The Value Of Blood Urea Nitrogen To Plasma Creatinine Ratio In Distinguishing Upper And Lower Sites Of Gastrointestinal Hemorrhage

Thesis
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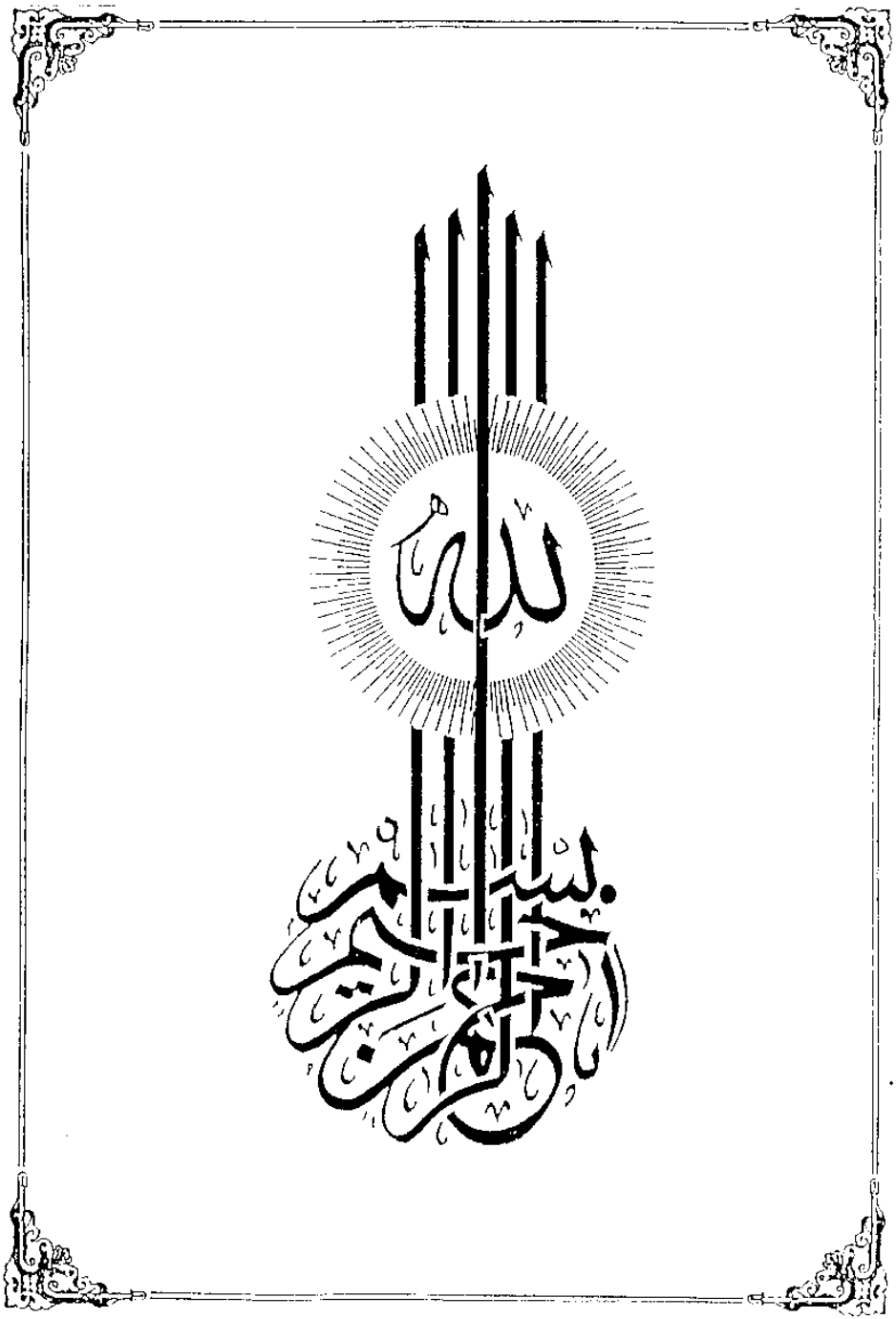

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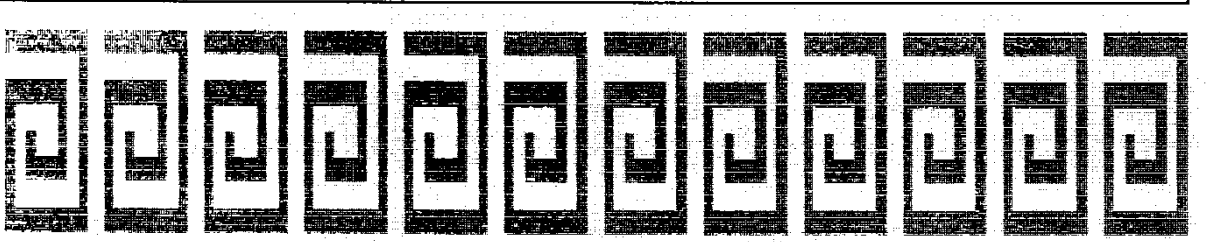


The value of blood urea nitrogen to plasma creatinine ratio in distinguishing upper and lower sites of gastrointestinal hemorrhage

Introduction :-

Inspite of the great advances in the procedures investigating gastrointestinal tract bleeding, in a good number of cases, the differentiation between upper and lower sites of bleeding represent a problem, especially in emergency cases. Also, in cases passing altered blood per rectum the diagnosis may be reached only after extensive and costly investigations of the whole GIT. ***Richardson et al., (1975)*** reported that the color of the blood passed per rectum is related to transit time within the bowel rather than the site of original bleeding, and so the color of the stool is not usually indicative for the site of bleeding.

Hence, great interest was directed towards the research for simple and reliable biochemical methods which can differentiate upper from lower sites of GIT hemorrhage.

A high serum blood urea nitrogen is a well recognized feature of gastrointestinal tract hemorrhage. The mechanism has not been firmly established, but one hypothesis implicates hepatic catabolism of an absorbed amino acid load ***(Peterson, 1985).*** Other hypothesis correlated the degree of elevation of urea in blood with volume loss. The last one may explain the rise of serum urea associated with

hemorrhage arising distal to the absorptive surface of gastrointestinal tract ***(Pumphrey and Beck, 1980).***

In the last decade, many authors suggested plasma BUN / creatinine ratio as a simple and valuable screening biochemical test for the differentiation. ***Snook et al., (1986)*** reported that plasma BUN / creatinine concentration ratio proved highly accurate in distinguishing upper and lower GIT sources of hemorrhage and the overall accuracy was 90%.

Aim of the work :-

Rational investigation of gastrointestinal tract bleeding demands the fewest, least invasive investigations to establish the diagnosis. In the present study, we try to evaluate the BUN / creatinine ratio as a reliable, simple, and cheap biochemical test for differentiating upper and lower sources of GIT bleeding.

Review of Literature

CATABOLISM OF AMINO ACID NITROGEN AND UREA BIOSYNTHESIS

Biosynthesis of urea is divided into 4 stages :

(1) Transamination,

(2) Oxidative deamination,

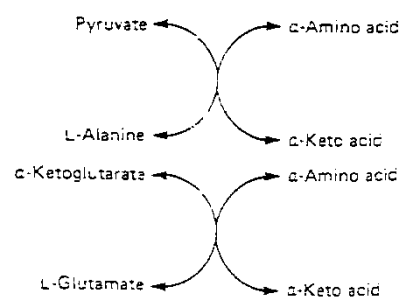
(3) Ammonia transport, and

(4) Reactions of the urea cycle.

Although each stage also plays a role in amino acid biosynthesis, what following is discussed from viewpoint of amino acid catabolism.

♦ Transamination :

Transamination, catalyzed by enzymes termed trans-aminases or amino transferases, inter-converts a pair of amino acids and a pair of ketoacids. These generally are α-amino and α-ketoacids ***(Torchi-nsky, 1987).***



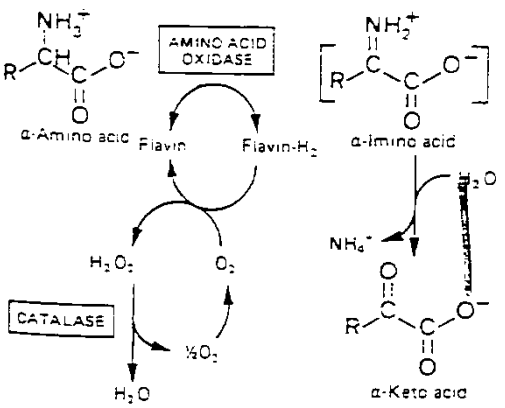
Alanine (*top*) and glutamate (*bottom*) trans-aminases.

Two transaminases, alanine-pyruvate transaminase (alanine trans-aminases) and glutamate α-keto glutarate transaminase (glutamate trans-aminase) catalyze transfer of amino groups from most amino acid to form alanine (from pyruvate) or glutamate (from α-keto glutarate).

Most, but not all, amino acids are substrates for transamination. Exceptions include lysine, threonine, proline and hydroxyproline ***(Torchi-nsky, 1987).***

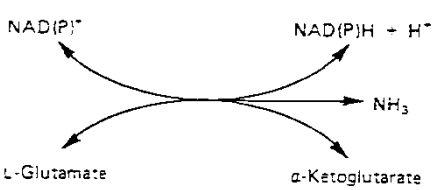
♦ Oxidative deamination :

Many amino acids are subjected to oxidative deamina-tion in the liver and kidney. Although most of the activity toward L-α-amino acids is due to coupled action of transamina-ses plus L-glutamate dehydro-genase, both L- and D-amino oxidases activities occur in the liver and kidney, but the physio-logic function of it is unknown.



Oxicative deamination catalyzed by L-amino acid oxidase (L-α-amino acid: O_2 oxicoreductase). The α-imino acid, shown in brackets, is not a stable intermediate.

The amine groups of most amino acids ultimately are transferred to α-keto glutarate by transamination forming L-gluta-mate. Release of this



The L-glutamate dehydrogenase reaction. NAD(P)$^+$ means that either NAD$^+$ or NADP$^+$ can serve as cosubstrate. The reaction is reversible, but the equilibrium constant favors glutamate formation.

nitrogen as ammonia is catalyzed by L-glutamate dehydrogenase ***(Robert et al., 1988).***

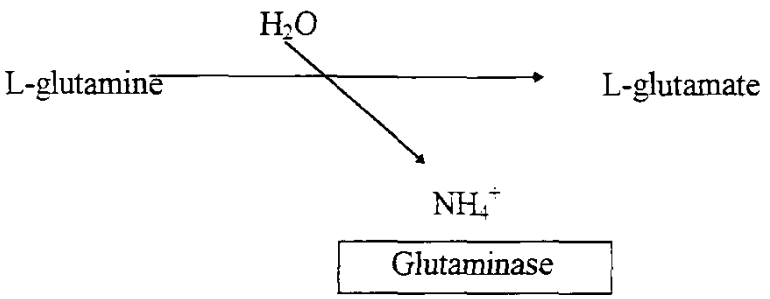
Formation of ammonia : ***(Robert et al., 1994)***

In addition to ammonia formed in tissues, a considerable quantity is produced by intestinal bacteria from dietary protein and from urea present in fluids secreted into the gastrointestinal tract. This ammonia is absorbed from the intestine into portal venous blood, which characteristically contains higher levels of ammonia than does systemic blood. Under normal circumstances, the liver promptly removes the ammonia from portal blood, so that blood leaving the liver (and indeed all of the peripheral blood) is virtually ammonia-free.

With severely impaired hepatic function, development of collateral communications between the portal and systemic veins and surgically produced shunting procedures (portacaval shunts), portal blood may bypass the liver and ammonia may thus rise to toxic levels in the systemic blood, particularly after ingestion of proteins or after gastrointestinal hemorrhage, which provides blood proteins to colonic bacteria.

Ammonia is formed also by the kidney added to the blood and excreted in urine. Ammonia production is considered as an important renal tubular mechanism for regulation of acid-base balance and conservation of cations, is markedly increased in metabolic acidosis and depression in alkalosis. This ammonia is derived, not from urea, but

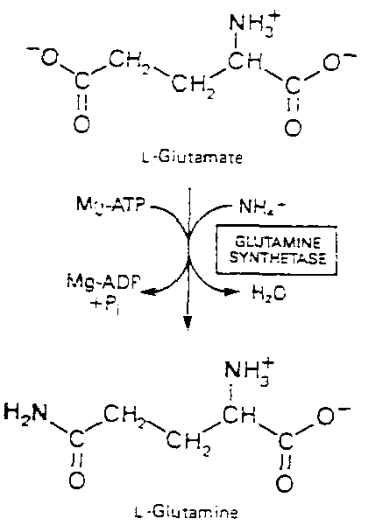
from intracellular amino acids, particularly glutamine, a reaction catalyzed by glutaminase.



Transport of ammonia : ***(Robert et al., 1994)***

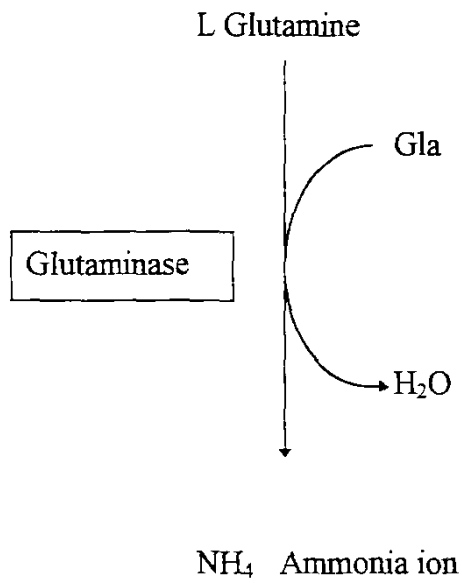
Although ammonia may be excreted as ammonium (NH_4^+) - particularly in metabolic acidosis - the vast majority is excreted as urea, the principle nitrogenous component of urine. Ammonia is constantly produced in the tissues but present only in traces in peripheral blood (10-20 µg/dL), is rapidly removed from the circulation by the liver and converted to glutamate, to glutamine, or to urea.

Removal of ammonia via glutamate dehydrogenase was mentioned above. Formation of glutamine is catalyzed by glutamine synthetase, a mitochondrial enzyme present in highest quantities in renal tissue.



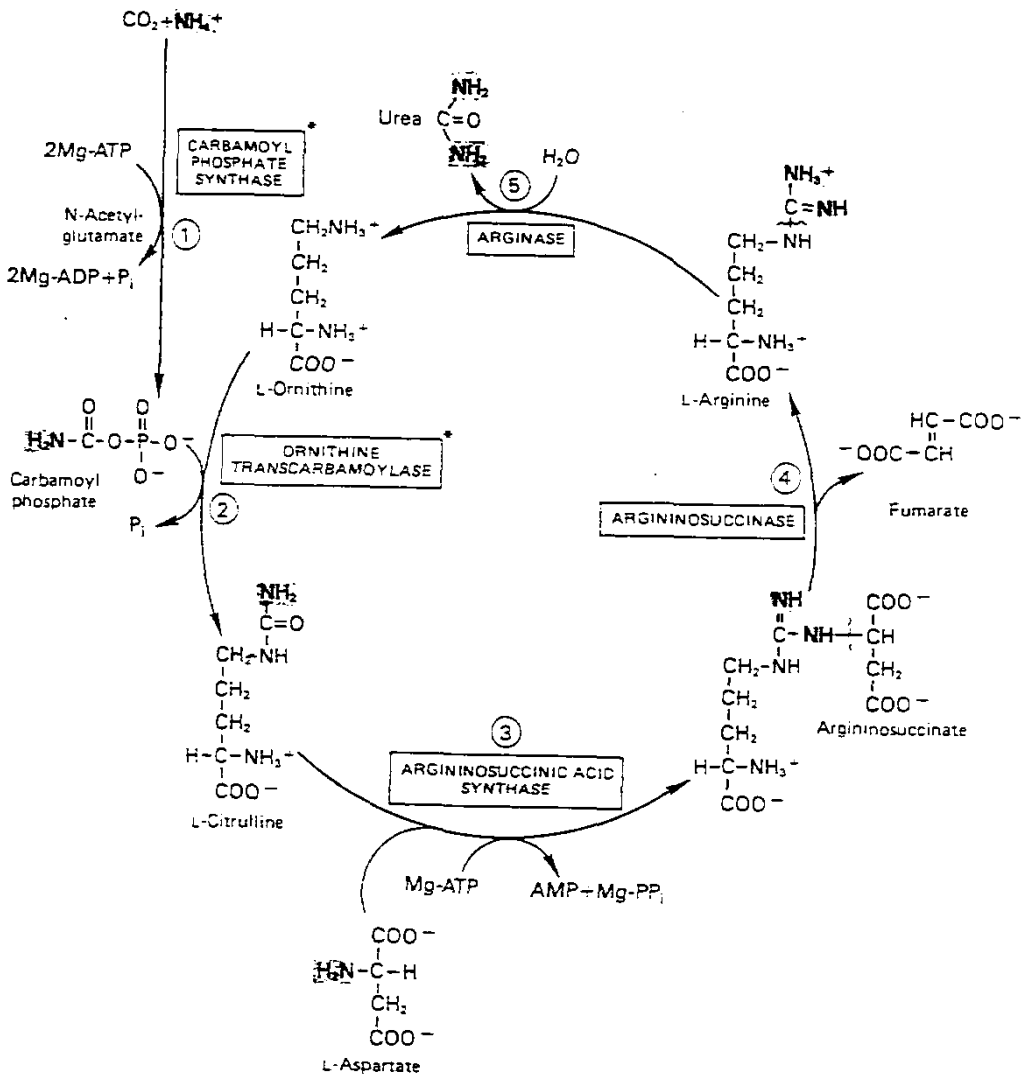
The glutamine synthetase reaction. The reaction strongly favors glutamine synthesis.

Liberation of the amide nitrogen of glutamine as ammonia occurs by hydrolytic removal of ammonia catalyzed by glutaminase. The glutaminase reaction, unlike the glutamine synthetase reaction, does not involve adenine nucleotides, strongly favors glutamate formation and does not function in glutamine synthesis. Glutamine synthetase and glutaminase, thus, catalyze interconversion of free ammonium ion and glutamine.



Biosynthesis of urea : ***(Robert et al., 1994)***

A moderately active man consuming about 300 g of carbohydrate, 100 g of fat and 100 g of protein daily must excrete about 16.5 g of nitrogen daily. 95% is eliminated by the kidneys and 5% in the feces. The major pathway of nitrogen excretion in humans is as urea synthesized in the liver, released into the blood and cleared by the kidney. In humans eating an accidental diet, urea constitutes 80-90% of the nitrogen excreted.



Reactions and intermediates of urea biosynthesis. The amines contributing to the formation of urea are shaded. *Mitochondrial enzymes.

The reactions and intermediates in biosynthesis of 1 mol of urea from 1 mol each of ammonium ion, of carbon dioxide (activated with Mg^{2+} and ATP), and of the α-amino nitrogen of aspartate. The overall process requires 3 mol of ATP (2 of which are converted to ADP + Pi and 1 to AMP + PPi) and the successive participation of 5 enzymes catalyzed the numbered reactions. Of the 6 amino acid involved in the urea formation, one (N-acetyl glutamate) functions as an enzyme activator rather than as an intermediate. The remaining 5-aspartate, arginine, ornithine, citruline, and arginino-succinate - all function as carriers of atoms which become ultimately urea. Two (aspartate and arginine) occur in proteins, while the remaining 3 (ornithine, citruline and arginino-succinate) do not. There is no net loss or gain of ornithine, citruline, arginino-succinate, or arginine during urea synthesis; however, ammonium ion, CO_2, ATP and aspartate are consumed.

Creatine and creatinine : ***(Victor et al., 1994)***

Creatine is present in muscle, brain and blood, both as phospho-creatine and in the free state. Traces of creatine are also normally present in urine. Creatinine, the anhydride of creatine, is formed largely in muscle by irreversible non-enzymatic dehydration of creatine phosphate.