TECHNICAL REPORT

DETERMINATION OF TRANSAMINASES AND CREATINE KINASE LEVELS IN PATIENTS WITH MUSCULAR DYSTROPHY AND MUSCULOSKELETAL DISEASES

ABSTRACT

BACKGROUND
The transaminases, ALT and AST (alanine and aspartate transaminases, respectively), that are generally considered to be the hepatic enzymes, also found in skeletal muscles. Continual elevated levels of both enzymes in patients with several forms of muscular dystrophy and musculoskeletal diseases have been documented in several studies.

AIM AND OBJECTIVES
The present study is undertaken to examine the possibility of highlighting transaminases elevation in muscular dystrophy as an indicator of concomitant muscular damage, rather than hepatic injury due to medications, and relate its significance with underlying myofibrillar damages.

MATERIALS AND METHODS
Data of a total of 52 patients (males = 38, females = 14) were obtained during December 2006 to December 2011 and complied as per criteria. Plasma CK enzyme and transaminases (AST and ALT) levels were performed by enzymatic methods on Hitachi 912. A specific hepatic marker gamma glutamyl transpeptidase (GGT) was also measured to assess the extent or presence of hepatic damages. All enzymatic data were analyzed using regression correlation analyses with significance level of $P < 0.05$.

RESULTS
Cumulative as well as individual data analysis showed significant correlation of transaminases with CK, which is the distinct indicator of muscle damage. ALT R^2 correlation with CK showed linear regression correlation of $R^2 = 0.796$ and for AST $R^2 = 0.814$. Cumulative mean of CK was 406.83 ± 20.15 IU/L; ALT = 70.86 ± 10.21 IU/L, AST = 68.78 ± 8.30 IU/L and ɣGT = 20.13 ± 4.30 IU/L.

CONCLUSION
The present study describes the elevated level of transaminase, ALT and AST in patients of muscular dystrophy and myopathies. It was also exhibited that both transaminases concentration linearly correlated with muscle marker CK. No hepatic damage was noted in all patients as manifested by normal levels of GGT, a distinct marker of hepatic origin.

KEY WORDS
Creatine Kinase, Alanine transaminase (ALT), Aspartate Transaminase-(AST), Muscular Dystrophy, Myopathy, Regression.

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INTRODUCTION

Continual elevated levels of serum transaminases (Alanine transaminase-ALT; Aspartate transaminase-AST) in patients with several forms of muscular dystrophy and musculoskeletal diseases have been documented in earlier studies[1-5]. Additionally, similar biochemical manifestations has also been observed in inflammatory myopathies[1,6]. The transaminases, ALT and AST, generally considered to be the hepatic enzymes, are also found in skeletal muscle[1,6,7]. However, the concentration or activity of both in skeletal musculature is one tenth of those occur in hepatocyte origin. Creatine kinase (CK) or creatine phosphor-kinase (CPK), on the contrary, is a susceptible marker of skeletal muscle dystrophy, such that its concentration reaches 100 times higher in muscle than in hepatocytes after onset or progression of a disease[1,8]. Previous studies regarding determination of transaminases in patients with muscular dystrophies and myopathies suggested that ALT and AST elevation might also be due to myofibrillar damages, which causes their release in the blood stream[7,9]. It was also pointed out that restricting ALT/AST in the determination of the hepatocyte damages, which might be caused by usage of myopathy treating medications, such as steroids, azathioprine and methotrexate, could sometimes be misleading and may end in halting the treatment[9-12].

The present study is undertaken to examine the possibility of highlighting transaminases elevation in muscular dystrophy as an indicator of concomitant muscular damage, rather than hepatic injury due to medications, and relate its significance with underlying myofibrillar damages.

MATERIALS AND METHODS

Study Design and Data Collection

The study design followed for the presented research was established methods and protocols documented earlier[13]. Briefly, the inclusion period for this cohort study was from December 2006 to December 2011, of which data were collected retrospectively from November 2006 to December 2004 and prospectively from December 2006 to Dec 2011. Patients who met the following criteria were eligible for the study. Thus the inclusion criteria were patients aged > 20 years to <75 years and had a diagnosis of myopathies as per description of reported earlier[14,15]. Data of total 52 patients (males = 38, females = 14) were obtained and complied as per criteria. Data was also collected from LIS and HIMS archives, where possible.

Blood sample Collection and Analysis

Blood samples were collected by venipuncture on Li-heparinate 5 ml tubes from patients after 72 hours of resting and an overnight fasting. Plasma CK enzyme and transaminases (AST and ALT) levels were performed by enzymatic methods at admittance and at the diagnosis of myopathy. AST, ALT and CK levels were measured on Hitachi 912 (Roche Diagnostics-Basel) using commercial kits and both internal and external quality controls. A specific hepatic marker Gamma Glutamyl Transpeptidase (GT) was also measured to assess the extent or presence of hepatic damages. The normal ranges for enzymatic analytics are plasma CK/CPK, males > 18 years: 52-336 IU/L, females > 18 years: 38-176 IU/L; AST, 8-48 IU/L; and ALT, 7-45 IU/L, and ɣGT Males = 12-48 IU/L and females = 6-29 IU/L, respectively.

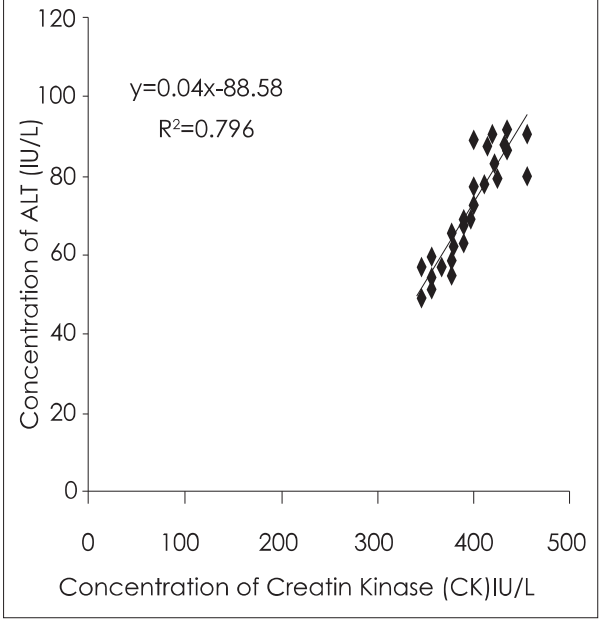
Statistical analysis

All enzymatic data obtained were analyzed using SPSS 13 (USA), considering significant level of $P < 0.05$. Additionally, regression analysis was also performed to correlate AST and ALT levels with that of CK.

RESULTS

A total of 52 patients (males = 48, females = 14) were selected for the present study. Initially over the period of December 2006 to December 2011, data sets of around 160 patients (Males = 103 and females = 57) were screened and analyzed, out of them 52 falls into our required criteria. Cumulative as well as individual data analysis showed significant correlation of transaminases with CK, which is the distinct indicator of muscle damage. ALT R^2 correlation with CK showed linear regression correlation of $R^2 = 0.796$ (Fig 1) and for AST $R^2 = 0.814$ (Fig 2). To distinguish the fact that the correlation of transaminases determined in serum/plasma was that from muscle injury and not from hepatocyte damage, a prominent hepatocyte marker ɣGT was also estimated and analyzed for correlation with CK. Interestingly, no significant relationship was obtained, as ɣGT levels were found to be mostly within the normal ranges and thus manifested R^2 values of less than 02 (R^2 CK versa ɣGT = 0.016) (Fig 3). Cumulative mean of CK = 406.83 ± 20.15 IU/L; ALT = 70.86 ± 10.21 IU/L, AST = 68.78 ± 8.30 IU/L and ɣGT = 20.13 ± 4.30 IU/L.

Fig 1: Correction between CK and ALT in patients (n=52) with muscular dystrophy and myopathies



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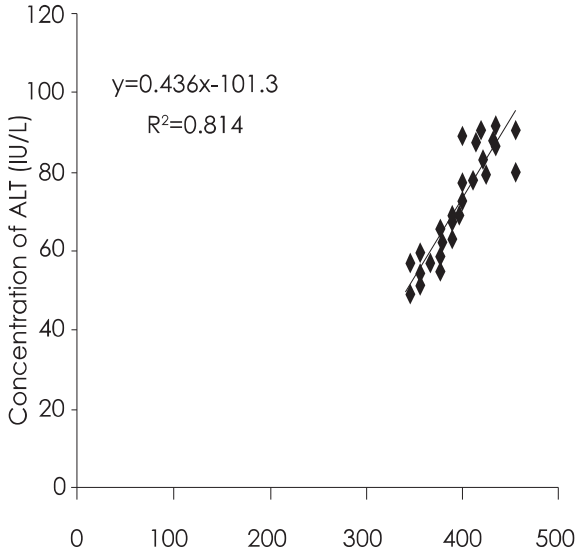

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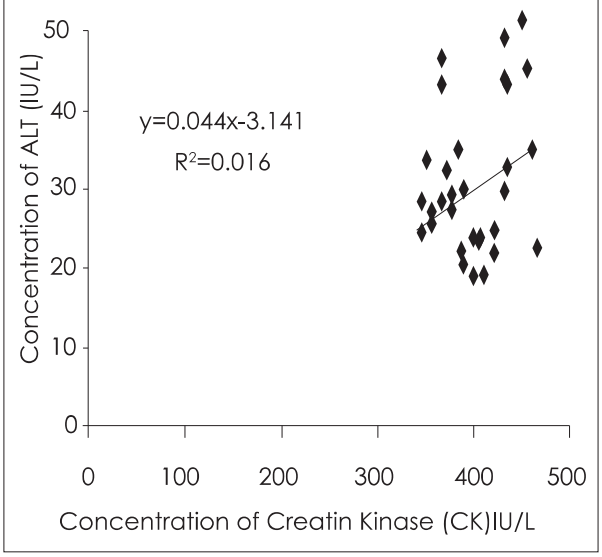

DISCUSSION

It was discussed in several studies and even proven that high transaminase levels in patients with muscular dystrophy and myopathies, and also in those undergoing treatments, were from muscle damage rather than hepatocyte injury[1,9,16].

The researcher have argued that evidently manifesting proximal muscle weakness with high CK level in patients also suggests that occult muscular dystrophy or inflammatory myopathy might also be responsible for the same[1,4,5]. In our study high levels of transaminases correlated well with elevated levels of CK, with mostly normal levels of ɣGT, a prominent hepatic injury marker, thus suggesting evidently, that transaminases leakage in blood stream was from muscular cells rather than hepatocytes. Moreover, several past studies also noted that, without taken into consideration the linearly correlated high levels of transaminases with CK, or establishing the fact that there might be some underlying, undiagnosed myopathies, without any hepatic damages due to medications; treatments were halted or altered, thus causing hardships for patients[9-12,17].

It was reported earlier that elevated transaminase levels were noted in myositis9-12 and muscular dystrophy[17,18]. High transaminase levels, especially that of ALT upto 50% (and AST upto 17%) were reported in a study carried out in patients with myotonic dystrophy type 2[16]. Similarly another study documented that transaminase performs several metabolic functions in many cells, including that of muscles, and its leakages into the blood stream might be due to myofibrillar damages, as usually observed in case of elevated LDH and CK concentrations[9,19].

In conclusion, the present study describes the elevated level of transaminase, ALT and AST in patients of muscular dystrophy and myopathies. It was also exhibited that both transaminases concentration linearly correlated with muscle marker CK. No hepatic damage was noted in all patients as manifested by normal levels of ɣGT, a distinct marker of hepatic origin.

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