Original Article

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Influence of Stress on Quality of Sleep and QT Interval Variables among Young Adult Medical Students- A Cross-sectional Study

Physiology Section

AFREEN BEGUM H ITAGI[1], AMUDHARAJ DHARMALINGAM[2], SATISH DIPANKAR[3], AKSHAY BERAD[4], SENTHIL M VELOU[5], SENTHIL KUMAR SUBRAMANIAN[6]

ABSTRACT

Introduction: Stress affects different cardiovascular responses and trigger arrhythmias through Autonomic Nervous System (ANS) activation. Medical students generally tend to reduce their sleep, in order to adjust and cope with their stressful and demanding workload.

Aim: To assess the correlation of QT intervals variables with quality of sleep and stress among young adult medical students.

Materials and Methods: This cross-sectional study was undertaken in All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India, among 60 medical students taken as internal match for collection of data at the beginning of the academic year (unstressed) and three weeks before the term-end examination (stressed) during October 2019 to March 2020. Two validated questionnaires namely, Pittsburgh Sleep Quality Index (PSQI) to assess sleep quality and the Medical Student Stress Questionnaire (MSSQ) to measure the stressors and the intensity of stress were used among the medical students. Short-term Electrocardiogram (ECG) recording was used to measure QT interval variables. Descriptive statistics and paired t-test were applied using Statistical Package for the Social Sciences (SPSS) version 19.0. The $p \leq 0.05$ was considered significant.

Results: Academic Related Stress (ARS) showed a highly significant increase during the stressed conditions ($p<0.001$). The mean global PSQI score of 6.03±2.76 was significantly higher (p-value <0.001; PSQI >5) during the stressed conditions indicating poor quality of sleep, when compared to 4.50±2.87 recorded in unstressed conditions. In stressed conditions, QT interval measures had moderate correlation with ARS. Quality of sleep had negative correlations with all QT interval measures except for corrected QT interval (QTc) and QTC_{min}.

Conclusion: Stress affects the sleep quality and induced QT changes which reflected difference in variability between 'stressed' and 'unstressed' times. However, there is no significant impact on QT duration among the young adult medical students.

Keywords: Academic stress, Education, Electrocardiogram, QT variability, Undergraduate

INTRODUCTION

Sleep is an inherent and essential physiological phenomenon that contributes to the health and well-being of an individual. The American Academy of Sleep Medicine and the Sleep Science Society in their recent consensus statement had stated that to attain a good and healthy life, every individual on daily basis should acquire a minimum of seven or more hours of sleep every night. The consensus statement also throws light on the adverse outcomes of sleep deprivation and states that sleep of less the seven hours every night might result in depression, impaired performance, increases chances of error or accidents, and even jeopardises human life by impairing bodily immune functions [1,2].

Stress is characterised as the non specific reaction or response of the body to demands made on it or because of environmental events that are too disturbing. It is not just a stimulus or a rational response, but it is a manner in which we perceive and comply with threats and challenges to the environment [3,4]. Stress that can stimulate and encourage learning is called favourable stress, whereas unfavourable stress can hinder and suppress learning. Various studies have revealed that unfavourable stress levels shown to have a potential correlation with higher anxiety and depression levels of medical students, difficulties in solving interpersonal disputes, increased intake of alcohol and other drugs coupled with sleeping disorders [5-8].

Many times it has been observed that medical students prefer to minimise their sleep in an attempt to adapt and cope with their workload and stressful environment [9]. Little has been published about pre clinical medical students' sleep habits, a potentially modifiable factor in student wellness. Unlike resident physicians or medical students in clerkships, pre clinical medical students' sleep is not yet determined by call schedules or patient care workload. However, the enormous volume of information they must master places high demands on the students' time, leaving relatively little time for rest. High aspirations may cause students to sacrifice sleep for better grades. These pre clinical years would ideally set the foundation for time management and self-care in the future [4,5]. Unfortunately, by the end of the first year of medical school, many students already report changes in health habits such as decreased sleep, decreased exercise, and an increase in substance abuse [7,8].

A stressor is defined as a personal or environmental event that causes stress. Medical student stressors can usually be split into six types: stressors related to academics, those related to teaching and learning, those related to intrapersonal and interpersonal reasons, those related to social-related, those related to drive and desire, and ultimately those related to group activities [10,11].

Stress influences multiple cardiovascular responses and the stress-induced activation of the ANS might also trigger fatal arrhythmias by altering neural transmissions to the heart [12,13]. Epidemiologic evidence suggests that there is a relationship between stress and cardiac morbidity and mortality in susceptible individuals. The QT interval represents the time between the onset of electrical stimulation and its recovery and is called the duration of repolarisation [14-17]. Several variables such as genetic, physiological, patho-physiological, etc., influence the QT interval in a person, whereas the earlier published studies provide conflicting evidence on the effects of mental stress on the QT interval and dispersion [18-20]. It has been observed that QT interval is prolonged in physicians when alarm calls are received and awakened in the night with bad news.

Various laboratory based study on the other hand had observed the shortening of QT interval during stressful interviews. However, the effect of stress on QT interval and QT dispersion (SDQT) is subject to speculation in healthy young adults. These previous reports provide conflicting data on the effect of stress on QT interval and also there exists a paucity of literature about the stress, quality of sleep, and their QT variables among young adults [17-22]. Hence, this observational study aims to assess the correlation of quality of sleep, stress with QT intervals, SDQT, and other QT variables among young adults.

MATERIALS AND METHODS

This cross-sectional observational study was undertaken in the Electrophysiology Laboratory setting of All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India, from October 2019 to March 2020. Ethical approval was obtained before conducting the research, from the Institutional Ethical Committee (IEC/AIIMS/Mangalagiri/2020-21/11). Written informed consent was obtained from the participants after explaining the objectives and the procedure in the language they could comprehend.

Sample size calculation: The sample size determination was carried out by using G power statistical software for analysis. With an effect size of the study at 0.5 (Desired=<1), keeping the power of the study as 0.95 (95%) and significance level (p-value) at 0.05, the minimum required sample was estimated to be 54. In this study, however, the whole sample/total population sample was used i.e., first and second year medical students aged 18-24 years were approached to participate in the research.

Inclusion criteria: Apparently normal young adult medical students with no history of depression who provided written informed consent were included in this study.

Exclusion criteria: Participants with any established obstructive coronary artery disease, unstable coronary syndromes, or those with obstructive sleep apnoea were not considered to be part of this research.

A purposive sampling technique was adopted to recruit the participants in the study. A Guided-self-administered structured questionnaire proforma was designed to include four sections viz., socio-demographic details; MSSQ; PSQI and QT interval recording format.

Medical Student Stress Questionnaire (MSSQ)

MSSQ was developed to recognise the stressors of medical students and assess the stress level induced by these stressors. It is a self-reported, self-scoring instrument with 40 items categorised into six domains namely the ARS, Teaching and Learning Related Stress (TLRS), Interpersonal/Intrapersonal Related Stress (IRS), Social Related Stress (SRS), Desire Related Stress (DRS) and Group Activities Related Stress (GARS), these were measured as domains of stress by the MSSQ [11]. The investigator held few face-to-face sessions with the students related to a guided self-administered questionnaire and asked the participants to fill in the MSSQ, the answered questionnaires were collected on the same day. The students rate the intensity of stress caused by each item on a scale of 0-4 (causing no stress to causing extreme stress). The cumulative mean values for each of the six domains were taken to calculate the MSSQ score.

Pittsburgh Sleep Quality Index (PSQI)

PSQI has diverse utilisation in research and clinical settings, including the assessment of quality of sleep and identifying/classifying the sleep problems during the previous month [23]. It can also be used to screen for sleep disorders at night and to monitor the development of sleep disorders. The PSQI consists of 21 questions categorised into seven components and each scored 0 (no difficulty) to 3 (severe difficulty). The cumulative component scores were obtained ranging from 0 to 21 to produce a global score, where higher ratings indicate a worse quality of sleep. A global PSQI score of >5 has shown that it has high diagnostic sensitivity and specificity in measuring the poor sleep quality, relative to clinical and laboratory measures and hence the same was used in this study to differentiate between good sleepers (<5) and bad sleepers (>5) [23,24].

Measurement of QT Interval

The skin preparation, electrode placement, and associated protocols were identical to the developed guidelines. Physiograph- three channels and MLU268/8 LabChart software were used for recording 5-minute 12-lead resting ECG and QT interval, corrected QT interval (QTc), SDQT respectively. Volunteers were assuming the supine position. Vital parameters like resting heart rate, blood pressure were recorded. Twelve lead ECG was taken while resting in a room with a comfortable temperature of 22-25°C at a speed of 25 mm/sec with a gain of 10 mm/mV. Uncorrected QT interval, Corrected QT interval, SDQT were calculated from 12 lead ECG. The uncorrected QT interval was identified from the beginning of the Q wave to the end of the T wave. QTc was calculated by Bezett's formula $QTc=QT/\sqrt{RR}$ and QTd was calculated as the difference between shortest and longest QT interval recorded utilising a standard 12 lead ECG.

A semi-automated berger template matching algorithm was used for the reliable estimation and description of QT interval variability. The QT intervals was calculated as the difference between the Q wave onset and the T wave endpoint (i.e., QT end interval).

Unstressed/Prestress (T1) and Stress (T2) Time Periods for Data Collection

All the parameters were assessed at two different time points (T1 and T2). T1 being the unstressed (or) Prestress measures, were taken at the beginning of the academic year and T2 measures were taken during "stressed time", three weeks before the term-end examination.

STATISTICAL ANALYSIS

The collected data was compiled systematically in a Microsoft Excel sheet. All statistical tests were carried using version 19.0 of SPSS (IBM SPSS, Chicago, USA). The distribution of the data was determined by the Kolmogorov-Smirnov test. Demographic data observations and QT variables were expressed as mean, Standard Deviation (SD), and range values for both the comparable classes. The difference in parameters between prestress and during stressed conditions was analysed using paired t-test. In case the data was found to be showing a non normal distribution, the Mann-Whitney U test was used for statistical inference. At a confidence interval of 95%, the test was considered "Highly Significant" if it yielded p<0.001. The p-value <0.05 was taken as 'Significant'.

RESULTS

A total of 68 medical students participated in the study. Eight participants were not available for the data collection during the T2 (stress time) assessment of variables. The mean age of 60 (34 males and 26 females) participants who completed the study was 19.8±1.19 years. The Mean GPSQI score of 4.50±2.87 was recorded in unstressed conditions was well under limits to rule out poor quality of sleep. However, the mean score of 6.03±2.76 during the stressed conditions was significantly higher indicating poor quality of sleep (p-value <0.001; PSQI >5). The "stressed" mean scores of QT, QTc, QT_{min}, and QTc_{min} measured were significantly higher compared to the "unstressed" mean scores among the medical students. Although, there was a comparative increase in mean scores of ARS, TLRS, SRS, DRS, and GARS, but only ARS showed a highly significant increase during the stressed conditions (p<0.001) [Table/Fig-1].

All the stressor domains of MSSQ showed a weak correlation with sleep quality during the unstressed times, however there was a significant

	Unstressed	Stressed	Paired differences			t	Sig. (2-tailed)
	Mean±SD	Mean±SD	Mean	SD	SE mean		
GPSQI	4.50±2.87	6.03±2.76	-0.1533	1.307	0.1689	-3.159	0.001*
ARS	1.34±0.56	1.59±0.67	-0.2551	0.5785	0.0746	-3.527	0.001*
IRS	1.70±0.80	1.71± 0.7	-0.01433	0.1138	0.0146	-.975	0.333
TLRS	1.21±0.77	1.23±0.75	-0.01421	0.0679	0.0087	-1.621	0.110
SRS	1.55±0.7	1.56±0.69	-0.01250	0.0549	0.0070	-1.762	0.083
DRS	1.22±0.79	1.24±0.76	-0.02490	0.1005	0.0129	-1.918	0.060
GARS	1.41±0.87	1.42±0.86	-0.01128	0.1055	0.0136	-.828	0.411
QT	0.33±0.02	0.34±0.03	-0.0095	0.0192	0.0024	-3.849	0.001*
QTc	0.36±0.02	0.37±0.02	-0.0099	0.0207	0.00268	-3.720	0.003*
QT_{max}	0.36±0.02	0.36±0.03	-0.0037	0.0232	0.0030	-1.255	0.215
QT_{min}	0.30±0.06	0.32±0.04	-0.0145	0.0483	0.0062	-2.329	0.023*
QT_{cmax}	0.42±0.05	0.43±0.05	-0.0078	0.0397	0.0051	-1.526	0.132
QT_{cmin}	0.31±0.06	0.32±0.06	-0.0078	0.0207	0.0026	-2.931	0.005*
SDQT	0.007±0.00	0.006±0.004	0.0006	0.0063	0.0008	0.810	0.421
SDQTc	0.017±0.01	0.017±0.008	0.0004	0.0072	0.00093	0.465	0.643

[Table/Fig-1]: Quality of sleep (GPSQI), Stress and QT variables measures at unstressed and stressed times among the study participants.
Paired t-test was used and Mann-Whitney U test was used to compare the difference in mean values of QT interval measures; *p-value ≤0.05='Significant'; SDQT: Standard deviation of all QT intervals; SDQTC: standard deviation of all QTc intervals; GPSQI: Global pittsburgh sleep quality index; ARS: Academic related stress; IRS: Intrapersonal related stress; TLRS: Teaching- and learning related stressors; SRS: Social related stress; DRS: Desire elated stress; GARS: Group activities related stress

moderate positive correlation observed between ARS and DRS with sleep quality during the term-end examination period indicating that academic stress influences the low quality of sleep [Table/Fig-2].

	Unstressed			Stressed		
GPSQI	Mean±SD	r	Sig.	Mean±SD	r	Sig.
ARS	1.34±0.56	0.181	0.167	1.59±0.67	0.289*	0.025*
IRS	1.70±0.8	0.094	0.473	1.68±0.70	0.141	0.283
TLRS	1.21±0.77	0.211	0.106	1.23±0.81	0.247	0.057
SRS	1.54±0.70	0.165	0.207	1.55±0.67	0.22	0.091
DRS	1.22±0.79	0.227	0.082	1.28±0.87	0.260*	0.045*
GARS	1.40±0.87	0.156	0.233	1.43±0.58	0.242	0.063

[Table/Fig-2]: Correlation of quality of sleep with MSSQ scores among the study participants.
Pearson's correlation test; * Correlation is significant at the 0.05 level (2-tailed); ARS: Academic related stress; IRS: Interpersonal/intrapersonal related stress; TLRS: Teaching related stress; SRS: Social related stress; DRS: Desire related stress; GARS: Group activities related stress

During the initial "unstressed" period, Global PSQI had a moderate negative correlation with QT interval measures. QT, QT_{max}, QT_{min}, QTc_{max}, and QTc_{min} measures had a weak negative correlation with ARS, while QTc, SDQT, and SDQTc had a weak positive correlation with the MSSQ scores. Overall, compared to the MSSQ scores, which failed to reach a significant correlation with QT interval measures; quality of sleep (GPSQI) had a significant negative correlation with QTc, SDQT, corrected SDQT, QT_{max}, QTc_{max} and QTc_{min} [Table/Fig-3].

During the "stressed" period, QT interval measures had a moderate correlation with academic-related stress scores. Quality of sleep had negative correlations with all QT interval measures except for QTc and QTc_{min} [Table/Fig-4].

DISCUSSION

In this study, authors found insignificant elongation of the QT interval in 'stressed' medical students, which is in line with many studies

	QT		QTc		SDQT		SDQTc		QT_{max}		QT_{min}		QTc_{max}		QTc_{min}	
	r	Sig.	r	Sig.	r	Sig.	r	Sig.	r	Sig.	r	Sig.	r	Sig.	r	Sig.
ARS	-0.046	0.729	0.098	0.456	0.001	0.993	0.001	0.993	-0.161	0.218	-0.199	0.127	-0.194	0.139	-0.075	0.571
IRS	-0.053	0.689	0.214	0.101	0.1	0.448	0.1	0.448	-0.023	0.863	-0.36**	**0.005**	-0.144	0.272	-0.034	0.799
TLRS	-0.11	0.403	0.002	0.991	-0.128	0.328	-0.128	0.328	-0.239	0.066	-0.208	0.11	-0.238	0.068	0.152	0.246
SRS	0.133	0.311	0.199	0.128	0.175	0.181	0.175	0.181	-0.029	0.824	-0.118	0.37	0.029	0.827	0.075	0.57
DRS	-0.088	0.503	0.013	0.924	-0.095	0.471	-0.095	0.471	-0.234	0.072	-0.183	0.161	-0.39**	**0.002**	0.003	0.979
GARS	-0.013	0.92	0.093	0.48	-0.165	0.206	-0.165	0.206	-0.017	0.9	-0.031	0.816	-0.118	0.37	0.127	0.332
GPSQI	-0.004	0.975	-0.314*	**0.014**	-.378**	**0.003**	-0.38**	**0.003**	-0.40**	**0.002**	-0.061	0.641	-0.302*	**0.019**	0.286*	**0.027***

[Table/Fig-3]: Correlation of quality of sleep and stress with the QT measures at unstressed time.
**Correlation is significant at the 0.01 level (2-tailed); *Correlation is significant at the 0.05 level (2-tailed)

	QT		QTc		SDQT		SDQTc		QT_{max}		QT_{min}		QTc_{max}		QTc_{min}	
	r	Sig.	r	Sig.	r	Sig.	r	Sig.	r	Sig.	r	Sig.	r	Sig.	r	Sig.
ARS	0.269*	**0.037**	0.197	0.132	-0.075	0.567	-0.245	0.059	0.053	0.689	0.124	0.345	-0.211	0.106	0.107	0.416
IRS	0.064	0.626	0.062	0.64	-0.13	0.324	-0.082	0.536	-0.104	0.43	-0.143	0.276	-0.134	0.307	0.055	0.675
TLRS	-0.008	0.951	-0.074	0.575	-0.158	0.227	-0.234	0.072	-0.185	0.158	-0.093	0.478	-0.183	0.162	0.186	0.155
SRS	0.195	0.136	0.14	0.287	0.003	0.982	0.033	0.803	0.024	0.858	0.006	0.964	-0.016	0.902	0.093	0.478
DRS	-0.056	0.672	-0.073	0.58	-0.263*	**0.042**	-0.241	0.064	-0.293*	**0.023**	-0.09	0.492	-0.357**	**0.008**	0.073	0.578
GARS	0.172	0.189	0.078	0.554	-0.038	0.772	-0.256*	**0.048**	0.046	0.727	0.084	0.525	-0.046	0.727	0.179	0.171
GPSQI	-0.032	0.81	0.083	0.528	-0.021	0.872	-0.33**	**0.009**	-0.168	0.198	-0.137	0.297	-0.349**	**0.008**	0.24	0.065

[Table/Fig-4]: Correlation of quality of sleep and stress with the QT measure after exposure to stress.
**Correlation is significant at the 0.01 level (2-tailed); *Correlation is significant at the 0.05 level (2-tailed)

reporting significant QT interval prolongation in stress [13,20,25,26]. However, this finding contradicts with the other similar researches, reporting significant QT interval shortening under stress [15,27-29].

This study showed that both stress and sleep quality correlated with the prolongation of QT interval measures. Perceived stress has been recognised as one of the major factors resulting in poor sleep quality, delay in onset of sleep, increased daytime dysfunction as a result of sleepiness, and decreased quality of subjective sleep. In the present study at both (unstressed and stressed) time points, stress levels correlated with the GPSQI-score, supporting previous findings suggesting a close inter-relationship between these two factors [30]. Various researches had found evidence regarding the close link of sleep and stress with the Hypothalamic-Pituitary-Adrenal (HPA) axis, which explains the near inter relationship between these two variables [31-33].

Mental stress can result in imbalance of the ANS, adrenergic release, increased sympathetic tone, contributing to heterogeneity of ventricular depolarisation resulting in prolonged QT interval. The QT interval has proved its clinical significance as a reliable clinical index in assessing the length of ventricular repolarisation, as prolonged QT and QTc reflects an increased risk of primary cardiovascular events among persons without clinically recognised heart disease [26,28,34]. Prolongation of the QT interval is considered as one of the markers of such an imbalanced distribution of the activity of the sympathetic nervous system in the heart and is also assumed to be linked with a lower threshold for ventricular fibrillation and a risk of sudden cardiac death [26,35]. Routine monitoring of the QT-related parameters such as QT, QTc, QT variability, QTd may help prevent a major cause of cardiovascular impairment and allowing for more efficient preventive intervention by identifying early changes in otherwise safe subjects' biological parameters [28]. This aspect might have important public health implications, by reducing the direct and indirect costs of cardiovascular disease in medical personnel. A cognitive behavioural approach, such as meditation or progressive muscle relaxation, might help medical students, reducing stress and thus increasing the quality of sleep.

This study has several strengths. First, a cross-sectional research design was used, which was able to investigate the possible correlation between the medical students' sleep quality, stress, and QT interval measures. Second, to measure stress among medical students, the MSSQ is a valid, reliable, and well-established measurement instrument. Thus, a comparison can be made with previous studies. Considering the limitations and strengths, this study should be interpreted with caution and within its context. However, the present study can be used as the basis for planning longitudinal or cross-sectional studies with a larger sample size.

Limitation(s)

Despite these promising results, this research has some limitations. First, this study involved a relatively small number of study subjects that might compromise the accuracy of the results obtained from the analysis. Second, this study was limited to the cohort of only medical students studying in a medical institution, restricting the generalisability of its findings. The majority of the correlation coefficients were below/nearly 0.3 in this study which can be considered as small to medium effect size and may not have reached significance with a smaller size. The association between GPSQI and QT interval measures seemed slightly stronger than stress (ARS) and the QT interval measures, especially noticeable in the partial correlations QT, QTc, SDQTc, and QTcmax. ARS scores and QT remained significant with the correlation between stress and the QT interval during the stressed time. The causal relationship between sleep, stress, and QT interval measures remains unknown and cannot be determined by this study. The findings, however, further underline the critical interaction between these variables. Last, authors did not explore the possible causes of poor sleep quality and poor general health; also both PSQI and MSSQ assess participants during the past month or less and hence authors could not discriminate between acute and chronic problems.

CONCLUSION(S)

In this study, authors have highlighted the influence of stress, quality of sleep on QT interval measures. The findings indicate that stress primarily influences the QT variability, but there is no major effect on the duration of QT. Both standard deviation of QTc and QT measure reflects the difference in variability between 'Stressed' and 'Unstressed' times among the medical students. Present study findings suggest the possibility of a mechanism linking emotional stress to changes in autonomic balance and ventricular repolarisation as indicated by QT interval prolongation. However, as such, no definitive conclusions have so far been drawn as to the specific QT interval response to stress conditions and poor quality of sleep. Authors supposed that further insight into QT changes related to these two distinct psychophysiological entities would help us to explain the varying reports on the effects of poor sleep quality and stress-induced QT changes in medical students.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Physiology, All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India.
2. Associate Professor, Department of Physiology, All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India.
3. Associate Professor, Department of Physiology, All India Institute of Medical Sciences, Patna, Bihar, India.
4. Assistant Professor, Department of Physiology, Government Medical College, Nagpur, Maharashtra, India.
5. Assistant Professor, Department of Physiology, All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India.
6. Assistant Professor, Department of Physiology, All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Afreen Begum H Itagi,
All India Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India.
E-mail: afreen.itagi@gmail.com

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