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CHAPTER

10

An ensemble approach for evaluating the cognitive performance of human population at high altitude

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CHAPTER OUTLINE

1 Introduction

Hypobaric hypoxia at high altitude can cause the loss of memory, recall, and learning resulting in cognitive impairment in addition to the acute mountain sickness (AMS), high-altitude pulmonary edema (HAPE), high-altitude cerebral edema (HACE), and neurophysiological disturbances with insomnia and dizziness (Bahrke and Shukitt-Hale, 1993; Lieberman et al., 1994; Ray et al., 2019) (Fig. 1).

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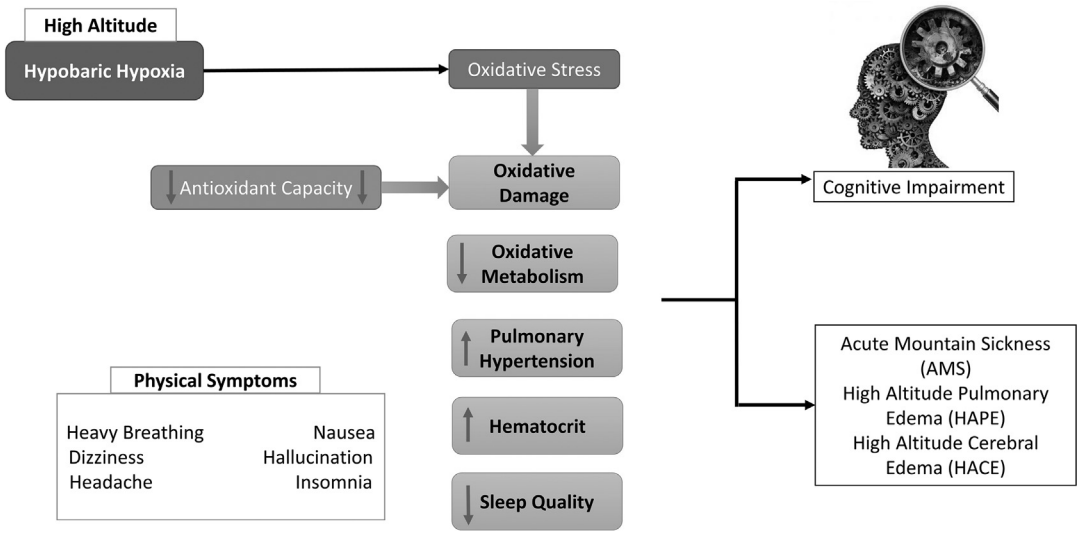

f0010 **FIG. 1**

In hypobaric hypoxia, the body is deprived of sufficient oxygen supply. At high altitude, there is fall in the atmospheric pressure and oxygen, which leads to oxidative stress. This impacts the physiology and metabolism causing oxidative damage, reduction in oxidative metabolism, and sleep quality, along with an increase in pulmonary hypertension and the hematocrit values. An individual may have an early stage cognitive impairment and develop acute mountain sickness, which if not clinically addressed may cause high-altitude pulmonary edema or high-altitude cerebral edema.

The neurological symptoms are due to lack of proper oxygen supply to brain that can alter neurotransmitter synthesis, uptake, and release and free radical generation and related excitotoxic neuronal damage (Askew, 2002; Benveniste et al., 1984; Hota et al., 2010; Rossi et al., 2000). Changes in gene expression and protein functions are also associated with hypoxia and ischemia (Chandel et al., 1998; Gorter et al., 1997; Hartman et al., 2005; Nalivaeva and Rybnikova, 2019; Pellegrini-Giampietro et al., 1992). Ascent to high altitude also increases sensory discrimination, delay in the evaluation process, and impairment of short-term memory (Hayashi et al., 2005; Nation et al., 2017; Singh et al., 2003). Chronic hypoxia exposure of volunteers residing at high altitude also revealed impairment in verbal working memory (Ray et al., 2019; Yan et al., 2011).

p0095 In the trans-Himalayan region, an early stage of cognitive impairment is commonly observed in the population who have been residing at an altitude $\geq$4300 m for a period of at least 12 months. This form is called the mild cognitive impairment (MCI), which is characterized by a decline in cognitive abilities [mental processes regulating perform day-to-day functions] including memory, thinking, and decision-making (Fig. 2).

p0100 Some of the cognitive domain tests commonly used for screening MCI are Multidomain Cognitive Screening Test (MDCST) (Hota et al., 2012; Sharma et al., 2014), Mini Mental State Examination (MMSE) (Folstein et al., 1975; Pan et al., 2020), Montreal cognitive Assessment (MoCA) (Nasreddine et al., 2005; Pan et al., 2020), Mini-Cog (Borson et al., 2000), Computer Administered

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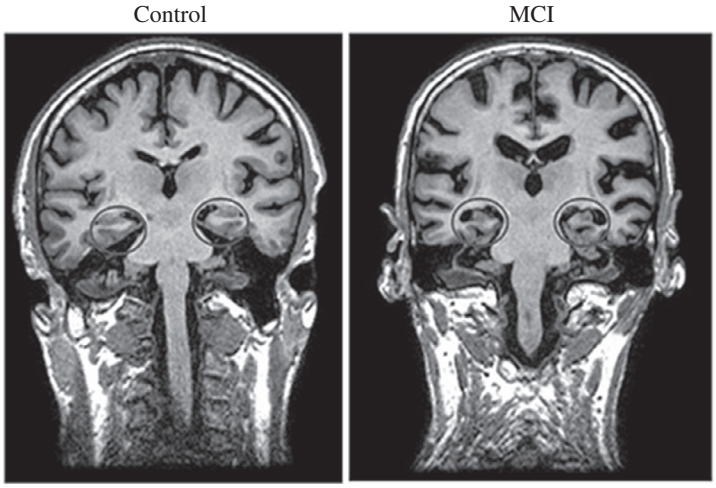

f0015 **FIG. 2**

Brain imaging studies show shrinkage of hippocampus region in MCI, which plays an important role in learning and memory (Aurtenetxe et al., 2016). Existing medical conditions like diabetes, high blood pressure, etc. increases the risk for an individual developing MCI at high altitude.

Neuropsychological Score (CANS-MCI) (Tornatore et al., 2005), and Patient Reported Outcomes in Cognitive Impairment (PROCOG) (Frank et al., 2006). Majority of these tests lack the required screening specificity and sensitivity. A few of them specifically screen for a deficit of domains, while others are bulky and time consuming. In addition, they often have a complex scoring system, which needs the expertise of a trained person. A study by Hota et al. showed MDCST to be the most effective for MCI assessment among the listed cognitive tests (Hota et al., 2012). It is most promising in particular for the demographic studies, as it exhibits excellent psychometric properties in terms of sensitivity and test-retest reliability. Considering the limitations of MMSE and MoCA, MDCST was designed to establish an easy to administer and a more reliable test for detection of MCI at early stages (Hota et al., 2012). Moreover, it is based on findings that suggest involvement of several brain regions in cognitive function. MDCST is comprehensive as it covers nine domain assessments: Orientation, Memory Registration, Visuospatial Executive, Object Recognition, Attention, Recall, Coordination & Learning, Language and Procedural Memory and, in comparison, has a better specificity with sensitivity. Thus, it provides an opportunity to increase the scope of cognitive assessment to domains like procedural memory, mindbody coordination, attention, and learning of complex tasks through improvised and customized psychometric tests. Beck Depression Inventory (BDI) with insomnia may further help in identification of hitherto concealed depression (Beck et al., 1961).

p0105 There are no demographic studies that measure the prevalence of MCI with Beck Depression Inventory (BDI), insomnia, and clinical features collected from routine assessments [like blood glucose level, blood pressure, blood cholesterol, complete blood count, kidney, and liver functionality]. A rule-based study can assist in analyzing and identifying risk factors specific to population cohorts for their cognitive decline at higher altitude ($\geq$4300 m). It has been a common practice in clinical practice to ignore the rigor and sophistication of a data mining, and rather focus on results with an interpretation

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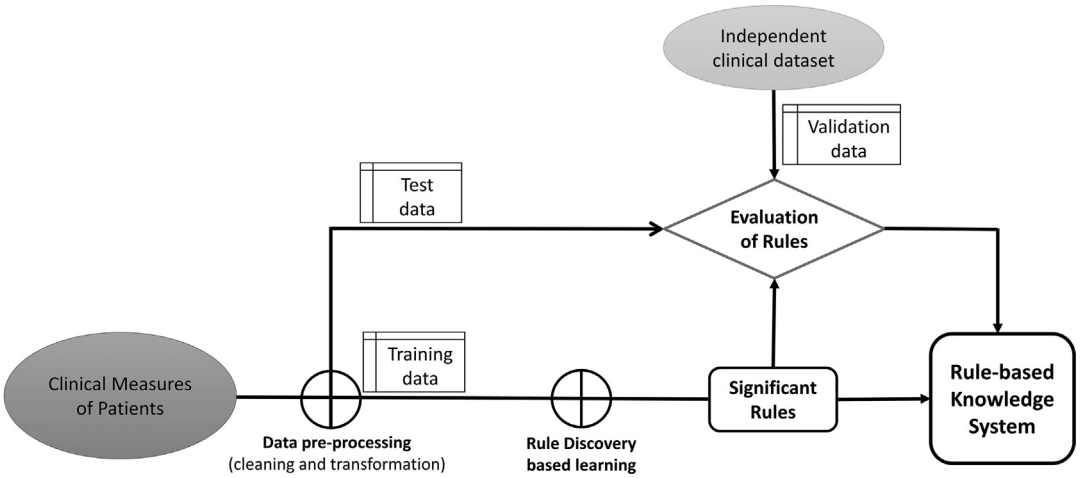

f0020 **FIG. 3**

Schematic representation for development of rule-based knowledge systems for clinical applications.

(Anhøj, 2003; Beckmann and Lew, 2016; Handelman et al., 2018). "Rule-based" analysis has been fairly promising in the domain, being a human-comprehensible knowledge system, and therefore suitable for deciphering new rules for clinical applications (Fig. 3). Association rule mining is a general-purpose rule discovery scheme of finding disease cooccurrences in electronic health record data that has been widely used to find disease-disease, disease-finding, and disease-drug cooccurrences (Agrawal et al., 1993; Brossette et al., 1998; Chen et al., 2008; Hanauer et al., 2009; Said et al., 2018; Sengupta and Naik, 2013).

p0110 In this study, we evaluate the cognitive parameters identified by MDCST along with the clinical features, which can be associated with MCI, BDI and sleep. Based on the native's residence altitude, there are two population cohorts which are been compared in this study: Highlanders (natives of altitude $\geq$1500 m but $<$4300 m) and Lowlanders (natives of altitude $\leq$350 m), who have been residing at an altitude $\geq$4300 m for at least 18 months. We apply an ensemble technique combining differential expression analysis with unsupervised machine learning technique to augur rules for the two cohorts. These rules help in the identification of the cognitive and clinical features which can be used for early identification of mild cognitive impairment and depression among the respective population cohorts.

s0015 2 Methodology

s0020 2.1 Data collection

p0115 Fig. 4 illustrates the overall methodology of this study in a logical flow diagram. Data used in this study was collected as a field research [August 2009–January 2011] of High-Altitude Physiology Division, Defence Institute of High-Altitude Research (DIHAR), DRDO, Leh. Data collection and subsequent studies are based on the ethical approval of the institutional ethics committee DIHAR (Hota et al., 2012).

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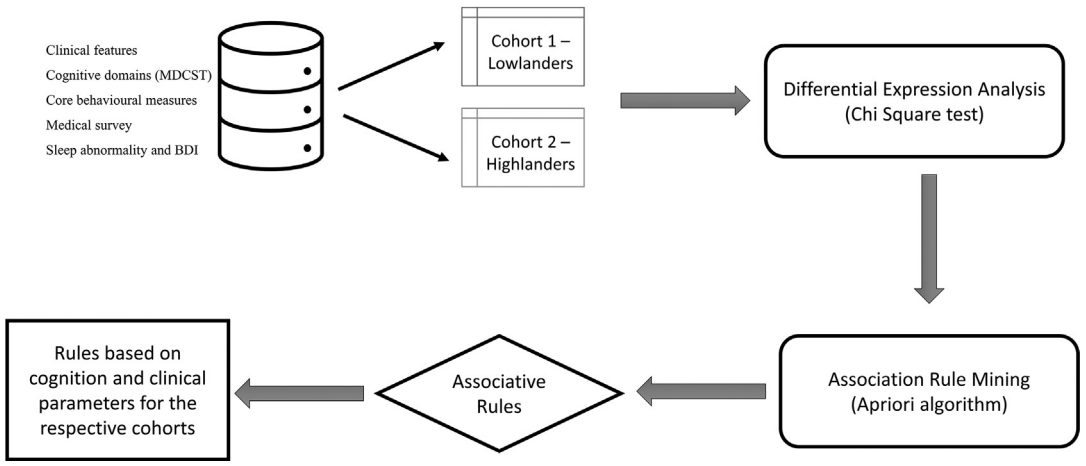

f0025 **FIG. 4**

Schematic representation of knowledge discovery process used for the identification of key cognitive parameters and clinical features for mild cognitive impairment.

p0120 The clinical features along with the parameters from MDCST were obtained from a group of volunteers in the age group of 25–40 comprising of Lowlanders and Highlanders, who have been residing at high altitude ($\geq$4300 m) (Table 1). All the participants were informed about the study purpose, protocol, and expected outcome (Hota et al., 2012). Baseline recordings were collected for both the population categories with the onset of study at an altitude of less than 350 m. Furthermore, there was a longitudinal follow-up of the cohort that ascended to high altitude (>4300 m) and lived there for the duration of 18 months (Hota et al., 2012).

p0125 Clinical features in this study include results from lipid profiling, kidney function test (KFT), liver function test (LFT), sugar level, blood pressure, and pulse rate. MDCST was performed independently on all the volunteers. The scores were compared to establish the subjective dependability in this scoring. Additionally, a medical survey of all the volunteers was performed via a questionnaire related to the occurrence of chronic diseases, physical and physiological ailments, heart problems, stroke, epilepsy, head injury, drug abuse, psychological disorders, and general health status (Hota et al., 2012). Data for core behavioral measures (CBM) such as the alcohol consumption, tobacco use, diet, and physical activity were also collected from all the subjects in accordance with the WHO guidelines (WHO, 2020). All the tests were administered by field investigators under the supervision of a clinical psychiatrist.

t0010 **Table 1 Inclusion criteria of human subjects for this study.**

Parameter	Value
Age (in years) (mean $\pm$ SEM)	36.3 $\pm$ 6.84
Education (in years) (mean $\pm$ SEM)	12 $\pm$ 2
Geographical location	Jammu & Kashmir, India
Ethnic origin of all participants	India

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2.2 Data processing and feature selection

p0130 Respective cohort subjects with underlying heart disease, chest pain, stroke/infarction/cerebral hemorrhage, renal failure, diabetes, viral hepatitis, chronic disease, and gastro-esophageal reflux disease (GERD) were excluded from this study. Also, subjects with previous neurologic/psychiatric symptoms, major surgery, and familial disorders were ruled out. Nevertheless, the respective elimination steps ensured inclusion of only healthy subjects in the study. Data of 200 healthy volunteers, 100 each for Lowlander, and Highlander were randomly sampled for the study.

p0135 Following clinical features were measured under the supervision of registered medical practitioner: blood glucose (BS), systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate (PR), blood urea nitrogen (BUN), serum creatinine, serum glutamic oxaloacetic transaminase (SGOT), serum pyruvic transaminase (SGPT), total cholesterol (TC), triglycerides (TGL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), TC/HDL cholesterol ratio, LDL/HDL ratio, homocysteine, vitamin B-12, and folic acid. The value for each of these parameters was normalized into an ordinal form and scaled as low, normal, and high, respectively, based upon the prescribed range (Marshall et al., 2014).

p0140 MDCST includes screening for nine cognitive domains: Orientation, Memory Registration, Visuospatial Executive, Object Recognition, Attention, Recall, Coordination & Learning, Language, and Procedural Memory (Hota et al., 2012). Each of these parameters are scored in magnitude of five with max MDCST cumulative score of 45. A cumulative MDCST score $\leq$34 indicates onset or presence of MCI. For the subjects who qualified inclusion criterion, Sleep abnormality and Beck Depression Inventory (BDI) (Beck et al., 1961) were applied to assess activities of daily living and to investigate the presence of hitherto undetected depression. Sleep was measured in scale of 0/1, with 1 indicating abnormality, while for BDI, value $\geq$7 indicates abnormality.

2.3 Differential expression analyses

p0145 The statistical significance between the anticipated and observed frequencies was assessed performing a chi-square test comparing the two cohorts. This test enables the comparison of observed and expected frequencies objectively since it is not always possible to judge from the data whether they are different enough to be considered statistically significant (Bailey et al., 1982). Multivariate statistical analysis was performed on the significant factors to identify the independent clinical and cognitive risk factors for the onset of cognitive impairment. The level of statistical significance was defined by the criteria, P-value $<.05$. All the statistical analysis was performed using STATISTICA DATAMINER 9.1 (StatSoft, Inc., 2010).

2.4 Association rule mining

p0150 Association mining, the task of finding associative rules between items in a data set, has received considerable attention, particularly since the publication of the AIS and apriori algorithms (Anand Hareendran and Vinod Chandra, 2017; Sarıyer and Öcal Taşar, 2020; Sengupta and Naik, 2013a). This study uses an apriori algorithm to obtain the information related to clinical and cognitive screening parameters to be associated with onset of cognitive impairment. It is a popular data mining technique that attempts to find interesting patterns in large databases (Agrawal et al., 1993; Borgelt, 2010; Goethals, n.d.).

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p0155 The apriori algorithm exploits the downward closure property, which states that if an item-set is infrequent, all of its supersets must be infrequent (Sengupta and Naik, 2013a). Facilitates filtering item-sets but is limiting while mining infrequent item-sets. Each of the filtered item-set is backed by a statistical measure called support. For an item-set $X \subset I$, support$(X) = s$, if the fraction of transactions in the data set D containing $X = s$ (Agrawal and Srikant, 1994). The classic framework for association rule mining uses support and confidence as thresholds for constraining the search space. The confidence or accuracy of an association rule $X \Rightarrow Y$ in D is the conditional probability of having Y contained in a transaction, given that X is contained in that transaction: confidence $(X \Rightarrow Y) = P(Y \mid X) =$ support(XY)/support(X) (Goethals, n.d.). In general, support represents the ratio of samples among the data set that simultaneously satisfies both, condition X in the antecedent part and condition Y in the consequent part of a rule, while confidence represents the ratio of samples that satisfy both conditions X and Y, but only among those that satisfy condition X in the antecedent part (Jung et al., 2013). A confidence value of 100 for a certain rule means that the possibility of obtaining outcome Y when X in a given condition $(X \rightarrow Y)$ is 100% (i.e., certain rule); if not, the possibility of $A \rightarrow B$ is defined as a value (possible rule) between 0 and 100.

s0040 2.5 Experimental set-up

p0160 All the experiments in this study were implemented via STATISTICA 9.1 (StatSoft, Inc., 2010) software. It is grueling to predispose appropriate criteria for any two parameters in association rule mining, since information is acquired centered on a minimum threshold for support and confidence. Therefore, the minimum confidence level was subjected to at least 30%, with a minimum support of 10%; domain specialists (human cognition and physiology) were consulted for the association rules generated, while the final confidence level was determined considering physician's opinion. Total cognitive score, BDI score, and sleep were declared as the response indicators and the remaining parameters were defined to be as categorical indicators. For maximum components for any deciphered rule, the antecedent and precedent iteration rate was set to 10.

p0165 The described experiment was set up and executed on a Dell precision workstation (M4700), with Intel(R) Core(TM) i7-3820QU CPU @ 2.70 GHz 8M cache, 4 cores and 8 threads, NVIDIA(R) Quadro(R) K1000M with 2 GB GDDR3, 32 GB RAM, and 1 TB hard disk.

s0045 3 Results and discussion

s0050 3.1 Differential analyses—Cognitive and clinical features

p0170 Table 2 represents Visuospatial Executive, Attention, and Coordination & Learning to be statistically significant screening parameters for Lowlanders in reference to the cumulative MDCST score, whereas Object recognition is significantly impaired corresponding to BDI as represented in Table 3. The Orientation parameter is found to be significantly associated with sleep abnormality (Table 4). In contrast, the results observed for Highlander population suggests Procedural Memory, Coordination and Learning, Visuospatial Executive, and Recall are statistically significant parameters against the cumulative MDCST score (Table 2), whereas no parameter is significant corresponding to BDI (Table 3) and sleep abnormality (Table 4).

p0175 Among the clinical features, the chi-square test reveals that although there is not a significant parameter for Lowlanders corresponding to either cumulative MDCST score, BDI, or sleep abnormality.

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Table 2 Cognitive screening parameters against cumulative MDCST score.

	Lowlanders		Highlanders	
	Chi-square	***P*-value**	**Chi-square**	***P*-value**
Visuospatial executive	22.5195	.0002	15.1725	.0044
Attention	15.2778	.0016	2.0888	.5542
Coordination and learning	14.2017	.0067	16.4056	.0058
Language	6.6546	.1553	10.7607	.0563
Recall	5.9658	.3096	12.2461	.0156
Object recognition	3.4211	.3311	3.7738	.1515
Memory registration	3.0049	.2226	0.8685	.6477
Orientation	2.2338	.5253	3.9102	.4183
Procedural memory	2.0308	.1541	20.4540	.0000

t0020

Table 3 Cognitive screening parameters against BDI score.

	Lowlanders		Highlanders	
	Chi-square	***P*-value**	**Chi-square**	***P*-value**
Object recognition	9.5439	.0229	4.7122	.0948
Coordination and learning	6.0168	.1979	6.4409	.2657
Recall	4.7749	.4440	2.2947	.6817
Visuospatial executive	3.9827	.4084	5.1914	.2682
Memory registration	3.1067	.2115	1.0602	.5885
Attention	2.3175	.5092	2.2973	.5130
Orientation	1.9394	.5851	2.6340	.6208
Language	0.7826	.9408	2.9747	.7039
Procedural memory	0.6769	.4106	0.0002	.9880

t0025

Table 4 Cognitive screening parameters against sleep abnormality score.

	Lowlanders		Highlanders	
	Chi-square	***P*-value**	**Chi-square**	***P*-value**
Orientation	9.1667	.0272	6.1027	.1916
Attention	4.0908	.2518	3.0841	.3788
Object recognition	3.0829	.3790	1.9799	.3716
Language	2.4253	.6581	6.4835	.2620
Coordination and learning	1.9974	.7362	1.8216	.8732
Visuospatial executive	1.7417	.7831	1.3404	.8545
Recall	1.6155	.8994	1.2922	.8627
Memory registration	1.5109	.4698	1.3980	.4971
Procedural memory	0.0677	.7947	0.4686	.4937

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However, a significant parameter observed for Highlanders is vitamin B-12 level (P-value = .0099) that corresponded to cumulative MDCST score; total cholesterol level (P-value = .0094) that corresponded to BDI, and folic acid level (P-value = .0023) that corresponded to sleep abnormality.

3.2 Discovered associative rules

p0180 Table 5 enlists the associative rules observed among the Lowlander population within the defined criteria. Item-sets satisfying the support-percentage were subjected for discovery of association rules within the specified criteria. The rules suggest association of high vitamin B-12, HDL, BUN, and folic acid levels for MDCST, BDI, and sleep abnormality. Also, the alcoholic Lowlander population (alcoholic/nonalcoholic == A) tend to have a low cumulative MDCST score, which indicates it may be a key factor to be analyzed in MCI screening.

p0185 While Table 6 enlists the association rules discovered within the defined criteria for the Highlander population. For Highlander population, item sets that satisfied the support-percentage were subjected to discovery of association rules within the specified mining criteria. The discovered rules showcase association of high values of vitamin B-12, HDL, VLDL, BUN, cholesterol, triglycerides, and folic acid for MDCST, BDI, and sleep abnormality. In comparison to Lowlander, the alcoholic Highlander population (alcoholic/nonalcoholic == A) tend to show normal sleeping habit.

3.3 Discussion

p0190 Results from the study emphasizes that varied set of MDCST domains and clinical features should be used for the analyzing MCI and undetected depression (via BDI and sleep abnormality) for the respective population cohorts. MDCST considers nine different domains for analyzing cognitive performance in an individual. However, the statistical significance from our observations suggest that Visuospatial Executive, Attention, Coordination & Learning, Object recognition, and Orientation are the major cognitive screening parameters that need to be regularly monitored for Lowlanders. Whereas Procedural Memory, Coordination and Learning, Visuospatial Executive, and Recall are the key screening

t0030 **Table 5 Associative rules for the Lowlander population.**

Association rule	Support %	Confidence %	Correlation %
Alcoholic/nonalcoholic == NA == > BDI == Normal_BDI	40.91	54.55	68.38
Alcoholic/nonalcoholic == A == > Abnormal_MDCST	31.82	60.87	62.24
BDI == Normal_BDI == > sleep == Normal_Sleep	47.73	87.50	74.62
Normal_MDCST == > BDI == Normal_BDI	36.36	48.48	59.38
Vit-B12 == High_VitB12, HDL == High_HDL == > Abnormal_MDCST	50.00	100	74.16
Blood Urea Nitrogen == High_BUN, Vit-B12 == High_VitB12, Vit-B12 == High_VitB12 == > Abnormal_Sleep	52.27	100	76.79
Folic Acid == High_FA, Blood Urea Nitrogen == High_ BUN == > Abnormal_BDI	61.36	64.28	78.73
VLDL == Normal_VLDL == > Normal_BDI	61.36	64.28	80.17

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t0035 **Table 6 Associative rules for the Highlander population.**

Association rule	Support %	Confidence %	Correlation %
Normal_MDCST == > BDI == Normal_BDI	41.30	76.00	66.15
Alcoholic/Nonalcoholic == A == > sleep == Normal_Sleep	43.48	58.82	67.27
Sleep == Normal_Sleep == > BDI == Normal_BDI	47.83	88.00	75.46
Sleep == Normal_Sleep == > Normal_MDCST	50.00	69.70	68.66
HDL == High_HDL, VLDL == High_VLDL, Blood Urea Nitrogen == High_BUN, Vit-B12 == High_VitB12 == > Abnormal_MDCST	50.00	58.97	72.22
Total_Cholesterol == High_TC == > Abnormal_BDI	52.17	96.00	73.19
Creatinine == High_Creatinine, Triglycerides == High_TGL, HDL == High_HDL, Folic_Acid == High_FA, Vit-B12 == High_VitB12 == > Abnormal_Sleep	50.00	58.97	72.22

parameters for the Highlanders. Furthermore, Lowlanders exhibit a higher rate of cognitive impairment and sleep abnormality compared to Highlanders at an altitude of 4300 m or more. There are no significant clinical features observed from goodness of fit for Lowlanders, whereas vitamin-B12, total cholesterol, and folic acid levels are found to be significantly associated with Highlander's cognitive performance.

p0195 Rules deduced from association mining suggests the alcoholic Lowlander population show low cognitive response with 60.87% of confidence. Also high levels of vitamin B-12 and HDL are associated with cognitive impairment (100% confidence), high vitamin B-12 and BUN are associated with sleep abnormality (100% confidence), and high levels of folic acid is associated with BDI (64.28%). Associative rules observed for Highlander population are significantly different compared to Lowlander population. The alcoholic Highlander population did not represent any significant rule corresponding to MDCST, but an important statistical observation suggests that they had normal sleep with 88% confidence. In Highlander population, high level of HDL, VLDL, BUN, and vitamin B-12 is found to be associated with cognitive impairment (58.97% confidence), while a high level of total cholesterol is associated with BDI (96%) and high level of creatinine, HDL, vitamin B-12, and folic acid to the sleep abnormality (58.97%).

s0065 4 Future opportunities

p0200 Data and research in this study were kindly supported by DIHAR, DRDO, India. The study identifies cognitive analyzers and clinical features for the Low ($\leq$350 m) and Highlander ($\geq$1500 m) population staying at higher altitudes (>4300 m) for a prolonged duration, which can be used for early screening of mild cognitive impairment and depression. Visuospatial Executive, Attention, Coordination & Learning, Object recognition, Procedural Memory, Recall, Language for Lowlander population, while Procedural Memory, Coordination and Learning, Visuospatial Executive, Recall, Language for Highlander population, respectively, are the key MDCST parameters identified for analyzing the

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cognitive performance with observed P-value $\leq .05$. These rules were evaluated by the human cognition and physiology experts from DIHAR, DRDO, India.

p0205 An interesting direction to further work upon would be longitudinal analysis of the identified features at an individual and population (Lowlander and Highlander) level, in association with early detection of mild cognitive impairment, beck depression inventory, and insomnia. Furthermore, a comparative analysis of the Lowlander and Highlander cohorts with the native population living at an altitude $\geq$4300 m [e.g., Hikkim and Karzok in India, Dingboche in Nepal, etc.] can provide insights into the physiological and cognitive differentiation among the population.

p0210 Besides the unsupervised methodology discussed in this chapter, analyzing such biomedical longitudinal data sets using supervised learning approaches, like convolutional neural networks (CNN), random forests, gradient boosting trees (Zhao et al., 2019), regression-based linear mixed-effects model (Bandyopadhyay et al., 2011; Jensen and Ritz, 2018), or the most recent likelihood contrast model (Klén et al., 2020) can help in discovering new insights.

s0070 5 Conclusions

p0215 In this study, we have made first of an attempt to investigate the effects of prolonged stay at high altitudes ($\geq$4300 m) for the respective Lowlander, as well as Highlander populations on their cognitive performance based on clinical features and cognitive screening parameters from MDCST. The parameters from MDCST are coupled with clinical features to analyze high-altitude-induced cognitive impairment and sleep abnormality. Healthy individuals with no clinical antecedents of depression were recruited to negate the influence of these factors on the cognitive performance. The subjects were recruited randomly for both the high-altitude and low-altitude location population.

p0220 Our data and the analyses identify the MDCST domains and clinical features that need to be analyzed for the identification of early onset cognitive impairment at high altitudes ($\geq$4300 m) among Lowlander and Highlander populations. In principle, these parameters need to be further tested and validated clinically to be used for screening human subjects from their native geographical altitudes, planning their relocalization at higher altitudes.

ac0010 Acknowledgment

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Non-Print Items

Abstract

Hypoxic stress at high altitude can lead to cognitive disorders. One of the key tests developed in recent years for analyzing the onset of such cognitive impairment is the Multidomain Cognitive Screening Test (MDCST). In this study, we identify the key MDCST and clinical features among the Lowlander ($\leq$350 m) and Highlander ($\geq$1500 but $<$4300 m) populations, staying at an altitude $\geq$4300 m for a prolonged duration. Analyzing these measures ensembled with the Beck Depression Inventory (BDI) and sleep factors gives an opportunity to analyze cognitive performance, which can be associated with the early discovery of undetected depression.

A goodness-of-fit test was applied to the two population cohorts for identifying independent significant measures. This was followed by rule-based mining to discover associative rules between the clinical, behavioral, and cognitive screening parameters. The most significant MDCST parameters identified (P-value $\leq$.05) for analyzing the cognitive performance among the Lowlander population are Visuospatial Executive, Attention, Coordination & Learning, Object recognition, and Orientation, while for the Highlander population, Procedural Memory and Recall are identified in addition to Visuospatial Executive, Coordination, and Learning. Conclusively, a unique set of association rules have been identified with at least 30% support and more than 60% confidence in behavioral and clinical features associated with the cognitive parameters.

Keywords: Beck Depression Inventory (BDI), Cholesterol, Folic acid, Ensemble learning, Mild cognitive impairment (MCI), Multidomain Cognitive Screening Test (MDCST), Rule-based mining, Vitamin B-12