Evaluation of Biochemical Parameter Alteration in Alcohol Dependence Ethnic Nepalese

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Abstract

Alcohol consumption is a major health problem in Nepal leading to both serious morbidity and mortality. Alcohol abusers may exhibit several clinical and biochemical change. A case-control study was conducted to evaluate the biochemical changes and determine the diagnostic efficacy of these biochemical parameters in alcohol dependence. A total of 100 alcohol dependence subjects diagnosed by psychiatrist using ICD-10 and screening tool AUDIT as case and 100 healthy non-alcoholics as control were included in the study. Clinical parameters were recorded and biochemical parameters including hemoglobin, MCV, glucose, urea, creatinine, uric acid, cholesterol and liver function parameters were measured. After approval from IERB, BPKIHS consent was obtained from participants of both groups. An independent t-test was used to compare the parametric data and Mann-Whitney U test for the non-parametric data. Chi-square test (χ^2) was for the categorical data. Receiving operating characteristics (ROC) curve was used to find the diagnostics performance of parameters. Data were analyzed by using IBM SPSS Statistics version 20. Statistical significance is considered at $p \leq 0.05$. Alcohol dependence had significant low level of weight, BMI, hemoglobin, total protein, albumin, urea and creatinine and high level of MCV and liver enzyme activities (γ-GT, AST, ALT, AST/ALT ratio and alkaline phosphatase) compared to control ($P<0.001$). γ-GT had the highest diagnostic efficacy followed by AST, MCV, AST/ALT ratio and ALT as marker of alcohol dependence. Some of biochemical results in conjunction with the clinical history would be useful in diagnosing and management of alcohol related disorders.

Keywords: Alcoholism, Liver Enzymes, Analytical Systems

Alcohol-related problems are typically associated with medical, economic and social issues. Alcohol consumption causes or aggravates many medical conditions including liver disease, pancreatitis, diabetes, hypertension, stroke, cardiomyopathy, cardiac arrhythmia, breast cancer, depression, insomnia and others.7-9 Physicians are likely to identify only 20-50% patient with alcohol use disorders who are attending medical care.[10] The biochemical, clinical and social effects of alcohol abuse high light the urgent need for objective and specific marker for alcohol related disease and for early detection of potential alcohol abusers. The history is the most important means for detecting alcohol misuse. The history should cover current and past alcohol intake, identify quantity and frequency of intake. Pradhan B et al reported that the Nepali version of self-response AUDIT (Alcohol Use Identification Test) is reliable and valid screening tool to identify individual with alcohol use disorder in Nepalese population.[6] Although self-report has been shown to be reliable and valid, it is subjective and often, intentionally or unintentionally leads to an underestimate due to the inherent nature of the problem.

There is growing awareness of the wide spread metabolic effect on metabolism that form the basis of the laboratory test for alcohol abuse. Metabolic responses to alcohol ingestion are unlikely to be an all or none effect, their magnitude may depend on the extent and duration of drinking. To use such responses as the basis for diagnostic test, it is necessary to determine the changes in relation to the extent of drinking and then to determine the efficiency of such test in detecting alcohol abuse. However, there has been a great deal of controversy over the usefulness of biochemical marker. These tests are influenced by nutritional status, ethnicity, environmental and genetic factors.11 Many

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tests have only limited sensitivity and specificity and there have been doubt whether there is sufficient benefit to warrant their use.12 There is limited study about biochemical change in alcohol dependence of Nepalese population. Thus, this study aims to see the changes in biochemical parameter and to evaluate the diagnostic efficacy of these tests in alcohol dependence in comparison to healthy control.

Table 1: Demographic and anthropometric variables among alcohol dependence cases and controls

Parameter		Case (N=100)	Control (N=100)	P value
Age (yrs)		43.22±10.23	44.12±9.43	0.51
Sex	**Male (N)**	78	76	0.73
	Female (N)	22	24	
Weight (Kg)		58.23±8.19	65.22±10.27	0.001
Height (M)		1.64±0.074	1.62±0.079	0.14
BMI (Kg/m^2)		21.66±2.90	24.69±3.28	0.001

Table 2: Hematological and biochemical profile in alcohol dependence and control.

Parameter	Case (N=100)	Control (N=100)	P value
Hemoglobin (g/L)	127.4±16.3	142.8±17.0	0.001
MCV (fl)	96.30±7.54	87.78±4.76	0.001
Glucose (mmol/L)	5.56±0.97	5.23±0.98	0.01
Urea (mmol/L)	101.52±45.48	138±45.54	0.001
Creatinine (µmol/L)	60.99±18.56	78.67±22.1	0.001
Uric acid (mmol/L)	0.33±0.10	0.35±0.08	0.159
Cholesterol (mmol/L)	4.40±1.11	4.55±0.93	0.31

Materials and Methods

This was a case control study conducted in the Department of Biochemistry with collaboration of Department of Psychiatry and Internal medicine of BPKIHS, Dharan, Nepal. A total of 100 alcohol dependence and 100 healthy controls were enrolled in the study. Subjects visiting Psychiatry OPD and ward diagnosed as alcohol dependence by Psychiatrist using the ICD-10 and exceeding the AUDIT score were included as case in this study. The control subjects were recruited from both the community and the hospital. All subjects were interviewed using the same clinical interview tool for alcohol dependence. Subjects who did not have any alcohol related problem (either never drank or drank occasionally) were included as control. The subjects between 25-65 years of age willing to participate in the study and with no history of long-term medical condition like diabetes, hypertension, cancer, renal failure etc. were recruited in the study. This study was carried out after obtaining the approval of the Institute Ethical Review board (IERB). Consent was obtained from all subjects.

Blood sample (5ml) was drawn in EDTA and plain vial for hematological and biochemical test. Hematological parameter (Hb and MCV) were determined by hematology auto analyzer Lab life D5 Supreme. Biochemical parameter (glucose, urea, creatinine, cholesterol, uric acid, total protein, albumin, total bilirubin, direct bilirubin, ALT, AST, γ-GT, alkaline phosphatase) were determined by Cobas C 311 by using Roche reagent on fresh serum sample by IFCC recommendation method.

Data were expressed as mean±SD, median, frequency and percentage. An independent t-test was used to compare the parametric data and a Mann-Whitney U test for the non-parametric data. Chi-square test (χ^2) was for the categorical data. Receiving operating characteristics (ROC) curve has been used to find the diagnostics performance of study parameter. Data were analyzed by using IBM SPSS Statistics version 20. Statistical significance is considered at $p \leq 0.05$.

Results

A total of 100 alcohol dependence and 100 controls were included in this study. The mean differences of age, height, weight, BMI and sex distribution among alcohol dependence and control are depicted in Table1. The mean age, height and sex distribution were not statistically significant among alcohol dependence cases and controls. Alcohol dependence subjects had significantly lower weight and BMI compared to control (p<0.001).

The mean hemoglobin, MCV, glucose, urea, creatinine, cholesterol and uric acid level of alcohol dependence cases and control subjects is shown in table 2.

Alcohol dependence had significantly lower level of hemoglobin and higher level of MCV compared to control subjects (p<0.001). Although glucose, urea and creatinine levels were found within the reference limit in both groups; the increase in glucose, decrease in urea and creatinine level i n alcohol dependence were significantly different as compared to control group (p<0.01, p<0.001). The increased but not statistically significant level of uric acid and cholesterol were found

Table 3: Liver function parameter in alcohol dependence and control.

Parameter	Case (N=100)	Control (N=100)	P value
Total protein (g/L)	72.2±6.7	78.9±5.5	0.001
Albumin (g/L)	41.7±6.2	47.4±3.8	0.001
Total bilirubin (µmol/L)	19.665±20.862	9.918±4.959	0.001
Conj. Bilirubin (µmol/L)	7.524±8.892	3.42±1.368	0.001
ALT (U/L)	42 (27,69)	24 (16,35)	0.001
AST (U/L)	74 (38,135)	24 (18,30)	0.001
AST/ALT	1.75 (1.12,2.38)	0.96 (0.78,1.30)	0.001
γ –GT (U/L)	151 (80,323)	24 (16,35)	0.001
ALP (U/L)	87 (74,112)	76 (64,87)	0.001

Table 4: ROC analysis of different parameters.

Parameter	Best cut off value	Sensitivity (%)	Specificity (%)	AUC
MCV (fl)	93	75	90	0.84
γ –GT (U/L)	35	91	76	0.92
AST (U/L)	34	77	90	0.88
ALT (U/L)	35	63	80	0.77
AST/ALT	1.4	63.5	84	0.79
ALP (U/L)	87	50	73	0.67

in alcohol dependence compared to control subjects.

Table 3 indicates the liver function parameter in study group. The total protein, albumin, total bilirubin and conjugated bilirubin levels were found within normal range. The mean of total protein and albumin were significantly lower in alcohol dependence subjects compared to control (P<0.001). Similarly; the total bilirubin, and conjugated bilirubin were found higher in alcohol dependence subject compared to control (P<0.001). The data regarding liver enzymes were expressed in median and inter-quartile range because they were not normally distributed. The liver enzyme of AST, ALT, AST/ALT, γ-GT and alkaline phosphatase activities were significantly increased in alcohol dependence compared to control. All the biochemical tests were not statistically significant within the alcohol dependence group having AUDIT score 9-20 and 21to 40.

The ROC analyses of different parameters were shown in Fig1. γ-GT was having highest diagnostic efficacy followed by AST, MCV, AST/ALT ratio and ALT as marker of alcohol dependence.

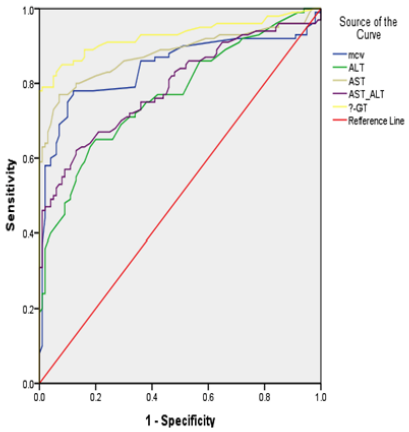

Figure 1: ROC curve of different parameters

Discussion

Alcohol consumption results in profound alteration in the metabolism of various nutrients resulting in several clinical and biochemical changes. Clinical anthropometric parameters weight and height were recorded and biochemical parameter like hemoglobin, MCV, glucose, urea, creatinine, uric acid, cholesterol and liver function parameters were determined in this study. The aim of present study is to see the changes of biochemical and clinical parameter in alcohol dependence compared to control and to evaluate the diagnostic efficacy of these parameters for alcohol dependence.

In the present study, the mean age, height and sex distribution between both groups were almost similar and not statistically significant which confirms matching between alcohol dependence and control group. Alcohol dependence had significant low body weight and BMI compared to control (P<0.001). Addolorato *et al* (1998) observed that alcoholics, as compared with social drinker showed lower body weight due essentially to fat mass reduction.[13, 14] World *et al* also reported that fall in body weight was the best clinical indicator of apparently continuing alcohol use.[15]

It has been well established that many hematological and biological abnormalities occur in chronic alcoholic liver disease. A number of studies have shown that chronic alcohol use is associated with significant decrease in hemoglobin concentration while significant increases are seen in MCV.[11,12,16] The results of our study also support this observation. Interestingly, although hemoglobin was elevated significantly in alcohol dependence compared to control, it remained within the normal limit. Alcohol has a variety of pathologic effects on hematopoiesis. It directly damages erythroid precursors, thereby contributing to macrocytosis and the anemic state. It also interferes with heme synthesis and induces sideroblastic anemia. Furthermore, chronic alcohol ingestion can lead to various types of hemolytic anemia due to alteration in erythrocyte membrane lipid.[17]

The MCV estimates the average erythrocytes volume and serves as an indicator of macrocytosis. Increased MCV has been long used as part of the screening procedure for detecting alcohol abuse. It responds slowly to abstinence as a RBC survives for 120 days after it has been into circulation; its normalization may require 2-4 months. However, it is relatively less sensitive and less

specific indicator of alcohol problem. An increase in MCV has also been reported in thyroid disease, recent blood loss and number of other conditions. Our results showed the mean level of glucose, urea, creatinine, uric acid and cholesterol are within the normal range in both groups. Similar findings were observed in other studies.[12,18,19] Some studies reported higher level of uric acid and cholesterol in alcohol dependence compared to control.[20] Urea concentration is often reduced because alcohol inhibits enzymes in the urea cycle.[17]

Alcohol is a known liver toxin. It is metabolized by the liver and resultant metabolic disturbances are implicated in hepatic damage. Our result showed a significant alteration of liver function parameters in alcohol dependence compared to control. The mean of total protein, albumin and bilirubin were within the normal range in both groups but there was a significant difference between the groups. Similar findings were reported in some studies.[12,16, 20]

Liver enzymes are important indicators of liver dysfunction, possibly as marker of alcohol dependence. Various studies reported that liver enzymes are traditional markers of alcohol use disorder with varying diagnostic efficacy. γ-GT is early and sensitive marker increased in alcohol dependence. It is induced by ethanol and our result shows a sensitivity of 91% and specificity at cut off value 35 U/L in distinguishing alcohol dependence from control. These results were similar to the results of others[7,21,22], but the major problem is that a raised serum γ-GT is also caused by other factors including microsomal inducing agents like antiepileptic drugs, non-alcoholic liver disease and biliary tract disease. Nonetheless, it is a well-established laboratory assay, is cheap and compares reasonably well with some of the newer more expensive assays.[23]

The serum transaminase (ALT and AST) are common routine liver function tests, and chronic alcohol consumption can lead to raised level due to increased cell permeability and cell necrosis. The present study indicated the sensitivity of AST (77%) and ALT (63%) is poorer than γ-GT to discriminate alcohol dependence from non-alcoholic. The best cut off value of AST/ALT ratio is ≥1.4 with sensitivity (63%) and specificity (84%) to distinguish alcohol dependence. Some studies in our context as well as in other setting reported similar usefulness of these enzymatic markers with varying diagnostic efficacy.[24-26] Some interrelated reasons have been reported for the high AST/ALT ratio in alcohol dependence: (a) decreased hepatic ALT activity (b) pyridoxal 5' phosphate depletion in the liver of alcoholics (c) mitochondrial damage leading to an increase in the serum activity of mitochondrial AST in patient with chronic alcohol users.[27] Our results also displayed mild increased activity of alkaline phosphatase in alcohol dependence in agreement with other study.[12]

Conclusion

The estimation of the biochemical parameters is essential for the rational understanding of the alcohol effect in alcohol dependence for the effective diagnosis and treatment of alcohol related disorder. However, further studies with greater sample size are necessary to generalize the finding.

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