Prevalence and associations of depression in orthopedic trauma patients at 4-weeks since admission: a prospective cohort study at a tertiary care center in Northern India

Santosh Kumar[1], Vikas Verma[2], Umesh Kushwaha[3], Amit Arya[4]

[1]Professor, [3]Senior Resident, Department of Orthopaedics, [2]Associate Professor, Department of Paediatric Orthopaedics, [4]Associate Professor, Department of Psychiatry, King George Medical University, Lucknow, Uttar Pradesh, India

ABSTRACT

Background: Depressive symptoms have been reported in admitted patients of musculoskeletal trauma. However, prevalence and associations of depression have not been reported after definitive management of injury. **Aims and Objectives:** The objectives of this study were to document the presence of depressive symptoms in adult musculoskeletal injury patients and identify factors associated with an abnormal score on the depression sub-scale of HADS at 4-weeks since admission. **Materials and Methods:** A longitudinal cohort study was undertaken on musculoskeletal injury patients admitted in the orthopedics department. Patients were enrolled on a randomly chosen day of the week. Subjects were excluded if they suffered from conditions known to preclude the assessment of the mental status. Age, sex, injury severity score, matrimonial status, insurance status, educational status, economic condition, support from family, alcohol abuse, and cannabis abuse were recorded at the time of admission. At 4-weeks after admission, enrolled subjects were screened for depression using the depression subscale of Hospital anxiety and depression scale score. Pain was recorded using visual analogue scale (VAS). Bivariate and multivariate analysis was used to identify predictors of an abnormal HADS score. **Results:** One-hundred ninety subjects were included. Average age of the subjects was 33.8 years. Thirty nine (21.53%) were females. At 4-weeks, 49 (25.79%) had an abnormal HADS score. A higher VAS score for pain, a younger age, living in a nuclear family and cannabis abuse were associated with an abnormal HADS score. **Conclusion:** Depressive symptoms are common in musculoskeletal injury patients at 4-weeks after admission.

Key words: Depression; India; Injuries; Musculoskeletal; Prevalence

INTRODUCTION

Management of orthopedic trauma patients has undergone significant improvements on account of development of new techniques of fixation, better implants, and a better understanding of the biomechanics of fixation. Orthopedic surgeons are trained to focus on the physical aspects of treatment of injured patients. Trauma care facilities are lacking in rural India causing many patients to travel great distances to receive treatment. Injury places the patient at a huge risk of psychological morbidity on account of physical injury, anxiety related to uncertainty of recovery, monetary requirements of treatment, long distance transfers, and a strange hospital environment.

Depression is a common mood disorder. Depression as a co-morbid condition is known to worsen outcome in chronic conditions.[1] High prevalence of depression has been reported among general trauma patients[2,3] as well as orthopedic trauma patients.[4-7] To return to pre-injury

levels of performance, a time and effort consuming rehabilitation protocol is required for patients of musculoskeletal injuries. Poor outcome in orthopedic injury patients is recognized to be associated with psychiatric illness.[5]

The Hospital Anxiety and Depression Scale (HADS) is a uniformly accepted instrument to screen for depression.[8] HADS has been validated on Indian population.[9] A cutoff value of >7 on HADS to identify a case of depression has been reported to have a sensitivity of 0.67, a specificity of 0.97.[10] A mean Cronbach's alpha of 0.82 for the depression subscale of HADS has also been reported which implies that the depression subscale score has a high level of internal consistency and reliability.[10] The same review reported HADS to perform well in assessing the severity of symptoms and recognition of cases of depression in general population as well as somatic, psychiatric, and primary care patients.[10]

Few studies have focused on identifying factors associated with depressive symptoms in musculoskeletal injury patients. Factors known to be associated with a HADS score >7 in admitted musculoskeletal injury patients after initial stabilization are female gender, a lower age, greater pain score, and a nuclear family.[7] A retrospective study done on admitted patients has reported visual analog scale (VAS) for pain, injury severity score and matrimonial status to have a significant association with a Huawie emotional distress score >8.[11] A study that investigated factors associated with depression in musculoskeletal injury patients reporting to OPD on follow-up found female gender, lack of social support, development of complications, loss of limb, and pain to be significant associations.[12] Since the patients were followed up in OPD, they had a variable time duration since injury.

A study has identified associations for depressive symptoms in admitted patients after stabilization of the general condition of the patient[7] in India and another retrospective study done in China.[11] However, it is possible that the factors associated with depression may vary with time, type of treatment and the socio-cultural milieu of the subjects which is very different in India compared to China. Therefore we decided to do a study to record the presence of depressive symptoms in patients with musculoskeletal injury and identify factors associated with an abnormal score on the depression sub-scale of HADS score at 4-weeks since admission. We chose to investigate the effect of type of treatment (operative vs. non-operative) as a variable of interest on depressive symptoms. Since patients in our setup receive definitive treatment (including 2nd surgery if required) by 4 weeks, we chose 4 weeks as the time to assess the patients.

Aims and objectives

The aim of this study was to determine the factors associated with an abnormal HADS score in musculoskeletal injury patients at 4 weeks since admission

MATERIALS AND METHODS

This manuscript adheres to STROBE guidelines. The study was a part of thesis of one of the authors and was cleared by the departmental research committee. A longitudinal cohort study was undertaken enrolling musculoskeletal injury patients admitted to the department of Orthopedics King George Medical University, Lucknow. A list of random days in a week was generated using the command =TEXT(RANDBETWEEN(1,7), "dddd") in Microsoft Excel (Microsoft corp., Redmond, USA), which was used to select a random day of the week. All the patients being admitted from 8 am of the randomly chosen day to 8 am of the following day were considered for enrollment. This was done to make sure that our sample was representative. Patient interviews, examination of past and current medical records were used to determine the eligibility for the study. Eligibility was determined after stabilization of the general condition of the patient. Patients meeting the eligibility criteria were offered enrolment in the study. Only those patients who agreed to a give a written informed consent were included in the study. Enrolled patients were followed up for a period of 4-weeks either within the hospital or called for follow-up in the OPD.

Inclusion criterion was adult musculoskeletal injury patients admitted to the department of Orthopedics, KGMU. The exclusion criteria for the study were head trauma (history of head injury, or an abnormal GCS score), senile dementia, Parkinson's disease, a history of psychiatric illness, continuing medication or counseling for psychiatric conditions, chronic, or terminal medical illness known to cause cognitive impairment (motor neuron disease, advanced cancer, chronic renal disease, cardiomyopathy, chronic hepatic disease, and acquired immunodeficiency syndrome) and intellectual disability confirmed by a psychiatrist.

Sample size was calculated using the formula

$$N = \frac{Z^2 P\ (1 - P)}{D^2}$$

The prevalence of depression in orthopedic trauma patients has been reported in the literature.[12] For calculating the sample size, P was kept at 36.1%, confidence interval at 95%, and relative error at 20% for 80% power of study

and 10% loss to follow-up. The sample size was calculated to be 187 which were rounded to 190.

Patients were interviewed by a single investigator (after stabilization of the general condition of the patient) to record demographic data, duration since injury, matrimonial status (married or unmarried), insurance cover (present or not), level of education, socioeconomic condition, familial support, tobacco abuse, alcohol abuse, and cannabis abuse. Educational status was recorded as illiterate, primary, intermediate, and college. Socioeconomic condition was measured by recording whether the subject had a below poverty line (BPL) card or not. A BPL card holder is entitled to free healthcare in India. Degree of familial support was recorded as nuclear family, joint family, or no support. Criteria for recording use of cannabis as abuse were its consumption more than once a day for at least 20 days in a month.[13] Criteria of alcohol abuse was defined as at least 14 drinks in a week. A drink was defined as five ounces of wine, or 12 ounces of bear or one and half ounces of distilled beverages (like rum, whisky, tequila, or vodka).[14] Diagnostic and Statistical Manual of mental disorders-5 criteria were used to define tobacco abuse.[15] Patient records including examination findings, per-operative findings and X-rays were used to record abbreviated injury scale codes which were used to calculate ISS. Inpatients as well as discharged patients were assisted by a single investigator. Pain score was recorded at 4-weeks using VAS.

A HADS score of 0–7 was taken as normal, 8–10 as doubtful, and ≥11 as depression.[16] Data were recorded using Microsoft EXCEL (Microsoft corp., Redmond, USA) on a password protected computer. To maintain confidentiality, identifiers were not recorded in the data sheet. Abnormal HADS score was taken as >7 on the depression subscale of HADS as it is reported to have an ideal balance of sensitivity and specificity.[10] Factors associated with >0.25 significance on bivariate analysis were used to make a logistic regression model to predict an abnormal HADS score at 4-weeks after admission.

RESULTS

Two-hundred forty-six musculoskeletal injury patients were admitted to the orthopaedics department on a randomly selected day in the duration September1, 2017,to March31, 2018. Twenty-eight patients had suffered from head injury in the past or had a Glasgow Coma Scale Score of <15. Five patients had a history of psychiatric illness and another three were under active psychiatric treatment. Three patients had chronic liver disease. Therefore, we excluded 39 patients as they met the exclusion criteria. Two-hundred

and seven patients met the inclusion criteria. Of these, 190 consented to be enrolled. One-hundred eighty-four of the enrolled 190 patients were discharged before 4-weeks. These reported back to OPD for follow-up at 4-weeks where HADS score and VAS score for pain was recorded. Six of the enrolled 190 patients were still admitted in the hospital at 4weeks after admission. Inpatients as well as those reporting back in the OPD were assisted by a single investigator trained in HADS questionnaire to complete the HADS questionnaire.

Means of age, pain score (VAS) and ISS were 33.8 years, 4.9 and 6.8, respectively Table 1. Forty-nine (25.79%) had an abnormal HADS score (>7). A HADS score in the range of 8–10 was recorded in forty-five (23.68%) patients. A HADs score of >10 was recorded in four patients (2.1%). Average duration since injury to admission was 75.62 h.

Three patients did not turn up for follow-up and therefore HADS score and VAS score for pain werenot available for these patients. Missing data points were accounted using single mean imputation. On bivariate analysis, we

Table 1: Base line characteristics of enrolled patients	
Variable name	n (%)
Sex	
Male	151 (79.47)
Female	39 (21.53)
Education	
Illiterate	3 (1.5)
High school	24 (12.63)
Higher secondary	95 (50)
Graduate and above	68 (35.79)
Family support	
None	6 (3.16)
Nuclear family	74 (38.95)
Joint family	110 (57.89)
Insurance status	
Covered	11 (5.79)
Not covered	179 (94.21)
Type of treatment	
Operated	161 (84.74)
Not operated	29 (15.26)
Marital status	
Married	123 (64.76)
Not married	67 (35.24)
BPL* card	
Holder	6 (3.16)
Non-holder	184 (96.84)
Tobacco abuse	
Yes	92 (48.42)
No	98 (51.58)
Cannabis abuse	
Yes	54 (28.42)
No	136 (71.58)
Alcohol abuse	
Yes	67 (35.26)
No	123 (64.76)

*BPL: Below the poverty line

found a lower age, greater ISS, higher pain score, nuclear family, alcohol abuse, and cannabis abuse to be significant associations of (P<0.05) an abnormal HADS score at 4-weeks since admission. Tables 2-4 insurance status, type of treatment (operative vs. non-operative), duration since injury, level of education, gender, matrimonial status, socioeconomic status (BPL card), and tobacco abuse were not found to be significant on bivariable analysis.

Multivariable analysis using the stepwise logistic regression identified a greater pain score, a lower age, being a part of a nuclear family and cannabis abuse to be significant associations of an abnormal HADS score Table 5.

DISCUSSION

In this study, the 25.79% of the enrolled subjects had an abnormal HADS score. Depressive symptoms have been reported in 8.1–56% of orthopedic trauma patients in

Table 2: Results of bivariable analysis of continuous/discrete variables

Variable	HADS≤7 n (Mean±SD)	HADS>7 n (Mean±SD)	P value
Age	141 (35.75±12.46)	49 (30.20±11.61)	0.042
ISS*	141 (6.51±2.56)	49 (7.71±2.57)	0.005
Pain	141 (4.60±1.56)	49 (5.69±1.23)	<0.001
Duration since injury**	141 (68.61±119.27)	49 (95.80±228.60)	0.291

*ISS: Injury Severity Score. **Duration since injury-Mann–Whitney U-test was used as the data were not normally distributed

Table 3: Results of bivariable analysis of categorical variables

Education	HAD≤7 n (%)	HADS>7 n (%)	P value
Illiterate	2 (1.4)	1 (2.0)	0.630
Primary	18 (12.8)	6 (12.2)	
Inter	67 (47.5)	28 (57.1)	
Graduate	54 (38.3)	14 (28.6)	
Total	141 (100)	49 (100)	
No Support	6 (4.3)	0 (0.0)	<0.001
Nuclear Family	41 (29.1)	33 (67.3)	
Joint Family	94 (66.7)	16 (32.7)	
Total	141 (100)	49 (100)	

literature.[4-7,11,12,17,22] The percentage of musculoskeletal trauma patients with depressive symptoms reported in this study is higher compared to 3.1–3.6% with depressive symptoms in general population reported by a study that investigated the prevalence of mental disorders in India.[18]

Results of bivariable analysis in this study identified a lower age, greater injury severity score, being a part of nuclear family, alcohol abuse, and cannabis abuse as significant associations of (P<0.05) a HADS score of >7 at 4-weeks since admission. However, on logistic regression we found a lower age, being a part of nuclear family and cannabis abuse to be significant associations of a HADS sore of >7. Loss of limb and a higher Gustilo Anderson grade of compound fractures have been reported to significantly correlate with BDI score.[19] We have found ISS to be significantly associated with HADS score on bivariate analysis but the significance was lost on logistic regression. Since we did not look into the aftermath of Gustilo Anderson grade or loss of limb on HADS score, we are unable to comment on its effect. A study conducted on Orthopedic trauma patients reporting for follow-up identified female gender, lack of social support, occurrence of complications, loss of limb, and pain as factors associated with depression.[12] A previous study at KGMU on admitted orthopedic trauma patients reported a greater pain, nuclear family, and female gender to associated with a HADS score of >7.[7] However, this study enrolled patients after primary stabilization of the patient. Another study using multivariable analysis to recognize factors associated with HEI score of >8 in admitted patients has identified a higher pain score, being single and a higher ISS to be significant associations of >8 HEI score.[11]

We have not found female gender to be significant association of an abnormal HADS score which is in contrast to the results reported by other studies.[7,12] We also found that a higher proportion of females were present in the HADS >7 group (26.6%) compared to HADS ≤7 group (18.4%). However, the difference was not found to be significant. This could be because of a smaller proportion of female patients in our cohort (20.52% females) compared to the proportion of females in the

Table 4: Results of bivariable analysis of qualitative variables

Exposed parameter	HADS≤7 n (%)	HADS>7 n (%)	OR (95% CI)	P value
Female sex	26 (18.4)	13 (26.6)	1.6 (0.74–3.43)	0.227
Single (n=67)	48 (34)	19 (38.8)	1.23 (0.63–2.40)	0.550
No Insurance coverage (n=179)	131 (92.9)	48 (98.0)	3.66 (0.45–29.39)	0.192
Operative treatment	118 (85.72)	43 (86.04)	1.39 (0.52–3.66)	0.236
No BPL card (n=184)	137 (97.2)	47 (95.9)	0.69 (0.12–3.87)	0.668
Smoking tobacco (n=92)	68 (48.2)	24 (49.0)	1.03 (0.54–1.97)	0.928
Alcohol (n=67)	43 (30.5)	24 (49.0)	2.19 (1.13–4.25)	0.020
Cannabis (n=54)	32 (22.7)	22 (44.9)	1.03 (0.54–1.97)	0.003

Type	Variable	B	P-value	Exp (B)/OR
Age		−0.051	0.005	0.950
VAS at 4-weeks		0.550	<0.001	1.733
Type of Family	Overall		<0.001	
	No Support	−17.882	0.999	0.000
	Nuclear Family	1.826	<0.001	6.210
Cannabis	Yes	−1.592	0.001	0.203
Constant		−2.294	0.032	0.101

Table 5: Logistic regression analysis showing the relationship of significant factors with HADS Status at 4-weeks

n=190, Pseudo (Nagelkerke) R²=0.394, Log likelihood: 157.66

population of India (47.36% females). A lower proportion of female patients in this study is likely to result in the study missing the effect of female sex on occurrence of outcome of interest which is a HADS score >7.

This study identified pain to an independent predictor of HADS score at 4-weeks. An association of pain with HADS score has been reported in follow up orthopedic trauma patients[14] as well as in admitted orthopedic trauma patients after stabilization of the general condition.[7] The fact that pain has a significant association with an abnormal HADS score raises the possibility that controlling pain might be helpful in preventing the development of depressive symptoms in patients with musculoskeletal injury. Pain has been reported to be a significantly associated with the resultant disability in orthopedic injury cases.[20] Since disability was not investigated by us, we are not in a position to draw any conclusion regarding the effect of pain on resultant disability.

An inverse correlation has been reported between social support from friends as well as family and depression.[5,21] We found that being a part of a nuclear family is an independent predictor of a HADS score of >7. Other studies have also reported an association between nuclear family and depression.[4,7,21] The level of social support provided by joint families is likely to be higher than in a nuclear family and that may be the reason for depression being associated with being a part of nuclear family.

In this study, we report a lower age as a significant association of a HADS score >7 at 4-weeks on bivariable analysis as well as multivariable analysis. A younger age has been reported to be a significant predictor of abnormal HADS score in orthopedic injury patients.[7] In general population a "U" shaped relationship between age and occurrence of depression has been described.[23] Since we did not do a correlation of age and HADS score we are unable to comment on the relationship of age with depressive symptoms.

We found an association between a HADS score of >7 and cannabis at 4-weeks after admission. However, another study that investigated the association of use of cannabis with HADS score at the time of admission did not find any association between the two.[7] Termination of excessive as well as extended use of cannabis is known to result in a depressed mood.[24] Consistent consumption of cannabis results in inactivation and downregulation of cannabinoid (CB_1) receptors in the brain of humans.[25] These receptors return to normal level of function at about 4 weeks of abstinence.[24] This explains the lack of association at admission reported in a previous study[7] and a positive association at 4-weeks as reported in this study. CB_1 receptor availability has been reported to be strongly correlated with cannabis withdrawal syndrome.

In this study, alcohol abuse was not found to be an independent predictor of an abnormal HADS score at 4 weeks. Association of alcohol with depression is still a matter of conjecture. At one end of the spectrum is a longitudinal study that has reported no association between alcohol abuse and depression.[26] On the other hand, a significant association has been reported between depression and alcohol use.[27] On the basis of the results of our study, it is not possible to make any definitive conclusion regarding the association of alcohol abuse with depression. Therefore, we suggest planning and execution of more robust longitudinal studies to answer the question regarding the association of alcohol abuse with depression in musculoskeletal injury patients.

Clinical depression is not the same as occurrence of depressive symptoms or an abnormal HADS score. It is imperative that an abnormal HADS score on screening followed by a referral to psychiatry for conclusive diagnosis and treatment.

Limitations of the study
A short coming of using HADS score is that it uses questions pertaining to physical condition of the subject. This raises the possibility of confounding due to impaired activities of daily living, chronic pain or the consumption of narcotics. To overcome this shortcoming, we used logistic regression to delineate the independent predictors of abnormal HADS score. A limitation of our study is that we did not explore the effect of co-morbidities on depression. Another study with characterization of co-morbidities using the Van Walraven Index or the Charlson Comorbidity Index may be planned to explore the effect of co-morbidities on depression. Our study is limited by our lack of ability to gather information regarding the extent of depressive symptoms in our patients before sustaining injury. This precludes our capacity to draw conclusion regarding the effect of injury on depressive symptoms. To

overcome this shortcoming, we did not include patients with a history of psychiatric illness as they are at high risk of pre-existing depression. The present study is also limited in the sense that we did not look into the role played by Gustilo Anderson grading of compound fractures on HADS score.Another limitation of our study is that we have not investigated the effect of place of residence (rural vs. urban) due to which we cannot comment as to whether an association exists between the place of residence and an abnormal HADS score. Another shortcoming of the present study is that we did not check for intra-observer reliability. Checking for intra-observer reliability and reporting correlation coefficients for the same would have increased the strength of the study. The present study is also limited by lack of a well-defined referral pathway to a trained psychiatrist for further diagnostic assessment and management.

CONCLUSION

Using logistic regression to test for factors associated with an abnormal HADS score in orthopedic trauma patients at 4 weeks since admission, the present study found a younger age, lack of family support, and cannabis abuse to be independent predictors of an abnormal HADS score at 4 weeks. Since orthopedic surgeons are not trained to diagnose and treat depression, it is important to screen musculoskeletal injury patients for depression using screening tools like HADS and those found positive for an abnormal HADS score should be referred to a trained psychiatrist for conclusive diagnosis and treatment.

ACKNOWLEDGMENT

REFERENCES

1. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V and Ustun B. Depression, chronic diseases, and decrements in health: results from the world health surveys. Lancet. 2007;370(9590):851-858.
   https://doi.org/10.1016/S0140-6736(07)61415-9

2. McCarthy ML, MacKenzie EJ, Edwin D, Bosse MJ, Castillo RC and Starr A. LEAP study group. Psychological distress associated with severe lower-limb injury. J Bone Joint Surg Am. 2003;85(9):1689-1697.
   https://doi.org/10.2106/00004623-200309000-00006

3. Kovacevic J, Miskulin M, Degmecic D, Vcev A, Leovic D, Sisljagic V, et al. Predictors of mental health outcomes in road traffic accident survivors. J Clin Med. 2020;9(2):309.
   https://doi.org/10.3390/jcm9020309

4. Vincent HK, Hagen JE, Zdziarski-Horodyski LA, Patrick M, Sadasiva KK and Guenther R. Patient-reported outcomes measurement information system outcome measures and mental health in orthopedic trauma patients during early recovery. J Orthop Trauma. 2018;32(9):467-473.
   https://doi.org/10.1186/s13018-020-02132-4

5. Weinberg DS, Narayanan AS, Boden KA, Breslin MA and Vallier HA. Psychiatric illness is common among patients with orthopedic polytrauma and is linked with poor outcomes. J Bone Joint Surg Am. 2016;98(5):341-348.
   https://doi.org/10.2106/JBJS.15.00751

6. McCrabb S, Baker AL, Attia J, Balogh ZJ, Lott N, Palazzi K, et al. Comorbid tobacco and other substance use and symptoms of anxiety and depression among hospitalised orthopedic trauma patients. BMC Psychiatry. 2019;19(1):28.
   https://doi.org/10.1186/s12888-019-2021-y

7. Kumar S, Verma V, Kushwaha U, Hynes EJ, Arya A and Agarwal A. Prevalence and association of depression in in-patient orthopedic trauma patients: A single centre study in India. J ClinOrthop Trauma. 2020;11(Suppl 4):S573-S577.
   https://doi.org/10.1016/j.jcot.2019.12.010

8. Zigmond AS and Snaith RP. The hospital anxiety and depression scale. ActaPsychiatr Scand. 1983;67(6):361-370.
   https://doi.org/10.1111/j.1600-0447.1983.tb09716.x

9. Thomas BC, Devi N, Sarita GP, Rita K, Ramdas K, Hussain BM, et al. Reliability and validity of the Malayalam hospital anxiety and depression scale (HADS) in cancer patients. Indian J Med Res. 2005;122(5):395-399.

10. Bjelland I, Dahl AA, Haug TT and Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002;52(2):69-77.
    https://doi.org/10.1016/s0022-3999(01)00296-3

11. Yang Y, Tang TT, Chen MR, Xiang MY, Li LL and Hou XL. Prevalence and association of anxiety and depression among orthopedic trauma inpatients: A retrospective analysis of 1994 cases. J OrthopSurg Res. 2020;15(1):587.
    https://doi.org/10.1186/s13018-020-02132-4

12. Srahbzu M, Yigizaw N, Fanta T, Assefa D and Tirfeneh E. Prevalence of depression and anxiety and associated factors among patients visiting orthopedic outpatient clinic at TikurAnbessa specialized hospital, Addis Ababa, Ethiopia, 2017. J Psychiatry 2018;21:450.
    https://doi.org/10.4172/2378-5756.1000450

13. Hoch E, Bonnet U, Thomasius R, Ganzer F, Havemann-Reinecke U and Preuss UW. Risks associated with the non-medicinal use of cannabis. DtschArztebl Int. 2015;112(16):271-278.
    https://doi.org/10.3238/arztebl.2015.0271

14. Ngasa, SN, Sama CB, Dzekem BS, Nforchu KN, Tindong M, Aroke D, et al. Prevalence and factors associated with depression among medical students in Cameroon: A cross-sectional study. BMC Psychiatry. 2017;17:216.
    https://doi.org/10.1186/s12888-017-1382-3

15. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-5®). 5th ed. Washington DC, USA: American Psychiatric Association; 2013.

16. Stern AF. The hospital anxiety and depression scale. Occup Med (Lond) 2014;64(5):393-394.
    https://doi.org/10.1111/j.1600-0447.1983.tb09716.x

17. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: Results from the national comorbidity survey replication (NCS-R). JAMA. 2003;289(23):3095-3105.
    https://doi.org/10.1001/jama.289.23.3095

18. India State-Level Disease Burden Initiative Mental Disorders Collaborators. The burden of mental disorders across the states of India: The global burden of disease study 1990-2017. Lancet

Psychiatry. 2020;7(2):148-161.

https://doi.org/10.1016/S2215-0366(19)30475-4

19. Secinti, E, Selcuk B and Harma, M. Personal and familial predictors of depressive feelings in people with orthopedic disability. Health Psychol Rep. 2017;5(3):227-239.

https://doi.org/10.5114/hpr.2017.65206

20. Albert PR. Why is depression more prevalent in women? J Psychiatry Neurosci 2015;40(4):219-221.

https://doi.org/10.1503/jpn.150205

21. Nota SP, Bot AG, Ring D and Kloen P. Disability and depression after orthopedic trauma. Injury. 2015;46(2):207-212.

https://doi.org/10.1016/j.injury.2014.06.012

22. Becher S, Smith M and Ziran B. Orthopedic trauma patients and depression: A prospective cohort. J Orthop Trauma. 2014;28(10):e242-e246.

https://doi.org/10.1097/BOT.0000000000000128

23. Sutin AR, Terracciano A, Milaneschi Y, An Y, Ferrucci L and Zonderman AB. The trajectory of depressive symptoms across

the adult life span. JAMA Psychiatry. 2013;70(8):803-811.

https://doi.org/10.1001/jamapsychiatry.2013.193

24. Bonnet U and Preuss UW. The cannabis withdrawal syndrome: current insights. Subst Abuse Rehabil. 2017;8:9-37.

https://doi.org/10.2147/SAR.S109576

25. Hirvonen J, Goodwin RS, Li CT, Terry GE, Zoghbi SS, Morse C, et al. Reversible and regionally selective down regulation of brain cannabinoid CB1 receptors in chronic daily cannabis smokers. Mol Psychiatry. 2012;17(6):642-649.

https://doi.org/10.1038/mp.2011.82

26. Haynes JC, Farrell M, Singleton N, Meltzer H, Araya R, Lewis G, et al. Alcohol consumption as a risk factor for anxiety and depression: results from the longitudinal follow-up of the national psychiatric morbidity survey. Br J Psychiatry. 2005;187:544-551.

https://doi.org/10.1192/bjp.187.6.544

27. McHugh RK and Weiss RD. Alcohol use disorder and depressive disorders. Alcohol Res. 2019;40(1):1.

https://doi.org/10.35946/arcr.v40.1.01

Orcid ID:
Santosh Kumar- https://orcid.org/0000-0002-9548-8349
Vikas Verma - https://orcid.org/0000-0002-0973-126X
Umesh Kushwaha - https://orcid.org/0000-0002-2735-9721
Amit Arya - https://orcid.org/0000-0002-7496-3462