RESEARCH

PROSPECTIVE STUDY ON FACTORS ASSOCIATED WITH RELAPSE IN ALCOHOL USE DISORDER

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Abstract
Background: Alcohol related disorders are highly prevalent in the South Indian State of Kerala. This study looks into the relapse rate & factors associated with relapse in Alcohol Use Disorder (AUD). The aim are to follow up patients diagnosed with AUD at a tertiary care hospital and to assess relapse rates and factors associated with relapse at periodic time intervals, To examine the association between relapse and various factors like (demographic variables, clinical parameters, comorbid psychiatric disorders, motivation at discharge, stressful life events & perceived social support), Comparison of these factors in patients who were in relapse versus in those who abstained from alcohol. **Materials and Methods:** Hundred inpatients meeting DSM5 Criteria for AUD were included in this study. After 2 weeks of detoxification, patients were assessed for socio-demographic and clinical variables. Comorbid psychiatric illness is diagnosed using DSM5.SOCRATES, PSLES, SSQ Scales were applied at baseline. After discharge these patients were followed up at 3, 6 & 12 months for relapse. The correlation of various psychosocial factors with relapse is also assessed. **Result:** Eighty-seven patients completed the study, among which 32.2% remained abstinent for a year. The relapse rate at 3, 6 and 12months were 37.9%, 25.3% and 4.6% respectively. The annual relapse rate was 67.8% (in all groups) and the major relapse occurred in the first 3 months. Low relapse rates were noted in sub groups having higher education and from urban backgrounds. Disulfiram helped to decrease relapse significantly. Motivation and stressful life events were also found to be important factors associated with relapse. **Conclusion:** Our study shows that relapse rate is almost similar to most of the outcome studies of alcohol dependent patients with maximum relapse rate within 3 months of treatment.

INTRODUCTION

Alcohol is one of the most widely used psychoactive substances in the world.[1] In a country wide national survery the Drug Abuse Monitoring System, found that the substances most commonly abused were alcohol (43.9%), opioids (26%) and cannabis (11.6%).[2] Alcohol related disorders are a major health and social problem worldwide and has a waxing and waning course which makes it a chronic disease.[3]

It is difficult to get an exact figure on the prevalence of AUD in India, as most of the studies published as much data were regional in nature.[4] In 1998, a meta-analysis conducted by Reddy and Chandrashekhar, showed an overall substance use prevalence of 6.9/1000 for India; with urban and rural rates of 5.8 and 7.3/1000 population respectively. As seen globally the rates among men were more (11.9%) as

compared to the opposite sex (1.7%).[5] Another study conducted in southern rural India showed that 14.2% of the population surveyed had hazardous alcohol use on the audit.[6] The prevalence of alcohol use was found to be different in different states of India (current use ranged from as low of 7% in Gujarat (the state under prohibition laws on alcohol sale) to 75% in Arunachal Pradesh.[2] In Kerala, prevalence of alcohol consumption in Thiruvananthapuram city was estimated to be significantly high (38.4%).[7]

Relapse is a complex process, which appears to be determined by various factors including individual, psychosocial and biological factors. Nearly a couple of decade ago, relapse was originally seen as a failure of treatment and failure of the individual in recovery.[8] This concept has changed over time. Currently relapse has been considered as a transitional process changing over time.[9] The occurrence of relapse is so prevalent that some

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clinicians accept relapse as an inevitable part of the disease process.[10]

Relapse is common following treatment and thus research into the nature and determinants of relapse in AUD is highly relevant clinically. A vast majority of patients relapse within a year of starting treatment, the first 3 months being the most vulnerable period.[10,11] About 50% of the detoxified alcohol users relapse within 3 months, the estimated long term relapse rates have varied between 20% and 80%.[8,12] Statistical study proves that approximately 90% of alcohol dependents are likely to experience at least one relapse within the 4 year period following treatment.[13]

Relapse prevention is a major challenge in the treatment of alcoholism. Better knowledge of the factors associated with relapse enable clinicians to offer better individualized treatment and to predict which patients are likely to relapse and hence to prevent relapses in persons at risk.

As literature suggests Alcohol related disorders are highly prevalent in the South Indian State of Kerala. With this in mind we aim to look into the relapse rate and factors associated with relapse in AUD thereby helping the psychiatrist on effective relapse prevention strategies in the management of alcohol use disorder. We have conducted a prospective study to assess the relapse rate and various factors associated with relapse in alcohol use disorder. The aim of this study was to examine the association between relapse and factors like demographic variables, clinical parameters, comorbid psychiatric disorders, motivation at discharge, stressful life events and perceived social support among patients with AUD and to compare these factors in those who were in relapse (at time points 3months, 6months and 1 year) and those who remained abstinent.

MATERIALS AND METHODS

This prospectively evaluated longitudinal study was conducted in the De-addiction Clinic, of a tertiary hospital in Kerala, India. All consecutive in- patients meeting DSM5 Criteria for AUD and all the inclusion criteria were recruited over a period of 6 months, starting from January 2015. Study duration including follow up was extended to a period of 20 months. Adult Patients in the age group of 18- 60 years, male in-patients and who gave informed consent were taken in for the study. Patients with history of organic brain disease and history of polysubstance abuse were excluded.

Assuming a significance level of 5% and a power of 80% and an expected relapse rate at 3 months to be 50% the sample size was calculated to be 100. A convenience sampling technique was used.

Post enrollment patients underwent detoxification, and two weeks later they were assessed for socio-demographic variables including age, education, occupation, marital status, community and socioeconomic status. Patients were also assessed for clinical variables including age of onset of alcohol use, duration of alcohol use disorder, previous attempt at de-addiction, family history of alcohol use. Comorbid psychiatric illness if any is diagnosed using DSM 5 criteria.

Motivation was assessed in the included sample at discharge using The Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES) V-8 (Local Language – Malayalam Version) designed by Miller, W. R., & Tonigan, J. S.[14] Stressful life events were determined using the Presumptive Stressful Life Events Scale(PSLES) by Singh G,Kaur D, Kaur H.[15] A scale consisting of 51 life events commonly experienced by the normal Indian adult population.A score of 100 with the highest stress score and 0 with no perceived stress. In this 51 item scale, Malayalam version was used with a reliability of the scale at 0.8.[16] Perceived social support was measured using the Social Support Questionnaire(SSQ) by Nehra R, Kulhara P.[17] The items were written in Malayalam, contained 46 items. This scale has approximately the same number of items from each area. Answering to each item was on 4 point scale of extreme agreement,[4] quite a bit,[3] a little,[2] and not at al.[1] The test retest reliability is 0.89.[16]

Once discharged from the hospital, these patients were followed up at 3, 6 and 12 months to look for any relapse. Patients were divided into two cohorts, in relapse and those who maintained abstinence. The relapsed group consists of patients who had maintained in a remitted state for at least two weeks following treatment, but had then restarted drinking. Those who restarted drinking within 2 weeks of discharge were considered dropouts. An episode of relapse was defined as the person meeting DSM 5 criteria for alcohol use disorder for a minimum period of 1 month. Abstinent patients will be those who had not taken alcohol since previous hospital discharge confirmed from a reliable bystander and without features suggestive of alcohol intake during evaluation. The relationship of relapse with various parameters were assessed. Comparison was done on various parameters between patients who were abstinent and those who had relapsed.

The data was entered and analyzed using IBM SPSS Version 20. Continuous variables were summarised in the form of mean and standard deviation. The categorical variables were presented as frequency and percentages, comparisons between the quantitative data were done by t-tests and categorical variables were done by chi-square tests. Percentages were worked out and tabulated for analysis. Variables with p values of <0.05 are to be considered significant. Multivariate time dependent analysis for relapse was carried out using Cox Regression and the survival curves were plotted for the most significant variable.

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RESULTS

Relapse Rates

Out of 100 patients, 87 patients completed the study among which 32.2% (28 subjects) remained completely abstinent for 1 year.

37.9% (33subjects)relapsed at 3 months follow up, 25.3% (22subjects) relapsed at 6 months follow up and 4.6% (4subjects) relapsed at 12 months follow up. Thus the total relapse rate is 67.8% (59 subjects) at 1 year and majority has relapsed within the first 3 months of treatment

Demographic Profile

Age Group

Majority of subjects in the study and those who relapsed belong to the 31-45 years age group (Table 1), but it was not statistically significant (p-value 0.521).

Education

Majority of patients had high school and intermediate education and there were no illiterates in the study (Table 2). The relapse rate was found to be lower in those with higher education which was statistically significant (p-value 0.034)

Occupation

Most of the subjects belong to skilled worker group but there was no significant correlation between relapse and occupational status (Table 3).

Marital status

77% of subjects were married and there was no significant correlation between marital status and relapsed drinking (Table 4).

Socioeconomic status

53 patients belonged to APL and 47 patients belong to BPL class. No significant correlation between relapse and socioeconomic class was noted

Rural Urban Distribution

78 patients belonged to rural population and 22 to urban population and in the 87 patients who completed study there was increased relapse in rural population than urban population which was statistically significant (p=0.017). (Table 5)

Clinical Profile

Age of onset of alcohol use

81% of subjects started drinking at the age group of 11-20 yrs with only 1% less than 10yrs.The minimum age of onset of drinking was 9yrs and maximum was at 28yrs with mean 18.42 yrs and SD 3.782. (Table 6). There was no significant correlation between age of onset of drinking and relapse

Duration of alcohol use disorder

63% has duration of AUD from 1 to 10 yrs, and 30% from 11- 20yrs.Very few has a total duration of>20yrs.No statistical significance could be noted between relapse and duration of AUD (p=0.252)

Family History

66% of cases had positive family history. Relapse was found to be high in those with positive family history but not statistically significant.(Table 7)

Previous Deaddiction Treatment

53% of patients had history of previous Deaddiction Treatment. (Table 8). Those patients with a previous deaddiction treatment had increased relapse but no statistically significant association could be established

Duration of Hospital Stay

Minimum duration of hospital stay was 4 days while the maximum was 80 days with mean of 12.8 and SD of 8.432. 80% of patients left hospital within 2 weeks (Table 9). Only 2% stayed for > 30days.There was no significant correlation between relapse and hospital stay (P= .861). No statistically significant correlation was found between duration of hospital stay and relapse

Comorbid Psychiatric Disorders

34% of subjects had comorbid psychiatric illness, most frequent association was found with bipolar disorder. Pearson Chi-Square 1.290 DF 1 P = .256. Relapse rate was found to be high in those with comorbid psychiatric disorders but was not statistically significant (p-value at 0.256)

Disulfiram Treatment

Disulfiram was started in 20 out of the 100 subjects.(Table10). Patients treated with Disulfiram had lesser relapse rate when compared to those not initiated with disulfiram and it was found to be statistically significant (p value < 0.05)

Socrates score

SOCRATES score was found to be high in those who remained abstinent (Table 11) and was statistically significant with p-value <0.05. PSLES Life time score was found to be significantly associated with high relapse at p- value < 0.05, relapse rate was also high among those with stressful life events in the past 1 year but it was not statistically significant (Table 12).

Social Support

The difference in social support in the relapse group and abstinent group was not found to be statistically significant. Multivariate time dependent analysis for relapse was carried out using Cox Regression and the survival curves was plotted for SOCRATES score which was the most significant variable (Table13). It had been found that the time period for relapse was shortened in those with poor motivation (low SOCRATES score)

Table 1: Age group and Relapse

			Relapsed Age Group (Relgp)						Total
			Lost to	Drop Out	Relapsed in 3 mo	Relapsed in 6 mo	Relapsed in 12 mo	Abstinent	
AGE Group Years	18-30	Number	0	1	1	5	1	3	11
		% within RELGP	0.0%	12.5%	3.0%	22.7%	25.0%	10.7%	11.0%
	31-45	Number	3	5	23	9	2	13	55
		% within RELGP	60.0%	62.5%	69.7%	40.9%	50.0%	46.4%	55.0%
	46-60	Number	2	2	9	8	1	12	34
		% within RELGP	40.0%	25.0%	27.3%	36.4%	25.0%	42.9%	34.0%
Total		Total Number	5	8	33	22	4	28	100
		% within RELGP	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Table 2: Correlation between Education and Relapse

Education group (edu gp)		Relapsed status		Total
		No	Yes	
Primary school	Number	1	3	4
	% within EDU GP	25.0%	75.0%	100.0%
Middle school	Number	2	8	10
	% within EDU GP	20.0%	80.0%	100.0%
High School	Number	9	30	39
	% within EDU GP	23.1%	76.9%	100.0%
Intermediate/ HSE	Number	11	18	29
	% within EDU GP	37.9%	62.1%	100.0%
Graduate/PG	Number	5	0	5
	% within EDU GP	100.0%	0.0%	100.0%
Total	Number	28	59	87
	% within EDU GP	32.2%	67.8%	100.0%

Table 3: Annexures Correlations between Occupation and Relapse

Occupation Group (OCCU GP)		Relapsed		Total
		No	Yes	
UNEMPLOYED	Number	7	10	17
	% within OCCU GP	41.2%	58.8%	100.0%
UNSKILLED	Number	6	18	24
	% within OCCU GP	25.0%	75.0%	100.0%
SEMISKILLED	Number	1	0	1
	% within OCCU GP	100.0%	0.0%	100.0%
SKILLED	Number	9	25	34
	% within OCCU GP	26.5%	73.5%	100.0%
SHOP OWNER/ FARMER/ CLERK	Number	3	5	8
	% within OCCU GP	37.5%	62.5%	100.0%
SEMIPROFESSIONAL	Number	2	1	3
	% within OCCU GP	66.7%	33.3%	100.0%
Total	Number	28	59	87
	% within OCCU GP	32.2%	67.8%	100.0%

Table 4: Annexures: Marital Status and Relapse Rate

Marital Status		Relapsed Status		Total
		No	Yes	
UNMARRIED	Number	3	9	12
	% within MAR CODE	25.0%	75.0%	100.0%
MARRIED	Number	22	46	68
	% within MAR CODE	32.4%	67.6%	100.0%
SEPARATED	Number	3	2	5
	% within MAR CODE	60.0%	40.0%	100.0%
DIVORCED	Number	0	2	2
	% within MAR CODE	0.0%	100.0%	100.0%
Total	Count	28	59	87
	% within MAR CODE	32.2%	67.8%	100.0%

Table 5: Annexure, Correlation between Place of Residence and Relapse

			Relapsed status		Total
			No	Yes	
Rural/Urban	Rural	Count	18	51	69
		% within Rural/Urban	26.1%	73.9%	100.0%
	URBAN	Count	10	8	18
		% within Rural/Urban	55.6%	44.4%	100.0%
Total		Count	28	59	87
		% within Rural/Urban	32.2%	67.8%	100.0%

Pearson Chi-Square 5.680 DF 1 P = .017

Table 6.Correlation between Age of Onset of Drinking and Relapse

			Relapsed Status		Total
			NO	YES	
AGE ONSET Group	1-10	Count	0	1	1
		% within AGE ONSET GP	0.0%	100.0%	100.0%
	11-20	Count	23	47	70
		% within AGE ONSET GP	32.9%	67.1%	100.0%
	21-30	Count	5	11	16
		% within AGE ONSET GP	31.2%	68.8%	100.0%
Total		Count	28	59	87
		% within AGE ONSET GP	32.2%	67.8%	100.0%

Pearson Chi-Square .496 , DF 2, P = .781

Table 7: Family History and Relapse

			Relapsed Status		Total
			NO	YES	
Family History	ABSENT	Count	13	18	31
		% within Family History	41.9%	58.1%	100.0%
	PRESENT	Count	15	41	56
		% within Family History	26.8%	73.2%	100.0%
Total		Count	28	59	87
		% within Family History	32.2%	67.8%	100.0%

Pearson Chi-Square- 2.098, DF 1, P = .147

Table 8: Previous Deaddiction treatment and Relapse rates

			Relapsed Status		Total
			.00	1.00	
Previous Deaddiction treatment	NIL	Count	15	23	38
		% within Previous Deaddiction	39.5%	60.5%	100.0%
	YES	Count	13	36	49
		% within Previous Deaddiction	26.5%	73.5%	100.0%
Total		Count	28	59	87
		% within Previous Deaddiction	32.2%	67.8%	100.0%

Pearson Chi-Square 1.643 , DF 1, P = .200

Table 9: Duration of Hospital Stay and Relapse rates

			Relapsed Status		Total
			NO	YES	
Duration of Hospital stay	0-15Days	Count	22	47	69
		%	31.9%	68.1%	100.0%
	16-30Days	Count	5	11	16
		%	31.2%	68.8%	100.0%
	>30Days	Count	1	1	2
		%	50.0%	50.0%	100.0%
Total		Count	28	59	87
		%	32.2%	67.8%	100.0%

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Table 10: Impact of Disulfiram Treatment on Relapse

			Relapsed Status		Total
			No	Yes	
Disulfiram Treatment Status	No	Number	14	53	67
		% within disulfiram treatment	20.9%	79.1%	100.0%
	Yes	Number	14	6	20
		% within Disulfiram treatment	70.0%	30.0%	100.0%
Total		Number	28	59	87
		% within Disulfiram Treatment	32.2%	67.8%	100.0%

Pearson Chi-Square 17.016 DF 1 P = .000

Table 11: SOCRATES Score and Relapse Groups Correlation

			Relapsed Status						Total
			LOST	DROP OUT	REL IN 3 M	REL IN 6M	REL IN 12M	ABSTINENT	
SOCRATES SCORE	High	Count	0	0	1	4	1	17	23
		% within relapse code	0.0%	0.0%	3.0%	18.2%	25.0%	60.7%	23.0%
	Low	Count	3	7	15	3	0	2	30
		% within relapse code	60.0%	87.5%	45.5%	13.6%	0.0%	7.1%	30.0%
	medium	Count	2	1	17	15	3	9	47
		% within relapse code	40.0%	12.5%	51.5%	68.2%	75.0%	32.1%	47.0%
Total		Count	5	8	33	22	4	28	100
		% within relapse code	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square 62.199, DF 15, P = .000

Table 12: Correlation between PSLES and Relapse

		Sum of Squares	Df	Mean Square	F	Sig.
PSLES LIFE TIME	Between Groups	173.038	5	34.608	3.813	**.003**
	Within Groups	853.202	94	9.077		
	Total	1026.240	99			
PSLES 1 year	Between Groups	17.680	5	3.536	2.233	.057
	Within Groups	148.880	94	1.584		
	Total	166.560	99			

Table 13: Correlation of Various Factors of Relapse (Anova)

		Sum of Squares	Df	Mean Square	F	Significance (P value<0.05)
Age Groups	Between Groups	.876	5	.175	.424	.831
	Within Groups	38.834	94	.413		
	Total	39.710	99			
Level of Education	Between Groups	11.573	5	2.315	3.014	**.014**
	Within Groups	72.187	94	.768		
	Total	83.760	99			
Marital Status	Between Groups	1.378	5	.276	.955	.450
	Within Groups	27.132	94	.289		
	Total	28.510	99			
Occupation	Between Groups	24.235	5	4.847	2.208	.060
	Within Groups	206.325	94	2.195		
	Total	230.560	99			
Age of Onset of alcohol consumption	Between Groups	.540	5	.108	.652	.661
	Within Groups	15.570	94	.166		
	Total	16.110	99			
Duration of AUD	Between Groups	1.309	5	.262	.496	.778
	Within Groups	49.601	94	.528		
	Total	50.910	99			
SSQ SCORE	Between Groups	531.118	5	106.224	.785	.563
	Within Groups	12716.322	94	135.280		
	Total	13247.440	99			
SS Re	Between Groups	907.788	5	181.558	9.652	**.000**

	Within Groups	1768.212	94	18.811		
	Total	2676.000	99			
SS Ts	Between Groups	954.533	5	190.907	14.801	**.000**
	Within Groups	1212.457	94	12.898		
	Total	2166.990	99			
SS Am	Between Groups	280.823	5	56.165	8.177	**.000**
	Within Groups	645.687	94	6.869		
	Total	926.510	99			

Abbreviation: SSQ Score - SSRe- SS Ts SS Am

DISCUSSION

AUD is a significant stressor to one's life and the chronicity of this disorder and the high relapse rates has shown that it is a long battle to be won over time with patience and perseverance.

In our study, we had a good compliance of 95%, but with best of our efforts we were unable to trace 5 patients who were deemed lost to follow up.

The socio-demographic profile of the patients help us to understand their background and the relationship of the factors associated with relapse. Surprisingly, all of our patients were males and this could be due to the psycho-social stigma among women to approach a de-addiction clinic for help or probably due to the low rates of alcohol consumption in the population where this study was conducted. As noted in the results a majority of the patients were in the age group of 31-45 years, which is the most productive age group, but there was no correlation between age of the individual and relapse to alcohol consumption. The chances of relapse were high in unmarried and divorced individuals. Owing to the low sample size a statistical significance could not be proved, but the figures projected shows that a proper family support system is much needed in reducing relapse rates.

As this study was conducted in one of the most literate states of this country, there were no illiterate subjects and the majority of subjects had high school or intermediate level of education. The relapse rate was found to be lower in those with higher education (p-value 0.034). This could point to the important fact that it is easier to counsel the educated cohort of subjects and the pros and cons of abstinence was better understood in this group. We also noticed that the educated and employed patients (mostly skilled workers) were more receptive towards treatment, and they showed good compliance to medications and periodic hospital follow up visits. This could be the reason for improved outcome in those with higher educational and occupational status. The results of out study could be reflected to that done by Korlakunta et al, where in the employment status of alcohol relapse patients were analysed and majority were employed, hailed from rural area and were married.[18] The purchasing power, easy access to alcohol and independent lifestyle may be the reasons for relapse.

Similar study conducted among indian males, showed most patients were in the third decade of life, and were educated to secondary level and the marital status showed many to be unmarried or divorced.[19] Their findings were similar to ours.

Analysis into urban and rural populations, showed that relapse rate was significantly higher in rural areas and was also higher in patients living below the poverty line. Thus socioeconomic status and place of residence also play a role in relapse of alcohol use disorder.

Multiple studies have shown inconsistent results to show an association between short term remission and female gender, older age and marital status.[11,20] As one of our aims of the study was to look into factors associated with relapse we evaluated the clinical profiles of patients with AUD and relationship with relapse.

Only one patient started his habit of drinking below 10 years of age, while 81 patients started drinking between 11-20yrs, and the rest 18 patients started drinking between 21-30 yrs. Majority of patients had their first drink at a very early age. Even though we noted that relapse was higher in those who started drinking at an early age our study was not powered to show statistical significance. To substantiate these claims, studies by Korlakunta et al and Higson et al. also showed that individuals who began drinking at younger age were more likely to experience multiple relapses.[18,21] To note, was that in comparison to the western population majority of the patients in our study had their first drink at an early age (10-20years), and the age at first drink was at a later onset of age. In the west, the free culture and attitude towards alcohol consumption and the lack of stigma towards alcoholism could be the reason for an early onset of drinking habits.

After looking into the onset of drinking, we also analysed the duration of dependence towards alcohol. Sixty-three percent of patients had duration of Alcohol Use Disorder between 1-10yrs suggesting that most of the patients were dependent within 10 years of onset of drinking. This finding was in concordance to the studies done by Korlakunta et al and Higson et al, in which the majority of patients were dependent within 5 years and 10 years of onset of drinking respectively.[18,21]

Literature has suggested that a positive family history is associated with relapse and 66% of subjects gave a positive family history of alcohol consumptions and the relapse rates were found to be higher, but owing to the small sample size this was not proven statistically. This could be linked due to a genetic etiology of Alcohol use disorders. Hill et al. found that children with a high family history of alcoholism have a higher risk for early onset of alcohol use.[22] In another similar study conducted at Kerala it has been

noted that relapse is high in those with positive family history and with a high age of onset.[23]

The reason for relapse could be any underlying co – morbid psychiatric illness and our study had 34% of subjects with comorbid psychiatric disorders commonest being bipolar disorder. Relapse rate is found to be high in those with comorbid psychiatric disorders (p-value at 0.256). Hence, family members have a definite role in providing support and care to avoid a relapse in these patients who harbour a co-morbid psychaitric condition.[24] Another Indian study by with a smaller sample size of 37 patients, reported that 64.8% of patients had comorbid psychiatric illness.[25] In a review on co-occurring psychiatric disorders in Alcohol use Disorder it has been found that Alcohol use disorder have a particularly high rate of psychiatric comorbidities, most commonly with mood disorders, anxiety spectrum disorders and sexual dysfunction. While some studies focussed on specific psychiatric disorders such as ADHD, psychoses, mood disorders, anxiety disorders and sexual disorders, others have explored the prevalence of more than one psychiatric disorders. Diagnosis of multiple comorbidities is not infrequent, but multiple comorbidities were not found in our study.[26] There was significant association between the reasons for relapse and comorbid diagnosis of patients in another Indian study which is similar to our findings.[18]

Though not defined as an end point of this study, medical management of AUD patients were analysed as a subset and patients treated with disulfiram had lesser relapse rate when compared to those not initiated with disulfiram which is found to be statistically significant (p value < 0.05). Disulfiram is started only if the patient is sufficiently motivated and given written explained consent and this explains why patients initiated on disulfiram tend to remain abstinent. However controlled studies of disulfiram reveal a mixed outcome. In a meta-analysis, there is evidence in open-label studies of disulfiram efficacy in maintaining abstinence and preventing relapse. In terms of safety, there was no difference between the disulfiram and control groups in studies reporting deaths and serious adverse events requiring hospitalization.[27] Thus disulfiram was found to be effective compared to other treatment strategies.

Fifty-three percent of patients had a history of previous De Addiction treatment. Those patients with a previous de- addiction treatment had no correlation with relapse. However, failure of previous de-addiction treatment also indicates poor motivation and poor coping strategies.

Motivation was found to be the most important factor determining relapse in Alcohol use disorders which showed strong statistical significance in our study. This illustrates the importance of assessing and improving motivation through motivational interviewing and MET. The trials funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA)—Project MATCH and Project COMBINE, studies examining the combination of pharmacotherapy and psychosocial treatment—have included motivational measures and treatment components. Recent research strongly suggests the role of motivation, both intrinsic and extrinsic, in the treatment of addiction and relapse prevention.[15]

PSLES Life time score has significant association with high relapse. Relapses are also high among those with stressful life events in the past 1yr (not proven statistically). This illustrates stressful life events as another important determining factor for relapse. In a study analyzing the association between stressful life events and relapse, events like divorce and separation were found to be significantly associated with relapse. No other stressful life event was associated with relapse according to this study.[28]

There is no statistically significant difference in social support in the relapse group and the abstinent group, only few patients lacked social support found that psychosocial factors such as relapse precipitants (or high risk situations), coping, self-efficacy, social support and stressful life events appeared to be of greater importance in determining relapse.[10] Dixit et al. found that abstinent group perceived better social support than relapsed groups and patients in upper socio-occupational status and less alcohol related problems perceived more social support than patients with lower socio-economic status and more alcohol related problems.[29] Unfortunately, in our study no statistically significant correlation is found between social support and relapse.Perhaps a study with a larger sample size could be helpful in answering this question.

Long term follow up, till one year was done in these subjects and it was found that 87 patients completed the study among which 32.2% remained completely abstinent for 1 year, 37.9% relapsed at 3 months follow up, another 25.3% relapsed at 6 months follow up and another 4.6% relapsed at 12 months follow up. Thus the total relapse rate is 67.8% at 1 year and the majority had relapsed within the first 3 months of treatment. The results are similar to previous outcome study done in a Military Psychiatry setup which found that 1/3rdof patients were abstinent and 2/3rd of patients relapsed out of which 1/3rd showed partial improvement.[30]

The relapse rate reported in literature is above 60 % during a 12 month period and it is almost similar to our study population.

The limitation of our study is that there were many factors, which are associated with relapse in AUD, including the biological factors which are not assessed here. We also acknowledge the fact that smaller sample size has restricted us from getting statistically meaningful results. The lack of female population, getting enrolled into the study, shows that it is unequally weighted to one gender and hence the findings may not be generalized to the population.

Even with effective pharmacological and psychological management, relapse in AUD remains very high. Hence it is essential to focus on the biological as well as psychosocial factors associated with relapse, as relapse prevention is the goal in the

treatment of addiction. We also suggest a genetic analysis of the subjects who have AUD and the cause could be rooted to an individual's DNA which could be a subject of active research.

CONCLUSION

The results of our study shows that certain clinical and demographic variables were reliably and consistently associated with relapse in Alcohol use disorder. Along with the demographic and clinical variables, motivation at discharge, stressful life events and social support which are the major risk factors for relapse. Among socio-demographic variables age, occupation, marital status and socioeconomic status showed no significant correlation with relapse. The association of demographic factors including educational status and rural residence with relapse were found to be statistically significant.

The motivation of patients at discharge is found to be the most reliable and important factor determining relapse which was statistically significant in our study. Medical intervention in the form of Disulfiram treatment is found to reduce relapse. Stressful life events during lifetime of an individual contributes to relapse, which was identified in our study and ways to effectively cope with them must be addressed. Even though no significant correlation is found between social support and relapse in our study, we feel social support is the cornerstone to prevent relapse.

Our study shows that the relapse rate is almost similar to most of the outcome studies of alcohol-dependent patients with a maximum relapse rate within 3 months of treatment.

Thus addiction is a chronic relapsing and remitting disorder and "RELAPSE" is the rule in addictive disorders. Our study focusses on the importance of relapse prevention in the treatment of addiction and suggests various psychosocial and clinical factors which should be addressed in order to obtain the expected outcome in the management of Alcohol Use Disorders.

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PREVALENCE OF VITAMIN D DEFICIENCY AMONG POPULATION IN SOUTH INDIA: A CROSS SECTIONAL STUDY

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Abstract

Background: High prevalence of vitamin D deficiency is seen in general population in South India. Exposure to sun is the main source of vitamin D. But our present lifestyle provides very less sun exposure. Most people are confined to indoors leading a sedentary life. Our cultural and social practices do not provide enough sunlight exposure. Dietary source of vitamin D are animal products and food items fortified with vitamin D. But vitamin D fortification of food items is very rare. The aim is to assess the serum vitamin D levels in healthy individuals. **Materials and Methods:** A cross sectional study was conducted in ninety apparently healthy individuals attending Comprehensive health care clinic in a tertiary care hospital. Serum vitamin D was analyzed. **Result:** Among the ninety apparently healthy individuals included in the study, a high prevalence of hypovitaminosis D was noted. 70 percent of the people had vitamin D deficiency who were otherwise healthy. **Conclusion:** Hypovitaminosis D is highly prevalent in the general population.

INTRODUCTION

Vitamin D, the fat-soluble sunshine vitamin is a steroid hormone precursor and it is biologically inert.[1,2] Food items containing vitamin D are very few. The major source of vitamin D is sunlight. It is synthesized in the human skin through sun exposure. So vitamin D is rightly called the sunshine vitamin. On exposure to ultraviolet Blight, the initially synthesized vitamin D is biologically inactive and its half-life is 12-16 hours. Later it is converted to 25-OH vitamin D in the liver and in the kidney to 1,25(OH)2 vitamin D which is biologically active. Vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol) which are two important forms of vitamin D are hormone precursors which play a major role in metabolism of calcium and phosphate. Thus it plays an important role in maintaining bone health. 1,25 dihydroxy vitamin D is a steroid hormone and it acts by binding to the vitamin D receptor (VDR) seen inside the cell. Vitamin D receptors are seen all over the body and so it is involved in many physiological processes. Thus vitamin D deficiency will adversely affect the bone metabolism. Deficiency of the sunshine vitamin is also associated with a wide range of diseases. So vitamin D very much essential for maintaining normal health.

Hypovitaminosis D is a global issue and its consequences are widespread. Vitamin D deficiency need not be always symptomatic. Subclinical hypovitaminosis D is widely prevalent in general population. This can cause a major risk of developing health problems in the future. Alteration in bone mineral density can lead to osteoporosis. Hypovitaminosis D is also associated with various cardiovascular and metabolic disorders. This makes it important to study the prevalence of the deficiency of the sunshine vitamin.

MATERIALS AND METHODS

A cross sectional study was conducted in 90 apparently healthy individuals attending Comprehensive health care clinic in a tertiary care hospital in Kerala after obtaining written informed consent. The study was conducted between November 2015 and July 2017 after approval from Dissertation Review Committee and Ethical clearance. With 95% confidence and 20% relative error, the minimum sample size was calculated to 15. We included 90 healthy individuals in our study

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which would give a confidence of 99% and relative error of 15%. With 95% confidence and 80% power, the minimum sample size was 5. We included 90 healthy individuals giving 99% confidence and 90% power.

Inclusion Criteria
90 apparently healthy individuals between 18 and 65 years of age.

Exclusion Criteria
1. Individuals below 18 years and above 65 years of age.
2. Conditions known to affect the vitamin D levels like liver disease, renal disease, skeletal disease, cardiovascular disease and primary malnutrition.
3. Individuals on calcium and vitamin D supplementation
4. Individuals with malignancies or any other chronic illness

Study Tools
A detailed history, general examination and systemic examination was done on the first visit to the Comprehensive health care clinic. Blood pressure was measured in millimetres of mercury. A calibrated weighing machine was used to measure the weight in kilograms. A stadiometer was used to measure the height in centimetres. Body mass index was calculated. Other details like sunlight exposure, occupation, history of smoking and alcohol consumption, diet was collected using questionnaire. Laboratory test values like HbA1C, fasting blood sugar, renal function and liver function tests were collected from latest lab reports.

2ml blood was drawn by venepuncture and serum was separated by centrifuging at 3000 rpm for 5 minutes. Serum was stored at -200 Celsius until the analysis for the estimation of vitamin D which was done with Cobas E411 and vitamin D total Roche reagent based on Electro Chemiluminescent Immuno Assay (ECLIA).

Subjects were classified as vitamin D deficient, insufficient and sufficient based on the serum vitamin D concentration of < 20, 20-30 and >30 ng/ml respectively according to recent consensus.[3,4]

IBM SPSS version 20.0 was used for performing data analysis. Numerical variables were expressed as mean and standard deviation. Categorical variables were expressed as frequency and percentages. Karl Pearson correlation coefficient was applied to obtain the correlation between two numerical variables. Kruskal Wallis test was applied to test the statistical significance of serum vitamin D levels among Cambridge grades, since it is significant Dunn Bonferroni multiple comparison test was applied. p value of <0.05 was considered as statistically significant.

RESULTS

Serum vitamin D levels of 90 apparently healthy individuals were analyzed. Serum calcium levels, serum vitamin D levels and body mass index were correlated within the study group. Among the study group 45 were females and 55 were males. The mean age of subjects was 46.19+ 13.68 years. 47.5% were smokers and 45% were alcoholics among the study group. 38.5% of the study group was vitamin D deficient, 45% was vitamin D insufficient and 16.5% had normal vitamin D levels. Serum calcium and serum vitamin D levels positively correlated with each other. Duration of sunlight exposure had a negatively correlated with serum vitamin D levels. (p < 0.0001) Serum vitamin D and calcium levels were significantly lower in females as compared to males in our study.

We did not find any correlation between dietary habits and serum vitamin D levels. Family history also did not correlate with serum vitamin D levels.
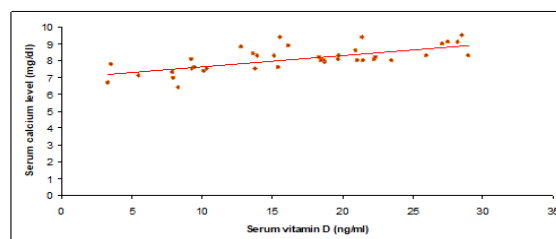

Figure 1: Correlation between serum vitamin D levels and serum calcium levels in study group

Table 1: Correlation between BMI and duration of sun exposure.

	Serum vitamin D (ng/ml)		
	n	Pearson Correlation	p Value
Duration (hours)	90	- 0.602	<0.001

Table 2: Comparison of serum Vitamin D levels between male and female subjects

Groups	n	Serum vitamin D (ng/ml)		p Value
		Mean	SD	
Females	45	16.91	7.17	<0.05
Males	55	22.43	6.09	

Table 3: Comparison of BMI between male and female subjects.

Groups	n	BMI (kg/m²)		p Value
		Mean	SD	
Males	55	19.98	1.40	<0.001
Females	45	24.36	1.87	

DISCUSSION

Hypovitaminosis D is an alarming concern that we are facing in the recent times. Our study showed that vitamin D deficiency is highly prevalent in the general population. 38.5% of the study group was vitamin D deficient, 45% was vitamin D insufficient and 16.5% had normal vitamin D levels. Serum calcium and vitamin D levels positively correlated with each other. This shows that vitamin D supplementation could possibly improve calcium levels too. Surprisingly we found that females were more likely to be having vitamin D deficiency as compared to the male population. This may be attributed to lesser exposure to sunlight as compared to males because females are more confined to indoors. We did not find any association between smoking and alcoholism and vitamin D deficiency. Dietary habits and family history also did not correlate with vitamin D deficiency in our study.

Studies conducted in Asian population reveals higher prevalence of vitamin D deficiency.[5] Lower serum calcium values may be due to serum vitamin D deficiency. Calcium is absorption is only 10% in Vitamin D deficient state.[6] Increased loss of calcium through urine may result from hypovitaminosis D. Poor dietary intake of vitamin D and less exposure to sunlight might also have contributed to the lower serum calcium levels in our study group.

Supplementation of the sunshine vitamin can be a solution to this problem. But an earlier study showed that intramuscular supplementation of vitamin D did not considerably improve the deficiency while vitamin D supplementation orally increased the serum levels.[7] Another study reported that only 40% of experimentally applied, radioactively labelled vitamin D3 is absorbed by the intestines of patients with pancreatic exocrine insufficiency,[8] contrary to 80-90% in healthy persons, exocrine pancreatic function gains significance. This leads us to the conclusion that vitamin D deficient individuals should also be screened for any malabsorption disorders.

Vitamin D is very important. It plays an important role in many physiological activities and is required for the proper functioning of different organ systems of the body. Vitamin D is essential for normal bone metabolism and so its deficiency is very well related to many musculoskeletal disorders. It is also seen that this can affect the bone mineral density, gradually leading to osteopenia, osteoporosis and pathological fractures in future. Thus timely intervention is very necessary to prevent such health problems.

Recent times it is known that the sunshine vitamin deficiency can also result in various other negative effects like adverse pregnancy outcomes.[9] Vitamin D has also been found to play a role in malignancies. Miriam PY et al. 2018 reported that vitamin D deficiency has a role in development of breast cancer.[10] Sunshine vitamin also has action in the respiratory system. Supplementation of vitamin D in asthmatics have been found to reduce exacerbation.[11] Vitamin D is also known to have a role in body's immune system. Some studies have shown relation of immune diseases to vitamin D. One such study was by Giorgia et al. 2017 which says patients affected with many immune disorders have very low levels of vitamin D.[12] But is vitamin D the causative factor of immune diseases or has the immune disorder resulted in vitamin D deficiency is still unknown.

India being a tropical country receive enough sunlight and it is presumed that vitamin D deficiency is rare in the subcontinent. But our study findings are totally against this presumption. This may be due to more people confined to indoors, having white collar jobs and also having a sedentary lifestyle. Clinically unrecognized Vitamin D deficiency in the long run can lead to complications like osteoporosis.[6,13,14,15,16,17] Timely intervention thus becomes very important. This can be done only if we screen for vitamin D deficiency.

CONCLUSION

It is high time vitamin D tests should be made part of the routine blood examination which will help us filter our those with deficiencies and take necessary measures. Time and financial constraints made it difficult for us to take a detailed diet history and do DEXA scan to find out the bone mineral density. Further studies with larger sample size must include bone mineral density screening to find out long standing cases of hypovitaminosis D so that timely intervention is possible. This would enhance the standard of living of the general population.

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