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Since last three decades introduction of intensive care units for the management of critically ill patients has shown steady improvement in both monitoring and vital organ support. In parallel fashion growing recognition of hazards of weight loss in the critically ill patients led to provide intravenous nutrition and ultimately to the introduction of total parenteral nutrition (TPN). Protein catabolism (negative nitrogen balance) and lipid catabolism occurs to fulfill the extra energy for wound healing, cellular inflammatory response and hepatic synthesis of acute-phase reactant proteins (Clowes, *et al.,* 1980). The past decade has been a shift in focus concerning the regulation of metabolic changes in injury and infection. The counter regulatory hormones have been considered responsible for the stress response. The role of insulin in the feed/fast cycle is used as background for the consideration of metabolic changes in injury and the related factors that contribute to Insulin resistance.

Biochemical analysis of various parameters in critically ill gives idea regarding existing metabolic state of the patient, degree of negative nitrogen balance, adequacy of treatment and nutrition.

The present study was carried out with a view to detect protein calorie malnutrition, effect of various disease processes on protein/carbohydrate metabolism and predicting outcome of the illness. In particular for the assessment of protein energy status (only one part of overall nutritional status), no single test or technique has been found to be both a sensitive and specific indicator of malnutrition. The present study is an attempt to reevaluate the routinely used methods of assessing nutritional status in two different hospitals and three groups of patients.

In patients having multiple fractures, or those who have undergone major surgery and those with multiple organ failure (MOF), plasma proteins like serum albumin and serum transferrin decreased significantly on second day as compared to the control group, this could be because of the increase in trans-capillary escape of proteins in extra-vascular space due to shock like state in critical illness. Also the circulating levels of these proteins are affected by large fluid shifts associated with shock and resuscitation (Fleck, 1988). The serial fall in serum albumin and serum transferrin observed in, multiple fractures and major surgery, groups in both the hospitals, can be explained by the fact that, fasting / undernourishment decreases availability of amino acids substrates to liver for synthesis of these proteins (Fleck, 1988). Moreover, the synthesis of acute phase reactant proteins occurs preferentially over that of visceral proteins regardless of nutritional status (Shaw *et al.*, 1987). Studies in rats and man have indicated that hypoalbuminemia which followed burn or bony injury was a consequence of increased catabolism and reduction in albumin synthesis together with a change in compartmentalization of body albumin. The data gathered showed that, serum transferrin level fell significantly from second to fourth day period but from fourth to eighth day it did not fall significantly, whereas in this period albumin continued

falling steadily (tables 1 and 3). This could be because of different molecular weights of these proteins (Transferrin 80,000, Albumin 65,000) that would not allow them to diffuse freely across the compartments of the body fluids (Shenkin *et al.,* 1980). Thus albumin may diffuse out of the intravascular compartment due to shock and continue giving low serum albumin and the same would not occur with transferrin because of the higher molecular weight of the latter.

Major surgery, multiple fractures and multiple organ system failure, all critical situations give similar impact on protein catabolism in form of almost identical fall in levels of serum albumin and transferrin in serial estimation among all three groups. In patients having malaria and other infestations, because the liver function was primarily impaired due to disease itself and the patients were hospitalized quite late in the intensive care unit, they had comparatively lower albumin and transferrin on second day of inclusion in study. Later on the serial fall in these protein levels in this subgroup of MOF was comparable to other groups of patients. Thus presence of liver disease itself decreases serum protein synthesis significantly so it becomes non-specific indicator of protein metabolism status in presence of liver dysfunction.

The magnitude of albumin and transferrin fall was almost similar in all three groups of patients in both the hospitals (Tables 2,4,8,10). Thus showing that both the proteins even-though having different molecular weight and half-life, are equal indicators of protein metabolism. Ingelbleek *et al*, (1975) showed that plasma transferrin is more sensitive to change in nutritional status than albumin. Our study showed that albumin is equally sensitive for change in protein metabolism.

Thus it becomes evident that protein calorie malnutrition alone is not the only factor that would decrease serum protein levels but, even

compartmentalization of body fluids with proteins, other diseases like sepsis, liver disease also affect levels of these proteins significantly in blood. Hence estimation of serum proteins in initial period of critical illness becomes poor indicator of nutritional status and similarly in presence of liver diseases or sepsis it does not correlate well with nutritional status. Thus serial measurements of these proteins in blood may be useful in monitoring the response to nutritional support later in the course of illness.

Hypoalbuminemia is frequently correlated with morbidity and mortality in critical illness. Harvey *et al*, (1981) showed association between hypoalbuminemia and occurrence of sepsis or prolonged recovery. We could not find such association. Morbidity and mortality was found only MOF group, where it was correlated well with the basic disease process like malaria, renal failure, cardiac failure, and septicemia.

Significant fasting hyperglycemia was observed in all groups of patients as compared to control group of patients (Table 11). This was associated with fasting hyperinsulinemia (Table 12). For a given plasma insulin levels the corresponding glucose levels were significantly higher in critically ill patients, that represents the state of *insulin resistance* as observed by Allison *et al.*, (1968) and Black *et al.*, (1982). Wolfe *et al* (1987) has documented increased glucose cycling in patients with burns and an enhanced glucose production seen in critically ill reflects both synthesis of new glucose from amino acids and recycled glucose from lactate. Kinney (1977) has speculated that the increased glucose production is adaptive, as it may provide a substrate for synthesis of acute phase glycoproteins and for connective tissue requirements of glucosaminoglycans and fibroblasts. Glucose also serves as a fuel for many cell types in healing wounds (Im *et al.*, 1970).

Insulin secretion shows parallel rise in response to hyperglycemia but other hormones like catecholamines, glucocorticoids antagonize the insulin activity and thereby results in the maintenance of a persistent hyperglycemic state. Glucocorticoids inhibit the ability of insulin to mediate the recruitment of glucose transport protein from the cell interior to the cell surface. It also causes decrease in number of insulin receptors and its affinity of receptors for insulin (Nordenstrom *et al.*, 1983). Thus despite the increased mass flow of glucose during critical illness, patients are usually intolerant to exogenous glucose administration (Wolfe *et al.*, 1979, 1980). This apparent limitation in the ability to utilize glucose during critical illness is related to severity of illness (Wolfe *et al.*, 1979, 1980, Black *et al.*, 1982). Therefore, in ICU the most seriously ill patients are progressively less able to utilize glucose to meet their total energy requirements. This forms the basis for formulation of parenteral nutrition in critically ill patients. In diabetic patients also the hyperglycemia is exaggerated due to critical illness as observed in three of our patients who had preexisting diabetes in MOF group. The existing state of insulin resistance correlated well with the increased dose requirements of insulin in the treatment of these patients.

Biochemical parameters like blood urea and / or creatinine represent the kidney function of an individual. In critical illness presence of shock like state can affect kidney perfusion and can cause elevations in blood levels of urea and creatinine (Azotemia). Azotemia was observed in some of the MOF patients. This is because in MOF group of patients the kidney function is pathologically affected by the existing disease state e.g. in patients having Malaria and Leptospirosis. The infecting organisms directly damage the kidneys and decrease glomerular filtration rate (GFR) thereby, decreases the clearance of nitrogen wastes (urea and

creatinine) in urine (Nicholas and James). In patients of cardiac failure also similar rise in urea and creatinine was observed. Here, reduced GFR was secondary to reduced renal perfusion resulting from diminished cardiac output.(Table 15).

As such serial measurement of urea and creatinine is very useful in critically ill because these patients are at higher risk of getting volume depletion, circulatory shock, infection, etc which affect kidney function; thus becoming a useful guide in evaluating the course of critical illness.

Serum electrolytes like Na^+ (sodium) and K^+ (potassium) are very important informants of fluid and electrolyte status in critical illness. Its serial measurement not only precludes the deadly complications like cardiac arrhythmia in case of hypokalemia (low serum K^+), but also helps in monitoring the response to fluid therapy and size of extra cellular fluid compartment. Hyponatremia (low serum sodium) (Table 16) seen in patients of pancreatitis was not really associated with the clinical features of low sodium levels, it could be an artifactual hyponatremia because of hyperlipemia occurring in pancreatitis, as in sever hyperlipemia part of any unit volume of plasma taken for analysis would be lipid which is sodium-free and therefore plasma sodium is measured falsely low (Norman, 1991).

High serum potassium (Table 16) was seen in all patients of MOSF except for pancreatitis in initial estimation could be because of acidosis that was present in most of these patients due to one or other cause. In metabolic acidosis potassium (a principally intracellular cation) comes out of the cell and hence its concentration is higher in plasma. Potassium plays important role in impulse conduction and muscle contraction of heart. Hypo/hyperkalemia both cause cardiac arrhythmia and sudden death. Thus frequent estimation of serum potassium is mandatory.

Arterial blood gas analysis (Table 17) done in critically ill patients in intensive care unit becomes a very important and basic investigation tool. It gives varied information regarding metabolism, respiratory system, kidney function and circulatory system. Acidic pH seen in patients with MOF with sepsis and in those having cardiac and respiratory failure was because of lactic acidosis resulting from anaerobic metabolism in hypoxemic tissues because of poor tissue perfusion. In septicemia there is shock and hypotension, which causes decrease in peripheral blood circulation, whereas in cardiac failure the same was caused by poor pumping function of heart. Since acidosis causes significant changes in electrolyte status of body fluids and causes direct myocardial depression it becomes mandatory to know pH of the blood repeatedly and precisely in these patients. Arterial blood pH also gives idea about adequacy of compensation mechanism (renal or respiratory) for acidosis or alkalosis and thereby the function of that particular organ.

Carbon dioxide (CO_2) in arterial blood mentioned as $PaCO_2$ was significantly found lower in all MOF patients. Low $PaCO_2$ almost always indicates CO_2 "WASH OUT" in respiration due to hyperventilation. In cardiac and respiratory failure hypoxia was responsible for reflex respiratory stimulation and hence the CO_2 "WASH OUT', the same occurred in metabolic acidosis as a respiratory compensatory mechanism to wash out an acid in form of CO_2. Thus arterial CO_2 is an important indicator of respiratory function.

Hypoxia in our patients of MOF was because of poor oxygenation of blood in lungs due either to infection in lungs or alveolar edema due to cardiac failure or non-cardiogenic edema of adult respiratory distress syndrome (ARDS). Hypoxia causes dysfunction of vital organs like heart, brain and many other tissues and if

not treated in time, it can lead to death. Thus serial measurements of PaO_2 (arterial oxygen) help in knowing the seriousness of disease, response to the treatment and outcome of the disease.

Bicarbonate in arterial blood is an important buffer system for acid base balance. In our study all patients who had acidosis were having metabolic acidosis showed low bicarbonate in blood, as the bicarbonate ion is used to neutralize excessive H^+ ions in body in acidotic state.

Even though biochemical parameters showed same variations among all three groups, the morbidity and mortality were seen only in MOF group. In this group the mortality was almost 35% and all other patients had long and morbid course of disease compared to patients of major surgery and multiple fractures. Among MOF patients, cardiac/ respiratory/ renal failure, septicemia, pulmonary edema, liver failure were important leading causes of death. Thus vital organ function is more important determinant of outcome of critical illness than mere biochemical parameters like serum proteins, blood sugar etc.