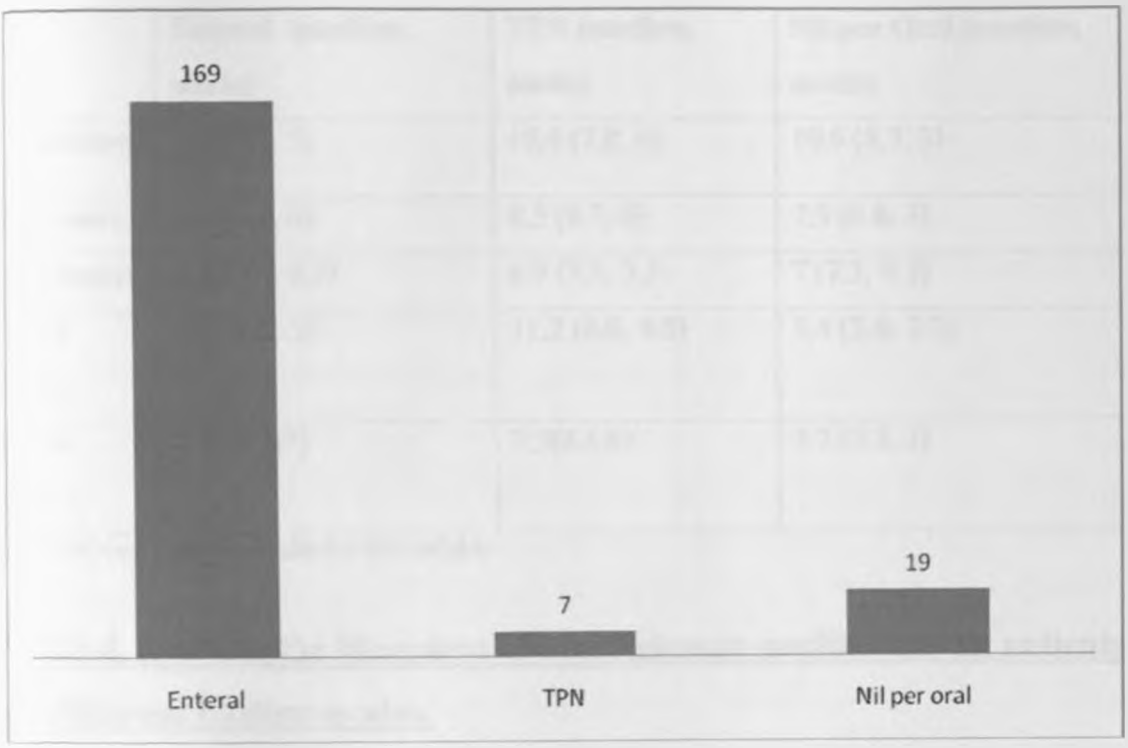

Figure 6. demonstrating the feeding mode amongst the study subjects.

The commonest mode of feeding was through enteral route representing 86.7%, followed by patients who were not on any mode of feeding with 9.7%. These were patients e.g. who were admitted from the operation theatre, had contraindications for enteral feeding such as gut surgery and TPN had not been initiated. Such patients were noted to have dextrose containing solutions included in their usual maintenance intravenous fluids. The rest were on total parenteral nutrition.

	Enteral (median, mode)	TPN (median, mode)	Nil per Oral (median, mode)
Admission	7.7 (7.3, 5)	10.4 (7.8, 6)	10.6 (8.3, 2)
0-6 hours	7.6 (6.7, 6)	8.3 (8.3, 6)	7.8 (6.8, 3)
6-12 hours	8.7 (7.6, 6.3)	6.9 (7.3, 5.5)	7 (7.3, 9.3)
12-18 hours	7.4 (6.6, 5)	11.2 (8.8, 4.8)	5.4 (5.4, 3.7)
18-24 hours	7.5 (7, 0*)	7.5(8.6,6)	3.7 (3.7, 3)

*=There were multiple modes for this variable

Table 4, showing the Measures of blood glucose profiles among patients on different feeding modes.

All the blood glucose values were non-fasting as the patients were on different modes of nutrition. Patients on nil per oral status were on continuous infusion with dextrose containing solutions.

Kruskal-Wallis test was used to determine if there was a statistically significant difference in the blood sugar levels of patients fed using different modes. There was no statistically significant difference in the blood sugar levels among the different feeding modes, (The p-value was 0.8596).

DISCUSSION

The study was carried out among the critically ill patients admitted in the critical care unit at Kenyatta National Hospital, (CCU-KNH). Approval to carry out the study was duly granted by the Kenyatta National Hospital/University of Nairobi Research and Ethics Committee. Data collection was carried out during the months of February, March and April, 2009. A total of 196 patients were recruited into the study. The majority of the patients in the study sample were male representing 56% of the total sample.

The mean age was 32.2 years with median of 30 years and a mode of 30 years. The range was 4 months to 89 years. This wide range reflects the wide variety of ages of the patients admitted to the critical care unit at Kenyatta National Hospital. This is because the CCU-KNH being in a tertiary and referral health facility receives patients of all ages. There are no sub-specialized critical care units in KNH, besides neonatal intensive care unit, to take care of special groups such as pediatric, neurosurgical, cardiac patients among others.

A total of a hundred and ninety three random blood sugars as measured at the time of admission of the patients to the CCU-KNH were done. Three patients recruited into the study did not have their admission random blood sugars done.

The mean of these was 8.1mmol/l with a median of 7.3mmol/l and a mode of 5.0mmol/l. The range was 2.1 to 30.6mmol/l. These glucose values were essentially non-fasting values as none of the patients recruited was fasting during the duration of follow up. The means of the random blood sugars at admission compares closely with those of patients in the conventional treatment group in a study on benefits of intensive insulin therapy in 1548 critically ill patients in a surgical intensive care unit by Greet Van Berghe[13] et al. The patients in the conventional treatment group received intravenous insulin only if their blood glucose levels exceeded 11.9mmol/l. Their morning blood glucose level was maintained at a value of 8.5mmol/l. This shows that majority of the patients admitted to the CCU-KNH have random blood sugars that largely within normal range at the time of admission into the unit.

Subsequently after admission into the CCU-KNH, a total of two hundred and sixty five random blood sugars were done on these patients. This translates to less than 2 blood glucose measurements per patient over a twenty four hour stay in the CCU-KNH.

This falls short of the expected total number of seven hundred and eighty four random blood glucose measurements that were anticipated if each patient was to have a random blood glucose done at least once every 6 hours while in the unit as recommended by some studies[21,32] and as per the expectations of this study. Some studies recommend blood glucose determinations to be done as frequently as one hourly. This is especially so in critical care units that tend to lean towards intensive glycaemic control and have adequate resources to avoid the relatively higher prevalence of blood glucose derangements and the associated adverse events[33,34].

There was no statistically significant difference between the random blood glucose done at admission and subsequent random blood glucose done while the patients were in the CCU-KNH within the first twenty four hours.

This could mean that the patients' glycaemic profiles did not change significantly when compared at the time of admission into the CCU-KNH and on subsequent follow up for twenty four hours of stay in the unit. With regard to the few cases of deranged blood glucose values encountered in this study, majority were hyperglycaemia as compared to hypoglycaemia. For in stance at admission, out of the one hundred and ninety three random blood glucose determinations done, 11.4% were hyperglycaemic and 1% was hypoglycaemic and the rest were within the normal range. The CCU-KNH staff on duty were duly informed by the researcher and/or his assistant about all the patients noted to have deranged blood glucose levels so as to take appropriate corrective measures.

Upon admission into the unit, almost similar pattern of glycaemia were noted, for instance at between 6 and 12 hours of admission, of the 77 random blood glucose determinations done, 2.6% were hypoglycaemic, 4.3% were hyperglycaemic while the rest were within normal range. These values are higher than the values in the conventional treatment groups in the NICE-SUGAR study[29] where hypoglycaemia occurred in 0.5% of the patients, and in 0.8% of the patients in the Greet Van Den Berghe study[13].

It is worth noting that the patients who had deranged blood glucose values at admission were not necessarily the same patients that had deranged blood glucose values later on follow up in the unit. This could imply that the factors predisposing critically ill patients to glycaemic derangements prior to admission to the CCU-KNH are not

necessarily the same factors that predispose the same patients to glycaemic derangement while in the CCU-KNH. It could also imply that sufficient corrective measures are taken on admission of the patients to the CCU-KNH soon after the deranged blood glucose levels are noted with the development of glycaemic derangement occurring in other patients on various stages of varied acute illnesses.

While a follow up duration of twenty four hours appears short to state that majority of the critically ill patients in the CCU-KNH have random blood glucose values that are mostly within normal range, further research incorporating longer follow-up duration combined with more regular and frequent measurement of the random blood glucose may need to be carried out to authoritatively arrive at such a conclusion[35].

It is also apparent from these findings, that there is need to do more frequent and regular blood sugars for the patients admitted in the CCU-KNH so as to have a more lucid picture of the blood sugar patterns for all the critically ill patients admitted in the unit[13,29]. This is because glycaemic levels can change suddenly and as such if there are no frequent and regular blood glucose determinations done, the staff at the critical care unit is bound to miss episodes of either hypoglycaemia or hyperglycaemia. These scenarios could be worsened by the fact that patients in the critical care unit may be sedated and /or paralysed or their neurological status could be depressed or altered by the illness that resulted in their admission into the unit. Hence they may not show overt or obvious signs and symptoms of either hypoglycaemia or hyperglycaemia[34].

The need to do more frequent blood glucose determinations was also recommended by Meijering S. et al[21] after a systemic review of literature regarding the implementation of a feasible glucose regulation protocol. Some of their recommendations were that first to choose a blood glucose target such as between 4 and 8 mmol/l. How low a target to set depended on local possibilities such as personel, workload, fast and accurate point-of-care blood glucose determination among other factors. Other factors to consider included the prevailing mean blood glucose level before starting a protocol. Secondly they suggested that it would be preferable to use a dynamic scale protocol with continuous insulin infusion combined with frequent determination such as hourly to four hourly and to use the last two blood glucose values to determine the insulin infusion rate. It was however found out that frequent blood glucose determinations imposed increased

nursing workload and acceptance of the protocol by the nursing staff is very important for successful implementation.

This is in contrast to the recommendation from the NICE-SUGAR study, (2006) by Atherton S. et al[29] on intensive versus conventional glucose control in critically ill patients. In this study they recommended that a blood glucose target of less than 10.0mmol/l or less resulted in lower mortality (24.9%) than a strict control at between 4.5- 6.0mmol/l, (mortality of 27.5%). The findings from their study therefore discouraged lower target of blood glucose control in the critically ill patients. This appears to favour the conventional glucose control practice at the CCU-KNH which is based in a resource-limited set up of a developing country.

The corrective measures taken when elevated random blood sugars were encountered in the critically ill patients included starting an infusion with soluble insulin or increasing the dosage if such an infusion was already in place (55%), administration of a stat dose of subcutaneous/intravenous soluble insulin (36%), and stopping the infusion of dextrose containing solutions if such a solution was running in a patient found to have hyperglycaemia (9%).

Corrective measures taken in those patients with episodes of hypoglycaemia mainly involved intravenous administration of varied strengths of dextrose containing solutions. These included the use of 50%, 25%, 10% or the 5% dextrose solutions. The 50% and 10% dextrose containing solutions were the more commonly used ones-both were used in 66% of the patients, with 25% and 5% dextrose containing solutions being used in the rest of the patients. The administration was either as a bolus infusion or initiation of a continuous intravenous infusion. Unfortunately there was no way of telling if these corrective were effective or not as only five entries were encountered during this study despite encountering a greater number of deranged random blood sugars. Analysis of these data would have yielded inaccurate results. Such a low number of entries might mean poor documentation of the measures taken or failure to recheck the patients' blood sugar levels after instituting the relevant corrective measures. Data on other possible measures taken such as review of the frequency, type or the amount of feeds given was not available.

This situation is worsened by the fact that in the CCU-KNH, there was no chart dedicated purely to the management of the patients' blood sugars at the time that this study was carried out. As a result, information such as the latest blood sugar levels and the current mode of treatment for deranged blood sugars are not available at a glance. Instead one had to check through the patients' pile of different charts to get the particular information on blood sugars. This was not easy and it increased chances of missing out on important opportunities to optimize on the glycaemic control. The KNH-ICU/HDU protocols do not stipulate any particular chart on which to record the regular/random blood glucose determinations[36].

It was also evident that the measures taken to correct deranged blood sugars were rather short term based. At the same time, some of the measures taken such as infusion of 5% dextrose in patients with hypoglycaemia may not be very effective especially if the underlying cause is not found and addressed. It was not always evident in this study that some of the underlying problems leading to deranged glycaemic control were conclusively and effectively addressed. For instance, in patients with hypoglycaemic episodes, besides administering intravenous dextrose solutions, endeavours aimed at identifying the root cause of the low blood sugars, such as inadequate or poorly planned nutritional plan, should be instituted. This holistic approach is more likely to curtail recurrence of similar episodes of deranged glycaemic levels and the associated complications[29,31].

The number of critically ill patients in this study who were confirmed to have diabetes mellitus was 7%. This is rather high compared to the prevalence of type 1 diabetes mellitus of 0.01% and 2.4% for diabetes mellitus type 2 in sub-Saharan Africa as found in some studies[28]. One of the possible explanations for this discrepancy could be the fact that the CCU-KNH is in a tertiary and referral health facility that is located in an urban setting where the prevalence of diabetes mellitus, especially type 2, are known to be higher[27]. At the same time, the unit also admits critically ill patients from other health facilities including those with complications of diabetes mellitus that call for management in the critical care unit. Another possibility is that diabetes mellitus could also be predisposing patients to be more likely to be admitted into the CCU-KNH because of the associated acute complications that warrant intensive care. Some of the

complications in the diabetic patients admitted in the critical care unit included diabetic ketoacidotic coma, acute renal failure and congestive cardiac failure. As such, the CCU-KNH patient population is unlikely to be representative of the general population. In view of the fact that the data between the patients with diabetes mellitus and those without was very asymmetrical, (13 versus 183 respectively), comparative analysis was not done as it would have resulted in inaccurate results.

There were 42 patients in the study who were on treatment with steroids. This was 21% of the total study population. The difference in glycaemic profile, both at admission into the CCU-KNH and the subsequent 24 hour profile, was not statistically significant between those on treatment with steroids and those who were not on treatment with steroids as demonstrated by p-values greater than 0.05. The only exception was in the 24 hour blood sugar profile at between 6-12 hours stay in the CCU-KNH between those on and without steroids where the difference was statistically significant with a p-value of 0.0351. A possible explanation for this statistically significant difference in blood glucose between those on steroids and those without is as follows; since the steroids are started at around the time of admission in to the unit and they take around 6 hours to take effect, the blood glucose levels are bound to be higher after 6 hours in those patients on steroids compared to those without.[30] After this time, corrective measures are bound to have been instituted in the patients with hyperglycaemia and hence the lack of a significant difference in blood glucose values between diabetics and non-diabetics 12-18 hours and 18-24 hours.

Majority of the patients, (86.7%), were on enteral mode of nutrition. This was well in line the recommendations that advocate for enteral nutrition in critically ill patients. In one study, clinical improvement was noted to be greater in patients with acute pancreatitis receiving enteral, (nasojejunal tube), feeding rather than total parenteral nutrition[37].

There was no statistically significant difference between the blood sugar profiles of the patients on the different modes of nutrition as demonstrated by the kruskal-Wallis test, (p-value 0.8596). This could be taken to imply that the two modes of feeding, i.e. enteral, total parenteral nutrition were achieving their primary objective of meeting the patients' glycaemic requirements. The fact that patients on nil per oral status also had

blood glucose levels that were not significantly different from those on other modes of feeding could mean this status was not allowed to be longer than necessary to predispose these patients to hypoglycaemia or that the intravenous dextrose these patients were put on was sufficient to meet their glycaemic needs.[31]

CONCLUSION

1. It's apparent from this study that critically ill patients admitted in the CCU-KNH have blood glucose levels that are largely within relatively normal range.
2. It is not possible, from this study, to tell the factors that could be contributing to glycaemic derangements in the few patients who were found to have deranged blood glucose values. However, mode of nutrition and whether or not the patients were on treatment with steroids did not seem to affect significantly the glycaemic control of the critically ill patients admitted at the CCU-KNH.
3. From this study, commonest corrective measure taken in patients with hyperglycaemia was stoppage of infusion with dextrose containing solutions. In patients with hypoglycaemia, the commonest corrective measure taken was to infuse dextrose containing solutions.
4. It was not possible to evaluate the effectiveness of the corrective measures so taken in those patients with deranged blood glucose levels because significant data on the same was missing from the patients records.
5. It was noted that there is no chart dedicated purely to recording details on glycaemic control in the critically ill patients.
6. In addition, the frequency at which random blood glucose determinations are done is rather on the lower side. As such there is need to come up with a chart to record details regarding blood glucose management and to optimize on frequency of blood glucose determinations.

RECOMMENDATIONS

The following recommendations were made as an attempt to fill in the gaps that might be in existence in the management of the critically ill patients at the CCU-KNH regarding the achievement of optimal blood glucose control.

1. There is need to do more frequent blood glucose measurements for each patient and/or on regular basis so as to pick episodes of either hypoglycaemia or hyperglycaemia. This is more applicable especially in patients with labile blood glucose levels. In this regard, guidelines on glycaemic control in the critically ill patients the CCU-KNH may need to set up for purposes of uniformity. Such guidelines should stipulate a target blood glucose range to achieve and the corrective measures to institute in cases where the glucose values get out of this target range.
2. It would be prudent to have proper documentation of blood glucose management plan. This can be achieved by having a chart that will indicate the blood glucose levels, dosage of insulin or oral hypoglycaemic agents the patient is on if any and measures taken in instances of blood glucose derangements. This visual charting tends to make sudden changes in blood glucose levels more obvious and therefore trigger appropriate relevant corrective measures.

STUDY LIMITATIONS

1. This was a cross-sectional study. As such the researcher did not determine the way blood glucose management is done at the CCU-KNH, e.g. the frequency at which blood glucose determinations are done or proper documentation of the same. Therefore in situations where, for instance, corrective measures were taken for deranged blood glucose and documentation was not done, this study may have missed out on such data.
2. The study did not factor in the various types or brands of feeds for the various modes of nutrition as these may have a bearing on blood glucose levels because of their varied composition.
3. The study did not consider the differences in the dosages and subtypes of the steroids that the patients were on as these may have a bearing on the glycaemic levels in those who were on steroid therapy.

APPENDIX 1a

CONSENT EXPLANATION

Dear participant

I am Dr. Ng'ang'a W. Kuria, a postgraduate student in Anaesthesia at the University of Nairobi. I am conducting a research study on blood sugar control at the critical care unit at Kenyatta National Hospital.

The findings of this research study will be useful in the management of the critically ill patients in this hospital and the country as a whole. The research study will be in the form of a data collection tool. Strict confidentiality will be maintained; the collected data will be used purely for research purposes.

Please, confirm that you have accepted to take part in this research study by completing the consent form provided to you.

APPENDIX 1b

UFAFANUZI WA MAKUBALIANO

Jina langu ni dak. Ng'ang'a W. Kuria, mwanafunzi katika chuo kikuu cha Nairobi. Ninafanya utafiti kuhusu jinsi vipimo vya sukari kwenye damu vinavyo thibitishwa katika wagonjwa mahututi katika hospitali kuu ya Kenyatta.

Habari ambayo itatokana na utafiti huu itakuwa ni ya maana sana kwenye matibabu ya wagonjwa mahututi hapa hospitali ya Kenyatta na nchi kwa jumla. Utafiti wenyewe utakuwa kwa njia ya fomu ya kuandikia habari. Habari hii itakuwa ni siri na itatumika kwa utafiti pekee.

Tafadhali onyesha ya kuwa umekubali kuhusika kwenye utafiti huu kwa kujaza fomu ya makubaliano utakayopewa.

APPENDIX 2a

INFORMED CONSENT FORM.

I .....agree to take part in this study/allow my relative to take part in this study, as explained to me by.....with all the risks and side effects that may occur. My participation is fully out of my own free will and not due to any benefits, direct or indirect, I may or may not gain from the study.

Participant's signature.....Date.....

I, the researcher, have explained fully to the participant/participants relative about the study, its benefits and side effects, and have not withheld any information regarding the study. I have also assured the participant of his or her confidentiality during the study, and in case he or she withdraws from the study.

Researcher's signature.....Date.....

APPENDIX 2b

FOMU YA MAKUBALIANO YA KUJIUNGA NA UTAFITI

Mimi.....

kutoka.....

nimeitikia kushiriki/nimeruhusu jamaa yangu kushiriki katika uchunguzi huu. Na ya kwamba hakuna pesa au mapato yoyote nitapewa ili kushiriki kwenye utafiti huu.

Nimeridhika na maelezo niliopewa na.....na najitolea kushiriki/kuruhusu jamaa yangu kushiriki kwa hiari yangu katika uchunguzi huu wa kuangalia jinsi vipimo vya sukari kwenye damu vinavyo thibitishwa katika wagonjwa mahututi katika hospitali kuu ya Kenyatta.

Sahihi ya mshiriki.....Tarehe.....

Anayeshiriki / mwangalizi amefahamishwa kuhusu aina ya uchunguzi huu,na kuwa habari ambayo itatokana na utafiti huu itakuwa ni siri kati ya daktari,mshiriki na hospitali hata ikiwa mshiriki ataamua kujiondoa kwenye utafiti huu.

Sahihi ya mtafiti.....Tarehe.....

APPENDIX 3

QUESTIONNAIRE

Code No. *001* Date of data collection.....

In-Patient Number _____

1. Age.....
2. Sex .....a. male .....b. female .....
3. Diagnosis _____
4. No. of days in the CCU _____
5. Random blood sugar (in mmol/l)
   a. on admission _____
   b. Post corrective measures (mmol/l) if deranged _____
6. 24-hour blood sugar profile (mmol/l) at;0-6hrs,6-12hrs,12-18hrs,18-24hrs.
7. If the random blood sugar is out of range, what corrective measures were taken for-
   a. hyperglycemia?
   b. hypoglycemia?
8. Known diabetes mellitus patient?
   a. Yes
   b. No
9. If yes, the current treatment for diabetes mellitus?
   a. Insulin
   b. Oral hypoglycemic agents
   c. Diet control
10. Treatment with steroids?
    a. Yes
    b. No
11. Mode of feeding
    a. Enteral
    b. Total parenteral nutrition
    c. Mixed.
    d. Nil per oral.

APPENDIX 4

Budget

Item	Cost per unit (ksh)	No. of units	Total cost (ksh)
Consultancy (Biostastician)	-	-	15,000
Research assistant	-	-	5,000
Printing paper & printing cost	-	-	4000
Flash disk	1500 (1GB)	2	3000
Photocopying cost	3	600	1800
E.R.C. Fee	-	1	1000
Binding	100	8	800
Pens & pencils	20	5	100
Miscellaneous			1900
TOTAL			**32,600**

APPENDIX 5

IMPLEMENTATION PLAN.

ACTIVITY	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr
Proposal Writing	√	√	√	√	√	√	√	√					
Presentation to Ethical Review Committee									√				
Pilot Study								√					
Data Collection									√	√	√		
Data Processing											√	√	
Report Writing												√	
Study Presentation													√

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Ref: KNH/UON-ERC/ A/177

31st March 2009

Dr. Ng'ang'a W. Kuria
Dept of Surgery
School of Medicine
University of Nairobi

Dear Dr. Ng'ang'a

RESEARCH PROPOSAL: "GLYCAEMIC CONTROL IN THE CRITICALLY ILL PATIENTS AT THE CRITICAL CARE UNIT, K.N.H." (P339/12/2008)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your above revised research proposal for the period 31st March 2009 –30th March 2010.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF. A N GUANTAI
AG. SECRETARY, KNH/UON-ERC

c.c. The Chairperson, KNH/UON-ERC
The Deputy Director CS, KNH
The Dean, School of Medicine, UON
The Chairman, Dept of Surgery, UON
Supervisor: Dr. T.M. Chokwe, Dept. of Surgery, UON

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