

## HOMA-IR INDEX IN INDUSTRIAL SHIFT WORKERS, A PRELIMINARY STUDY

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### ABSTRACT

There is strong evidence suggesting a probable association between shift work (SW) and insulin resistance (IR). Hence, it is crucial to evaluate this factor in therapeutic and preventive interventions. In a comparative cross-sectional study, serum fasting glucose levels and serum fasting insulin hormone levels were estimated, then Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index was examined among shift workers (SWs) employed in the industrial sector. An occupational surveillance framework included 60 industrial workers, who were classified as follows: thirty were shift workers (SWs) and thirty were non-shift workers (NSWs). Fasting blood sugar and fasting serum insulin hormone levels were estimated, and HOMA-IR Index was calculated for all participants and the results were investigated for a possible link with shift work. A significantly higher serum fasting insulin level as well as a high HOMA-IR index was observed among SWs as a result ( $p < 0.05$ ). Accordingly, Shift work may raise the potential for developing insulin resistance.

**Keywords:** Diabetes Mellitus; Insulin resistance; Workers; Night work; Shift work; Circadian clock.

### INTRODUCTION

The term "shift work" (SW) describes a work schedule that is different from the regular weekday hours (Nagaya *et al.*, 2002). In contemporary society, shift work plays a crucial role in various industries as manufacturing, transportation, hospitality, and emergency services (Boivin *et al.*, 2022). Shift work exposure has been assessed on a global scale by the International Labor Organization and the European Foundation for the Improvement of Living and Working Conditions, encompassing 187 nations and nearly 1.2 billion workers. Findings from the joint research in 2019

revealed that approximately 10% to 30% of workers globally engaged in night shifts for at least once a month (Eurofound, 2019). In other nations, 12% to 13% of the workforce reported working night shifts (Rydz *et al.*, 2020). It is worth noting that identifying and quantifying other forms of atypical shifts, such as split shifts, irregular shifts, and on-call shifts, is more challenging (Boivin *et al.*, 2022). Night shift work, characterized by the desynchronization between sleep and the natural light-dark cycle, is associated with sleep restriction and concurrent dysregulation of the circadian clock.

Extensive research has investigated the potential health implications of SW and has identified associations with chronic conditions such as diabetes, cancer, coronary heart diseases (CHD), and cerebrovascular disease (CVD) (Morris *et al.*, 2017). Epidemiological studies have indicated a heightened risk of type 2 diabetes mellitus (T2DM) among individuals engaged in SW (Monk and Buysse, 2013). Chronic sleep deprivation, commonly experienced by shift workers, detrimentally affects glucose tolerance and cardiovascular health (Cappuccio *et al.*, 2011).

Insulin resistance (IR) refers to an attenuated responding of insulin-target tissues to insulin hormone. The range of metabolic disorders associated with IR goes beyond T2DM and includes inflammation, hypercoagulability, dyslipidemia, and hypertension. These disorders are interconnected with metabolic syndrome (MS) and act as risk factors for cardiovascular diseases (Lebovitz, 2001). Nagaya *et al.* (2002) proposed a potential relationship between SW and metabolic syndrome. In the realm of therapeutic and preventive approaches, the assessment of metabolic syndrome holds significant importance. The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) technique is commonly employed to evaluate MS, using measurements of fasting insulin and fasting glucose levels to compute the HOMA-IR index (Barnosky *et al.*, 2014).

Thus, the objective of this study was to investigate the HOMA-IR index in shift workers to help determine the assessment of the economic impact of metabolic syndrome within this specific population.

## MATERIALS AND METHODS

**Study design:** Comparative cross-sectional study.

**Place and time interval of the study:** Sharqia governorate, Egypt during the period from March 2023 till September 2023.

### Sample size calculation

The sample size was calculated using Power Analysis and Sample Size Software (PASS 11) (Version 11.0.08). The power was set at 99% and the alpha error at 5%. Previous study results by Ledda *et al.* (2019) were reviewed, which showed that the mean HOMA-IR Index in healthcare workers with shift work was  $2.8 \pm 0.6$ , while in those without shift work it was  $1.5 \pm 0.4$ . Based on these findings, a sample size of at least 30 shift workers and 30 non-shift workers was determined to be sufficient for the study objective.

### Study sample

A convenient sample of 60 males who were industrial workers working in electric appliances factory with moderate physical activity level, were classified in accordance with the type of their work into:

- Non-shift workers (number=30) who work from 8.00 a.m.-5.00 p.m. for six days each week.
- Shift workers (number=30) who work from 11:00 p.m.-8:00 a.m. for six days per week, for two successive weeks. And afterwards, they work from 8:00 a.m.-5:00 p.m., for six days per week, for another two weeks.

### Study methods

A self-administered semi-structured questionnaire was used to collect data in this study, following the necessary requirements. The questionnaire covered the following aspects:

- **Socio-demographic data:** This included information as age, residency, marital status, and level of education.
- **Occupational history:** Details regarding shift work type, the number of working hours per day, and number of years of employment were recorded.
- **Anthropometric data:**

Weight and height measurements were obtained following the standard protocol established by the World Health Organization (WHO). Weight was measured by using a digital balance, and height was measured by using a mobile stadiometer.

The Body Mass Index (BMI) was calculated by dividing the measured weight in kilograms by the squared height in meters.

Waist circumference was estimated by locating the midpoint between the lower rib margin and the anterior superior iliac spine, and measurements were recorded in centimeters.

**Ethical considerations** were rigorously observed throughout the study. Verbal informed consent was obtained from the industrial workers, ensuring that participation was voluntary, and their data would be kept confidential. The consent form was designed in accordance with international ethical guidelines for medical research involving human subjects. The participants were provided with a comprehensive explanation of the study's nature, potential benefits, and possible risks. Verbal consent was obtained from those who accepted to take part in the study, following the guidelines provided by the WHO Research Ethics Review Committee on obtaining informed consent (WHO/ERC, 2010). The Declaration of Helsinki's guiding principles were followed in the planning and execution of the study.

#### **Laboratory Analysis**

Blood samples were collected from the shift workers after they had been shifted to day shift rotation four days prior. The collection took place in the morning after fasting overnight. Venous blood samples of 5 mL were obtained, and one tube of serum was collected. The serum tubes were then kept in a vertical position at room

temperature for a minimum of 30 minutes, but not more than sixty minutes. Then, the tubes were centrifuged at 3500 rpm for ten minutes to isolate the serum. Then, serum fasting glucose and insulin hormone levels were estimated to assess HOMA-IR Index.

The following methods were employed for the determination of glucose and insulin levels in the serum:

**1- Determination of blood glucose level in the serum:**

The quantitative measurement of glucose in the serum was carried out using the method described by (Trinder, 1969). A kit from Spinreact Co., Egypt, was used for this purpose.

**2- Determination of blood Insulin level in the serum:**

Insulin levels in serum were estimated using the method outlined by (Greenwald *et al.*, 2016), employing Enzyme-Linked Immunosorbent Assay (ELISA).

**3- Determination of HOMA-IR level in the serum:**

The HOMA-IR level was calculated using the following equation:

$$\text{HOMA-IR} = (\text{Serum fasting glucose level} * \text{Serum fasting insulin level}) / 405,$$

as described by (Matthews *et al.*, 1985).

**Statistical analysis**

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 21. Qualitative variables were presented as numbers and percentages, while quantitative variables were expressed as means and standard deviations. The  $\chi^2$  test for independence was used to compare proportions, and the independent sample t-test was employed for comparisons between two groups. A significance level of  $p < 0.05$  was considered statistically significant.

## RESULTS

The results of the present study presented in Table 1 revealed a significant difference in marital status between NSWs and SWs (NSWs: 80%, SWs: 53%) where married persons were significantly less among the SWs ( $\chi^2 = 4.8$ ;  $df = 1$ ;  $p = 0.028$ ). Yet, no significant difference was observed between the two groups as regarding education: illiterate workers (NSWs: 10%, SWs: 0%) were not significantly less in SWs group. Intermediate education (NSWs: 26.7%, SWs: 16.7%) was not significantly less in SWs group. Higher education (NSWs: 63.3%, SWs: 83.3%) was non significantly more in SWs group ( $\chi^2 = 4.51$ ;  $df = 2$ ;  $p = 0.105$ ). As for residency, the percentage of the city dwellers among the two groups was the same (83.3%) with no significant difference between the two groups ( $\chi^2 = 0.000$ ;  $df = 1$ ;  $p = 1.000$ ). Regarding smoking habit, the percentage of smokers was not significantly higher among SWs group (33.3%) than that among NSWs group (26.7%) ( $\chi^2 = 0.317$ ;  $df = 1$ ;  $p = 0.389$ ). There were no significant difference concerning the family medical history of DM, hypertension, and cardiovascular diseases, the following was observed: The percentage of DM was the same among the two groups (30%) ( $\chi^2 = 0.000$ ;  $df = 1$ ;  $p = 1.000$ ). Hypertension was higher among SWs group (36.7%) compared to the NSWs group (26.7%) ( $\chi^2 = 0.696$ ;  $df = 1$ ;  $p = 0.290$ ) and that of cardiovascular diseases was lower among the SWs group (10%) compared to the NSWs group (16.7%) ( $\chi^2 = 0.577$ ;  $df = 1$ ;  $p = 0.353$ ).

**Table 1.** Comparing socio- economic status, smoking habit, and family medical history of Diabetes Mellitus (DM), hypertension, and cardiovascular diseases between the non-shift workers and the shift workers.

VARIABLE		NON-SHIFT WORKERS (NSWS)		SHIFT WORKERS (SWS)		X <sup>2</sup> TEST	DF	P VALUE
		No	%	No	%			
<b>Marital Status</b>	<b>Single</b>	6	20.0	14	46.7	4.800	1	0.028
	<b>Married</b>	24	80.0	16	53.3			
<b>Level of education</b>	<b>Illiterate</b>	3	10.0	0	0.0	4.510	2	0.105
	<b>Intermediate</b>	8	26.7	5	16.7			
	<b>Higher education</b>	19	63.3	25	83.3			
<b>Residence</b>	<b>City</b>	25	83.3	25	83.3	0.000	1	1.000
	<b>Village</b>	5	16.7	5	16.7			
<b>Smoking</b>	<b>Yes</b>	8	26.7	10	33.3	0.317	1	0.389
	<b>No</b>	22	73.3	20	66.7			
<b>Family history</b>								
<b>DM</b>	<b>Yes</b>	9	30.0	9	30.0	0.000	1	1.000
	<b>No</b>	21	70.0	21	70.0			
<b>Hypertension</b>	<b>Yes</b>	8	26.7	11	36.7	0.693	1	0.290
	<b>No</b>	22	73.3	19	63.3			
<b>Cardiovascular diseases</b>	<b>Yes</b>	5	16.7	3	10.0	0.577	1	0.353
	<b>No</b>	25	83.3	27	90.0			

Results in Table 2 showed no significant difference ( $p > 0.05$ ) between the two groups regarding: **age** which was lower in SWs group ( $31.0 \pm 8.0$  years) than in NSWs group ( $32.0 \pm 7.0$  years); **height** which was higher in SWs group ( $172.0 \pm 7.0$  cm) than in NSWs group ( $171.0 \pm 7.0$  cm); **weight** which was lower among SWs group ( $73.3 \pm 11.1$  kg) than in NSWs group ( $74.6 \pm 12.6$  kg); **BMI** which was lower in SWs group ( $24.9 \pm 3.6$  kg/m<sup>2</sup>) than in NSWs group ( $25.5 \pm 4.0$  kg/m<sup>2</sup>); **waist circumference** which was lower in SWs group ( $88.0 \pm 10.0$  cm) than in NSWs group ( $90.0 \pm 12.0$  cm); **neck circumference** which was lower in SWs group ( $37.0 \pm 2.0$  cm) than in NSWs group ( $38.0 \pm 3.0$  cm); **years of working** which was non significantly higher in SWs group ( $7.0 \pm 6.0$  years) than in NSWs group ( $5.0 \pm 4.0$

years); **systolic BP** which was higher in SWs group ( $114.7 \pm 5.2$  mmHg) than in NSWs group ( $114.3 \pm 5.8$  mmHg); and **diastolic BP** which was higher in SWs group ( $74.1 \pm 4.0$  mmHg) than in NSWs group ( $73.8 \pm 4.5$  mmHg) ( $t= 0.278$ ;  $df= 56$ ;  $p= 0.782$ ).

**Table 2.** Comparing age, anthropometric data, years of working, systolic blood pressure (BP), and diastolic BP between the non-shift workers and the shift workers.

VARIABLE	NON-SHIFT WORKERS (NSWS)	SHIFT WORKERS (SWS)	VALUE OF T	DF	P VALUE
	Mean $\pm$ SD	Mean $\pm$ SD			
Age/years	32.0 $\pm$ 7.0	31.0 $\pm$ 8.0	0.446	58	0.657
Height/cm	171.0 $\pm$ 7.0	172.0 $\pm$ 7.0	-0.303	58	0.763
Weight/kg	74.6 $\pm$ 12.6	73.3 $\pm$ 11.1	0.408	58	0.685
Body Mass Index (BMI) kg/m <sup>2</sup>	25.5 $\pm$ 4.0	24.9 $\pm$ 3.6	0.563	58	0.576
Waist circumference/cm	90.0 $\pm$ 12.0	88.0 $\pm$ 10.0	0.695	58	0.490
Neck circumference/cm	38. $\pm$ 3.0	37.0 $\pm$ 2.0	1.049	58	0.298
Duration of working/years	5.0 $\pm$ 4.0	7.0 $\pm$ 6.0	-0.871	58	0.387
Systolic BP/ mmHg	114.3 $\pm$ 5.8	114.7 $\pm$ 5.2	-0.240	56	0.812
Diastolic BP/ mmHg	73.8 $\pm$ 4.5	74.1 $\pm$ 4.0	-0.278	56	0.782

As shown in Table 3 serum **fasting glucose level** was not significantly lower in SWs group ( $93.0 \pm 7.0$ ) than in NSWs group ( $95.0 \pm 11.0$ ) ( $t= 0.642$ ;  $df= 58$ ;  $p= 0.524$ ). Serum **fasting insulin level** was significantly higher in SWs group ( $5.2 \pm 0.8$ ) than in NSWs group ( $3.2 \pm 0.9$ ) ( $t= 9.175$ ;  $df= 58$ ,  $p$ -value= 0.0001), and **HOMA-IR index** was significantly higher in SWs group ( $1.18 \pm 0.2$ ) than in NSWs group ( $0.73 \pm 0.2$ ) ( $t = -8.804$ ;  $df= 58$ ,  $p= 0.0001$ ).

**Table 3.** Comparing lab results between the non-shift workers and the shift workers.

LAB RESULTS	NON-SHIFT WORKERS (NSWS) MEAN ± SD	SHIFT WORKERS (SWS) MEAN ± SD	T	DF	P
Fasting Glucose/mmol/L	95.0 ± 11.0	93.0 ± 7.0	0.642	58	0.524
Fasting Insulin/uIU/mL	3.2 ± 0.9	5.2 ± 0.8	-9.175	58	0.000
HOMA- IR/uIU/mL	0.73 ± 0.2	1.18 ± 0.2	-8.804	58	0.000

### DISCUSSION

Clinical data on the relationships between the shift/night work and MS has been published in recent years (Shah *et al.*, 2022). The relationships between SW and MS, diabetes, and dyslipidemia are the subjects of these investigations.

The current study showed no significant difference between SWs group and NSWs group in all of the following: The socio-demographic data (Marital status, education, residence), years of working, family medical history (HTN, DM, CVD), anthropometric measures (age, height, weight, waist circumference, neck circumference, BMI), smoking habits, and physical activity level.

Previous research has yielded partially inconsistent findings, particularly regarding the relationship between body mass index (BMI) and circadian misalignment. For instance, shift work (SW) has been associated with increased BMI in individuals with pre-diabetes, untreated individuals with existing T2DM, and female nurses engaged in SW, although the increase in BMI among the nurses was observed only after 1000 nights of work (Borrueal *et al.*, 2014). Another study indicated that circadian misalignment resulting from shift or night work, which disrupts the synchronization between endogenous and behavioral cycles, may impact metabolic parameters such as BMI and waist circumference (Schettini *et al.*, 2023).

The present study focused on male workers in the industrial sector, with half of the sample comprising shift workers and the other half non-shift workers. A significant difference was noticed between the two groups in both fasting serum

insulin levels and HOMA-IR index. These findings suggest that shift work may impact IR and contribute to the development of MS in males.

Similar findings were reported by Nagaya and associates. (2002), who identified a relationship between MS and shift work in labors under the age of 50. Furthermore, these current findings align with a study which investigated the potential link between SW and the HOMA-IR index in professional vehicles drivers. The study concluded that SW can be a risk factor for the development of MS and IR. (Sadeghniaat-Haghighi *et al.*, 2022). Similar results were observed in a cross sectional study conducted on working employees in Jordan University Hospital where night-shift workers showed higher levels of HOMA-IR index compared with daytime workers (Akour *et al.*, 2017). The current findings was in agreement with those of another study which noticed that rotating shift workers had more chances of developing MS than other types of workers (Khosravipour *et al.*, 2021).

However, our results revealed no significant difference in serum fasting glucose levels among the two groups. This was in disagreement with a study conducted on healthcare shift and non-shift workers which revealed a highly significant difference in fasting serum glucose levels between the two groups (Ledda *et al.*, 2019). A possible explanation for these differences regarding serum fasting glucose levels among the two studies may be related to the fact that the shift workers in the present investigation were rotatory shifted to the morning shift, four days before the blood samples were collected.

A study conducted by Wefers *et al.* (2018) demonstrated that shift work (SW) leads to circadian misalignment, which significantly reduces muscle insulin sensitivity. Previous epidemiological investigations have also indicated an increased risk of developing T2DM among individuals working at night (Leong, 2018). Additionally, animal models with disruptions in clock genes specifically in the liver or muscles have shown an increased susceptibility to metabolic syndrome (MS).

However, the metabolic consequences of circadian misalignment in human skeletal muscles remain largely unknown (Wefers *et al.*, 2018).

It should be noted that there were certain restrictions on this study. Firstly, the sample size was small. Secondly, it failed to take non shift workers' sleep issues into account, as well as the influence of physical activity level and job stress.

### **CONCLUSIONS AND RECOMMENDATIONS**

In conclusion, SWs had a significantly higher fasting insulin level as well as higher values of HOMA-IR index than NSWs. It is recommended to assess any potential associations between IR and clock gene expression in future research, and to study the effect physical activity level and/or eating behavior on IR and SW. It is also suggested to make further comprehensive studies on a large sample of workers, especially those working in heavy industries. A self-controlled-study design is recommended, where shift workers are studied during night shift weeks, and then re-examined during day shift weeks, and then compare the results with that of the control group (Non shift workers), so that the small sample size problem may be overcome, since the confounding factors will be controlled.

### **FUNDING**

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### **CONFLICT OF INTEREST**

The authors affirm that they have no financial or personal conflicts of interest that might influence the findings presented in this study.

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## نموذج التماثل الساكن لمقاومة الأنسولين في عمال المصانع العاملين بنظام الورديات - دراسة أولية

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### المستخلص

هناك أدلة دامغة تشير إلى وجود علاقة محتملة بين العمل بنظام الورديات ومقاومة الأنسولين. ومن ثم، فمن المهم أن يتم تقييم هذا العامل في التدخلات العلاجية والوقائية. في دراسة مقطعية مقارنة، تم قياس مستويات الجلوكوز في الدم أثناء الصيام، ومستويات الأنسولين في الدم أثناء الصيام، ثم فحص مؤشر تقييم نموذج التماثل الساكن لمقاومة الأنسولين بين عمال المناوبات الصناعية. في هذه الدراسة شمل إطار المراقبة المهنية 60 عاملاً صناعياً؛ من بين هؤلاء، كان 30 من العمال يعملون بنظام الورديات و30 كانوا من العاملين غير العاملين بنظام الورديات. تم قياس نسبة السكر في الدم أثناء الصيام لكل مشارك وقياس مستوى الأنسولين في أثناء الصيام. ثم تم قياس نسبة مؤشر نموذج التماثل الساكن لمقاومة الأنسولين بحثاً عن صلة محتملة مع العمل بنظام الورديات. كانت مستويات الأنسولين في الدم أثناء الصيام، وهو مقياس لاستقلاب الجلوكوز، بالإضافة إلى مستوى نموذج التماثل الساكن لمقاومة الأنسولين أعلى بكثير في العمال العاملين بنظام الورديات. ووفقاً لذلك، قد يؤدي العمل بنظام الورديات إلى زيادة خطر الإصابة بمقاومة الأنسولين. الكلمات المفتاحية: مرض السكري؛ مقاومة الأنسولين؛ عمال؛ عمل ليلي؛ العمل بنظام الورديات؛ إيقاع الساعة البيولوجية.