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Study Of Oxidative Stress And Insulin Resistance In Late Night Workers.

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ABSTRACT

Late night work hours can disrupt circadian rhythmandoxidative stress,leading toinsulin resistance and early development of type 2 diabetes in the absence of other risk factors. A better understanding of this model can have a potential non-pharmacological therapeutic implication. The present study was a descriptive cross-sectional design conducted among 120 individuals (60-night shift worker &60 days shift worker) working at a tertiary care hospital. The study involved estimating plasma glucose, insulin level,Malondialdehyde (MDA), and Super Oxide Dismutase (SOD) level. The Homeostatic Model Assessment of Insulin Resistance (HOMA IR) was calculated to assess insulin resistance. The mean Insulin level, HOMA IR level, MDA and SOD levelamong the night shift worker was higher when compared with day shift worker, and this was found to be, statistically significant after adjusting for possible confounders.Binary logistic regression to assess the fitness of model showed Nagelkerkel R square of 0.86 andAUC under the ROC curve for Insulin level was 0.89,HOMA IR level was 0.85, MDA level was 0.84 and SOD level was 0.71. Late-night work hours can lead to insulin resistance, which is a risk factor for diabetes.

Keywords: Late-night work, Insulin resistance, Oxidative stress, HOMA-IR, Diabetes

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INTRODUCTION

Night shift work lasts seven-hour and includes the interval between midnight and five o'clock in the morning[1].

This inversion of the sleep-wake pattern causes a change in the circadian rhythm and affects melatonin secretion, causing oxidative stress,viz-altering antioxidant enzyme activity. It also affects the GLUT4 expression and phosphorylation of the insulin receptor and can cause insulin resistance, which is a precipitating factor for the onset of diabetes[2]. The present intends to test the hypothesis that higher level of oxidative stress markers among night workers compared to day shift workersleads to insulin resistance after adjusting for potential confounders.

MATERIAL AND METHODS

The current study is a descriptive cross-sectionaldesign among 120 non-diabetic, non-obese participants working at a tertiary care hospital in Andhra Pradesh. The participants were divided into two groups. Group 1 consists of a voluntary night shift worker who has been in night shift work for more than six months. Group 2 consisted of the day shift workers who were not involved in night shift work for the last six months. The study participants were between the agesof 25 to 45 and had no pre-existing comorbidities. In each equal number of male and female study participants were enrolled. The study participants were informed about the study's objectives, and after they gave written consent, they were enrolled in the study. Diabetic, prediabetic, overweight, obese, and individual who consumed tobacco in any form or those who did not consent to be part of the study were excluded.A brief clinical history from all the subjects was recorded,anthropometric measurement, followed by estimating serum fasting glucose, MDA, and SOD level.The estimation of Malondialdehyde (MDA) in serum was done by the thiobarbituric acid reactive species method[17]. Super Oxide Dismutase (SOD) was assayed by Kakkaret al. method[18]. Plasma glucose was estimated by Glucose oxidase and peroxidase method[19] in an autoanalyzer, and plasma insulin by Chemiluminescent immunoassay.Fastingblood samples were collected and analyzed for plasma glucose and insulin levels—the homeostatic Model of Assessment of Insulin Resistance (HOMA IR) was calculated. The estimation of Malondialdehyde (MDA) in serum was done by the thiobarbituric acid reactive species method[17]. HOMA IR was calculated basing on plasma glucose and serum insulin levels using the formula, fasting glucose concentration (mg/dl) times fasting insulin concentration (IU/ml) divided by 405 [20].

Statistical analysis

Data areexpressed as mean and standard deviation (mean ± SD). Statistical significance among the subjects will be observed; thet-test was performed SPSS software version 26.Binary logistic regression and calculation for Nagelkerke R square were done.ROC curve was plotted to determine the AUC, and a value of more than 0.7 was suggestive of the good fitness of the model. The statistical significance was determined at 5% ($p < 0.05$) level.

RESULTS

The study subjects in both the groups shared similar characteristics (Table 1); there was no significant statistical difference found in age, SBP, DBP,waist circumference,and BMIamong both groups. It is seen that the fasting glucose,fasting insulin level, mean MDA, SOD level was higher among night shift workers (group 1) than the daytime worker, which was statistically significant. Mean HOMA-IR level was also higher among group 1 study subjects than group 2, which was statistically significant. Binary logistic regression to assess the fitness of the model (Table 2) showed a Nagelkerke R square of 0.86 .The AUC under the ROC curve (figure 1) for Insulin level is 0.89,HOMA IR levels are 0.85, the MDA level is 0.84, and the SOD level is 0.71 indicating a good to fairpredication probability of the present model.

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Table 1: Comparison between two groups

Variable	Group 1 Mean ± SD	Group 2 Mean ± SD	t Stat	df	p-Value
Age in years (yrs.)	31.43±3.47	30.27±3.60	1.79	118	0.7
SBP (mm Hg)	116 ± 4.7	114 ± 5.2	2.2	118	0.4
DBP (mm Hg)	78 ±1.6	82 ± 1.2	-7.7	118	0.02
Waist circumference(cm)	85 ±2.4	84 ± 2.7	-4.2	118	0.3
BMI (kg/m2)	22.45±1.2	21.68±1.4	3.2	118	0.2
Fasting Glucose(mg/dl)	85.1 ± 9.3	69.3±4.8	134.89	118	**<0.05**
Insulin (mU/L)	10.1 ± 2.2	6.7 ± 1.6	88.7	118	**<0.05**
HOMA-IR	2.16 ± 0.84	1.1 ± 0.47	66.5	118	**<0.05**
Malondialdehyde (MDA) (µmol/l)	4.6 ± 1.9	2.2 ± 1.4	56.0	118	**<0.05**
Superoxide dismutase (SOD) (U/ml)	9.1 ± 2.4	7.3 ± 2.1	19.0	118	**<0.05**

The above table shows mean value of demographic data, insulin, HOMA-IR, MDA and SOD.

Table 2: Binary Logistic regression for assessing the predication strength of the model

Variable	B	SE	Wald	df	p-value	Exp(B)	95% CI	
							Lower	Upper
Insulin	1.37	0.46	10	1	0.002	3.7	1.6	8.4
HOMA -IR	2.06	0.76	11.7	1	0.001	13.5	3.0	60.0
MDA	1.2	0.37	11.0	1	0.001	3.4	1.6	7.1
SOD	0.2	0.17	1.4	1	0.22	1.2	0.87	1.7
Constant	20.89	5.3	15.2	1	0.000			
Nagelkerke R square	**0.86**							

The above table shows Binary Logistic regression for assessing the predication strength of the model, insulin, HOMA-IR, MDA and SOD.

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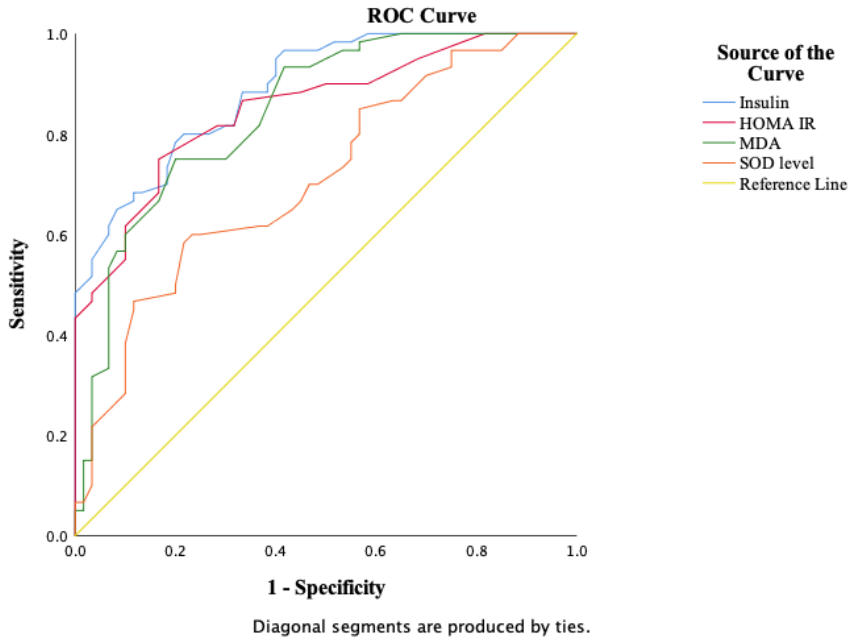
Figure 1: ROC Curve for fitness of the model



DISCUSSION

The inversion of the sleep/wake cycle causes stress for the circadian rhythms. The natural sleep hormone melatonin peaks at night, and this regulates the sleep cycle[3]. Late-night sleep or sleeplessness produces low melatonin[4], and it can cause oxidative stress, which hasbeen reported in various studies[5-10]; the finding of our study is similar to these studies. Various studies[11-16] suggest that night shift workers develop insulin resistance. We also report the same with HOMA IR level higher in late-night shift workers when adjusting for confounder like age, sex ,gender , waist circumference and obesity.

The present study's external validity can be questioned as its single centre study carried among a small group of individuals. It is impossible to remove all possible confounder, like genetic predisposing of development of the outcome, non-revelation of potential risk factors by the study participant. An arbitrary cut off of 6 months was made for the inclusion of the study subject for technical feasibility. The type of vocation adopted by night shift workers and the impact on outcome could not be ascertained as the study group subsets are small for statistical comparison. The result of the study did suggest that study subjects who work at night shift have higher oxidative stress marker and have higher HOMA -IR level, but did they develop Type 2 DM due to this, which can only be evaluated by different study design, and also raises a potential ethical question whether they should continue with the present shift. In the present study, we did not assess the inflammatory marker's level due to financial constraints, which could be the critical link between the oxidative stress stage and the development of Insulin resistance.

Late shift work needs the hour in 24X7 hours industries like medical care to provide quality care, but it is vital to have a healthy workforce. Haus et al.[21] in their study have provided specific recommendation which includes, a maximum of 4-night shift continuously and then one day off of having a 7-hour sleep per 24 hours and the central sleep starting just after finishing the night shift. It also recommended that night shift workers take 30 min to 2-hour nap before starting the night shift work and increase exposure to bright light in the first few night shift hours. The effect of these interventions can be a subject of future study. We also recommend that night shift workers be informed about the potential risk of prolonged late night work and a night shift in rotation.

CONCLUSION

Late-night shift work is an oxidative stress state that can elevate markers such as SAD and MDA, leading to insulin resistance, a risk factor for type 2 diabetes.

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