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Original Research Article

Alcohol state markers- facility and utility for clinical management of alcohol use disorders: study from a tertiary care centre in South India

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ABSTRACT

Background: Alcoholism is broadly any drinking of alcohol resulting in significant psychological and physiological health problems. As alcoholism is not a recognized diagnostic entity the detection and monitoring of the clinical manifestations of alcoholism is of great importance in the alcohol use disorders (AUD) treatment. Hence, the use of alcohol biomarkers plays a vital role in the diagnosis, treatment and prognosis of AUDs.
Methods: This study aimed to understand the utility of state markers in alcohol related distress, both for diagnosis and prognosis in a tertiary care centre. The relative number and the frequency of the alcohol biomarker tests such as AST (aspartate aminotransferase), ALT (alanine aminotransferase), MCV (mean corpuscular volume) and GGT (gamma-glutamyl transferase) investigated in the hospital departments (32 departments) were collected. Test requests and results in January to March on five consecutive years from 2016 to 2020 were analyzed, by comparing psychiatry department with all other departments and AUD with non-AUD cases.
Results: The study findings revealed that, the tests AST, ALT and MCV were well utilized for the AUD treatment procedure in the tertiary care centre, irrespective of the department the patient got admitted. Since GGT was the least preferred test, the figures of GGT could not be analysed because of the exceptionally low number.
Conclusions: The utility of the commonly available alcohol biomarker tests is especially useful for the clinical management of AUD patients and these are well utilized in an appreciable manner in the study centre. Development of more accurate, specific, and sensitive panel of biomarker tests may further motivate clinicians to better monitor individuals who suffer from alcoholism.

Keywords: Alcohol biomarkers, Alcohol use disorders, Aspartate aminotransferase, Alanine aminotransferase, Mean corpuscular volume, Gamma glutamyltransferase

INTRODUCTION

Biological markers in alcoholism include organ damage markers (state markers), markers of a genetic predisposition (trait markers) and novel markers. Among this State markers are biochemical tools indicative of recent alcohol consumption (acute or chronic) and the subsequent alcohol-induced organ damage. The Trait markers are markers indicative of a genetic predisposition which denotes the dependence of an individual on alcohol after a chronic long-term exposure.[1]

Although the direct alcohol biomarkers, such as the direct detection of ethanol in the serum, urine, breathe, or body fluids, are considered to be the gold standard in alcohol detection, these are valid only to test for very recent alcohol intakes as the ethanol is rapidly cleared from the body.[2] So, the use of indirect biochemical tools for the detection of both acute and chronic alcohol intake is of great importance in the diagnosis and prognosis in the treatment schedule of an alcoholic.[3] Biochemical state marker tests provide direct or indirect ways to estimate the amounts of alcohol consumed and the duration of ingestion, and to detect the harmful effects on body

functions resulting from long-term misuse.[4] These conventional biochemical panel of tests were used to identify chronic alcohol exposure, that include the liver function test, gamma-glutamyltransferase (GGT) and aspartate and alanine aminotransferase (AST and ALT) in serum, and the mean corpuscular volume of erythrocytes (MCV).[5] GGT, AST and ALT are standard diagnostic tools used in blood chemistry panels to indicate non-specific liver dysfunction, and MCV is often measured as part of a routine blood count.

Conventional biochemical tests like AST/ALT, MCV and GGT are reported to be widely used and relatively inexpensive and they provide valuable information on complications of drinking, comorbid conditions that may be affected by drinking and prognosis.[6-8]

The studies on the use of different biochemical markers for the determination of diagnostic tools for acute and chronic alcoholism, reports that serum GGTs level purely correlates with the period and duration of excessive alcohol consumption and was found elevated in 34-85% of cases.[9] An increased level of mean corpuscular volume (MCV) has been found in 31-96% of chronic heavy drinkers. Likewise, the ratio of AST to ALT was found to be exceeding by twofold in alcoholics and thus used to differentiate alcoholic and nonalcoholic liver injury.[10] Also, in 26-94% of patient, MCV levels was found to be elevated, and MCV in combination with the AST and ALT ratio could be used as biochemical tool of greater value in detecting the duration and extent of drinking episodes in heavy-drinkers than in screening for alcoholism.[11]

Recent studies indicate that combined measurement of GGT with other tests such as the early detection of alcohol consumption (EDAC) test panel viz., monocytes, high-density lipoproteins (HDL), AST, ALT, bilirubin results in improved diagnostic accuracy.[12-14]

These biochemical markers are useful in the identification of excessive drinking and give objective information on the degree and changes of alcohol consumption over time, and help the clinician to decide the possible role of alcohol in the clinical manifestations and disease process.[15] They enhance suspicion and could be combined with a clinical history, physical examination, and questionnaires and useful in follow-up treatment procedure of the patient.[16] An extensive review of state markers of alcohol was done by authors and published recently.[17]

The present study aimed to understand the utility of state markers in alcohol related distress both for diagnosis and prognosis in a tertiary care centre. The de-addiction treatment is offered by the psychiatry department of this centre. The number and the frequency of the alcohol biomarker tests investigated in the hospital departments were compared and analysed along with the data collected from psychiatry department.

METHODS

This was an observational retrospective study conducted in a tertiary care centre, Thrissur, Kerala, India using the data base of the study centre. The study aimed to explore the utility of state biomarkers of alcoholism in the departments of the hospital. Data was collected from all the 32 departments using survey sampling.

Inclusion criteria

The inclusion criteria used were the AST, ALT, MCV and GGT test requested from January to March in five consecutive years from 2016 to 2020 from all the departments.

Exclusion criteria

The repeated test request within three months of same year was excluded.

The database of the central laboratory was searched for the test reports of AST, ALT, MCV and GGT. Number of requisitions for these investigations from different departments and abnormal values were recorded. Both new cases and revisits were included. Each requisition slip with any one of these investigations or all the four is counted as one. Data from psychiatry department was taken and evaluated separately from other departments. Among the data from psychiatry department, the cases were sorted based on presence of alcohol use disorders (AUD). AUD is classified as per ICD (10^{th} revision) F10.0 to F10.9. Each category of AUD was collected in separate list from the hospital data base.

The data was entered in Microsoft Excel 2007. The frequency of investigations demanded from all departments and specifically from department of Psychiatry were noted and compared. The year wise and department wise distribution of abnormal test values were also compared similarly. The chi-square test was done to find association between; (i) test positivity and presence of AUD among patients from psychiatric department, and (ii) test positivity in AUD patients and their department.

RESULTS

In the present study we collected data regarding the test requests for state biomarkers of alcoholism, from central laboratory using hospital database during a period from January to March for the five consecutive years 2016, 2017, 2018, 2019 and 2020 respectively. Data of different years were selected for the study to avoid individual bias of any single consultant or team of consultants. Test requests from all the departments for the three months were tabulated. MCV was the most requested one (39.14%) and GGT the least (0.02%). The figures of GGT were not analyzed because of the very low number. The percentage of abnormal values for each test during each year is presented (Table 1).

Table 1: Year wise distribution of state biomarker tests and percentage of abnormal findings excluding psychiatry department.

State biomarkers		AST	ALT	MCV	GGT	Total
2016 (January- March)	Tests done	10578	12214	14044	14	36850
	>Normal values	31.7%	38%	40.4%	0	
2017 (January- March)	Tests done	11119	13212	15518	15	39849
	>Normal values	33.2%	30.1%	44.8%	0	
2018 (January- March)	Tests done	11676	13850	16464	7	41997
	>Normal values	33.8%	36.2%	40%	0	
2019 (January- March)	Tests done	11226	13006	16462	6	40700
	>Normal values	31%	29.8%	33.4%	0	
2020 (January- March)	Tests done	9952	12187	14200	9	36139
	>Normal values	32.1%	33.8%	23.7%	0	

Table 2: Year wise distribution of state biomarker test and abnormal values from psychiatry department.

Year	Total cases psychiatry dept.	AST		ALT		MCV		GGT	
		Test done	>Normal values	Test done	>Normal values	Test done	>Normal values	Test done	>Normal values
2016	4288	120	41%	118	31.4%	64	67.1%	3	0
2017	4169	121	44.6%	124	29%	53	47.2%	1	0
2018	4323	188	44.6%	175	45.7%	155	54.8%	0	0
2019	4558	183	40.4%	185	34.1%	137	46%	0	0
2020	3298	190	39.5%	191	31.9%	134	59.7%	0	0
Total	20636	802		793		543		4	

Table 3: Association of test positivity (AST, ALT MCV) of state biomarkers with, department and presence of AUD.

Total Cases	AST with abnormal values	ALT with abnormal values	MCV with abnormal values
All departments excluding psychiatry n=725772	17154 (31.91%)	21287 (33.43%)	27875 (36.60%)
Psychiatry department n=20636	335 (41.77%)	277 (34.23%)	296 (54.21%)
Psychiatry without AUD n=20622	225 (33.3%)	179 (26.1%)	214 (48.2%)
AUD in psychiatry n= 142	110 (89.4%)	98 (80.2%)	82 (80.3%)
AUD in other departments N=120	79 (83.1%)	75 (79.7%)	70 (80.4%)
P value (without AUD versus AUD in psychiatry)	<0.001	<0.001	<0.001
P value (AUD in psychiatry versus AUD in other depts.)	0.568	1.000	1.000

The total patients attended in the Psychiatry department were separately considered as it is more likely that alcohol related distress will be treated in this department. The number of requisitions from the department and the percentage of the biomarkers under study are presented (Table 2).

Requests for the index investigations were 1.3% to 5.8% of the total, of these 29% to 67.1% have reported abnormal values. MCV has reported the highest abnormal value (67.1%) in 2016 (Table 3).

We had explored the association of the test positivity with presence of AUD and department. There were statistically significant association found between presence of AUD and the test positivity of ALT (p=0.001), AST (p=0.001), MCV (p=0.001), in the cases from psychiatric department. There were no statistically significant association found between patient's test positivity of ALT, AST, MCV and their department.

DISCUSSION

The alcohol biomarkers serve vital functions in the prevention, screening both in the diagnosis and prognosis of treatment of AUD's, and thus helps in the monitoring of abstinence.[18] It has been reported that these clinical laboratory tests can be used to differentiate between the medically diagnosed alcoholics from non-alcoholics.[19] Moreover, distinguishing alcoholic from non-alcoholic

patients has an inevitable importance in the treatment and management for the wide spectrum of liver diseases.[20] In various treatment settings including primary care settings and trauma services, biomarkers were reported either not being used or being used sparingly.[21]

The present study was based on the use of alcohol state biomarkers in AUD management. The frequency of testing AST, ALT, MCV and GGT in the tertiary care centre is presented. No comparable data is available till date. However, the data from the psychiatry department shows lesser number of requests for these investigations compared to the other departments in the centre. On the other hand, on an average 43.8% of the tested samples showed abnormal values. This value is 34.1% when all departments were considered.

When analysing the data from the psychiatry department, it was interesting to note that the total number of biomarker test requisitions from the department for non-AUD patients were very few, giving a negligible average of 2.89%, whereas the requisitions given for AUD patients from the department gives an average percentage of 82.39%. Of these requests, 35.87% and 83.3% has reported to be abnormal values, for non-AUD patients and AUD patients, respectively. This finding is very remarkable in making a conclusion that, the state marker tests, which are widely and easily available at a comparatively fair charge, were well utilized in the treatment of alcoholics in the psychiatry department of the tertiary care centre. It is noted that, the utilization of alcohol biomarker tests in non-AUD patients in the psychiatry departments shows lesser number.

In AUD patient's data, it is interesting to note that the total number of biomarker test requests from all the departments except Psychiatry was found to be an average of 76.66%, whereas from the psychiatry department the average percentage of tests requests were 82.39%. Of these, 77.6% and 83.3% have reported abnormal values in the requisitions from all departments except psychiatry and department of psychiatry alone respectively. From these results we can conclude that, the alcohol state marker tests were well utilized for the treatment of AUD patients in this tertiary care centre, no matter in which department the patient got admitted.

This study showed that, the AUD patients were well differentiated from the non-alcoholics by utilizing the locally available clinical facilities, namely alcohol state biomarkers.

CONCLUSION

The study revealed that the utility of the commonly available lab tests is very useful for the clinical management of AUD patients and these are well utilized in an appreciable manner in the tertiary care centre. Development of more accurate, specific, and sensitive biomarker panel of tests may further motivate clinicians to better monitor individuals who suffer from problem drinking.

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