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The potential of reducing AST testing in hospital settings

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ABSTRACT

Background: Aspartate aminotransferase (AST) is regularly ordered with alanine aminotransferase (ALT) to assess liver integrity. In many situations, AST testing provides little or no added clinical value, since ALT is more specific and the both enzyme activities highly correlate. The objective of this study is to determine the potential reduction in AST testing, if not performed when ALT results are within reference intervals (RI).

Methods: Results for patients > 18 years of age for both AST and ALT from the same specimen were obtained for the period January 1, 2017 – December 31, 2017. We calculated frequency of AST and ALT results that had various combinations of results within and above the RI. We also investigated the clinical locations of origin for the samples.

Results: In total 87,704 paired samples with both AST and ALT test results were recovered. The total of 73.2% of AST tests for males and 66.9% for females would be eliminated if we performed AST testing only when ALT was increased. However, 7.4% of elevated AST tests would be missed for males and 3.8% for females due to ALT being within limits. Specifically in the outpatient clinics, 79% male and 73% females paired enzyme results were within RI. Only 4% of males and 3% of females had paired results where ALT was within RI while AST > RI.

Conclusions: The rate of test results with increased AST while ALT is within the RI is low enough to recommend limiting AST testing only to cases where ALT is above the RI. Our recommendation for AST restriction is to begin with the hospitals outpatient clinics.

1. Introduction

Aspartate aminotransferase (AST) is regularly ordered along with alanine aminotransferase (ALT) to assess liver integrity. Major clinical laboratory institutions list the enzyme AST solely as a useful test for diagnosing and monitoring liver disease, particularly diseases resulting in a destruction of hepatocytes. AST testing is, however, ordered in many situations where it provides little or no added clinical value, since ALT is more specific for the liver. AST is also present in high levels in skeletal and cardiac muscle, red and white blood cells, brain, pancreas, lung and kidney, and thus highly unspecific [1,2]. Moreover, both enzyme activities highly correlate [3]. Chronic alcohol intake causes the mitochondrial AST activity to rise in plasma, yielding the AST/ALT ratio > 1.5. The ratio, also called De Ritis ratio, has been used by clinicians to support the diagnosis of alcoholic hepatitis [4,5].

There have been ongoing initiatives in medical community to reduce unnecessary AST testing, such as omitting the test from the community laboratory requisitions. For example, the report made on behalf of the Government of Ontario in 2013 concluded that given the lack of specificity of AST compared to ALT, AST tests had limited utility in the community setting and testing should be restricted. The experts agreed that the AST/ALT ratio can, in some cases, provide important information to help differentiate between types of liver damage, in particular when determining if the damage is alcohol related. However, the experts felt that ALT, the more specific liver test, should be the primary test used in community-based laboratories with access through hospitals to those specialists who require the additional information that AST may provide [6]. However, a few years later after restriction implementation it was found that AST was being ordered in situations where the result was not useful in improving the health of a patient, deeming it thus as unnecessary. A report submitted to the Ontario Government suggested that almost 1.5 million AST tests conducted between April 2014 and March 2015 (costing about $3.8 million), potentially provided no clinical value [7]. In another report, from the Government of British Columbia Ministry of Health, the delisting of AST from the Laboratory Services Outpatient Payment Schedule was approved. This decision was made following a review of the clinical value of the AST test when compared with ALT test. It was stated that given that ALT was comparable to AST, and readily available to physicians and had an average test cost lower than AST, laboratory

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Table 1
All-department and outpatient clinics paired AST/ALT results for males and females.

	AST, ALT < URL (%)	AST > URL, ALT < URL (%)	AST, ALT > URL (%)	AST < URL, ALT > URL (%)
All departments - males	67	7	19	7
All departments - females	63	4	19	14
Outpatient clinics - males	79	4	10	7
Outpatient clinics - females	73	3	11	13

AST – aspartate aminotransferase; ALT – alanine aminotransferase; URL – upper reference limit.

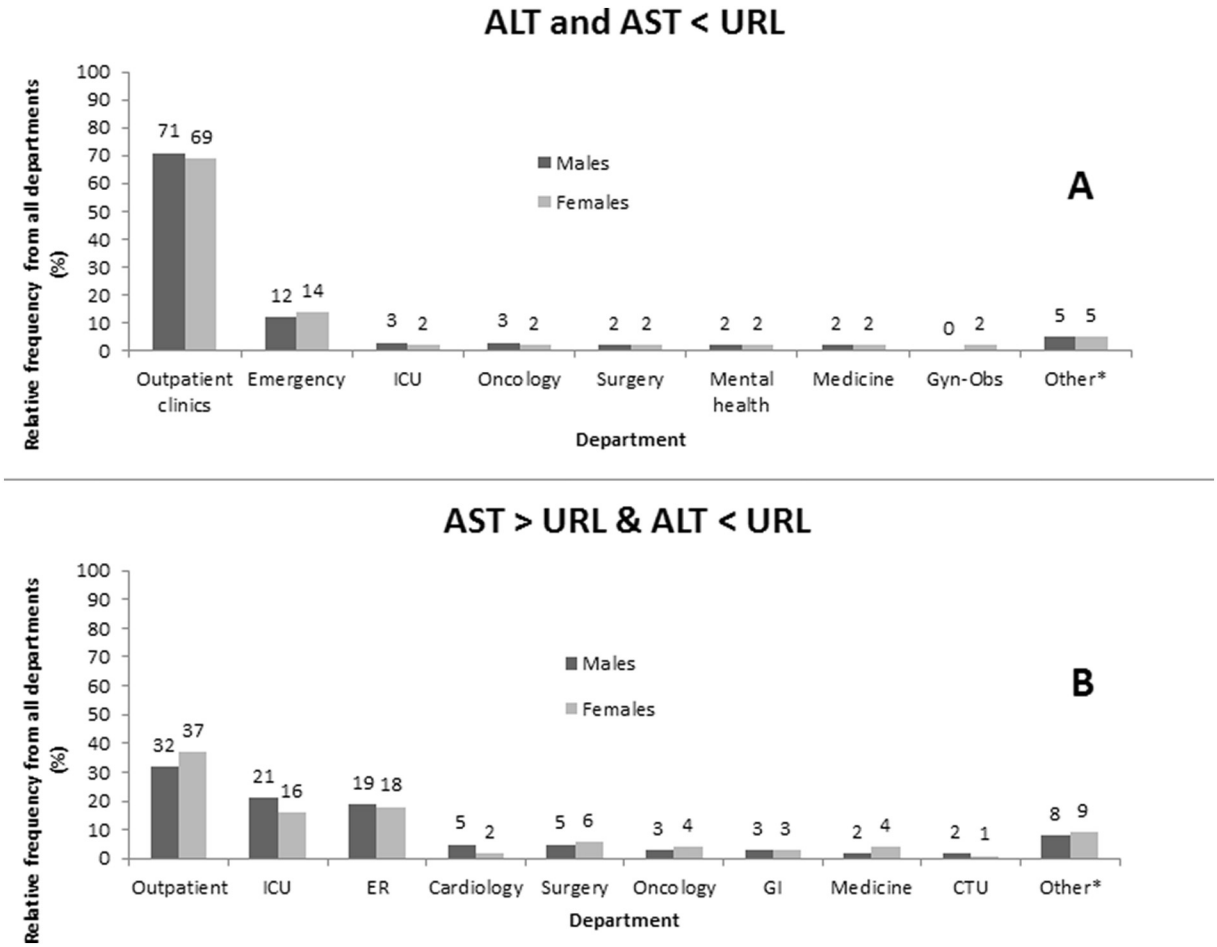

Fig. 1. Results of (A) ALT and AST < URL; and (B) ALT < URL and AST > URL, stratified by department.
AST – aspartate aminotransferase; ALT – alanine aminotransferase; URL – upper reference limit; ICU – intensive care unit; ER – emergency department, Gyn-Obs – Gynecology/obstetrics; GI – gastroenterology department; CTU – clinical teaching unit.

operators were to substitute any request for AST with ALT [8].

The objective of this study is to determine the potential for reduction in AST testing, if not performed when ALT results are within the reference interval (RI). Using data from the Hamilton Regional Laboratory Medicine Program (HRLMP), we seek the departments where the AST ordering reduction will add the most value and benefit to both patients and laboratory.

2. Methods

The results for AST and ALT, from the same specimen, were obtained from the Laboratory Information System (LIS) of HRLMP, which serves hospitals and clinics belonging to the Hamilton Health Sciences (HHS) and St. Joseph's Healthcare Hamilton (SJHH). These institutions provide a wide variety of patient care, from numerous outpatient clinics to tertiary-quaternary inpatient care. We analyzed AST and ALT results in the period of 12 months, from January 1, 2017 – December 31, 2017.

We analyzed data by creating four categories, in order to see the frequency of situations where AST and ALT results were in concordance (1) ALT and AST within RI, and (2) ALT and AST above RI; or the results showed discordant values (3) ALT within RI, AST > RI, and (4) ALT > RI, AST within RI. The categories (1) and (3) represent situations where AST testing could be omitted since ALT result is within RI and we focused our analyses on these two categories. Of our particular interest was the situation where AST was elevated while ALT was within the limits, since in this case elevated AST would be missed. Furthermore, the relative frequency of test results in each category was subdivided by location/department where the test order originated. The departments from different hospitals were combined to see the practice and results that are department specific [e.g. outpatient clinics, emergency department (ED), intensive care units (ICU), inpatient surgery etc.].

3. Results and discussion

The total number of paired AST/ALT test results of 87,704 (49.2% females) was analyzed after initial cleaning of the datasets. The results were excluded if: patient was < 19 years of age, no age information was given or there was an error with age information; or sex information was unknown considering different reference values for males and females for ALT. The RI for AST is < 35 U/L, while the RI for ALT is < 41 U/L in males and < 28 U/L in females. The paired test results of both enzymes for males and females in all departments together are presented in Table 1. Concordant AST and ALT results were present in 86% cases for males (n = 38,316) and 82% cases for females (n = 35,383). If ALT results within the RI had been used to eliminate AST testing, 74% AST tests in males (n = 32,970) and 67% in females (n = 28,911) would not have been run. In this situation, 7% of high AST in males (n = 3119) and 4% in females (n = 1295) would have been missed in the total population. The paired results where ALT was lower than the upper reference limit (URL), with concurrent increased AST, were further divided into categories regarding the extent of AST elevation. In only 10% of all cases, AST results were actually > 2× URL and likely clinically insignificant and only 1% > 20× URL, which strengthens our proposal for reducing its utilization without missing meaningful results.

The results where ALT < URL and AST either < URL or > URL were further investigated with respect to ordering department. This analysis gives us insight as to where the most aminotransferase orders come from, and if we omit AST testing when ALT is within RI, which departments we will need to focus on for the test reduction and consequently elimination. The results with respect to ordering location are presented in Fig. 1A for the results where both enzymes were within RI and in Fig. 1B for ALT < URL AST > URL. It can be clearly seen that the majority (70%) comes from various outpatient clinics, rendering an exemplary department where AST reduction may come in place. The outpatient clinics are followed by ED across our hospital network (13%). Other departments represented much lower number of paired, non-flagged, AST/ALT results. Similarly, the highest percentage where ALT was within RI while AST was high was observed in the outpatient clinics (32% males, 37% females), followed by ICU for males (21%) and ED for females (18%). The third place was occupied by ICU (16%) for females and ED for males (19%).

The outpatient clinics represented the majority of cases where both enzymes were not flagged by LIS, and we analyzed their relative frequency of non-flagged results. It can be clearly seen that more than two thirds (79% for males, 73% for females) paired enzyme results were within RI. Only 4% of cases for males and 3% for females had paired results where ALT was within RI while AST > URL (Table 1). The results where AST was elevated while ALT was within RI are clearly rare in the outpatient settings (< 5% for both sexes), providing a proof for potential restrictions in this area of clinical care. For that reason we endorse the restriction of AST ordering if ALT was within the reference limits, which could be location-based. With the respect to cost-reduction, this would result in approximately $6200 being saved for not running the AST test alone, considering only the reagent, quality control and calibrator costs (not considering fixed costs such as personnel and instrument).

Females have a lower RI for ALT and a higher proportion of cases with elevated ALT while AST is normal (14%) when compared to males (7%). The narrower RI may thus impact the proportion of AST high, ALT normal group. RI re-verification could provide answer whether this truly affects ALT results in females. Another noteworthy observation is comparison with the study done by Xu et al. [3], performed in Edmonton, Alberta. They analyzed 15 months of paired AST and ALT test results obtained from a large community laboratory (receiving all community samples from Northern Alberta) and Edmonton's five hospitals (a university hospital offering tertiary-quaternary care, a tertiary care hospital, and three general hospitals). Their results and suggestions agree with ours, while our study adds information regarding gender and specific medical departments. We plan to conduct the follow up study where we would assess the frequency of elevated AST that could be due to hemolysis, high leukocytes and muscle involvements, which would lay more evidence for implementing AST testing reduction.

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