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Original Article

People with dyssomnia showed increased vulnerability to CoVID-19 pandemic: a questionnaire-based study exploring the patterns and predictors of sleep quality using the latent class analysis technique in Indian population



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ABSTRACT

Introduction: CoVID-19 pandemic and the subsequent lockdown have impacted the sleep quality and the overall wellbeing of mankind. The present epidemiological study measured various aspects of sleep disturbance such as sleep quality, daytime impairments, negative emotionality, sleep hygiene, and wellbeing associated with CoVID-19 pandemic among the Indian population.

Methods: This cross-sectional voluntary online survey (using Google form) was communicated across the country from 4th June to 3rd July 2020 through mail and social media applications. The responses received (N = 450) were categorized and validated using the latent class analysis and logistic regression tests respectively, and the classes and subclasses derived were profiled. These techniques are used for the first time in a CoVID-19 sleep study.

Results: Out of the three classes derived from the LCA, people with severe dyssomnia belonging to class 1 (33.3%) showed high daytime impairments, negative emotionality and high vulnerability towards CoVID-19 pandemic measures. In addition, the two subclasses derived from the severe dyssomnia group; one with negative emotionality predominance and the other with excessive daytime sleepiness, were similarly affected by CoVID-19 measures. People with moderate dyssomnia (class 2, 28.5%) showed frequent arousals with daytime impairments and the majority (38.2%) which fell in to class 3, the 'no dyssomnia' category, were not impacted by CoVID-19 pandemic.

Conclusion: People with existing sleep problems or those who were vulnerable to the same were the ones affected by CoVID-19 pandemic. Those with inadequate emotional coping styles have showed heightened vulnerability. Proper medical and cognitive interventions are highly recommended for this population. No or moderate dyssomnia categories (class 3 and 2 respectively) were less impacted by CoVID-19.

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1. Introduction

The 2019–20 coronavirus (CoVID-19) outbreak caused by the SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2) has created one of the biggest unprecedented global crises in the

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21st century. The outbreak which was first reported at Wuhan, Hubei, China on December 1st 2019 is still continuing as a major public health issue globally. The disease *per se* as well as the subsequent lockdown and quarantine measures have contributed to an overwhelming physical and mental health burden among the public [1,2].

Sleep related issues have always been a major casualty at times of any stressful life event, whether its personal or social, especially in those who are highly vulnerable [3,4]. Sleep related disturbances observed during this pandemic have adversely affected the general wellbeing and the life quality of the public [5] which



Abbreviations: Latent class analysis (LCA), Excessive daytime sleepiness (EDS). * Corresponding author. National Institute of Mental Health and Neuro Sciences (NIMHANS), Hosur Road, Bengaluru, 560029, Karnataka, India.

includes the frontline task force [6-8] and those in the guarantine [9,10]. These sleep problems were also reported in several infectious epidemics in the past like severe acute respiratory syndrome (SARS) [11], swine flu (H1N1 influenza virus) [12] and Ebola viral disease [13]. In addition, during the COVID-19 pandemic, the prevalence of clinical insomnia has been reported to reach the upper limit of the worldwide prevalence [5.6.14–17]. A recent meta-analysis covering data from 13 countries showed a high global prevalence rate of sleep problems (35.7%); with CoVID-19 patients being the most affected group [18]. In a survey conducted on 18,147 individuals in Italy, 1301 (7.3%) were reportedly having insomnia within three to four weeks into the CoVID-19 lockdown measures [16]. The sleep disturbances, they reported, were associated with a number of CoVID-19-related risk factors. There are many studies on Chinese population reporting the association of CoVID-19 with poor sleep guality and short sleep duration [15,19]. Negative attitude towards CoVID-19 control measures, anxiety and depression are major risk factors as per their reports [15,19].

In India, the first case of CoVID-19 was reported on 30th January 2020 and as on 7th September 2020, India has the largest number of confirmed cases in Asia and second highest number of confirmed cases in the world [20]. However, the case fatality rate stands at 1.45% which is far lower than the world average. The lockdown period started-off on 24th March 2020 and extended till 31st May 2020. CoVID-19 and the control measures associated with it has heavily impacted the mental health of the general population including the frontline task force [21-27]. Sleep disturbance, as reported by Kochhar et al. was observed in 55.3% of the survey respondents in New Delhi during the lockdown period [28]. A shift in the bedtime to the later duration, delayed sleep onset, reduction in the night-time sleep duration and increased daytime napping were reported in an online survey (N = 1024) conducted on the general population [25]. They reported an association between sleeplessness and depressive symptoms. In a cross-sectional survey study using PSQI, the quality of sleep was found to be relatively decreased in the people (N = 50) suffering from chronic clinical problems like hypertension, diabetes and musculoskeletal conditions during the pandemic [29]. Furthermore, an ISI-based online survey on general population (N = 1015) reported moderate to severe insomnia in 21% (N = 213) of the respondents, with people residing in metros, people belonging to lower caste and women being more vulnerable [30]. Besides these, there are also studies reporting the prevalence of excessive sleepiness and increased nap duration in corporate sector professionals (N = 203) and university students (N = 325) during the CoVID-19 lockdown phase [9].

Most of the studies mentioned above have used various standardized and validated questionnaires such as ISI, PSQI that provides information on sleep quality and the severity of sleep problems but do not measure other aspects such as daytime impairments, negative emotionality, sleep habits and sleep hygiene. In the current study, the survey questionnaire was designed to collectively assess the sleep quality, daytime impairments, negative emotionality, sleep habits and hygiene of the general population. In addition, this study used the latent class analysis (LCA) technique to derive homogenous groups from a heterogenous population, as the latter is heavily influenced by sampling bias associated with any online survey study. Furthermore, the LCA technique also facilitate validating of a newly designed questionnaire for building a new global scale [31]. The current study attempts to identify the impact of CoVID-19 on sleep and other sleep disturbance-related consequences and risk factors. Importantly, the LCA technique was used to derive homogenous groups from the heterogenous survey response, followed by profiling the groups based on their characteristic features.

2. Methods

2.1. Participants

This was a cross-sectional online survey study presented in the google form in English language and communicated across the country from 4th June to 3rd July 2020. The present study is undertaken as a part of the ongoing sleep and cognition study on insomnia [Institutional Ethics approval No. NIMHANS/20th IEC (BS & NS DIV.)2019 dated 16-09-2019].

Snowball non-probability/convenient sampling was used in the study which relies on the referrals from the initial respondents to generate additional respondents. Non-probability sampling technique was used since the probability of every unit or respondent included in the sample cannot be determined and it is left to the respondents to choose whether to participate in the online survey or not [32]. The google form with the survey questions were sent to the participants *via* either mail or social media platforms. The form was sent along with the basic description and the purpose of conducting the survey. The response of the participants was automatically saved in an MS excel sheet. Inclusion and exclusion criteria of the study are presented in Table 1.

The survey was initially sent to people who were known to the authors. In the course of one month, a total of 450 responses were received from various parts of the country. Participation in the survey was voluntary and it was ensured that no personal identifiers or sensitive questions related to social taboos, cultural, political or religious elements were asked in the survey. Confidentiality of the responses was maintained.

Out of the 450 responses, 391 respondents disclosed their place of residence. Among them, 85.7% (N = 335) was obtained from the Southern states (majorly from Karnataka and Kerala), 6.1% (N = 24) from the Northern states, 3.3% (N = 13) from the Union Territories, 2.6% (N = 10) from the Western states, 1.5% (N = 6) from the Eastern states and 0.8% (N = 3) from the Central states. Response from the participants of the age less than 18 years were excluded from the analysis. Average and the median age of the respondents were 32.0 \pm 9.9 and 31 (24, 38) years respectively. 49.6% of the respondents were graduates or above and 68% were doing day shift jobs. No participants in this survey reported getting infected by CoVID-19.

Table	1
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Inclusion and exclusion criteria of the study.

	Inclusion criteria	Exclusion criteria
Gender	Males and females	Others
Age	Age \geq 18 years	Age <18 years
Nationality and place of residence	Indians staying within India	Non-Indians and Indians staying outside India
Survey response from the participants	Complete responses	Incomplete, repetitive, spurious and ambiguous
	(for 12 predictor variables)	responses (for 12 predictor variables)

2.2. Measures

Survey questionnaire was designed based on the theory of sleep problems. Few questions were adapted from the AIIMS insomnia evaluation questionnaire which the authors shared with us [33] and few others were pertaining to sleep problems and the general well-being during the current CoVID-19 situation. AIIMS insomnia evaluation questionnaire which is currently used at the comprehensive sleep disorder clinic, AIIMS, New Delhi, classifies insomnia patients based on their aetiology [33]. Questions were picked from the sections, insomnia diagnosis, 3 Ps and insomnia type [33]. We do not have permission from the authors to disclose further details on the psychometrics, specificity and the sensitivity of AIIMS insomnia evaluation questionnaire.

In the current survey, the participants were asked to respond to a total of 31 questions (variables) coming under 8 domains. Table 2 describes the domains and the variables with levels of response, assessed from the survey questionnaire. Questionnaire responses were screened based on the inclusion and exclusion criteria described in Table 1. Age of the respondents, their gender, nationality and place of residence were taken in to consideration while screening the responses. The dataset was further cleaned by removing the duplicate, incomplete and spurious responses and 412 responses were finally taken for the analysis. The responses for most of the variables had 3 levels (yes, sometimes, no). However, some variables which include dyssomnia features, reasons for davtime impairment, reasons for rumination, reasons for arousals and sleep hygiene issues were kept as checklists with multiple options. Supplementary Table S1 describes the options of checklists used in the survey questionnaire. Checklist response for daytime impairment and arousals were converted in to dichotomous levels (with and without) for the LCA.

The effect of CoVID-19 on life and sleep was also recorded from the participants in 3 levels (yes, maybe, no). Whereas, the life and the job satisfaction of the respondents coming under the life quality domain were measured on a Likert scale (1 is least satisfied and 10 is highly satisfied). This variable was converted in to dichotomous levels (those who rated ≤ 6 and > 6) for the analysis later on.

2.3. Procedure

The dataset was subjected to LCA using twelve variables which includes daytime sleepiness, daytime fatigue, worry about sleep, negative thoughts before sleep onset, sleep initiation problem, sleep maintenance problem, early morning awakening, feeling of worthlessness, sleep time variability, association of bed with purposes other than sleep/sex, arousals during sleep (dichotomous levels) and daytime impairments (dichotomous levels). Latent class analysis has been widely used in many sleep-related studies to subgroup the population based on their sleep quality, sleep duration, sleep difficulty and insomnia symptoms [34–37].

After prediction, the model goodness of fit was validated using logistic regression test [38]. The classes deduced from the latent class analysis were then profiled and compared.

2.4. Analysis

Latent class analysis was done in R (3.6.1) and the logistic regression and comparative statistics were done in SPSS for Windows, version 22 (SPSS Inc., Chicago, IL, USA).

LCA [39] is an exploratory process which identifies the confounding source between the observed variables, identify and characterize clusters of similar cases and approximate the distribution of observations across the many variables of interest [40,41]. There are no *a priori* assumptions regarding the number of classes derived from the LCA [38]. This technique estimates the posterior probabilities of class membership (probability of a respondent falling in to one of the classes) based on the class probability/prevalence (percentage of the respondents representing a particular class) and the item response probability (probability of each class member endorsing each item/variable) [38,42].

In the study, the LCA was primarily done to identify homogeneous groups within the heterogenous distribution based on twelve categorical variables pertaining to sleep-related problems. Multicollinearity among the variables was checked by creating a correlation matrix and all coefficients were ≤0.5. Correlation matrix is given in Supplementary Fig. S1. The LCA was done using the poLCA package in R [41]. poLCA is a software package implemented in R statistical computing environment for the estimation of latent classes and latent class regression models for multivariate categorical data (Fig. S2). poLCA uses expectation-maximization and Newton-Raphson algorithms to find maximum likelihood estimates of the model parameters [41]. The optimal class solution was selected based on three rules. First rule is based on the statistical fit index, Bayesian Information Criterion (BIC; [43]). Lower value of BIC indicates better fitting models [44]. Second, the classes should be distinct, meaningful and theory-based [38,44]. And, third is the parsimony rule wherein simple models are considered more preferable than the complex ones. All variables taken for the LCA were categorical and the maximum number of iterations (maxiter) through which the estimation algorithm cycled was 10,000. To automate the search for the global-rather than the local-maximum of the log-likelihood function, number of repetitions (nrep) was set to 100.

To validate the model and the classes derived from the LCA, logistic regression test was done. The significant predictor variables which can differentiate each class from the other was deduced and

Table 2

Domains and the variables (levels of response) assessed from the survey questionnaire.

Domains	Variables (levels of response)
Socio-demographic	Age, gender (male/female/others), education (undergraduate, graduate, postgraduate, above postgraduation)
Habits	Under regular medication (yes/no), morning/evening person (early/late)
Sleep quality	Perception about sleep problems (yes/maybe/no), sleep initiation problem (yes/sometimes/no), sleep maintenance problem (yes/ sometimes/no), early morning awakening (yes/sometimes/no), dyssomnia features (checklist), arousals (checklist), opportunity to sleep (yes/sometimes/no), daytime nap (yes/sometimes/no), sleep duration
Daytime impairment	Daytime sleepiness (yes/sometimes/no), daytime fatigue (yes/sometimes/no), reasons for daytime impairment (checklist)
Negative emotionality	Worry about sleep (yes/sometimes/no), negative thoughts before sleep onset (yes/sometimes/no), feeling of worthlessness (yes/no), reasons for rumination (checklist)
Sleep hygiene	Association of bed with purposes other than sleep/sex (yes/sometimes/no), sleep time variability (yes/sometimes/no), sleep hygiene issues (checklist)
Effect of CoVID-19	On life (yes/maybe/no) and sleep (yes/maybe/no)
Quality of life	Life satisfaction (1–10 scale), job satisfaction (1–10 scale)

the association was estimated using odds ratio and 95% confidence intervals (CIs; [38]).

Additionally, the LCA was performed for the second time on the three classes derived from the data obtained following the LCA conducted initially on the entire dataset. This was done to identify whether the same set of predictor variables can identify any latent subclasses within the classes derived. The procedure followed was the same with the optimal class solution selected based on the three rules explained before, followed by validation using logistic regression.

Internal consistency between the variables used for the LCA were assessed using the reliability test index Cronbach's (coefficient) alpha. Pearson's χ^2 goodness of fit test was done to analyse differences between the classes and the subclasses for various categorical variables including those not used for the LCA (external validators). For the variables having 3 levels of response, 2 levels (no and sometimes/maybe) were combined and then statistically compared with the third level of response (yes). This was done to make the chi square comparison more stringent. Difference in sleep duration and age (continuous variable) among the classes and subclasses were

Table 3

Profile of the total sample and the individual	l classes derived from the LCA.
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estimated using one-way ANOVA with Tukey's post-hoc test. A p-value \leq 0.05 was considered statistically significant.

3. Results

Characteristic features of the entire sample (N = 412) are given in Table 3. An equal representation of both the genders was obtained in the survey (approximately 50%). 74% of the respondents were active during the early phase and may be categorized as morning people. 57% of the respondents perceived sleep problems in them, 22.1% reported sleep initiation problems and 20.6% reported sleep maintenance problems. 59% had arousals in the night and 54.1% noticed some type of daytime impairments in them. Negative emotionality in the form of worries and negative thoughts were observed in 22–26% of the respondents.

26.5% felt that their life was affected by CoVID-19 pandemic and 15.1% attributed it to their sleep problems (Table 3). 26% of the people felt that the quality of their life is low and 15% responded that they are not satisfied with their job (Table 3).

Gender N Education U C F Morning/evenin; E	years) (Q3; in years) in hours) within each class in counts (in percentage) Male remale JIndergraduate Graduate Postgraduate Nove postgraduation	100 32.0 ± 10.0 $31 (24, 38)$ 6.9 ± 1.2 $204 (49.5)$ $207 (50.5)$ $36 (9.0)$ $169 (41.0)$ $149 (36.0)$ $55 (14.0)$	$\begin{array}{c} 33.3\\ 30.0 \pm 9.1\\ 29 \left(22, 35\right)\\ 6.6 \pm 1.4\\ \end{array}$ 61 (45.0) 75 (55.0) 11 (8.0) 65 (47.0) 48 (35.0) 13 (10.0)	28.5 32.2 ± 10.2 $31 (24, 38)$ 6.8 ± 1.1 $56 (48.0)$ $61 (52.0)$ $13 (11.0)$ $42 (36.0)$ $41 (36.0)$	$\begin{array}{c} 38.2\\ 33.7 \pm 10.2\\ 33 \ (27, \ 40)\\ 7.1 \pm 1.0^{**}\\ 45.0 \ (86)\\ 55.0 \ (71)\\ 8.0 \ (12)\\ 39.0 \ (62) \end{array}$
Average age (in Median age (Q1, Sleep duration (i Representation Gender M Education C G Morning/evenin, E L L	years) (Q3; in years) in hours) within each class in counts (in percentage) Male female Undergraduate Graduate Postgraduate Valove postgraduation g person Early	$31 (24, 38) 6.9 \pm 1.2 204 (49.5) 207 (50.5) 36 (9.0) 169 (41.0) 149 (36.0) 55 (14.0) \\ \\ $	$29 (22, 35) 6.6 \pm 1.4 61 (45.0) 75 (55.0) 11 (8.0) 65 (47.0) 48 (35.0) $	31 (24, 38) 6.8 ± 1.1 56 (48.0) 61 (52.0) 13 (11.0) 42 (36.0)	$\begin{array}{c} 33 \ (27, \ 40) \\ 7.1 \pm 1.0^{**} \\ 45.0 \ (86) \\ 55.0 \ (71) \\ 8.0 \ (12) \\ 39.0 \ (62) \end{array}$
Sleep duration (i Representation Gender Education C G Morning/evening L L	in hours) within each class in counts (in percentage) Male eemale Judergraduate Graduate Postgraduate Nove postgraduation g person Early	6.9 ± 1.2 204 (49.5) 207 (50.5) 36 (9.0) 169 (41.0) 149 (36.0) 55 (14.0)	6.6 ± 1.4 $61 (45.0)$ $75 (55.0)$ $11 (8.0)$ $65 (47.0)$ $48 (35.0)$	6.8 ± 1.1 56 (48.0) 61 (52.0) 13 (11.0) 42 (36.0)	7.1 ± 1.0** 45.0 (86) 55.0 (71) 8.0 (12) 39.0 (62)
Representation Gender Education C F Morning/evenin, L	within each class in counts (in percentage) Male remale Undergraduate Graduate Yostgraduate Vostgraduate Nove postgraduation g person Early	204 (49.5) 207 (50.5) 36 (9.0) 169 (41.0) 149 (36.0) 55 (14.0)	61 (45.0) 75 (55.0) 11 (8.0) 65 (47.0) 48 (35.0)	56 (48.0) 61 (52.0) 13 (11.0) 42 (36.0)	45.0 (86) 55.0 (71) 8.0 (12) 39.0 (62)
Gender N Education U C Morning/evenin, L	Male remale Jndergraduate Graduate Yostgraduate Yostgraduate Yostgraduate Yostgraduation g person Early	207 (50.5) 36 (9.0) 169 (41.0) 149 (36.0) 55 (14.0)	75 (55.0) 11 (8.0) 65 (47.0) 48 (35.0)	61 (52.0) 13 (11.0) 42 (36.0)	55.0 (71) 8.0 (12) 39.0 (62)
M F Education U C G A Morning/evenin, E L	remale Jndergraduate Graduate Postgraduate Nbove postgraduation g person Early	207 (50.5) 36 (9.0) 169 (41.0) 149 (36.0) 55 (14.0)	75 (55.0) 11 (8.0) 65 (47.0) 48 (35.0)	61 (52.0) 13 (11.0) 42 (36.0)	55.0 (71) 8.0 (12) 39.0 (62)
F Education C G Morning/evenin, E L	remale Jndergraduate Graduate Postgraduate Nbove postgraduation g person Early	207 (50.5) 36 (9.0) 169 (41.0) 149 (36.0) 55 (14.0)	75 (55.0) 11 (8.0) 65 (47.0) 48 (35.0)	61 (52.0) 13 (11.0) 42 (36.0)	55.0 (71) 8.0 (12) 39.0 (62)
Education C F A Morning/evenin, E L	Jndergraduate Graduate Postgraduate Nove postgraduation g person Early	36 (9.0) 169 (41.0) 149 (36.0) 55 (14.0)	11 (8.0) 65 (47.0) 48 (35.0)	13 (11.0) 42 (36.0)	8.0 (12) 39.0 (62)
L C F Morning/evening E L	Graduate Postgraduate Above postgraduation g person Early	169 (41.0) 149 (36.0) 55 (14.0)	65 (47.0) 48 (35.0)	42 (36.0)	39.0 (62)
C F Morning/evening E L	Graduate Postgraduate Above postgraduation g person Early	169 (41.0) 149 (36.0) 55 (14.0)	65 (47.0) 48 (35.0)	42 (36.0)	39.0 (62)
F A Morning/evening E L	Postgraduate Above postgraduation g person Early	149 (36.0) 55 (14.0)	48 (35.0)	. ,	
A Morning/evening E L	Above postgraduation g person Early	55 (14.0)		41 (36.0)	
Morning/evening E L	g person Carly		13 (10.0)		38.0 (60)
Morning/evening E L	g person Carly			19 (17.0)	15.0 (23)
E	Carly				
L	5	304 (74.0)	79 (58.0)	90 (76.0)	85.0 (117)*
		108 (26.0) \$\$\$	58 (42.0)	28 (24.0)*** ^{\$\$\$}	15.0 (2)*** ^{\$\$\$}
		85 (20.7)	31 (22.6)	28 (23.9)	26 (16.6)
Perception of po		118 (57.0)	89 (65.0)	22 (19.0)***	7 (5.0)***###
Adequate oppor		331 (80.3)	98 (71.5)	91 (77.1)	142 (90.3)**#
Daytime nap	jp	82 (19.9)	37 (27.0)	21 (17.8)	24 (15.3)
ncluded in the L	CA			()	_ ()
Sleep quality					
	leep initiation problem	91 (22.1)	71 (51.8)	14 (11.8)***	6 (3.8)***
	Sleep maintenance problem	85 (20.6)	68 (49.6)	15 (12.7)***	2 (1.3)***##
	Early morning awakenings	43 (10.4)	37 (27.0)	1 (0.8)***	5 (3.2)***
	Arousals	243 (59.0)	113 (82.5)	78 (66.1)**	52 (33.1)*** [#]
Daytime impairr		210 (0010)	110 (0210)	, e (een)	02 (0011)
	Daytime sleepiness	83 (20.2)	53 (38.7)	15 (12.7)***	15 (9.5)***
	Daytime fatigue	120 (29.1)	99 (72.3)	9 (7.6)***	12 (7.6)***
	Daytime impairments	223 (54.1)	128 (93.4)	73 (61.9)***	22 (14.0)*** ^{##}
Negative emotio		223 (31.1)	120 (33.1)	/3 (01.5)	22 (11.0)
	Norry about sleep	91 (22.1)	75 (54.7)	15 (12.7)***	1 (0.6)***###
	Vegative thoughts before sleep onset	105 (25.5)	81 (59.1)	19 (16.1)***	5 (3.2)***###
	Seeling of worthlessness	119 (28.9)	83 (60.6)	14 (11.9)***	22 (14.0)***
Sleep hygiene	centry of worthicsbicsb	113 (20.3)	05 (00.0)	14(11.5)	22 (14.0)
	sleep time variability	130 (31.5)	86 (62.8)	25 (21.2)***	19 (12.1)***
	Association of bed with other purposes	96 (23.3)	45 (32.8)	11 (9.3)***	40 (25.5) ^{###}
	ng assessment during CoVID-19 pandemic	50 (25.5)	-3 (32.0)	11 (3.3)	40 (23.3)
Quality of life	is assessment during covid-15 pundellite				
	ife satisfaction (rated \leq 6)	107 (26.0)	65 (47.4)	24 (20.5)***	18 (11.5)***
	ob satisfaction (rated ≤ 6)	135 (33.6)	74 (55.6)	33 (28.7)***	28 (18.2)***
J' CoVID-19		100 (0.00)	74 (33.0)	33 (20.7)	20 (10.2)
	CoVID-19 affected life quality	109 (26.5)	55 (40.1)	26 (22.0)**	28 (17.8)**
	CoVID-19 affected sleep quality	62 (15.1)	52 (37.9)	6 (5.1)***	4 (2.5)***

Average age and sleep duration are represented as mean \pm SD. Q1 indicates 25th percentile and Q3 indicates 75th percentile. * indicates the comparison of classes 2 and 3 with class 1, * indicates the comparison of classes 3 with class 2, ^S indicates the comparison between early and late phase (morning/evening person). Level of significance *[#]p \leq 0.05, **^{##}p \leq 0.01, ***^{###SSS} p \leq 0.001 (Pearson's χ^2 goodness of fit test for categorical variables and one-way ANOVA with Tukey's post-hoc test for sleep duration and average age).

Table 4	
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Model #	Maximum Log-likelihood	AIC	BIC
M1 (2 latent classes)	-4025.382	8148.765	8345.795
M2 (3 latent classes)	-3937.625	8023.250	8320.806
M3 (4 latent classes)	-3893.364	7984.727	8382.808
M4 (5 latent classes)	-3855.324	7958.647	8457.254
M5 (6 latent classes)	-3825.618	7949.237	8548.369

AIC is Akaike information criterion; BIC, Bayesian information criterion.

3.1. Latent class profiling

A 3-class model was found to satisfy all the rules for a best fit model (Table 4). The profile of the three classes derived from the LCA is shown in Fig. 1. When checked for the prevalence of each classes, 33.3% (N = 137) fell in to class 1, 28.5% (N = 118) of the respondents fell in to class 2 and 38.2% (N = 157) fell in to class 3.

First class comprised of the respondents showing highest probability of reporting sleep-related problems which includes sleep initiation problems, sleep maintenance problems, high arousals, high negative emotionality (worries and negative thoughts), daytime impairments, daytime fatigue and daytime sleepiness. They showed highest probability of reporting sleep hygiene issues which includes variability in sleep timing on different days (Fig. 1). Given the characteristics of this class, it was termed "the class with severe dyssomnia".

Second class comprised of respondents who had higher probability of reporting daytime impairments and arousals in the night (Fig. 1). This class was termed "the class with moderate dyssomnia".

Third class comprised of the respondents who reported negligible sleep-related problems (Fig. 1) and hence was termed "the class with no dyssomnia".

3.2. Latent class validation

Multinomial logistic regression was used to validate the latent classes derived from the LCA. Class 3 (no sleep-related problem group) was taken as the reference category and the odds ratios of the other two classes were compared with it. The contribution of each of the predictor variables/covariates used for the LCA was evaluated.

Deviance chi-square test ($\chi^2 = 173.8$, no significance) validated the model's goodness of fit. In the likelihood ratio test, except for daytime sleepiness, all the other predictor variables were found to contribute significantly ($\chi^2 = 725.9$, p < 0.001) in predicting the classes. Table 5 shows the comparison of three classes based on the odds ratio and the confidence interval (Cl). The percentage correct prediction (classification accuracy) of classes 1, 2 and 3 was 93.4, 85.6 and 96.2% respectively. For the set of variables used in the LCA, Cronbach's alpha (coefficient alpha) was found to be 0.81.

Based on the odds ratio, having sleep initiation and maintenance problems, arousals, higher daytime impairments, fatigue and high negative emotionality (worries and negative thoughts) increases the individual's likelihood of being grouped in to classes 1 and 2 in comparison to class 3 (Table 5). Also, having early morning awakening increases the likelihood of being grouped in to class 1 (Table 5).

3.3. Characterization of the classes

Three classes were profiled based on the predictor variables and the external validators (Table 3). Classes were not different from each other with respect to socio-demographic variables measured. Class 1 (the group with severe dyssomnia) comprised of more respondents who were active in the late phase in comparison to classes 2 ($\chi^2 = 10.5$, p = 0.001) and 3 ($\chi^2 = 16.2$, p < 0.001). However, no significant difference was observed between the early and the late phase respondents within class 1. Sleep duration was marginally higher for class 3 [F (2,407) = 6.336, p = 0.002] in comparison to class 1 (Table 3).

All classes reported that they had adequate opportunity to sleep with higher representation in class 3 (90.3%). However, people who perceived their sleep problems, were predominantly represented in class 1 (65%). Respondents who reported lower sleep quality with higher daytime impairments and negative emotionality were represented significantly in class 1 (Table 3). Sleep time variability was also reported predominantly by class 1 (class 1 > class 2, $\chi^2 = 33.5$, p < 0.001; class 1 > class 3, $\chi^2 = 42.8$, p < 0.001).



Fig. 1. Three classes derived from the LCA. The chart is plotted based on the item response probability values obtained in the LCA. Class 1 is represented in blue colour, class 2 in orange and class 3 is represented in grey. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 5

Validation of	Latent	classes.
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Predictor variables	Odds ratio (95% CI; lower bound-upper bound) Class 3 is the reference category		
	Class 1	Class 2	
Daytime sleepiness	2.6 (0.9-8.0)	1.4 (0.5–3.5)	
Daytime fatigue	112.9 (25.3-503.5)***	6.8 (2.3-20.3)***	
Daytime impairments	14.4 (4.9-42.4)***	5.9 (2.5-13.8)***	
Sleep initiation problems	26.1 (5.7-119.2)***	7.3 (1.9-27.6)**	
Sleep maintenance problem	229.7 (30.7–1716.8)***	154.9 (23.5–1021.1)***	
Early morning awakening	6.7 (1.9-23.5)**	1.9 (0.7-5.3)	
Arousals	7.1 (2.4-21.0)***	5.0 (2.0-12.1)***	
Worries about sleep	39.1 (8.1-189.3)***	14.6 (3.5-61.2)***	
Negative thoughts during sleep onset	30.7 (7.1–132.8)***	13.3 (3.4–51.9)***	
Feeling of worthlessness	2.0 (0.7-6.2)	0.3 (0.1-0.7)	
Sleep time variability	20.2 (5.5-73.7)***	11.6 (3.8-35.4)***	
Association of bed for other purposes	0.7 (0.2–1.8)	0.3 (0.1–0.8)	

Comparison of three classes based on odds ratio and confidence interval (CI): Level of significance **p $\leq 0.01,$ ***p $\leq 0.001.$

3.4. General well-being of different classes during CoVID-19 pandemic

40.1% (N = 55) of the class 1 respondents significantly reported that their life was affected by CoVID-19 pandemic (class 1 > class 2, $\chi^2 = 10.4$, p = 0.001; class 1 > class 3, $\chi^2 = 8.8$, p = 0.003) (Table 3). In addition, 37.9% of the respondents from class 1 also reported that their sleep was affected by CoVID-19 pandemic (class 1 > class 2, $\chi^2 = 36.5$, p < 0.001; class 1 > class 3, $\chi^2 = 41.1$, p < 0.001). However, only 36 respondents of the class 1 felt that CoVID-19 had affected both their life and sleep respectively.

In terms of life quality, respondents who rated ≤ 6 for life (47.4%; class 1 > class 2, $\chi^2 = 23.8$, p < 0.001; class 1 > class 3, $\chi^2 = 26.6$, p < 0.001) and job (55.6%; class 1 > class 2, $\chi^2 = 15.7$, p < 0.001; class 1 > class 3, $\chi^2 = 20.7$, p < 0.001) satisfaction, fell predominantly in to class 1 than classes 2 or 3 (Table 3).

3.5. Latent class analysis and profiling of class 1

Details of the indices used for computing the best fit model is given in Table 6. 2-class model was found to best fit the data (Fig. 2). The profile of the two subclasses derived from the LCA on class 1 is shown in Fig. 2. When checked for the prevalence of each subclasses, an absolute division based on the response for daytime sleepiness was observed. 61.3% (N = 84) of the respondents fell in to subclass 1 and 38.7% (N = 53) fell in to subclass 2.

All the respondents who reported that they do not have daytime sleepiness fell in to subclass 1. This subclass comprised of respondents who had higher probability of reporting negative thoughts before sleep onset. This subclass was termed "dyssomnia with negative emotionality predominance and no daytime sleepiness".

All the respondents who reported that they have daytime sleepiness fell in to subclass 2. This subclass comprised of

Table 6

Fit indices for computing the best fit model for class 1.

Model #	Maximum Log-likelihood	AIC	BIC
M1 (2 latent classes)	-976.1746.1746	2050.349	2193.428.428
M2 (3 latent classes)	-956.6588	2061.318	2277.396
M3 (4 latent classes)	-941.3421	2080.684	2369.760

AIC is Akaike information criterion; BIC, Bayesian information criterion.

respondents who had higher probability of reporting daytime sleepiness and fatigue; hence termed "dyssomnia with daytime sleepiness".

Binomial logistic regression was used to validate the 2 latent classes derived from class 1. Variable daytime sleepiness was removed from the validation process as it solely increased the explanatory power of the model with 100% variance (Nagelkerke pseudo r^2). Validation of the latent classes generated by the model (excluding daytime sleepiness) was established based on the chi-square goodness of fit test (Hosmer and Lemeshow $\chi^2 = 5.1$, p = 0.744). 34.2% of the variance in the data was explained by the model. Apart from daytime sleepiness, negative thoughts before sleep onset was found to be a good predictor variable based on this model. Having negative thoughts before sleep onset (Odds ratio = 3.0; 95% CI = 1.3–7.2) increases the individual's likelihood of being grouped in to subclass 1 as compared to subclass 2. Percentage correct prediction (classification accuracy) of subclasses 1 and 2 was 77.4 and 64.2% respectively and overall was 72.3%.

The subclasses derived from the classes 2 and 3 respectively, did not have any clear profile with respect to the predictor variables and hence were not included for further discussion.

3.6. Characterization of the subclasses derived from class 1

Two subclasses were profiled on the basis of the predictor variables and external validators (Table 7). Subclasses were not different from each other with respect to any socio-demographic variables measured.

Besides negative emotionality, subclass 1 comprised of respondents who perceived their poor sleep ($\chi^2 = 10.8$, p = 0.001) and reported more sleep maintenance problems ($\chi^2 = 4.8$, p = 0.030), daytime impairments ($\chi^2 = 8.0$, p = 0.005) and arousals in night ($\chi^2 = 8.5$, p = 0.004). People who reported that they are under some regular medication also fell predominantly ($\chi^2 = 3.9$, p = 0.048) into subclass 1 (Table 7). Furthermore, respondents who reported low daytime fatigue, fell predominantly in to subclass 1 ($\chi^2 = 26.9$, p < 0.001). Subclass 2 comprised of all respondents who reported daytime sleepiness.

Out of the various daytime impairments (Supplementary Table 1), mood disturbance (subclass 1: 60.7%; subclass 2: 62.3%), tensions, headaches or gastro-intestinal problems (subclass 1: 47.6%; subclass 2: 39.6%), motivation reduction (subclass 1: 50.9%; subclass 2: 27.4%), attention and memory problems (subclass 1: 26.2%; subclass 2: 32.1%) and anxiety (subclass 1: 25.0%; subclass 2: 30.2%) were found to be more prevalent (Supplementary Fig. S3A).

Out of the various dyssomnia features (Supplementary Table S1), disturbed sleep was observed in both subclasses 1 (69.0%) and 2 (64.1%) whereas increased sleepiness was high in subclass 2 (62.3%) (Supplementary Fig. S3B). Out of the various reasons for rumination, thinking excessively when lying on bed (subclass 1: 53.6%; subclass 2: 35.8%) and not being able to relax mentally when lying on the bed (subclass 1: 40.9%; subclass 2: 32.1%) were found to be predominantly reported by both the subclasses (Supplementary Fig. S3C). Usage of electronic gadgets and binge-watching videos before bedtime were the most commonly reported sleep-hygiene issues (Supplementary Fig. S3D).

4. Discussion

The present epidemiological study assessed sleep disturbances among the Indian population during CoVID-19 pandemic using a survey questionnaire. The LCA approach helped to reliably measure the sleep associated problems and related issues and also reduced the heterogeneity of the dataset. LCA approach helped us to identify three clear classes from the dataset-no, moderate and severe



Fig. 2. Two subclasses derived from the LCA on class 1. The chart is plotted based on the item response probability values obtained in the LCA. Subclass 1 is represented in blue colour and subclass 2 is represented in orange. . (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

dyssomnia with further classification of severe dyssomnia category into two meaningful subclasses-with EDS and with negative emotionality predominance respectively.

Not surprisingly, this online survey was responded mainly by the young population than the aged. This maybe primarily attributed to the ease of usage of electronic gadgets as well as the time spent on online surfing by the young or the "digital" generation [45]. An overestimation of the prevalence of sleep problems observed in the complete dataset is often seen in association with questionnaires, leading to incorrect epidemiological evidence [46]. However, the attribution of their sleep problems to CoVID-19 pandemic was minimal (15%). This is unlike many other studies which considered CoVID-19 measures as a major risk factor that aggravated sleep problems [5,6,14–17,20,21,24–26]. Existing sleep problems in these respondents or the lack of awareness about their vulnerability to stressful conditions might be the reasons for this inconsistency. This was further enumerated by the LCA conducted on the dataset, which minimized the effect of heterogeneity and bias associated with the sample.

The severe dyssomnia class exhibiting most of the classic features of dyssomnia [47–49] had a relatively high prevalence in the population screened, when compared to the world-wide prevalence during the pandemic [5,6,14–17]. Likewise, the daytime impairments and negative emotionality observed in this category are also reported widely in people with dyssomnia [47-52]. Furthermore, increased activity during the late phase shown by this category can be a consequence of their poor sleep hygiene or *vice-versa*. Notably, sleep/wake irregularities and waking distress are seen more among the insomniacs belonging to evening chronotype [53]. Moreover, many studies have shown a bidirectional relationship between sleep disturbance, excessive thinking or to an extent cognitive arousal before sleep onset with poor sleep hygiene [54-57]. Daytime sleepiness, observed in few members of this group, also shares a reciprocal relationship with sleep disturbance during night [48,58]. Apparently, this severe dyssomnia category was represented by those who were aware of their sleep problems and also those who perceived their vulnerability towards developing sleep problems due to stress or other factors.

Another interesting result of this study is the clear division of severe dyssomnia category on the basis of EDS. As reported previously, people who are vulnerable to sleep disturbances or with dyssomnias like acute insomnia, sleep apnoea, restless leg syndrome are more prone to having EDS and fatigue [58]. On the contrary, chronic/primary insomnia is found to be associated more with a state of increased cognitive and physiological arousal (hyperarousal), which may lead to hyper alertness as well as adaptation to sleeplessness in an individual [59-61]. Stressful events along with certain predisposing emotional factors and inadequate coping mechanisms are associated with the onset of chronic insomnia [62]. The second subclass of severe dyssomnia category is predominantly represented by those who are vulnerable to stress, leading to their increased rumination, worry, feeling of worthlessness and negative emotionality. As reported previously, negative emotionality heightens cognitive arousal, which in turn lead to anxiety and poor sleep quality [63–65]. There are also studies reporting significant association between feeling of worthlessness and sleep-related disorders [66–69]. Poor sleep hygiene observed in this category, such as excessive usage of electronic gadgets and binge-watching videos during CoVID-19 lockdown, might also have aggravated their sleep problems. A considerable increase in the usage of electronic gadgets and binge-watching videos have been reported elsewhere during CoVID-19 lockdown [70-72]. As reported before, the errors and accidents at work or while driving is evidently associated with EDS [73–76].

Majority of the respondents who perceived their sleep problems, fell predominantly in to the subclass with negative emotionality. This category of people had worries and rumination about their sleeplessness, which in turn reflected in their sleep habits and hygiene. This becomes a vicious cycle with poor sleep hygiene further damaging their sleep quality [57,77–79]. Additionally, this subclass also had major representation of respondents under some regular medication. As no further details on the medications were collected in the survey, discussing about the role

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Table 7

Profile of the class 1 and the individual subclasses derived from the LCA.

		Class 1	Subclass 1	Subclass 2
Prevalence in pe	rcentage (count)	100 (137)	61.3 (84)	38.7 (53)
Average age (in	years)	30.0 ± 9.1	29.7 ± 8.7	30.4 ± 9.8
Median age (Q1,	Q3; in years)	29 (22, 35)	29 (22, 33.2)	29 (22, 37)
Sleep duration (i	in hours)	6.6 ± 1.4	6.7 ± 1.4	6.4 ± 1.2
Representation	within each class in counts (percentage)			
Gender				
	Male	61 (45.0)	33 (39.0)	28 (54.0)
	Female	75 (55.0)	51 (61.0)	24 (46.0)
Education				
	Undergraduate	8.0	6(7)	5 (9)
	Graduate	47.0	39 (46)	26 (49)
	Postgraduate	35.0	29 (35)	19 (36)
	Above postgraduation	10.0	10 (12)	3 (6)
Morning/evening	g person			
	Early	79 (58.0)	47 (56.0)	32 (60.0)
	Late	58 (42.0)	37 (44.0)	21 (40.0)
Under regular m	edication	31 (22.6)	21 (25.0)	10 (18.9)*
Perception of po	or sleep	89 (65.0)	60 (71.0)	29 (55.0)***
Adequate opport	tunity to sleep	98 (71.5)	62 (73.8)	36 (67.9)
Daytime nap		37 (27.0)	15 (17.9)	22 (41.5)
Included in the L	CA			
Sleep quality				
	Sleep initiation problem	71 (51.8)	43 (51.2)	28 (52.8)
	Sleep maintenance problem	68 (49.6)	43 (51.2)	25 (47.2)*
	Early morning awakenings	37 (27.0)	21 (25.0)	16 (30.2)
	Arousals	113 (82.5)	72 (85.7)	41 (77.4)**
Daytime impairr	nent			
	Daytime sleepiness	53 (38.7)	0(0)	53 (100)
	Daytime fatigue	99 (72.3)	49 (58.3)	50 (94.3)
	Daytime impairments	93.4	80 (95.2)	48 (90.6)**
Negative emotio	nality			
	Worry about sleep	75 (54.7)	46 (54.8)	29 (54.7)*
	Negative thoughts before sleep onset	81 (59.1)	57 (67.9)	24 (45.3)***
	Feeling of worthlessness	83 (60.6)	55 (65.5)	28 (52.8)**
Sleep hygiene				
	Sleep time variability	86 (62.8)	51 (60.7)	35 (66.0)
	Association of bed with other purposes	45 (32.8)	27 (32.1)	18 (34.0)
General well-beir	ng assessment during CoVID-19 pandemic			. ,
Quality of life				
	Life satisfaction (rated ≤ 6)	65 (47.4)	38 (45.2)	27 (50.9)
	Job satisfaction (rated ≤ 6)	74 (55.6)	40 (48.8)	34 (66.7)
CoVID-19				. ,
	CoVID-19 affected life quality	55 (40.1)	34 (40.5)	21 (39.6)
	CoVID-19 affected sleep quality	52 (37.9)	29 (34.5)	23 (43.4)

Average age and sleep duration are represented as mean \pm SD. Q1 indicates 25th percentile and Q3 indicates 75th percentile. * indicates the comparison between subclasses 1 and 2. Level of significance * $p \le 0.05$, ** $p \le 0.01$, *** $p \le 0.001$ (Pearson's χ^2 goodness of fit test for categorical variables and one-way ANOVA with Tukey's post-hoc test for sleep duration and average age).

they play will be a mere speculation. However, it is emphasized that various psychiatric disorders like depression, generalized anxiety disorders, which are likely to emerge or worsen during any stressful conditions, can also be a causative reason for sleep disturbances and other associated problems [80–82]. Since this survey did not include any questions to measure the psychiatric disorders *per se*, any discussion related to this is beyond the scope of this paper.

CoVID-19 pandemic was found to majorly affect the people belonging to severe dyssomnia class and its subclasses. Any stressful conditions, internal or external, can be a potential risk factor for developing serious sleep problems [83,84]. Less perceived control over the stress associated with the pandemic and inadequate emotional coping styles [85] in these respondents would have led to an amplified negative emotionality with subsequent aggravation of their sleep problems. Hence, the respondents from this category are highly recommended to undergo relevant medical as well as cognitive interventions. If left untreated, sleep problems can potentially lead to major neuro-psychiatric disorders [80–82]. Moreover, the quality of life, which includes life and job satisfaction, day to day performance, motivation to work, socializing with people, is found to be highly sensitive to sleep problems [86–88]. As reported previously, sleep quality has a major role in determining the well-being of an individual [89–91]. In line with this, the respondents having severe dyssomnia predominantly rated their life and job satisfaction very low. The pandemic might also have contributed to worsen this, as currently both the life and the job securities of the people are at their nadirs [92–94].

The most prevalent class derived from LCA ie, the class with no dyssomnia (38.2%), reported minimal vulnerability towards COVID-19 and its measures. Good sleep hygiene and habits would have facilitated their quality sleep. It is emphasized that the people who suffer from dyssomnias like chronic insomnia perceive their sleep duration to be less, even when there is adequate opportunity to sleep [47]. Their poor sleep hygiene further aggravates their sleep problems [47–49]. Henceforth, the respondents falling under this category may be safe with no apparent sleep disturbance or associated problems.

The class (28.5%) with moderate dyssomnia features did perceive their poor sleep, however, majority were not aware of their vulnerability towards the negative impact of CoVID-19 on their sleep. The individuals with elevated sensitivity to stressinduced sleep problems [83] and maladaptive sleep beliefs [84] are predisposed to developing chronic sleep disturbance [83]. In light of this, improving sleep hygiene and habits can facilitate in reducing the chances of developing sleep problems of clinical concern, with cognitive behavioural therapeutic techniques being a good option [95–99].

4.1. Significance of the study

The major strength of this study is it acknowledges the importance of classifying a survey dataset before deriving at any conclusion as heterogeneity might lead to misinterpretation of epidemiological data. The LCA classification helped us to appreciate that those with severe dyssomnia were more vulnerable to COVID-19 as their sleep related issues were worsened during the pandemic. In unclassified dataset, such details will be either underor over-estimated. Moreover, this survey has covered multiple aspects of sleep problems, for instance, dyssomnia features, arousals, negative emotionality, daytime impairment, sleep hygiene, in single questionnaire.

The future direction will be to see the validity and the reliability of this survey questionnaire on clinical populations such as insomnia. On the basis of relevant predictor variables and with addition of few more questions on hyperarousal and EDS, this customised survey can be a potential prospective scale to screen and classify people with dyssomnia.

4.2. Limitations of the study

Convenient sampling technique is one of the major limitations of the current study. As reported previously, these online surveys are prone to sampling and self-selection biases and can be a skewed representation of the population in concern [100–102]. Online survey results predominantly favour the subsets who can access them with ease; mostly young as observed in the current study, and is heavily influenced by the medium of language. Because the medium was in English (second language), this survey might not have given enough motivation for the people who prefer to respond in their local languages. Moreover, these online surveys can also be biased towards the affluent with respect to the socio-economic status in a population [103–105]. Furthermore, the sample size of the study is low for the Latent Class Analysis with 12 variables (Effect size: Cohen's $\omega = 0.2$), and hence the conclusion may not be generalized to an entire population. Low response rate and the limited generalization of these findings may also attribute to the medium of language. Sub-classification of the severe dyssomnia group may require further validation as the conclusion drawn is from a small subset. Nevertheless, the technique of LCA is found to reduce the limitations associated with the lack of homogeneity of the sampling technique [106]. Also, to our advantage, we got an equal representation of the genders unlike other reports in which females respond more than males [45,103,105].

5. Conclusion

LCA conducted on the survey dataset from the Indian population revealed three classes based on the severity of sleep disturbance and associated problems. 33.3% of the respondents (class 1 with severe dyssomnia) had severe sleep problems with significant daytime impairments and negative emotionality. Adverse outcomes of CoVID-19 and its measures were predominantly impacting this category of respondents. Timely medical and cognitive interventions are crucial for them to prevent any further worsening of physical and mental health. Further classification of the severe dyssomnia category revealed two subclasses, one with EDS and the other with negative emotionality predominance. The subclass with high negative emotionality and no EDS perhaps indicates towards those people having a state of high cognitive arousal. The people in the other dyssomnia category are the ones having EDS and daytime fatigue as major symptoms, for instance, as in sleep-related breathing disorders. This classification, even though meaningful, needs further validation on a clinical population.

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CRediT authorship contribution statement

Arathi Radhakrishnan: Funding acquisition, Formal analysis, Writing - original draft, Conceptualization, Writing - original draft. **Ramajayam Govindaraj:** Formal analysis, Writing - original draft. **Arun Sasidharan:** Formal analysis, Writing - original draft. **P.N. Ravindra:** Conceptualization, Writing - original draft. **Ravi Yadav:** Conceptualization, Writing - original draft. **Bindu M. Kutty:** Conceptualization, Writing - original draft.

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Conflict of interest

All the authors have declared that there are no conflicts of interest in relation to the subject of this study.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2020.12.041.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2020.12.041.

Author contributions

A.R. carried out the data acquisition and analysis; R.G. and A.S. contributed to the data analysis; A.R., R.P.N., R.Y. and B.K. conceptualized the study; all authors critically evaluated the study and contributed to writing the manuscript.

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