
Serum Aspartate Aminotransferase and Alanine Aminotransferase in Newborn Libyan Babies

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Abstract:

Introduction: Transaminases are enzymes involved in transfer of amino groups from α -amino acid to α -keto acid using pyridoxal phosphate as a cofactor. Aspartate aminotransferase (AST) is widely distributed, whereas, alanine aminotransferase (ALT) is high in liver and to a lesser extent in skeletal muscle, kidney and heart. Both rise in serum after tissue damage. Bilirubin is an end product of the breakdown of haem, and its deposition leads to hyperbilirubinaemia which can cause brain damage, as a result long-life neurological disability. **Objective:** This study was carried-out to evaluate the ALT and AST activity, and the bilirubin (total and direct) level in newborn Libyan babies, as well as evaluating their inter-relationship. **Materials and Methods:** Blood was collected for routine investigation from 200 newborn Libyan babies, aged 1 to 18 days ($X = 6.3 \pm 4.0$ days), admitted in the neonatal unit, Sebha Teaching Hospital, Sebha, Libya. A part of this blood were used to investigate the ALT and AST activity, and the bilirubin level, which were performed by Kinetic test-IFCC recommended from Biomaghreb (Tunisa) and Biocon (Hecke, Germany) based on Jendrassik-Grof method, respectively. **Results:** In these two hundred newborn babies, the activity of ALT was 23.59 ± 13.5 U/l and AST was 58.20 ± 35.6 U/l. We observed a significant difference between the two means ($P < 0.001$), as well as a significant correlation ($r = 0.75$, $P < 0.001$). The ratio of ALT to AST was 1: 2.47. The total and direct bilirubin was 9.5 ± 4.9 mg/dl and 1.3 ± 1.5 mg/dl, respectively. We found no significant correlation between the activity of AST and ALT, and the bilirubin level. However, in group-I (41.5%) of these babies ($n = 83$, age = 5.9 ± 3.5 days) the total bilirubin was 9.2 ± 5.3 mg/dl and the direct bilirubin was 0.7 ± 0.5 mg/dl. While, the ALT activity was 19.1 ± 9.7 U/l and AST activity was 46.1 ± 17.2 U/l. The ratio of ALT to AST was 1 : 2.41. Again, we found , a significant difference between the means of AST and ALT activity ($P < 0.001$), as well as a significant correlation ($r = 0.44$, $P < 0.001$). In the other group-II, (58.5%, $n = 117$) the total bilirubin was 9.6 ± 4.7 mg/dl, but the direct bilirubin was 3.0 ± 2 mg/dl. While, the activity of ALT was 25.7 ± 15.7 U/l and AST was 65.9 ± 43.2 U/l. The ratio of ALT to AST was 1: 2.56. Interestingly, we observed a significant correlation between the activity of AST and ALT ($r = 0.78$, $P < 0.001$), and negative correlation between the activity of both AST and ALT, and the bilirubin ($P = NS$). **Conclusion:** Establishment of reference values for newborn babies would be helpful in achieving the most accurate diagnosis. **Key words:** Alanine aminotransferase, Aspartate aminotransferase, Bilirubin, Newborn babies.

Introduction:

The liver develops from progenitor cells into a well-differentiated organ in which bile secretion can be carried-out. Their full maturity takes up-to two years to be achieved (1). However, at birth, hepatocytes are already specialised and rapid induction of functions such as coagulation factors synthesis, glutamyl transferase, transamination, bile production and transport as soon as the umbilical supply is interrupted.¹

Transamination is the major process for removing nitrogen from amino acids.² It is carried-out by certain enzymes, termed "transaminases". These group of enzymes are

involved in transferring the amino group from α -amino acid to α -keto acid using pyridoxal phosphate as a cofactor.^{2,3} For most of these reactions, α -ketoglutarate and glutamate serve as one of the α -keto acid-amino acid pairs.²

Animal cells contain a variety of aminotranferases. But, there are only few clinically important transaminases: Aspartate aminotransferase (AST) (EC2.6.1.1; L-aspartate:2-keto-glutarate aminotransferase), is widely distributed, with high concentration in the heart, liver, skeletal muscle, kidney and erythrocytes. There are two iso-forms of mammalian AST; one mitochondrial (m-AST)

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and another of soluble cytosolic origin (s-AST).⁴ AST is one of the most active enzymes in the cell. It is measured in blood mainly for medical diagnostic purposes. Metabolically, it brings about amino groups between glutamate (the most common amino acid) and aspartate, the second major amino acid pool. The free movement of nitrogen between the glutamate and aspartate pools is an important balancing process that is vital for normal cellular metabolism.² The other important transaminase is called alanine aminotransferase (ALT) (EC2.6.1.2; L-alanine:2-keto-glutarate aminotransferase), which is mainly present in the cytoplasm. Its activity high found in liver and to a lesser extent in the skeletal muscle, kidney and heart.³ It is another active enzyme that has been used for medical diagnostic purposes too. Its main substrate is the amino acid alanine, which released from muscle tissue during starvation and used for hepatic gluconeogenesis, a process needed for maintaining fasting blood sugar concentration.² Usually, transaminases rise in serum after tissue damage.⁵ Cellular enzymes, as AST & ALT leak into the blood through the membranes of the cells that have been damaged as a result of the inflammatory process.² There are no known clinically important congenital metabolic disorders associated with these transaminases. However, their rise in serum has been associated with heart, liver diseases and other conditions as muscular dystrophy.^{5,6} Transaminases measurements in adult patient serum have proven to be in value in the diagnosis of hepatic diseases. Therefore it seemed of interest to apply them to the newborn babies.⁷⁻⁹ Conjugated hyperbilirubinaemia in newborn babies indicates neonatal liver disease which has numerous possible causes, classified as infective, anatomic/structural, metabolic, genetic, neoplastic, vascular, toxic, immune and idiopathic.¹⁰ High percentage of newborn babies develop a yellowish coloration of the skin, it is a result of accumulation of bilirubin.⁵ Bilirubin is an organic compound formed after the break down of red blood cells, mainly it comes from the haem compound.² Neonatal jaundice occurs when bilirubin builds up in the baby's blood. In most newborn babies, jaundice is a physiological event usually seen around the second or third day of life and disappears after few days,¹¹ often without special treatment.⁵ Treatment depends on the cause and the degree of elevation; definitive treatments include phototherapy by fluorescent

light (UV) and exchange transfusion.¹² Marked hyperbilirubinaemia can cause kernicterus, a syndrome of neurologic damage leading to long-life disability,^{2,12,13} it could be diagnosed by clinical examination and confirmed by measurement of serum bilirubin.

In general, hyperbilirubinaemia could be physiologic or pathologic, and always caused by increased production, decreased clearance, or increased enterohepatic circulation of bilirubin (prenatal physiology). Most of these cases involve unconjugated hyperbilirubinaemia, but liver dysfunction may cause conjugated hyperbilirubinaemia.¹¹ Preterm babies are at risk of hepatic decompensation because of their immaturity results in a delay in achievement of normal detoxification and biosynthesis function.¹ Recent concern is raised that partial or isolated neurologic sequelae, for example auditory neuropathy and other central auditory processing disorders, may result from excessive amount and duration of exposure to free, unconjugated bilirubin at different stages of neurodevelopment.¹⁴

Objective:

Therefore, this study was performed to evaluate the ALT and AST the transaminases enzymes activity and the bilirubin (total and direct) level in newborn Libyan babies, as well as evaluating their inter-relationship.

Materials and Methods:

Serum was collected from the blood has been sent for routine clinical investigation of two hundred full-term newborn babies, aged between 1 to 18 days ($X = 6.3 \pm 4.0$ days). They were admitted in the neonatal unit in Sebha Medical Centre, Sebha, Libya. The transaminases (ALT and AST) activity and the bilirubin (Total/Direct) level were performed using commercially standard kits from BioMerieux (Lyon, France) and Biocon (Hecke, Germany) based on Jendrassik-Grof method, respectively.

The statistical analysis was estimated by Student's test and correlation analysis (linear regression). Data were expressed as means \pm SD and the P-value of ≤ 0.05 were considered statistically significant.

Results:

As shown in Table 1, in the two hundred newborn babies, the mean of the activity of serum ALT was 23.59 ± 13.5 U/l and of serum AST activity was 58.20 ± 35.6 U/l, their

reference values are 6-37 U/L and 5-30 U/L, respectively.¹⁵ We observed a significant difference between the two means ($P < 0.001$), as well as a significant correlation between the two parameters ($r = 0.75$, $P < 0.001$). The calculated ratio of the serum ALT activity to serum AST activity was 1:2.47. The serum total and direct bilirubin values were 9.5 ± 4.9 mg/dl and 1.3 ± 1.5 mg/dl, respectively. We observed no significant correlation between the activity of serum AST and ALT, and the serum total bilirubin values. However, when the newborn babies results were divided upon their serum direct bilirubin level. In one group (41.5%) were the serum direct bilirubin values around 1.0 mg/dl ($n = 83$, age = 5.9 ± 3.5 days), the mean of serum total bilirubin was 9.2 ± 5.3 mg/dl and the mean of serum direct bilirubin was 0.7 ± 0.5 mg/dl, their reference values 0.2-1.0 mg/dl and 0-0.2 mg/dl, respectively.¹⁵ While, the mean of serum ALT activity was

19.1 ± 9.7 U/l and mean of serum AST activity was 46.1 ± 17.2 U/, the ratio of ALT to AST was 1:2.41. Again, we observed a significant difference between the means of AST and ALT activity ($P < 0.001$), as well as a significant correlation between them ($r = 0.44$, $P < 0.001$) (Table 2). However, in the other group (58.5%) where the direct bilirubin was far above 1.0 mg/dl ($n = 117$), the mean of total bilirubin was 9.6 ± 4.7 mg/dl, but the mean of direct bilirubin was 3.0 ± 2 mg/dl. While, the mean of serum ALT activity was 25.7 ± 15.7 U/l and the mean of serum AST activity was 65.9 ± 43.2 U/l, the ratio of ALT to AST was 1:2.56. Interestingly, we observed a significant correlation between the activity of serum AST and the serum ALT activity ($r = 0.78$, $P < 0.001$) (Figure 1), and we observed no correlation between the activity of both serum AST and serum ALT, and the serum bilirubin ($P = NS$) (Table 3).

Table 1: Comparison between the mean of serum ALT and AST activities, and the serum total Bilirubin level (Group-I plus Group-II).

Transaminases	Patients No.	Activity U/L	Ratio	r	P
AST vs ALT	200	$58.20 \pm 35.6^*$	1:2.47	0.75	<0.001
		$23.59 \pm 3.5^*$			
Bilirubin		Patients No.			
Total	200	9.5 ± 4.9 mg/dl**			
Direct		1.3 ± 1.5 mg/dl			

* No significant correlation between the mean of serum AST and ALT activity, and the mean of serum total bilirubin level.

Table 2: Comparison between the mean of serum ALT and AST activities. and the serum total Bilirubin level in group-I.

Transaminases	Patients No.	Activity U/L	Ratio	r	P
AST vs ALT	83	$46.20 \pm 17.20^*$	1:2.41	0.44	<0.001
		$19.10 \pm 9.70^*$			
Bilirubin		Patients No.			
Total	83	9.20 ± 5.30 mg/dl*			
Direct		0.70 ± 0.50 mg/dl			

*No significant correlation between the serum AST and ALT activity, and the serum total bilirubin level.

Table 3: Comparison between the mean of serum ALT and AST activities, and the serum total Bilirubin level in group-II.

Transaminases	Patients No.	Activity U/L	Ratio	r	P
AST vs ALT	177	$65.90 \pm 43.24^*$	1:2.56	0.78	<0.001
		$25.70 \pm 15.7^*$			
Bilirubin		Patients No.			
Total	117	9.60 ± 4.70 mg/dl*			
Direct		3.00 ± 2.00 mg/dl			

*No significant correlation between the activity of AST and ALT, and the serum total.

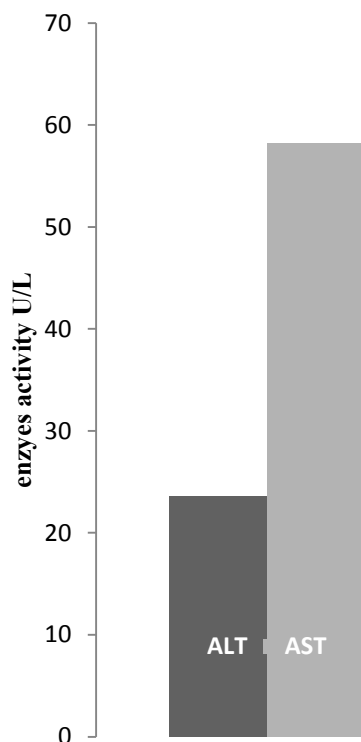


Figure 1: AST and ALT activities in Newborn Babies of 5 days old (n=200).

Discussion:

Most of the commonly used liver function tests are biomarkers for the investigation of liver diseases and not actual tests of function *per se*.¹⁶ In this study, the transaminases (AST & ALT) and total and, direct bilirubin were measured in a serum collected from Libyan newborn babies. Although, the total and direct bilirubin results were slightly high, the transaminases results were within the reference values at least in about 41.5% of these babies, which may indicate the possibility of physiological jaundice. Nonetheless, normal

values do not necessarily exclude diseases.¹⁶ On the other hand, the ratio of AST was more than twofold higher that of ALT. Diseases as muscular dystrophy and polymyositis may lead to high serum AST activity with normal ALT, a similar pattern may also seen in muscle trauma.⁴ Thus, further investigation of possibility of other abnormalities may be needed. **Conclusion:** We conclude that establishment of reference values for newborn babies would be helpful in achieving the most accurate diagnosis.

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