RESEARCH ARTICLE

Effect of Heavy Metals on the Activity Levels of Hepatic Enzymes in the Maternal and Embryonic Tissues of Viviparous Scorpion *(H. fulvipes)*

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ABSTRACT- An experimental study was performed with viviparous animal *Heterometrous fulvipes* to access the cumulative effect of chronic heavy metals exposure on the activity levels of the enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Chronic heavy metal exposure resulted in variation in the enzyme levels with increase in AST and decreases in ALT, contributed to the stress induced by the heavy metals. These changes in enzymatic activity of the maternal and embryonic tissue of *H. fulvipes* under the influence of heavy metal, mercury and lead is suggestive of the specific impact of mercury and lead on the enzymatic pathway, prompting a further study to consolidate the finding in human study. It is pertinent that the heavy metal toxicity be well documented and appropriate precaution taken in the mother and fetus to decrease its detrimental effects.

Key-words- Animal models, Enzymes, Heavy Metals, Hepatic Viviparous

INTRODUCTION

Heavy metals are believed to exert their influence on the activity of the enzymes playing a vital role in the biochemical transactions of a living system. Embryonic development is characterized by growth and formation of new tissues. The alterations in the activity of enzymes and/or embryonic tissues would invariably influence the developmental processes in viviparous animals as embryonic nourishment is provided by the maternal sources. Shift in the metabolism of either the maternal tissues or the embryos owing to changes in the enzyme activity influenced by heavy metals can be reflected in the form of deviations from the normal development. The metabolic levels of the embryo can, therefore, be expected to be different from those of the maternal animal. The metabolic state of the embryo relative to that of the mother would be reflected even at the molecular level in the enzymatic activity.

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Administration of 50, 100, 150 and 200 ppm cadmium chloride to male Sprague dawley rats, significantly increased aspartate aminotransferase (AST or AAT) and Alanine aminotransferase (ALT or ALAT) enzymes in the kidney, brain and liver tissues [1]. Exposure of the katelysia opima to 0.07 and 0.14 mg/l concentration of mercuric chloride elevated the activity of aminotransferase and reduced Na^+-K^+ ATPase activity [2]. The mother and the fetus of the mammals have been shown to have different enzyme status. Effects of cadmium at sub-lethal concentration in rainbow trout (*Oncorhynchus mykiss*) have significant responses on growth and biochemical parameters generally followed by an early elevation (or depression) and a return to baseline values in chronic exposure. This pattern is suggestive of acclimation to the toxicant over time. The levels of AST and ALT activity increased in the tissues of *Oreochromis mossambicus* exposed to cadmium chloride due to necrosis and increases in the permeability of cell membrane resulting in the damage of tissues after 7 and 14 days. These heavy metals may cause injury to the organisms and the damaged tissues subsequently causing malfunction. [3] Continuous exposure to sub-lethal cadmium concentrations resulted in significantly elevated levels of both AST and ALT activity in *Oreochromis niloticus*. It showed a linear

pattern of increasing ALP over time with cadmium exposure resulting in recognizable physiological and functional alterations. In contrast, *O. niloticus* exposed to 0.05 mg/l cadmium during 30-days showed reduction in ALP activity. [4] Transaminases like ALT and AST play significant role in amino acid and protein metabolism and they may release into the plasma following tissue damage and dysfunction. Different factors such as life history, water quality, exposure duration and cadmium concentration influence ALP activity. The decrease in ALP activity might be a result of disturbance of the membrane transport system, although the increase in the activity may be related to tissue damage. [5] There is distinctive evidence of significant effects in plasma enzymes (AST and ALT) by exposure to cadmium in marine fish *Mugil seheli* and after a transient reduction during the first few days, with an increase in the activity of enzymes reaching levels similar to the control value [6].

There have been multiple reports in alterations in the level of different enzyme levels apart from ALT and AST. A reduction in the activity of LDH was reported in the teleost fishes, *Channa punctatus* and *H. fossilis* when subjected to the heavy metal, mercury [7]. Mercuric chloride changed the levels of pyruvate and lactate dehydrogenase and inhibited the dehydrogenase activity in fresh water mussel, *Parreysia rugose* [8]. Exposure of *H. fossilis* to a sublethal concentration of 0.3 ug/l mercuric chloride inhibited the activity of alkaline phosphatase, adenosine triphosphate and glucose-6-phosphatase, but elevated the activity of succinic dehydrogenase, pyruvate dehydrogenase and cholinesterase in the brain tissue [9]. Exposure of teleost *Sarotherodon mossambicus* to mercury significantly decreased the activities of the succinate dehydrogenase, lactate dehydrogenase, glucose-6-phosphate dehydrogenase, alkaline phosphatase and acid phosphatase. Similarly, exposure of Tilapia mossambica to cupric chloride decreased the succinic dehydrogenase activity and significantly increased the lactate dehydrogenase activity.[10]

Heavy metals also have a profound effect in the embryos. Rao *et al.* [11] shown that the sub-lethal lose doses of mercury and lead brought about a reduction in the size of the embryos and even failure of parturition in the scorpion *H. fulvipes.* Changes in biochemical constituents induced by heavy metals, lead, and mercury have been held responsible for the reduction in the size of the embryos. In view of the paucity of information on the enzyme status of the embryos relative to the maternal animal in other viviparous forms and inter vertebrates in particular, a study of the levels of the activity of different enzymes in the maternal tissues and the embryos of *H. fulvipes* would prove valuable and reveal the metabolic gradients, if any, between the mother and the embryos. The sulfhydryl groups are known to have a very high affinity for mercury, lead and other heavy metals. Almost all proteins contain sulfhydryl groups that are metal reactive. As these groups are important in most protein functions, heavy metals can disturb almost all functions in which proteins are involved. Thus, almost every protein in the body is a potential target. In other words, heavy metals are potent but nonspecific enzyme poisons. Therefore an attempt is made here to examine the impact of the sub-lethal doses of mercury and lead on the selected enzymes (AST, ALT), which can account for the manifestations of the toxic effects of the heavy metals.

MATERIALS AND METHODS

A prospective experimental study was designed and performed in the Department of Zoology, Acharya Nagarjuna University, Andhra Pradesh, India in the year 2012 to 2014 using the animal model *H. fulvipes*. Three animal groups were formed based on heavy metal exposure: Group I (Control), Group II (Mercury exposure) and Group III (Lead exposure). Monthly samples were drawn from different groups after exposure to mercury and lead successively at the intervals of one month. Enzyme levels were estimated in the maternal tissues (hepatopancreas, pedipalpal tissues) and the whole embryos in the samples drawn from Group I, II, and III. Samples drawn every month from Aug to April received one sub lethal dose per month; hence the sample from the month of Aug represented the effect of a single dose, whereas samples taken in September represented cumulative effect of two doses. In the same order samples at the month of April represent the effect of nine sub lethal doses of the heavy metals. 10% homogenate of muscle, 7% homogenate of liver and 2% homogenate of embryo were made in 0.25 M sucrose solution at 5^{o}C. Supernatants obtained after centrifugation at 3000 rpm for 15 minutes, were used as the enzyme source for the assay of AST and ALT.

Estimation of AST and ALT- The activity levels of AST and ALT were estimated employing the method of Reitman and Frankel [12], after completing the protocol to determine optimal conditions for the enzyme activity. The reaction mixture contained 100 umoles of phosphate buffer (pH 7.4), 50 µmoles of L-aspartate for AST or 40 µmoles of DL-alanine for ALT, 2 µmoles of 1-Oxoglutaric acid and 0.3 ml of homogenate in a final volume of 1.5 ml. This reaction mixture was incubated at 37 37^{o}C for 30 minutes and the reaction was arrested by the addition of 1 ml of 2–4 dinitro phenyl hydrazines prior to the addition of the homogenate. The color developed by the addition of 10 ml of 0.4N sodium hydroxide was read at 545 µ against a blank. The specific activity was expressed as micromoles of pyruvate /mg protein/h. The protein content in the enzyme extract was estimated by the method of Lowry *et al*. [13].

The activity levels of AST and ALT were calculated from a standard graph using sodium pyruvate as standard. Colorimetric readings for all the estimations were taken. In the view of the occurrence of the marked diurnal rhythmic activity in *H. fulvipes,* all the estimations were carried out between 9 am to 12 pm noon.

RESULTS

Effect of mercury and lead on the levels of activity of aspartate aminotransferase (AST) in the maternal tissues and embryos

Maternal Hepatopancreas- The activity of the AST continuously increased throughout the gestational period from Aug to March followed by a reduction in the last two months. For animals treated by sub-lethal doses of mercury and lead, the pattern of variation in the levels of activity of AST during the gestation period remained essentially the same (Table 1; Fig. 1). However, the activity of the enzyme was elevated in each of the samples of scorpions treated with the sub-lethal doses of mercury, statistically insignificant up to November and significant beyond up to March. In scorpions treated with sub-lethal doses of lead, the elevation in the AST activity was statistically significant throughout, and nearly dose dependent.

Table 1: Effect of mercury (Hg) and lead (Pb) on the activity levels of aspartate aminotransferase (AST) in the hepatopancreas of *H. fulvipes* during the gestation period

Month of Treatment	AST umoles of pyruvate formed/mg protein/hr		
	Control	Experimental	Percent change
AUG	0.76±0.02	Hg 0.82±0.02*	7.02
		Pb 0.86±0.02[a]	12.22
SEP	0.81±0.02	Hg 0.87±0.03*	7.01
		Pb 0.91±0.02[b]	12.54
OCT	0.83±0.02	Hg 0.94±0.02*	8.72
		Pb 0.96± 0.03[b]	13.38
NOV	0.86±0.03	Hg 1.00±0.03*	11.47
		Pb 1.11±0.03[b]	16.22
DEC	0.97±0.03	Hg 1.19±0.04*	14.83
		Pb 1.15±0.04[c]	22.65
JAN	0.99±0.03	Hg 1.20±0.04*	16.12
		Pb 1.18±0.04[c]	21.65
FEB	1.03±0.02	Hg 1.22±0.04*	15.13
		Pb 1.24±0.04[c]	18.91
MAR	1.08±0.04	Hg 1.29±0.04*	15.43
		Pb 1.05±0.04[c]	19.68
APR.	0.97±0.04	Hg 1.11±0.05*	8.18
		Pb 0.240±0.04[a]	14.31

a_p< 0.05; b_p<0.01; c_p<0.001;*- Insignificant
Values represent mean ± S.E., Number of observations (N)= 6

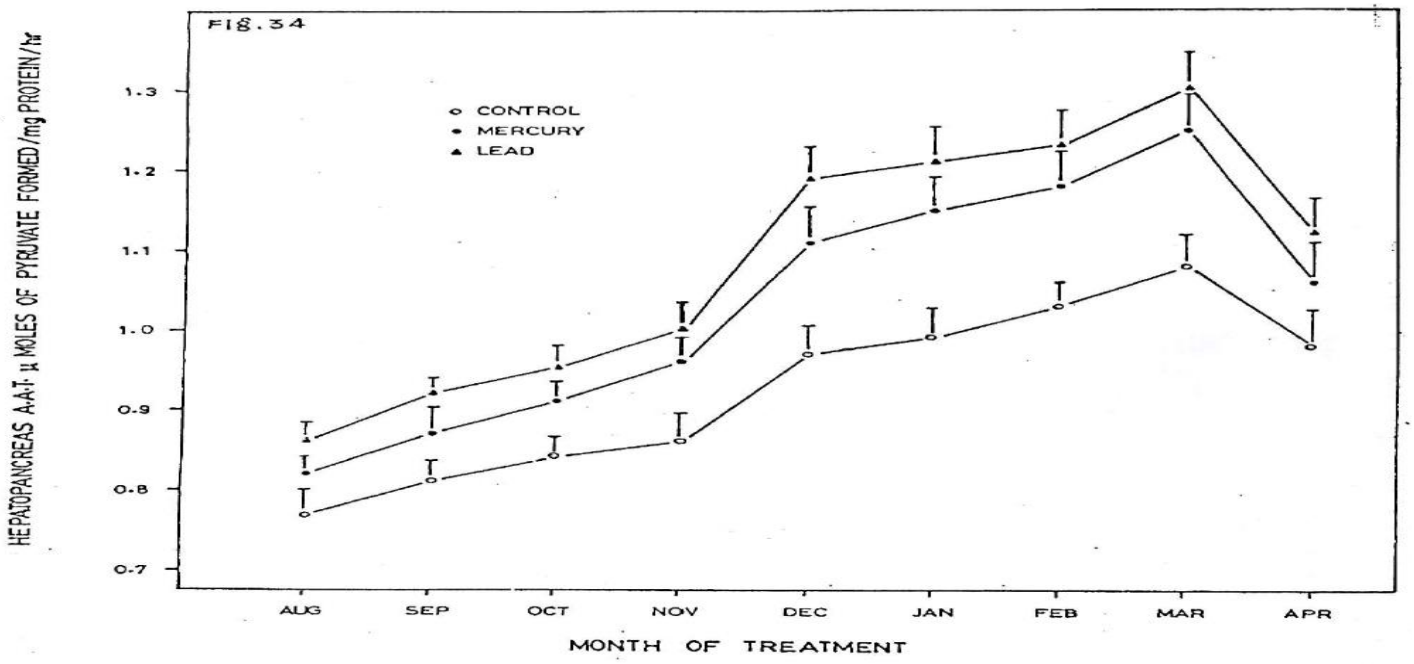

Fig. 1: Effect of mercury (Hg) and lead (Pb) on the activity levels of aspartate aminotransferase in the hepatopancreas of *H. fulvipes* during the gestation period

Pedipalpal muscle- The variation of activity of AST in the pedipalpal muscle of the maternal animal during different months of gestation period remained essentially the same both in the controls and the experimental animals.

But both mercury and lead at the sub-lethal concentrations administered, increased the activity of the enzyme in a dose dependent manner (Table 2; Fig. 2). The effect of mercury was not statistically significant up to four doses (except the august sample) beyond, which the effect was found to be significant statistically. The dose dependent impact is obvious with the gradually increasing percentage of elevation in the activity of the enzyme from 7.39% in Aug to 18.69% in April.

A similar effect of lead resulting in a statistically significant elevation in the enzyme activity in a dose dependent fashion from the beginning to the end of gestation period was noted.

Table 2: Effect of mercury (Hg) and lead (Pb) on the activity levels of aspartate aminotransferase (AST) in the pedipalpal muscle of *H. fulvipes* during the gestation period

Month of Treatment	AST umoles of pyruvate formed/mg protein/hr		
	Control	Experimental	Percent change
AUG	0.90±0.02	Hg 0.97±0.0[a]	7.39
		Pb 1.01±0.02[b]	12.03
SEP	1.11±0.03	Hg 1.18±0.02*	6.21
		Pb 1.22±0.01[b]	10.53
OCT	1.08±0.04	Hg 1.15±0.05*	7.03
		Pb 1.23± 0.05[b]	14.15
NOV	1.04±0.03	Hg 1.17±0.05*	12.40
		Pb 1.24±0.05[b]	18.89
DEC	1.31±0.04	Hg 1.51±0.02c	14.79
		Pb 1.58±0.03[c]	19.95
JAN	1.63±0.05	Hg 1.89±0.02c	15.78
		Pb 1.94±0.03[c]	19.02
FEB	1.49±0.04	Hg 1.76±0.02c	18.06
		Pb 1.81±0.02[c]	21.67
MAR	1.55±0.05	Hg 1.83±0.02c	18.34
		Pb 1.87±0.02[c]	20.91
APR	1.57±0.04	Hg 1.86±0.02c	18.62
		Pb 0.90±0.02[c]	21.23

a_p< 0.05; b_p<0.01; c_p<0.001; *- Insignificant
Values represent mean ± S.E., Number of observations (N) = 8

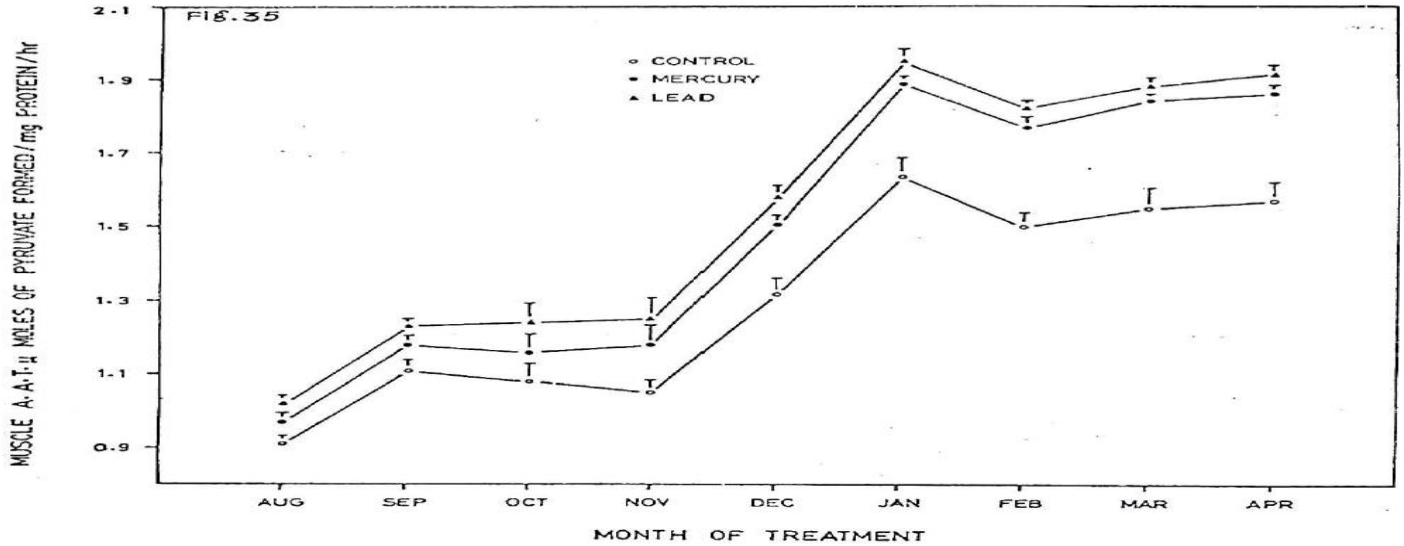

Fig. 2: Effect of mercury (Hg) and lead (Pb) on the activity levels of aspartate aminotransferase (AST) in the pedipalpal muscle of *H. fulvipes* during the gestation period

Embryos- The levels of activity of AST in control and experimental animals continuously increased all through the gestation period in a similar way (Table 3, Fig. 3).
It is however noted that the heavy metals mercury and lead elevated the levels of the enzyme activity, to increase in the number of doses of the sub-lethal concentrations of the two heavy metals, a dose dependent effect was not perceived, as the percent elevation of the activity did not steadily increase.

Table 3: Effect of maternal treatment with mercury (Hg) and lead (Pb) on the activity levels of aspartate aminotransferase in the embryos of *H. fulvipes* during the gestation period

Month of Treatment	AST umoles of pyruvate formed/mg protein/hr		
	Control	Experimental	Percent Elevation
SEP	0.91±0.031	Hg 0.96±0.02*	5.14
		Pb 0.99±0.03[a]	9.08
OCT	0.95±0.02	Hg 1.02±0.03*	6.88
		Pb 1.07± 0.03 [a]	12.20
NOV	1.07±0.02	Hg 1.12±0.02*	5.31
		Pb 1.18±0.02 [c]	10.35
DEC	1.23±0.01	Hg 1.32±0.02[b]	7.79
		Pb 1.36±0.02[c]	11.04
JAN	1.67±0.04	Hg 1.74±0.04*	4.00
		Pb 1.81±0.03[c]	8.60
FEB	2.13±0.10	Hg 2.25±0.09[c]	5.91
		Pb 2.27±0.09 [c]	6.71
MAR	3.55±0.10	Hg 3.87±0.07[a]	8.79
		Pb 4.07±0.05 [c]	14.55
APR	4.41±0.10	Hg 4.74±0.21*	7.42
		Pb 4.95±0.16 [b]	12.06

a_p< 0.05; b_p<0.01; c_p<0.001; *- Insignificant
Values represent mean ± S.E. Number of observations (N) =8

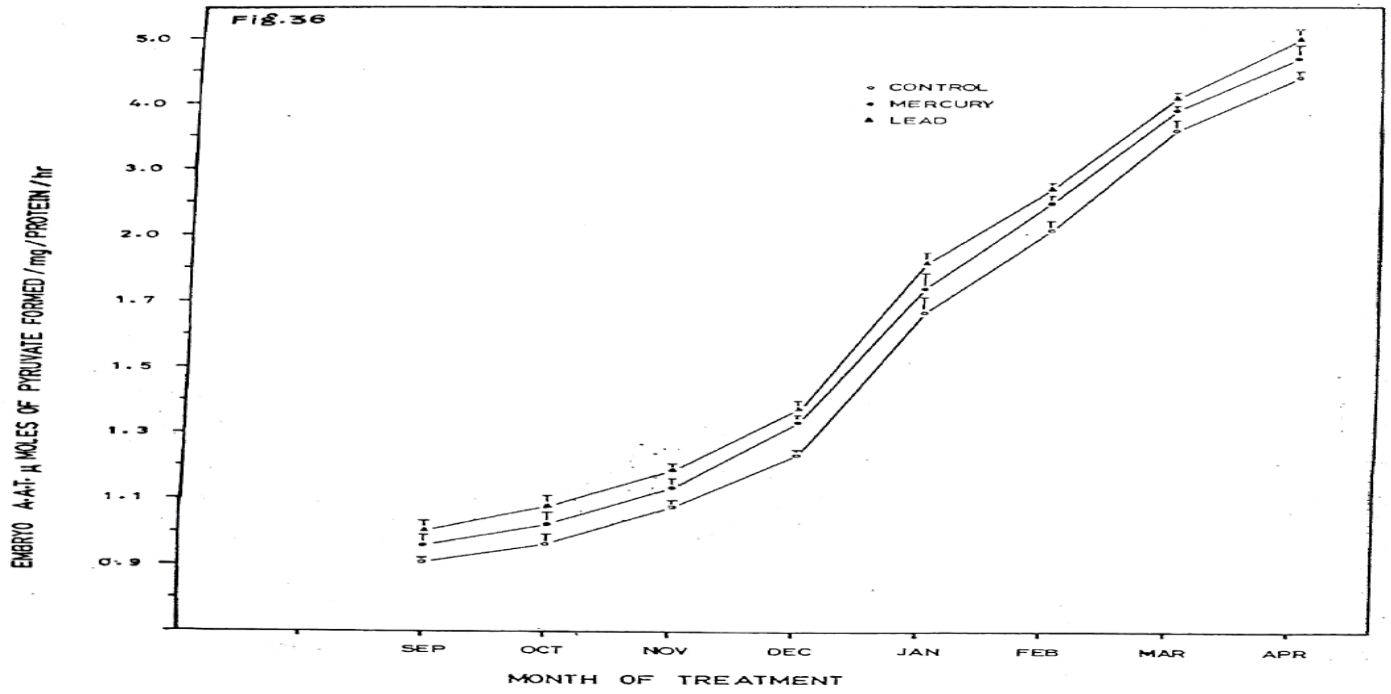

Fig. 3: Effect of maternal treatment with mercury (Hg) and lead (Pb) on the activity levels of aspartate aminotransferase in the embryos of *H. fulvipes* during the gestation period

Effect of mercury and lead on the levels of activity of alanine aminotransferase (ALT) in the maternal tissues and embryos

Maternal hepatopancreas- The activity of the alanine aminotransferase exhibited an initial rise in September month followed by a sudden decline in October beyond which there was a slow, steady progressive elevation up to March samples and a decline in April month samples.

Administration of monthly sub-lethal doses of mercury during the gestation period did not alter the pattern of variation, but depleted the levels of activity of the enzyme, though, statistically not significant for the samples of October, November, December and April (Table 4, Fig. 4).

A similar effect of lead resulting in statistically significant depletion in the enzyme activity from the beginning to the end of gestation period was noted except in April month sample.

Table 4: Effect of mercury (Hg) and lead (Pb) on the activity levels of alanine aminotransferace in the hepatopancreas of *H. fulvipes* during the gestation period

Month of Treatment	ALT umoles of pyruvate formed/mg protein/hr		
	Control	Experimental	Percent Depletion
AUG	0.90±0.02	Hg 0.81±0.03[a]	9.97
		Pb 0.79±0.03[b]	12.19
SEP	1.15±0.01	Hg 1.05±0.03[b]	8.76
		Pb 0.99±0.04[b]	13.36
OCT	0.91±0.05	Hg 0.84±0.02*	7.74
		Pb 0.78± 0.02 [a]	14.28
NOV	0.94±0.05	Hg 0.85±0.02*	9.41
		Pb 0.79±0.03 [a]	15.47
DEC	0.98±0.05	Hg 0.88±0.02*	9.98
		Pb 0.83±0.02[a]	14.66
JAN	1.11±0.01	Hg 0.98±0.04c	10.99
		Pb 0.96±0.05[c]	12.88
FEB	1.19±0.03	Hg 1.04±0.03[b]	12.21
		Pb 1.02±0.04 [b]	14.05
MAR	1.22±0.02	Hg 1.04±0.03[c]	15.03
		Pb 1.02±0.04 [c]	16.58
APR	1.05±0.04	Hg 0.97±0.04*	7.02
		Pb 0.94±0.05 *	10.63

a_p< 0.05; b_p<0.01; c_p<0.001; *- Insignificant
Values are representing mean± S.E. Number of observations (N) =8

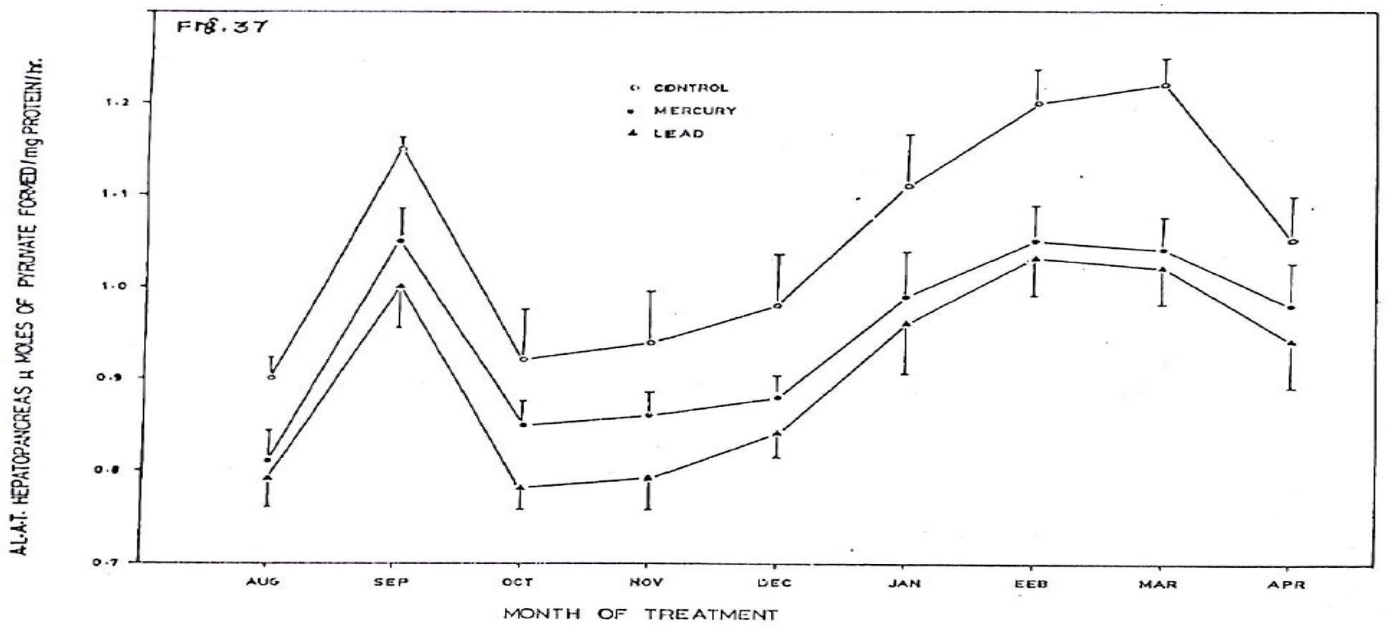

Fig. 4: Effect of mercury (Hg) and lead (Pb) on the activity levels of alanine aminotransferace in the hepatopancreas of *H. fulvipes* during the gestation period

Pedipalpal muscle- In the scorpion treated with sub-lethal doses of mercury and lead, the pattern of variation in the levels of activity of ALT during the gestation period remained essentially the same as controls (Table 5; Fig. 5).

However the activity of the enzyme was depressed in each of the samples of scorpions treated with sub-lethal doses of mercury, though statistically insignificant in august October and November month samples but significant in the rest of the samples. Sub-lethal dose of lead exerted a significant effect through its depressant action which was statistically significant in all the samples except in October month.

Table 5: Effect of mercury (Hg) and lead (Pb) on the activity levels of alanine aminotransferace in the pedipalpal muscle of *H. fulvipes* during the gestation period

Month of Treatment	ALT umoles of pyruvate formed/mg protein/hr		
	Control	Experimental	Percent Depletion
AUG	0.37±0.02	Hg 0.31±0.01*	15.01
		Pb 0.31±0.01[a]	16.62
SEP	0.39±0.02	Hg 0.32±0.01[a]	17.93
		Pb 0.32±0.041[b]	18.68
OCT	0.30±0.02	Hg 0.27±0.01*	10.82
		Pb 0.26± 0.01 *	14.75
NOV	0.31±0.02	Hg 0.27±0.01*	12.14
		Pb 0.26±0.01 [a]	15.97
DEC	0.32±0.01	Hg 0.28±0.01[a]	12.80
		Pb 0.27±0.01[a]	15.24
JAN	0.35±0.01	Hg 0.30±0.01[a]	13.92
		Pb 0.30±0.01[b]	16.15
FEB	0.31±0.01	Hg 0.26±0.01[a]	15.28
		Pb 0.25±0.01 [b]	20.38
MAR	0.40±0.02	Hg 0.34±0.01[a]	14.18
		Pb 0.33±0.01 [b]	16.17
APR	0.29±0.01	Hg 0.25±0.01[a]	13.85
		Pb 0.24±0.01 [b]	17.90

a_p< 0.05; b_p<0.01; c_p<0.001; *- Insignificant
Values are representing mean± S.E. Number of observations (N) =8

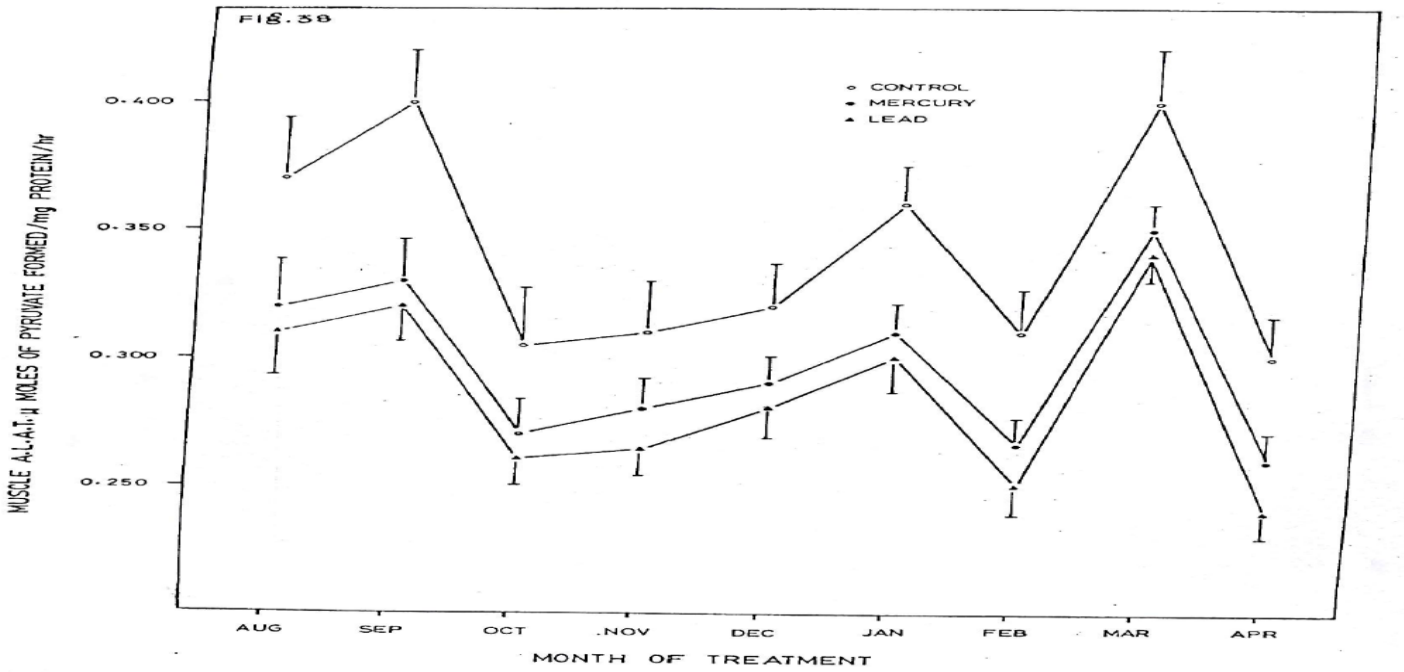

Fig. 5: Effect of mercury (Hg) and lead (Pb) on the activity levels of alanine aminotransferace in the pedipalpal muscle of *H. fulvipes* during the gestation period

Embryos- The level of activity of ALT in embryos increased continuously all through the gestation period both in the controls and the experimental animals with no change in the pattern of variation during the gestation period (Table 6; Fig. 6). However both the heavy metals depress the activity of the enzyme, through statistically significant, only during the later stages of gestation period.

Table 6: Effect of maternal treatment with mercury (Hg) and lead (Pb) on the activity levels of alanine aminotransferase in the embryos of *H. fulvipes* during the gestation period

Month of Treatment	ALT umoles of pyruvate formed/mg protein/hr		
	Control	Experimental	Percent Depletion
SEP	1.21±0.005	Hg 1.16±0.05*	4.52
		Pb 1.15±0.05*	5.02
OCT	1.30±0.06	Hg 1.23±0.04*	5.30
		Pb 1.21± 0.04 *	6.52
NOV	1.49±0.08	Hg 1.35±0.06*	9.60
		Pb 1.33±0.06 *	10.74
DEC	1.87±0.11	Hg 1.65±0.04[a]	11.76
		Pb 1.62±0.05[a]	13.20
JAN	2.20±0.12	Hg 2.09±0.04[a]	5.03
		Pb 2.06±0.04*	6.48
FEB	3.56±0.07	Hg 3.38±0.05*	4.83
		Pb 3.32±0.04 [a]	6.54
MAR	3.92±0.10	Hg 3.65±0.06[c]	6.90
		Pb 3.58±0.06 [c]	8.59
APR	3.98±0.11	Hg 3.72±0.06[c]	6.42
		Pb 3.59±0.06[c]	9.76

a_p< 0.05; c_p<0.001; *- Insignificant
Values are representing mean± S.E. Number of observations (N) =8

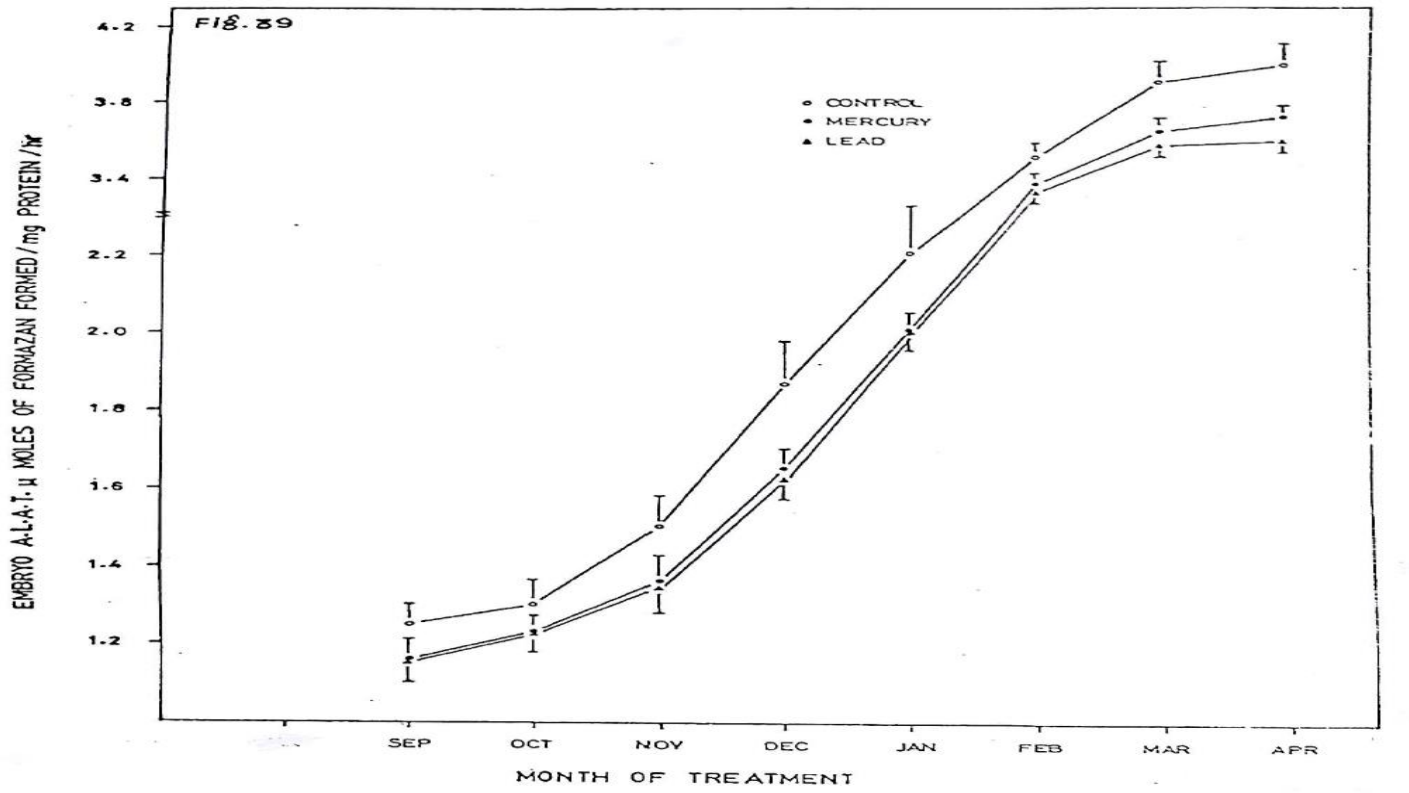

Fig. 6: Effect of maternal treatment with mercury (Hg) and lead (Pb) on the activity levels of alanine aminotransferase in the embryos of *H. fulvipe* during the gestation period

DISCUSSION

Heavy metals are known to interfere with the metabolism of many animals by directly interfering with the enzymatic system in internal homeostasis. Even low dose can result in increased morbidity and mortality in the long run. The combination of different heavy metals can have an added toxicity due to its additive effects. Lead is found to have a toxic effect in a very low dose [14]. There was a significant alteration in the liver function of Cadmium treated mice attributed to the modification in the hepatic genes, lipid metabolism, oxidative phosphorylation and cell death cascade. Heavy metals like Cadmium can result in protein oxidation and activation of inflammatory signaling. Cadmium burden has been associated with the nonalcoholic fatty liver disease (NAFLD) in the humans. [15] Similarly hepatic zinc deficiency has been linked to the liver toxicity in Wistar rats' due to uncontrolled activation of the internal cell death cycle. [16]

Elevation in the levels of AST in the maternal tissue of *H. fulvipes* can be considered a response to the stress induced by the heavy metals, mercury and lead to generate keto acids like alpha-ketoglutarate and oxaloacetate for contributing to gluconeogenesis and/or energy production necessary to meet the excess energy demand under the toxic manifestations. The elevation of AST activity provides the oxaloacetic acid required for the gluconeogenic pathway, to meet the additional supply of glucose for the production of energy under the reduced phase of oxidative metabolism. The inhibition of the activity of alanine aminotransferase in the maternal tissue of *H. fulvipes* under the heavy metal treatment is suggestive of the specific impact of mercury and lead of different enzymes.

The depletion of proteins under the stress of the heavy metals, mercury and lead observed in the maternal tissues of *H. fulvipes,* indicating proteolysis, prompted the suggestion that the proteins are utilized for meeting the excess energy demand imposed by the toxic stress [11]. The alterations in the levels of activity of glutamate dehydrogenase and aminotransferases induced by the heavy metals, mercury and lead, clearly indicate that the stress brings about the metabolic reorientations in the maternal tissues by raising energy resources in transaminase system.

The responses of the enzyme system in the embryos of the maternal animals treated with sub-lethal doses of mercury and lead are basically similar to, and not much different from, the responses observed in the maternal tissues. This probably suggests that the embryo behaves as an integral part of the maternal tissues and cannot be considered to reflect any autonomous status. The reduction in the size of the embryo observed, when the maternal animal was treated with the heavy metals during the gestation period, can hence be attributed to the excessive utilization of the biochemical constituents for energy needs, mediated by their enzyme systems, both by the mother and embryos, apart from the consequences lowered supplies of nutrients from the mother to the embryos.

Heavy metal toxicity is the public health concern, resulting in significant public health expenditure. Cadmium, chromium, lead, and mercury are the most toxic heavy metals, ranking highest in the priority metals related to the general public health. Experimental animals have shown varied clinical symptoms with lead exposure, ranging from cognitive, behavioral, and learning abnormalities. [14] Cadmium exposure has been lined to some cancers [17]. Nickel compound exposure has been associated with hypersensitivities and nephrotoxicity [18]. Zinc exposure can interfere with hematopoietic and endocrine balance [19]. Copper, essential heavy metals, can result into intestinal disturbances and liver toxicity. Heavy metals have profound toxic properties that can cause widespread damage to multiple organs in our body. [20] But the study of the effects of heavy metals in pregnancy, and in utero is still limited. Pregnancy is an enhanced and distinct physiological scenario. Therefore, it is necessary to study and establish the effects of heavy metals in humans, including mother and fetus, to prevent the morbidity and mortality associated with it. This can be achieved through further studies with heavy metals targeted specifically to mother and fetus to strengthen, consolidate, and replicate the findings for the formulation of effective public health program.

CONCLUSIONS

Heavy metal exposure in animals can have a profound effect on the growth and development with alteration in biochemical constituents and enzyme levels. There were significant changes in the activity levels of the enzymes aspartate aminotransferase and alanine aminotransferase with chronic exposure to heavy metals in animal models. It is pertinent that the heavy metal toxicity be well documented and appropriate precaution taken to decrease its detrimental effects. Therefore, further research is warranted in humans to study the impact of heavy metals in growth and development and develop prevention strategies.

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