Prevalence of major depressive disorder in adult patients with alcohol use disorder admitted in the psychiatric ward at the Jigme Dorji Wangchuck National Referral Hospital, Thimphu, Bhutan

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ABSTRACT

INTRODUCTION The increasing prevalence of major depressive disorder (MDD) in alcohol use disorder (AUD) is associated with detrimental consequences, affecting the course and outcome of each disorder. The objective of this cross-sectional study was to study the prevalence and severity of MDD and associated risk factors in Bhutanese adult patients with AUD admitted to the psychiatric ward, YJigme Dorji Wangchuck National Referral Hospital, from March 2020 to February 2021.

METHODS All patients with AUD presenting for alcohol detoxification for the first time with MDD as the only associated psychiatric comorbidity were administered a sociodemographic questionnaire and Patient Health Questionnaire-9 (PHQ-9). Multivariate binary logistic regression was carried out to determine factors associated with depression using two models. All independent variables were computed for multivariate logistic regression in Model 1. For Model 2, variables with p<0.2 from Model 1 were included. Akaike information criterion (AIC) score was used to construct our final multivariable model.

RESULTS The overall prevalence of major depression (PHQ-9 score ≥10) among the participants was 38% (59/155). Participants with mild depression (PHQ-9 score = 5–9) were excluded. Participants with family history of alcohol and substance use disorder demonstrated higher prevalence of depression (p=0.03). In the multivariate binary logistic regression, female participants (AOR=2.19; 95% CI: 1.01–4.75) and respondents with family history of psychiatric illness (AOR=4.63; 95% CI: 1.17–18.44) were more likely to develop MDD.

CONCLUSIONS This study demonstrated a high prevalence of MDD in AUD patients. Female gender, having a positive family history of psychiatric illness and a positive family history of alcohol and drug use were associated with increased likelihood of developing depression. Routine screening, initiating appropriate treatment, referral and follow-up of MDD in AUD patients may improve the prognosis of both the disorders.

INTRODUCTION

Nearly half of the 322 million people living with major depressive disorder (MDD) in the world are in the South-East Asia Region and Western Pacific Region[1]. With the increasing number of people suffering from depression, it will be a major contributor to the global disease burden by 2030 without further interventions[2]. In Bhutan, 11.69% of all psychiatric patients were diagnosed with MDD in 2017[3].

According to the World Health Organization (WHO) global report on Alcohol and Health 2018, the harmful use of alcohol resulted in an estimated 3 million deaths (5.3% of all deaths) globally in 2016[4]. Alcohol-related liver disease remains the top cause of mortality in Bhutan[2]. In 2017, 21.5% of all psychiatric patients had alcohol use disorder

(AUD) in Bhutan[2]. Patients with common mental disorders such as depression, anxiety, and difficulty in expressing emotions have been shown to have a higher risk of alcohol use disorder[5].

MDD is the most common psychiatric comorbidity among AUD patients[6]. They are reciprocal risk factors, and the presence of either disorder doubles the risk for the second[7-9]. The prevalence of MDD in alcohol use disorder is reported to be as high as 35%[7], and the lifetime prevalence of alcohol use disorder in people with major depressive disorder is as high as 40%[7,10-13]. The co-occurring nature of the two disorders has been explored using developmental and causal approaches, neurobiological theories and emotional dysregulation theories.

Studies have explained the developmental pathways in which AUD increases the risk for depressive disorder and, in turn, how depressive disorders increase the risk for AUD. Both disorders may share a common pathophysiology or set of risk factors[7,14].

Patients with comorbid MDD and AUD have a significant craving for alcohol after detoxification and rehabilitation[15]. The risk of relapse is higher and onset earlier with the comorbidity[16]. The co-existence of these two disorders poses a higher risk of delayed diagnosis and more severe psychopathological symptoms. Treatment adherence is lessened, and the treatment outcome is poorer. There is a greater impairment of social functioning. Admissions to emergency departments are more frequent and the incidence of suicidal ideation is higher. Medical comorbidity is greater[10,17,18]. Significant economic burden is incurred socially with high levels of healthcare resource consumption, inadequate treatment outcomes, high work absenteeism and lost productivity[18].

Screening of depression in AUD patients is essential for the appropriate management of dually diagnosed individuals. The prevalence of MDD among patients suffering from AUD in Bhutan is not known. There have been no studies conducted to the author's knowledge to date. Establishing the prevalence of this comorbidity will serve to increase awareness among the clinicians and health professionals, and facilitate more appropriate and successful treatment outcomes.

This study was conducted to establish the prevalence of MDD and associated risk factors in adult Bhutanese patients admitted with a primary AUD diagnosis to the inpatient psychiatric ward, Jigme Dorji Wangchuck National Referral Hospital, from March 2020 to February 2021.

METHODS

This cross-sectional study was carried out in the psychiatric ward of the Jigme Dorji Wangchuck National Referral Hospital, Thimphu, Bhutan. It is the only center providing specialized psychiatric services in Bhutan. The alcohol detoxification protocol was a standardized, tapering dose, fixed regimen of benzodiazepines over the course of 10 days. This study was carried out for a period of one year, from 1 March 2020 to 28 February 2021.

Study population

The sample in this study were Bhutanese adult patients with AUD admitted for alcohol detoxification in the psychiatric ward, fulfilling the following inclusion and exclusion criteria.

Inclusion criteria

Patient diagnosed as AUD and admitted for detoxification were included. Patients with AUD were included only once during the study period to avoid redundancy associated with multiple hospitalizations of an individual patient.

Exclusion criteria

Excluded were those patients with existing co-morbid psychiatric illnesses apart from MDD. This is because patients with comorbid schizophrenia and other psychotic illnesses, bipolar affective disorder, other substance use disorders apart from alcohol, personality disorders, and intellectual disability disorders could present with symptoms overlapping major depressive disorder, or their presentations could mask the symptoms of major depressive disorder.

Sample size

The sample size in this study was calculated using the Krejcie and Morgan formula[19] to determine the sample size for a finite population. After substituting the values into the formula, the required sample size for this study was 153 participants. A total of 155 participants were recruited over the study period.

Sampling method and study procedure

All the patients fulfilling the criteria from the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) AUD, who were admitted for alcohol detoxification during the specified time frame, were recruited for the study after obtaining informed written consent.

The principal investigator assessed patients admitted for alcohol detoxification through a detailed psychiatric history and selected only those patients fulfilling the inclusion criteria. Eligible participants were interviewed by the principal investigator after 5th detoxification day and administered the PHQ-9 and sociodemographic questionnaire. This process avoided confounding assessment factors of acute intoxication, delirium, sedation and transient cognitive impairment from withdrawal or medication burden.

Research instruments

The research instruments used in this study were a sociodemographic questionnaire and Patient Health Questionnaire (PHQ)-9.

Sociodemographic questionnaire

A self-designed questionnaire including basic demographic variables such as age, gender, marital status, education level, employment status, annual income, family history of psychiatric illness and family history of alcohol and substance use disorder, was employed in gathering the demographic profile of the participants.

The Patient Health Questionnaire (PHQ)-9

The PHQ-9 is a self-administered questionnaire designed to screen for major depressive disorder and its severity. Its 9-item questions coincide with the 9 symptoms of major depressive disorder described in the DSM-5 (Supplementary file).

A summary score ranging from 0–27 was calculated. Each of the 9 items is scored on a scale of 0 to 3: Not at all=0, Several

Table 1. Sociodemographic characteristics of participants admitted with AUD in the psychiatric ward, Jigme Dorji Wangchuck National Referral Hospital, and differences in distribution of depression among participants, March 2020 – February 2021 (N=155)

Characteristics	Admitted with AUD (N=155) n (col %)	AUD with depression (N=59) n (%)	p[a]
Total	155 (100)	59 (38.1)	
Gender			
Male	118 (76.1)	39 (33.1)	0.02 *
Female	37 (26.9)	20 (54.1)	
Age (years)			
18–29	29 (18.7)	11 (37.9)	0.35
30–39	66 (42.6)	22 (33.3)	
40–49	38 (24.5)	19 (50.0)	
≥50	22 (14.2)	7 (31.8)	
Marital status			
Never married	28 (18.1)	7 (25.0)	0.25
Married/living together	89 (57.4)	35 (39.3)	
Divorced/separated/widowed	38 (24.5)	17 (44.7)	
Education level			
No education	28 (18.1)	10 (35.7)	0.43
Formal education	117 (75.5)	47 (40.2)	
Non-formal education/monastic school	10 (6.5)	2 (20.0)	
Employment status			
Employed	119 (76.8)	43 (36.1)	0.37
Not employed	36 (23.2)	16 (44.4)	
Income per year (BTN)			
No income	25 (16.1)	10 (40.0)	0.26
1–99999	15 (9.7)	7 (46.7)	
100000–199999	57 (36.8)	16 (28.1)	
≥200000	58 (37.4)	26 (44.8)	
Family history of psychiatric illness			
Yes	12 (7.7)	9 (75.0)	0.01*
No	143 (92.3)	50 (35.0)	
Family history of alcohol and drug abuse			
Yes	83 (53.5)	38 (45.8)	0.03*
No	72 (46.5)	21 (29.2)	

a Two-tailed χ^2 analysis conducted for significance testing.*p<0.05. BTN: 1000 Bhutan Ngultrum about 12 US$.

days=1, More than half the days=2, and Nearly every day=3.

The severity of major depressive disorder is measured as follows: total score of 0–4=normal, 5–9=mild major depressive disorder, 10–14=moderate major depressive disorder, 15–19= moderately severe major depressive disorder, and 20–27=severe major depressive disorder.

Participants with PHQ-9 scores of ≥10 were considered to meet the criteria for MDD, as the sensitivity and specificity for PHQ-9 scores ≥10 is 88% for the diagnosis of MDD[20]. Participants with mild depression (PHQ-9 score of 5–9 were not included in the assessment of the overall prevalence.

Data management and analysis

Data were entered, double entered and validated using EpiData Entry version 3.1. The data were analyzed using statistical software (SPSS version 21). Descriptive statistics (frequency, percentage, mean and standard deviation (SD) were used to present the sociodemographic characteristics. Multivariate binary logistic regression was carried out to determine factors associated with depression using Model 1 and Model 2. All independent variables were computed for multivariate logistic regression in Model 1. For Model 2, variables with p<0.2 from Model 1 (gender, family history of psychiatric illness and family history of alcohol and drug abuse) were included. Variables with p>0.2 from Model 1 (age, marital status, education level, employment status, and income per year) were excluded. Akaike information criterion (AIC) score was used to construct our final multivariable model.

RESULTS

Sociodemographic characteristics

Table 1 describes the sociodemographic characteristics of the participants. The majority of the participants were male (76.1%) aged 30–39 years (mean=38.07; SD=9.71). More than half (57.4%) of the participants were married, and 75.5% of them had attended formal education. Most of the participants were employed (76.8%), and their annual income was >100000 BTN (1000 Bhutan Ngultrum about 12 US$); 7.7% of the participants had a family history of psychiatric illness, and 53.5% reported having a family history of alcohol and drug abuse.

Prevalence and severity of MDD in those with AUD

The overall prevalence of MDD (PHQ-9 score ≥10) among the participants was 38% (59/155). According to the PHQ-9 score, 29.7% of the participants had mild depression (PHQ-9 score = 5–9), 23.3% of the participants had moderate depression (PHQ-9 score = 10–14), 10.3% of the participants had moderately severe depression (PHQ-9 score = 15–19) and 4.5% of the participants had severe depression (PHQ-9 score = 20–27). The cut-off score for major depressive disorder is ≥10, although scores from 5–9 are considered as mild depression. Mild depression does not require active interventions, but they can be followed up and monitored for an increase in their subsequent PHQ-9 scores, so participants with mild depression are not included in the overall prevalence.

As shown in Table 1, female (54.05%) participants had a higher prevalence of depression than male (33.05%)

Table 2. Univariate binary logistic regression analysis of risk factors associated with depression among patients with AUD admitted in the psychiatric ward, Jigme Dorji Wangchuck National Referral Hospital, March 2020 – February 2021 (N=155)

Variables	Depression	
	OR (95% CI)	p
Gender		
Male (Ref.)	1	
Female	2.38 (1.12–5.05)	0.02*
Age (years)		
18–29 (Ref.)	1	
30–39	1.31 (0.41–4.22)	0.65
40–49	1.07 (0.38–3.01)	0.90
≥50	2.14 (0.71–6.44)	0.17
Marital status		
Never married (Ref.)	1	
Married/living together	0.41 (0.14–1.20)	0.10
Divorced/widowed/separated	0.80 (0.37–1.73)	0.57
Education level		
No education (Ref.)	1	
Formal education	0.83 (0.35–1.95)	0.67
Non-formal education/ monastic school	0.37 (0.08–1.83)	0.22
Employment status		
Employed (Ref.)	1	
Not-employed	1.41 (0.66–3.01)	0.37
Income per year (BTN)		
<150000 (Ref.)	1	
≥150000	1.15 (0.60–2.21)	0.67
Family history of psychiatric illness		
No (Ref.)	1	
Yes	5.58 (1.44–21.54)	0.01*
Family history of alcohol and drug abuse		
No (Ref.)	1	
Yes	2.05 (1.05–3.99)	0.04*

*p<0.05 (statistically significant). BTN: 1000 Bhutan Ngultrum about 12 US$.

(p=0.02). The prevalence of depression was significantly higher among participants with a family history of psychiatric illness (p=0.01) and participants with a family history of alcohol and substance use (p=0.03) compared to their counterparts.

Risk factors associated with depression

In unadjusted analysis (univariate binary logistic regression), female participants (OR=2.38; 95% CI: 1.12–5.05), participants with a family history of psychiatric illness (OR=5.58; 95% CI: 1.44–21.54) and those with a family history of alcohol and drug abuse (OR=2.05; 95% CI: 1.05–3.99) were significantly associated with depression compared to their counterparts as shown in Table 2.

Table 3 shows factors associated with depression among the study participants through multivariate logistic regression analysis. All independent variables were

Table 3. Multivariate binary logistic regression analysis of risk factors associated with depression among patients with AUD admitted in the psychiatric ward, Jigme Dorji Wangchuck National Referral Hospital, March 2020 – February 2021 (N=155)

Variables	Model 1		Model 2	
	AOR (95% CI)	p	AOR (95% CI)	p
Gender				
Male (Ref.)	1		1	
Female	2.03 (0.83–4.96)	0.120	2.19 (1.01–4.75)	0.04*
Age (years)				
18–29 (Ref.)	1			
30–39	1.16 (0.28–4.75)	0.84	NA	NA
40–49	1.05 (0.33–3.32)	0.94	NA	NA
≥50	2.21 (0.67–7.27)	0.19	NA	NA
Marital status				
Never married (Ref.)	1			
Married	0.40 (0.11–1.40)	0.15	NA	NA
Divorced/widowed/separated	0.78 (0.31–1.94)	0.59	NA	NA
Education level				
No education (Ref.)	1			
Formal education	0.75 (0.25–2.26)	0.61	NA	NA
Non-formal education/monastic school	0.48 (0.09–2.70)	0.41	NA	NA
Employment status				
Employed (Ref.)	1			
Not employed	1.58 (0.64–3.87)	0.32	NA	NA
Income per year (BTN)				
<150000 (Ref.)	1			
≥150000	1.32 (0.59–2.93)	0.50	NA	NA
Family history of psychiatric illness				
No (Ref.)	1		1	
Yes	5.23 (1.13–24.17)	0.03*	4.63 (1.17–18.44)	0.03*
Family history of alcohol and drug abuse				
No (Ref.)	1		1	
Yes	1.82 (0.88–3.76)	0.11	1.69 (0.84–3.38)	0.14
AIC score	198.96		197.77	

AOR: adjusted odds ratio. AIC: Akaike information criterion. *p<0.05 (statistically significant); NA: not applicable. Model 1: all independent variables were computed for multivariate logistic regression. Model 2: only those variables with p<0.2 from Model 1 were included. BTN: 1000 Bhutan Ngultrum about 12 US$.

computed for multivariate logistic regression in Model 1. For Model 2, only those variables with p<0.2 from Model 1 were included. After adjusting for confounding factors, the findings show that females had a more than two times (AOR=2.19; 95% CI: 1.01–4.75) likelihood of developing depression than male patients with AUD. In addition, participants with a family history of psychiatric illness had nearly five times (AOR=4.63; 95% CI: 1.17–18.44) the likelihood of developing of depression compared to those without a family history of psychiatric illness.

DISCUSSION

Prevalence of MDD in those with AUD

The association between depression and AUD is well established, and each disorder is a risk factor for the other. This study shows the occurrence of depression in AUD in the studied population to have an overall prevalence of 38%. This prevalence rate is consistent with other studies[6,7,21-23]. Studies conducted by Becker et al.[17,24,25], Cho et al.[17,24,25] in Korea, and Bott et al.[17,24,25] in Germany, however, reported lower prevalence rates. These differences could be due to different study designs and sample size, psychometric tools used in the study and different timing of the administration of the study tools. Studies conducted by Luitel et al.[22,26] in Nepal and Charnsil and Aroonrattanapong[26] in Thailand using the same study tool (PHQ-9) demonstrated that the prevalence of MDD in AUD was around 40% and 32.2% respectively. Mchugh and Weiss[6] reported that AUD patients are 3.7 times more likely to have MDD whereas Becker et al.[17] reported that the presence of alcohol dependence increases the risk for depression by 5 times (OR=4.7).

Alcohol is a central nervous system depressant, and prolonged alcohol use could precipitate symptoms of depression. Patients with depression may be self-medicating with alcohol to alleviate their symptoms of depression. Maladaptive coping skills in depressed patients could result in using alcohol as a coping strategy. Furthermore, social and environmental stressors could trigger both AUD and MDD simultaneously. MDD could also result from the consequences of alcohol through its effect on an individual's social, occupational and financial life. Finally, both disorders could be independent of each other and yet may present as comorbidity[10].

According to the literature, AUD and MDD share bidirectional causality[7,14]. In Bhutan, the prevalence of AUD was reported to be high[3]. Hence, a possible reason for the high prevalence of MDD among our participants could be linked to a high prevalence of AUD among the Bhutanese population. Further, high prevalence of AUD in Bhutan is attributed to easy access of alcohol, its cultural acceptance in routine religious rituals and social gatherings, and its relative inexpensiveness[27].

The validity of PHQ-9 was not checked in the Bhutanese context; however, similar studies using PHQ-9 have been done in India and Nepal. The translated and validated version of PHQ-9 used in Nepal had a sensitivity of 94% and specificity of 88% in diagnosing depression with a PHQ-9 score >10[28,22]. It has also been used in India for similar studies[29,30]. Bhutan shares its geographical boundaries with the two countries, and there are also some sociocultural, ethnic and religious similarities between these countries.

The co-occurrence infers that there are two deadly co-occurring psychiatric problems with multiple detrimental consequences. Some of the consequences, as explained in many studies, are a higher risk of delayed diagnosis, more severe psychopathological symptoms, less compliance with treatment, poorer effects of treatment, more impairment of social functioning, increased admissions to emergency department, and higher prevalence of physical comorbidity[10,17,18]. In addition, it can also cause a significant economic burden to society due to high levels of healthcare consumption, inadequate treatment outcomes, high work absenteeism, and lost productivity[18].

Gender differences in MDD in those with AUD

The majority of the participants in this study were males (76.1%). AUD is more common in males than females[31]. Males are more readily exposed to alcohol than females. They tend to drink more frequently and in greater amounts and this behavior is partly enforced by cultural factors, stigma against women who are drinking alcohol or abusing substances, and underrepresentation of females with AUD in research[31,32]. However, evidence suggests that the prevalence of AUD is increasing in females and is associated with greater severity of consequences of alcoholism[31,32].

In the current study female participants were more than two times likely to develop MDD (AOR=2.19; 95% CI: 1.01–4.75). A similar finding was demonstrated in Thailand by Suttajit et al.[33] where females with AUD had increased risk for MDD (OR=4.09; 95% CI: 2.31–7.26) compared to their male counterparts (OR=2.49; 95% CI: 1.76–3.53). There are epidemiological studies supported by genetic studies which suggest that the comorbidity of depression and AUD is more prevalent among females[34]. Twin studies have also shown a strong association between depression and AUD in females[34].

Family history as a risk factor for MDD in those with AUD

According to the present study, participants with a positive family history of psychiatric illness were nearly 5 times more likely to develop MDD (AOR=4.63; 95%CI: 1.17–18.44). This occurrence could be possibly due to genetics. According to Edwards et al.[35], genetic hereditability and the occurrence of comorbidity of depression and AUD have been established by family, twin and adoption studies, and the genetic influences account for at least 50% of their phenotypic association. It is associated with earlier onset and recurrent depression, which is greater in severity[9]. People with alcohol use problems who attempt suicide also tend to have a family history of alcoholism[32].

Considering the high prevalence of MDD among AUD

patients in our study, healthcare workers (HCWs) across the country are recommended to routinely screen for MDD when they are providing alcohol detoxification to AUD patients. Identified patients with MDD should be administered proper treatment or referrals to higher health centers when indicated. Further, HCWs should focus more on females and people with a family history of psychiatric illness as per our findings.

Strengths and limitations

This study is the first study known to date to examine the prevalence of MDD in AUD patients in Bhutan. The findings of the study could be used as a baseline prevalence for future studies. Owing to the study design, we could not determine the temporal nature and could not establish the causality of the two disorders. Moreover, we recommend conducting further studies to determine the temporal nature and to find out the association between the risk factors identified in this study.

CONCLUSIONS

This study demonstrated a high prevalence of depression in AUD patients, with an overall prevalence of 38%. Female participants and respondents having a positive family history of psychiatric illness were associated with an increased likelihood of developing depression among the AUD patients.

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DATA AVAILABILITY
The data supporting this research are available from the authors on reasonable request.

AUTHORS' CONTRIBUTIONS
All authors contributed to study designs, analyses, and drafting of the manuscript. All authors agreed and gave final approval for the manuscript to be submitted.

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