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MEASUREMENT OF ARGINASE ACTIVITY IN ERYTHROCYTES IN NEWBORNS AND CHILDREN AND ITS CORRELATION WITH PLASMA AMMONIA CONCENTRATION

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Abstract:
Background- *Arginase an enzyme of urea cycle which catalyzes the cleavage of L-arginine to urea and L-ornithine. This is an inherited genetic disorder. In blood elevated level of ammonia refers the condition of hyperammonemia which is protein degradation product. In blood lack of arginase enzyme can result in excessive accumulation of nitrogen in form of arginine and ammonia.* ***Methods-*** *In this study, along with plasma ammonia concentration erythrocyte arginase activity is measured in children and newborns. In this study 133 subjects were selected and based on ammonia level these all were divided into two groups. In group 1 (92) patients were kept who had normal level of ammonia whereas in group 2 number of patients were 41 who had high level of ammonia.* ***Results-*** *It was found that in high level of ammonia group there was significant decrease in arginase group as compared to the normal ammonia group. In both groups between ammonia and arginase negative correlation was observed.* ***Conclusion-*** *It was concluded that the reason behind hyperammonemia can be the deficiency of arginase. Therefore, in children, infants, newborns deficiency of arginase can be detected through the screening of arginase activity.*

Keywords: *Newborn screening, urea cycle, hyperammonemia, arginase*

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INTRODUCTION:

Arginase an enzyme of urea cycle which catalyzes the cleavage of L-arginine to urea and L-ornithine. This is an inherited genetic disorder. In blood elevated level of ammonia refers the condition of hyperammonemia which is protein degradation product. In blood lack of arginase enzyme can result in excessive accumulation of nitrogen in form of arginine and ammonia. Arginase can exist in two isoforms. First form is Arginase-1 which is a cytosolic protein found in liver and primarily expressed in erythrocytes. It is responsible for the nitrogen homeostasis and ureagenesis. The common source for ornithine which is present in plasma is erythrocyte arginase activity. For peripheral tissues of bone and cartilage, the availability of ornithine is very significant as these tissues have low arginase activity.

Second form is arginase-2 which is a mitochondrial protein can be found in many extrahepatic tissues that is mammary gland, small intestine, kidney, spinal cord and brain. Due to the deficiency of arginase- 1 Hyperargininemia can happen but it is a treatable urea cycle error in newborns. Normally this condition present in newborn period. Normally this condition present in early 2 to 4 years of childhood but if it remains untreated then it leads to the neurological disorder.

Hyperammonemia:

In blood elevated level of ammonia refers the condition of hyperammonemia which is protein degradation product. In blood lack of arginase enzyme can result in excessive accumulation of nitrogen in form of arginine and ammonia. The serious hyperammonemia saw in other urea cycle abandons is once in a while seen in patients with arginase inadequacy for in any event two recognizable reasons. The principal reason is that framed arginine, which contains two waste nitrogen atoms, can be discharged from the hepatocyte and discharged in pee. The absence of the arginase chemical outcomes in extreme gathering of nitrogen, as smelling salts (hyperammonemia) and arginine (hyperargininemia) in the blood. Untreated kids may show seizures, spasticity, short height, and mental disability. Be that as it may, no efficient investigations are accessible with respect to the erythrocyte arginase action and its relationship with plasma alkali levels.

METHODS:

Ethics:

For this study ethical clearance certificate of ethical number IEC/52 2017 was obtained

Study Subject:

For this study children and babies of age 0-15 years were selected. The total number of subjects taken were 133.

Specimen:

Erythrocytes separated from blood sample collected with ethylenediamine tetraacetic acid (EDTA). Study duration was 6 months.

Selection Criteria:

For this study children having age less than 15 years old were selected and their blood sample were sent for ammonia estimation.

Arginase activity estimation:

For estimation of arginase activity, arginine was taken as a substrate and then by its reaction with ninhydrin the produced product i.e. ornithine is measured calorimetrically. To extract red cells from collected blood this is centrifuged in EDTA tube at 4°C and 2000g. These extracted cells were then washed 3 times with 5mmol/L Tris buffer ad normal saline at pH 7.5. This obtained suspension was used for hemoglobin concentration and arginase activity estimation.

Statistical analysis:

For statistical analysis SPSS version 16 was used.

RESULTS:

In this study 133 subjects were selected and based on ammonia level these all were divided into two groups. In group 1 (92) patients were kept who had normal level of ammonia whereas in group 2 number of patients were 41 who had high level of ammonia. In plasma the reference value of ammonia is 0–70µg/dl and any value above than this is categorized as high level of ammonia and any value less than 70µg/dl categorized as normal level of ammonia as presented in below figures

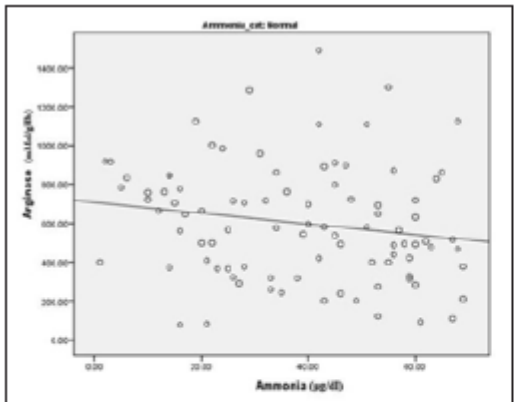

Figure 1: Correlation between ammonia and arginase activity in normal ammonia group. n=92, r=0.22, P=0.03.

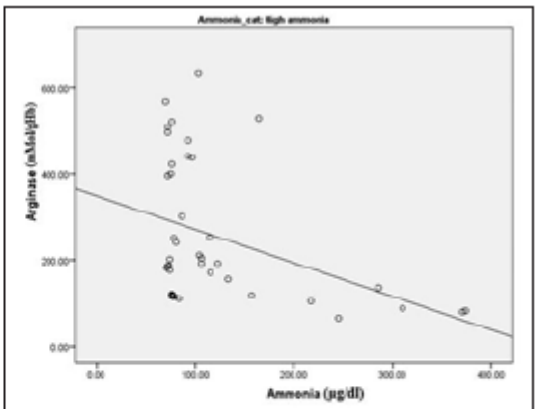

Figure 2: Correlation between ammonia and arginase activity in high ammonia group. n=41, r=0.39, P=0.01.

It was found that in high level of ammonia group there was significant decrease in arginase group as compared to the normal ammonia group. In both groups between ammonia and arginase negative correlation was observed.

Table 1: Erythrocyte arginase activity in the two groups

Groups	Arginase (mMol/gHb)median (Q1, Q3)
Normal ammonia group (n=92)	571.22 (375.37, 793.15)
High ammonia group (n=41)	*191.74 (117.84, 411.16)
*P-value is <0.001	

Table 2: Group-wise correlation analysis between arginase and ammonia

Groups	r	P
Normal ammonia group (n=92)	0.22	0.03*
High ammonia group (n=41)	0.39	0.01*
*P-value-significant		

DISCUSSION:

Arginase an enzyme of urea cycle which catalyzes the cleavage of L-arginine to urea and L-ornithine. This is an inherited genetic disorder. In blood elevated level of ammonia refers the condition of hyperammonemia which is protein degradation product. In blood lack of arginase enzyme can result in excessive accumulation of nitrogen in form of arginine and ammonia.

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CONCLUSION:

It was found that in high level of ammonia group there was significant decrease in arginase group as compared to the normal ammonia group. In both groups between ammonia and arginase negative correlation was observed. It was concluded that the reason behind hyperammonemia can be the deficiency of arginase. Therefore, in children, infants, newborns deficiency of arginase can be detected through the screening of arginase activity.

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