Review Article

Effect of Rotating Shift on Biomarkers of Metabolic Syndrome and Inflammation among Health Personnel in Gaza Governorate

Running title:

Shift work and metabolic syndrome

ABSTRACT

Background: Shift work has been hypothesized to associate with increase the risk of metabolic syndrome (MetS). It is a complicated syndrome that demonstrated as a common precursor for developing cardiovascular diseases and/or type 2 diabetes mellitus. The study was conducted to estimate the prevalence of MetS among health personnel and to examine the effect of rotating shift work on biomarkers of MetS and inflammation.

Methods: A comparative analytical cross-sectional study was conducted on a sample of 310 health care personnel, 100 current daytime workers compared with 210 rotating shift workers. A questionnaire on socio-demographic (sex, age, marital status, job), health-related behaviors such as physical activity) and occupational history about shift work, health examination including anthropometric and arterial blood pressure measurements, and laboratory investigations. We used the Adult Treatment Protocol III National Cholesterol Education Programme of America (ATPIII) indicators for diagnosis and determination of MetS. Statistical analysis was performed using SPSS version 20.

Results: The overall prevalence of MetS among healthcare workers was 8.4% (9.0% among current daytime workers and 8.1% among rotating shift workers) without significant difference between males and females, and shift category. The most frequently altered component among healthcare workers was elevated C- reactive protein (44.5%), followed by high triglyceride (35.5%), increased total cholesterol (24.8%), and elevated BMI>30 (20.6%). The main risk factors for MetS in both sexes among rotating shift workers in descending order were as follow: high Blood pressure (OR = 59.5; 95% CI, 16.4- 215.8), high fasting blood sugar (OR= 43.9; 95% CI, 12.9- 149.1), high triglyceride (OR = 42.3; 95% CI, 5.5- 326.6), obesity (elevated body mass index >30) (OR = 11.8; 95% CI, 4- 34.6), and low level of high-density lipoprotein cholesterol (HDL) (OR = 1.6; 95% CI, 0.3- 6.1).

Conclusion: MetS was prevalent among health care personnel in Gaza Strip, with a steady increase in its prevalence through age and BMI. There was no direct relationship between shift category and the occurrence of MetS and inflammation, other factors as genetic, lifestyle factors, the job itself may have more effects on the occurrence than shift category.

Keywords: Metabolic syndrome, current daytime workers, rotating shift workers, inflammation, risk factors.

1. INTRODUCTION

Metabolic syndrome (MetS) is multifaceted syndrome that usually occurs in general population, mainly in adults over 50 years of age [1]. This syndrome has been described as a ‘‘clustering’’ of multiple risk factors for cardiovascular disease (CVD) [2, 3] such as hypertension (HTN), dyslipidemia specifically high triglycerides (TG), low levels of high-density lipoprotein (HDL), and increased small dense low-density lipoprotein (LDL), obesity (particularly central or abdominal obesity), insulin resistance, and impaired glucose tolerance (IGT) or diabetes mellitus (DM) [4]. MetS was also known as syndrome X, cardio metabolic syndrome, insulin resistance syndrome, Reaven’s syndrome, CHAOS (an abbreviation for coronary artery disease, hypertension, atherosclerosis, obesity, and stroke) [5, 6]. Patients with MetS have a twofold increased risk of mortality from coronary heart disease (CHD) [7].

The increased prevalence of MetS has been attributed to changes in lifestyle, particularly with regard to new eating patterns and sedentarism [8, 9]. However, modern life has also brought changes to the work environment. Working hours that occurred during the daytime were extended in the last decades for a large number of services and production areas [10].

The vast majority function of the circadian system is the internal cycling of physiological and metabolic events [11]. In fact, many physiological processes display day–night rhythms, in addition to lipid and carbohydrate metabolism and blood pressure (BP) are subject to daily variation.

The circadian rhythm and environmental conditions may become asynchronous in rotating shift workers whose night activity is out of leading to desynchronization of the normal phase relationships between biological rhythms within the circadian system [12].

Recent epidemiological studies have reported an association between inflammation and thrombogenesis as a cause for CVD in patients suffering from the MetS [13].

In addition, several studies have shown a positive relationship between elevated leukocyte count and risk of CHD suggesting that leukocyte count is related with metabolic and hemodynamic diseases typical of the MetS [14].

To that end, we aimed to find out the prevalence of MetS among rotating shift workers and to explore the effect of rotating shift work schedule on biomarkers of MetS and inflammation among Palestinian medical staff working in Gaza-governorate hospitals. According to our best knowledge and published literature there is no studies in Gaza investigated the prevalence of MetS and its biomarkers among healthcare workers and the potential effect of rotating shift work on MetS and inflammation biomarkers.

2. MATERIALS AND METHODS

2.1 Study design

This study is quantitative approach; the design is comparative analytical cross sectional that use to determine the prevalence and effect of rotating shift work on biomarkers of MetS and inflammation. A cross sectional study is usually rapid, quick, cheap, and easily undertaken. It is generally carried out at a point of time or over a short period. In addition, it gives more insight into the association between variables in the study. However, it is limited by the fact that it is carried out at one point and gives no indication of the sequence of events whether exposure occurred before, after or during the onset of the disease outcome. This being so, it is impossible to infer causality [15].

2.2 Study setting

This study was conducted in two governmental hospitals, Al-Shifa Hospital (ASH) and Al- Nassir Pediatric Hospital (ANPH). The researchers chose these hospitals for several reasons including the following: the ASH hospital is the largest and general hospital in the Gaza strip, has the largest number of rotating shift health care workers (approximately 714), and is located in the Gaza city. ANPH hospital is one of the main general pediatric hospitals that located in the Gaza city and has nearly 141 rotating shift health care workers.

2.3 Study population

The study population consisted of health care workers who work in these aforementioned selected hospitals in total 1474 healthcare workers (1268 from ASH and 206 from ANPH) including physicians (470 from ASH, 55 from ANPH), nurses (680 from ASH, 120 from ANPH), medical technologists, radiologists, and radiologic technologists (118 from ASH, 31 from ANPH).

2.4 Eligibility criteria

2.4.1 Inclusion criteria

It included rotating night shift and daytime health care workers (male and female) in ASH and ANPH hospitals.

2.4.2 Exclusion criteria

1- Permanent night shift health care workers at the selected hospitals.
2- Health care workers with previous T2DM, CVD, and inflammatory disease.
3- Health care workers with type1 diabetes mellitus.
4- Health care workers with familial hyperlipidemia.

2.5 Period of the study

The study took 10 months in execution; it started in April, 2016 and completed by February 2017. This study was initially proposed in April, 2016. The research proposal has been submitted to and defended in the front of SOPH assigned committee in May 2016. At its development, the research proposal described the entire process and provided information and design of the data collection and data analysis methods and tools. Upon the approval, the researchers prepared the required tools of his study in addition to the demographic question. The researchers has consulted a group of 12 experts at arbitration stage before the finalization of the tool. The arbitration stage lasted for two weeks including refining of tools in the light of reviewers and the academic supervisor's feedback.

In October 2016, the tool was ready to go for data collection. Piloting took place between 2 and 6 October 2016. Actual data collection started on 16 October through 30November 2016. The researchers identified daily work hours to start at 07.15 am through 01.00 pm in order to increase the likelihood of distributing the questionnaires as many participants as possible.

Initial analysis of quantitative data was done between December 2016 - January 2017. The researchers extracted findings, created descriptive tables and performed inferential statistical analysis. The drafted report "thesis" has been frequently enriched and edited by the research supervisor. The final draft for defense was handed on 30 March, 2017.

2.6 Sampling

The sampling frame was from the governmental hospitals (Al- Shifa Hospital and Al- Nassir Pediatric Hospital).

Convenient sampling method was proposed because the mentioned hospitals consider the main and largest hospitals and nearly has the largest number of health care workers.

2.7 Sample size and sample process

In order to calculate the required sample, the researchers gathering the needed data. The researchers used Epi –Info version 7 to calculate the sample size, the number of all healthcare workers (physicians, nurses, radiologists, radiologic technologists and, medical technologists) work at ASH and ANPH are nearly 1474. The highest estimate of sample size was when both categories exposed and non-exposed reporting the outcome with 50%, and by considering the confidence interval was 95%, the power was 80, so the sample size was 305 health care workers. To overcome non-respondents, 310 health care workers were including in the study. The sampling of Self-administering questionnaire includes two governmental hospitals in the Gaza Strip (ASH and ANPH), then proportional sample was chosen from each health care workers in the two selected hospitals according to their number.

2.8 Research instrument

In this study the researchers used 2 main types of instruments:

2.8.1 Direct instrument

• Self-administering questionnaire

Self-administering questionnaire administered to health care worker in the selected hospitals. Most questions were the yes/no questions, which offer a dichotomous choice. The questionnaire includes questions on the personal data (sex, age, marital status, job). The questions covered social data, demographic data to detect the presence of diseases as HTN, CHD, DM and inflammation, lifestyle variables such as (physical activity, and the occupational history including questions about shift work.

2.8.2 Laboratory investigations and clinical tests

• Biochemical tests were measured from serum sample using chemistry kits in spectrophotometer including:

1- Triglyceride
2- HDL, LDL, Cholesterol
3- Fasting Blood glucose
4- CRP

• CBC

• Anthropometric measurements including:

– Length
– Weight

• Blood pressure

2.9 Data and sample collection

Data collection is defined as the precise, systematic gathering of information related to the research purpose or specific objectives, questions, or hypothesis of the study [16]. The health examinations included anthropometric measurements, a questionnaire on health-related behaviors and biochemical determinations, information about the years of work, either shift work or day work duration and past medical history was included. Overnight fasting for at least 10 hours required prior to blood sampling for all participants who agreed to be included in the study. Venous blood samples (5 ml) were collected from the fasting individuals in serum vacutainer tubes without anticoagulant, and EDTA tubes for CBC test under quality control and safety procedure. The serum was separated from blood samples by centrifugation at 3500-4000 rpm for 10 min. The separated serum was placed in new plain tubes and sealed for biochemical analysis. Blood in EDTA tube was used to measure leukocyte count and its differential count.

2.10 Diagnostic criteria for the MetS

For the diagnostic criteria of MetS, we used the NCEP/ ATPIII definition. The syndrome was met if an individual had three or more criteria:

1- Waist circumference >102cm in men and >88cm in women

2- Fasting plasma glucose ≥110mg/dl.

3- Blood pressure ≥130/85 mmHg

4-Serum triglycerides ≥ 150mg/dl

5-Serum HDL cholesterol <40mg/dl in male and <50mg/dl in female.

Because the participants refused to measure the WC, we measured the BMI instead of it for obesity, in which the participant considered obese if BMI >30.

2.11 Ethical and administrative consideration

The researchers committed to all ethical considerations required to conduct research which include:

- An official letter of approval was obtained from public health school at Al Quds University.
- An official letter of request was obtained from the general director of Ministry of Health in Gaza Strip.
- An official letter of approval to conduct this study was obtained from the Helsinki Committee in the Gaza Strip.
- To guarantee participants rights, a covering letter indicating that the participation is voluntary and the right to refuse was preserved.
- The confidentiality of the responses from the respondents was assured by explaining how the information shall be recorded and used.

2.12 Pilot study

Before starting the actual data collection process, a pilot study of 20 health care workers outside the selected clinics was done prior to the beginning of data collection to check applicability, identify problems in research questionnaire of data collection for validity and reliability. Pilot study was used to examine the clarity and ambiguity, length and suitability of questions before the data collection process starts [17].

2.13 Data entry

After checking and reviewing all filled questionnaires on the same way, data were entered in the computer using SPSS (Statistical Package for Social Science) software version 20 to be analyzed. After finishing the data entry process, check codes were used to avoid double entries. Pretesting of the tools

were done to eliminate inconsistencies and made the questions relate to the local settings. Data cleaning were done to account for missing values in a bid to ensure integrity and reliability.

2.14 Statistical analysis

- Statistical Package for the Social Science (SPSS, version 20) was used for data processing and analysis.
- Description of variables was presented as follows:
- Data were normally distributed, as determined using Kolmogorox-Smirnov test.
- Description of quantitative variables were presented as the following: Normally distributed data were expressed as mean ± SD.
- Description of qualitative variables was in the form of numbers (No.) and percent (%).
- Comparison between quantitative variables was carried out by student T-test of two independent samples. Results were expressed in the form of P-values.
- Comparison between qualitative variables was carried out by Chi-Square test (χ^2). Fisher exact test was used instead of Chi- square test when one expected cell or more were ≤ 5.
- Binary correlation was carried out by Spearman correlation test. Results were expressed in the form of correlation coefficient (R) and P-values. The following points are the accepted guidelines for interpreting the correlation coefficient:
    - 0 indicates no linear relationship.
    - +1 indicates a perfect positive linear relationship: as one variable increases in its values, the other variable also increases in its values via an exact linear rule.

4. RESULTS

The represented sample of the health care workers included in the study was 310 healthcare workers who were distributed in regard to selected hospitals and socio-demographic characteristics including, gender, marital status, age, job, governorate, as shown in Table 4.1. The study sample consisted of 310 healthcare workers who work at ASH and ANPH in the Gaza Strip, where (100) were currently daytime workers (32.3%), and (210) were rotating shift workers (67.7%). The socio-demographic characteristics of participants were depicted in table (4.1).

Table (0.1): Distribution of the study population by socio demographic characteristics (N= 310)

Variable	Category	Current daytime workers (N=100, 32.3%)		Rotating shift workers (N=210, 67.7%)		Total (N=310, 100%)	
		N	%	N	%	N	%
Gender	Male	56	56.0%	156	74.3%	212	68.4%
	Female	44	44.0%	54	25.7%	98	31.6%
Marital status	Single	19	19.0%	48	22.9%	67	21.6%
	Married	81	81.0%	162	77.1%	243	78.4%
Age	30 years & less	17	17.0%	99	47.1%	116	37.4%
	31-40 years	31	31.0%	68	32.4%	99	31.9%
	41 years & above	52	52.0%	43	20.5%	95	30.6%
Job	physicians	31	31.0%	91	43.3%	122	39.4%
	Practical nursing	51	51.0%	105	50.0%	156	50.3%
	Radiologists, radiologic technologists, and medical technologists	18	18.0%	14	6.7%	32	10.3%
Governorate	North	13	13.0%	30	14.3%	43	13.9%
	Gaza	72	72.0%	147	70.0%	219	70.6%
	Middle zone	14	14.0%	29	13.8%	43	13.9%
	Khan Younis	1	1.0%	3	1.4%	4	1.3%
	Rafah	0	0.0%	1	.5%	1	.3%

A total of 310 healthcare workers who work at ASH and ANPH in the Gaza Strip were included in this study, where (100) were currently daytime workers (32.3%), and (210) were rotating shift workers (67.7%). The socio-demographic characteristics of participants were depicted in table (4.1). The majority of daytime and rotating shift workers were males and married with percent (56.0%vs.74.3%), (81.0%vs.77.1%) respectively. A greater part of daytime workers were 41 years and above (52.0%), however 47.1% of rotating shift workers were 30 years and less.

According to the profession, 51.0% of daytime workers were practical nursing, 31.0% were physicians, while 18.0% were radiologists, radiologic technologists, and medical technologists, and for the rotating shift workers, 50.0% were practical nursing, 43.3% were physicians, while 6.7%, were radiologists, radiologic technologists, and medical technologists. Most daytime and rotating shift workers from Gaza with percent of (72.0% vs.70.0%) respectively, while (13.0% vs.14.3%) respectively from North

area, and (14.0% vs. 13.8%) from middles zone respectively. Only (1.0% vs.1.4%) were from Khan Younis.

Table (0.2): Relationship between the different risk factors and shift category among daytime and rotating shift healthcare workers (N=310)

Risk factors	Level	Current daytime workers (N=100, 32.3%)		Rotating shift workers (N=210, 67.7%)		Total (N=310, 100%)		Chi-Square (x^2)	OR	95% CI	*P*-value
		N	%	N	%	N	%				
BMI >30 (Obese)	No	73	73.0%	173	82.4%	245	79.4%	3.64	0.6	0.3-1.0	0.056
	Yes	27	27.0%	37	17.6%	64	20.6%		0.7	0.4-1.2	0.172
Blood pressure (BP) (mmHg)	<130/85	84	84.0%	187	89.0%	271	87.4%	1.57	0.7	0.3-1.3	0.210
	≥130/85	16	16.0%	23	11.0%	39	12.6%		1.6	0.8-3.1	0.210
Fasting blood sugar (FBS) (mg/dl)	<110	83	83.0%	188	89.5%	271	87.4%	2.62	1.8	0.9-3.5	0.105
	≥110	17	17.0%	22	10.5%	39	12.6%		0.6	0.3-1.1	0.105
T. Cholesterol (TC) (mg/dl)	< 200	67	67.0%	166	79.0%	233	75.2%	5.27	0.5	0.3-0.9	0.022*
	≥200	33	33.0%	44	21.0%	77	24.8%		1.9	1.1-3.2	0.022*
Triglyceride (TG) (mg/dl)	Normal	59	59.0%	141	67.1%	200	64.5%	1.96	0.7	0.4-1.2	0.161
	Abnormal	41	41.0%	69	32.9%	110	35.5%		1.4	0.9-2.3	0.161
High density lipoprotein (HDL-C) (mg/dl)	Normal	82	82.0%	193	91.9%	275	88.7%	6.64	0.4	0.2-0.8	0.010*
	Abnormal (decreased)	18	18.0%	17	8.1%	35	11.3%		2.5	1.2-5.1	0.010*
low density lipoprotein (LDL-C) (mg/dl)	Normal	70	70.0%	182	86.7%	252	81.3%	12.37	0.4	0.2-0.6	0.001*
	Abnormal (increased)	30	30.0%	28	13.3%	58	18.7%		2.8	1.6-5.0	0.001*
C- Reactive Protein (CRP)	Normal	48	48.0%	124	59.0%	172	55.5%	3.35	0.6	0.4-1.0	0.067
	Abnormal	52	52.0%	86	41.0%	138	44.5%		1.6	1.0-2.5	0.067
Leukocyte count	Normal	51	100.0%	249	96.1%	300	96.8%	0.99	-	-	0.321
	Increased	0	0.0%	10	3.9%	10	3.2%		-	-	
Neutrophil count	Normal	50	98.0%	253	97.7%	303	97.7%	0.13	-	-	0.719
	Increased	1	2.0%	6	2.3%	7	2.3%		-	-	
Lymphocyte count	Decreased	0	0.0%	1	0.4%	1	0.3%	0.82	-	-	0.365
	Normal	51	100.0%	258	99.6%	309	99.7%		-	-	
Metabolic syndrome	Absent	91	91.0%	193	91.9%	284	91.6%	0.07	0.9	0.4-2.1	0.788
	Present	9	9.0%	17	8.1%	26	8.4%		1.1	0.5-2.6	0.788

** Significant at 0.05*

Our findings demonstrated that 8.4% of health personnel had MetS with higher prevalence among day worker 9.0% than rotating shift workers 8.1%, with no statistical relationship ($\mathbf{x^2}$= 0.07, *P*-value>0.05) between MetS and shift category, which mean that daytime and rotating shift workers had the same opportunity to have MetS.

The most common abnormalities among study population in our study were as follow: elevated CRP, high level of TG, elevated level of TC, increased BMI >30, high level of LDL-C, increased FBS and BP, and low HDL-C, increased WBC count, increased neutrophil count, and decreased lymphocyte count with 44.5%, 35.5%, 24.8%, 20.6%, 18.7%, 12.6%, and 11.3%, 3.2%, 2.3%, 0.3% respectively. This study was the first that explored the prevalence and the effect of rotating shift on biomarkers of MetS and inflammation among health personnel in the Mediterranean countries.

The relationship between shift category and the related risk factors were studied. Table (4.2) showed that 27.0% of daytime workers were obese (BMI > 30) vs. 17.6% of rotating shift workers, without statistical relationship ($\mathbf{x^2}$= 3.64, *P*-value> 0.05). For FBS, 17.0% of the daytime workers had elevated FBS vs. 10.5% in rotating shift workers with no statistical relationship ($\mathbf{x^2}$= 2.62, *P*-value>0.05). Also16.0% of the daytime workers had elevated BP vs. 11.0% of rotating shift workers without statistical relationship ($\mathbf{x^2}$= 1.57, *P*-value > 0.05).

Also, the study revealed that 33.0% of the daytime workers had elevated cholesterol, while 21.0% from the rotating shift workers had elevated cholesterol, with statistically significant difference, (OR=1.9, 95% CI= 1.1-3.2). For TG, 41.0% of the daytime workers had elevated TG vs. 32.9% of the rotating shift workers with no statistical relationship ($\mathbf{x^2}$= 1.96, *P*-value>0.05). As well as 18.0% of the daytime workers had low level of HDL vs. 8.1% of rotating shift workers, and the difference was statistically significance (*P* = 0.010).

About 30.0% of daytime workers had high LDL while 13.3% of the rotating shift workers had elevated LDL with statistical relationship, (OR= 2.8, 95% CI=1.6-5.0). Finally, 52.0% of daytime workers had elevated CRP vs. 41.0% of rotating shift workers without statistical relationship (*P*-value>0.05). Moreover, there were no statistical differences in the CBC results including WBC and its differential counts between daytime and rotating shift workers. Our results showed that the obesity in daytime workers was higher than in current shift workers.

Table (0.3): Prevalence of MetS by age and work category (N=310)

Work category	variable	Category	Metabolic syndrome						OR	95 % CI	*P*-value
			Present		Absent		Total				
			N	%	N	%	N	%			

Daytime workers	Age	30 years & less	0	0.0%	17	18.7 %	17	17.0%	-	-	-
		31-40 years	3	33.3 %	28	30.8 %	31	31.0%	1.1	0.3-4.8	0.874
		41 years & above	6	66.7 %	46	50.5 %	52	52.0%	2.0	0.5-8.3	0.356
		Total	9	9.0%	91	91.0 %	100	100.0 %	(Fisher-exact x^2=1.78, *p*-value=0.512)		
Rotating shift workers	Age	31 years & less	1	5.9%	98	50.8 %	99	47.1%	0.1	0-0.5	0.001 *
		31-40 years	8	47.1 %	60	31.1 %	68	32.4%	2.4	0.8-62	0.117
		41 years & above	8	47.1 %	35	18.1 %	43	20.5%	4.5	1.6-12.9	0.002 *
		Total	17	8.1%	193	91.9 %	210	100.0 %	(Fisher-exact x^2=15.53, *p*-value=0.001*)		

** Significant at 0.05*

According to our results, in the daytime workers and shift workers, respectively, MetS increased from 0% and 5.9% within less than 30-year-old group to 66.7% and 47.1% in the participants of more than 41 years of age. There was a statistically significant relationship (*p*-value<0.05) between MetS and age (30 years & less, 31- 40 years, 41 years & above) among rotating shift workers. In addition, for rotating shift workers the result showed that the ratio of having MetS for 41 years and above equals 4.5 times of other age groups and their percent of susceptible ranging between 1.6 to 12.9 times.

Table (0.4): Relationship between metabolic syndrome and previously exposed night shifts among both groups (N=310)

Work category	Variable	Category	Metabolic syndrome						OR	95% CI	*P*-value
			Present		Absent		Total				
			N	%	N	%	N	%			
Daytime workers	Years	not exposed	1	11.1%	16	17.6%	17	17.0%	0.6	0.1-5.0	0.622
		1-5 years	2	22.2%	19	20.9%	21	21.0%	1.1	0.2-5.6	0.925
		more than 5 years	6	66.7%	56	61.5%	62	62.0%	1.3	0.3-5.3	0.762
		Total	9	100.0%	91	100.0%	100	100.0%	(Fisher-exact x^2=0.25, *p*-value=0.999)		
Rotating shift	Years	not exposed	0	0.0%	5	2.6%	5	2.4%	-	-	-

workers	1-5 years	3	17.6%	83	43.0%	86	41.0%	0.3	0.1-1.0	0.042*
	more than 5 years	14	82.4%	105	54.4%	119	56.7%	3.9	1.1-14.0	0.026*
	Total	17	100.0%	193	100.0%	210	100.0%		((Fisher-exact x^2=4.57, *p*-value=0.099)	

* Significant at 0.05

Table (4.4) showed that 66.7% of the daytime workers who have MetS had been exposed to night shifts previously for more than 5 years without statistical significant relationship vs. 82.4% in the rotating shift workers with statistical significant relationship (*P*-value= 0.026 OR= 3.9, 95% CI= 1.1-14), this mean that rotating shift workers who have night shifts more than 5 years have four times to have MetS than workers who had night shifts less than 5 years, while 22.2% of daytime workers who have MetS had been exposed to night shifts previously from one year to five years without statistical relationship vs. 17.6% in the rotating shift workers and the difference was statistical significance (*P*- value= 0.042) between MetS and the exposed night shifts among rotating shift workers.

Table (0.5): Relationship between elevated CRP and previously exposed night shifts among day and shift workers (N=310)

Work category	Variable	Category	CRP						OR	95% CI	*P*-value
			Elevated		Normal		Total				
			N	%	N	%	N	%			
Daytime workers	Years	not exposed	5	9.6%	12	25.0%	17	17.0%	0.3	0.1-1.0	0.040*
		1-5 years	8	15.4%	13	27.1%	21	21.0%	0.5	0.2-1.3	0.151
		more than 5 years	39	75.0%	23	47.9%	62	62.0%	3.26	1.4-7.6	0.005*
		Total	52	100.0%	48	100.0%	100	100.0%	(Fisher-exact x^2=7.95,*p*-value=0.018*)		
Rotating shift workers	Years	not exposed	1	1.2%	4	3.2%	5	2.4%	0.4	0-3.2	0.335
		1-5 years	34	39.5%	52	41.9%	86	41.0%	0.9	0.5-1.6	0.728
		more than 5 years	51	59.3%	68	54.8%	119	56.7%	1.2	0.7-2.1	0.572
		Total	86	100.0%	124	100.0%	210	100.0%	(Fisher-exact x^2=1.01,*p*-		

value=0.598)

** Significant at 0.05*

According to the results presented in table (4.5), most of daytime and rotating shift workers who have elevated CRP had been exposed to night shifts for more than 5 years (75.0%, and 59.3%) respectively, with statistically significant relationship among day workers (OR=3.26, 95% CI =1.4-7.6), but the differences did not reach the statistical significance among rotating shift workers (*P* =0.572), this may related to their ages (mean of their age was 33.2) and we know that CRP affected by age after 40 years.

Table (0.6): Prevalence of different factors that define metabolic syndrome (According to ATPIII definition) and inflammation among current daytime workers (N= 100)

Components of MetS	Level	Metabolic syndrome						OR	95% CI	*P*- value
		Present		Absent		Total				
		N	MetS%	N	%	N	%			
FBS (mg/dl)	**≥110**	5	55.6%	12	13.2%	17	17.0%	8.2	1.9-35.0	0.001*
	<110	4	44.4%	79	86.8%	83	83.0%	0.1	0-0.5	0.001*
BP (mmHg)	**≥130/85**	6	66.7%	10	11.0%	16	16.0%	16.2	3.5-75.1	0.001*
	<130/85	3	33.3%	81	89.0%	84	84.0%	0.1	0-0.3	0.001*
Obesity (BMI > 30)	**Yes**	6	66.7%	21	23.1%	27	27.0%	6.7	1.5-29.0	0.005*
	No	3	33.3%	70	76.9%	73	73.0%	0.2	0-0.7	0.005*
TG (mg/dl)	**≥150**	8	88.9%	33	36.3%	41	41.0%	14.1	1.7-117.4	0.002*
	<150	1	11.1%	58	63.7%	59	59.0%	0.1	0-0.6	0.002*

HDL-C (mg/dl)	**<50 for women < 40 for men (Abnormal)**	4	44.4%	14	15.4%	18	18.0%	4.4	1.1-18.4	0.030*
	> 50 for women > 40 for men (Normal)	5	55.6%	77	84.6%	82	82.0%	0.2	0.1-1.0	0.030*
CRP (mg/L)	**Abnormal**	4	44.4%	48	52.7%	52	52.0%	0.7	0.2-2.8	0.634
	Normal	5	55.6%	43	47.3%	48	48.0%	1.4	0.4-5.5	0.634

* Significant at 0.05

From table (4.6) the researchers computed the odds ratio and the confidence interval of daytime workers with MetS, by comparing the measurement of each component of the MetS for the normal and the abnormal level. In our study, 55.6% of participants with high-level of FBS had MetS vs. 44.4% with normal FBS, this difference was statistically significant (OR = 8.2, 95% CI =1.9-35.0). For Bp, 66.7% of daytime workers who had high Bp had MetS vs. 33.3% with normal Bp and the difference was statistically significant, (OR= 16.2, 95% CI = 3.5-75.1).

Moreover, 66.7% of daytime workers with BMI>30 had MetS vs. 33.3% with BMI <30 and the difference were statistically significant OR 6.7 CI 95% (1.5-29.0), then the study showed that 88.9% of daytime workers with high TG had MetS vs. 11.1% with normal level of TG OR (95% CI) 14.1 (1.7-117.4). Additionally, 44.4% with low level of HDL cholesterol had MetS vs. 55.6% with normal level, and the difference reached a statistically significant level (*P*= 0.030). Finally, 44.4% of participant with elevated CRP had MetS vs. 55.6% with normal level but the difference didn't reach the statistically significant level (*P*= 0.634).

We concluded that the risk factors of MetS among daytime workers based on value of OR in our sample is in descending order were as follow: high BP, high level of TG, high FBS, elevated BMI >30, and low HDL cholesterol level.

Table (0.7): Prevalence of different factors that define metabolic syndrome (According to ATPIII definition) and inflammation among rotating shift workers (N=210)

Components of MetS	**Level**	**Metabolic syndrome**						**OR**	**95% CI**	***P*- value**
		Present		**Absent**		**Total**				
		N	**MetS %**	**N**	**MetS%**	**N**	**%**			
FBS (mg/dl)	**≥110**	12	70.6%	10	5.2%	22	10.5%	43.9	12.9-149.1	0.001*
	<110	5	29.4%	183	94.8%	188	89.5%	0.02	0-0.1	0.001*
BP (mmHg)	**≥130/85**	13	76.5%	10	5.2%	23	11.0%	59.5	16.4-215.8	0.001*
	<130/85	4	23.5%	183	94.8%	187	89.0%	0.01	0-0.1	0.001*

Obesity (BMI >30)	**Yes**	11	64.7%	26	13.5%	37	17.6%	11.8	4.0-34.6	0.001*
	No	6	35.3%	167	86.5%	173	82.4%	0.1	0-0.3	0.001*
TG (mg/dl)	**≥ 150**	16	94.1%	53	27.5%	69	32.9%	42.3	5.5-326.6	0.001*
	<150	1	5.9%	140	72.5%	141	67.1%	0.02	0-0.2	0.001*
HDL-C (mg/dl)	**<50 for women < 40 for men (Abnormal)**	2	11.8%	15	7.8%	17	8.1%	1.6	0.3-6.1	0.562
	> 50 for women > 40 for men (Normal)	15	88.2%	178	92.2%	193	91.9%	0.6	0.1-3.0	0.562
CRP (mg/L)	**Abnormal**	10	58.8%	76	39.4%	86	41.0%	2.2	0.8-6.0	0.118
	Normal	7	41.2%	117	60.6%	124	59.0%	0.5	0.2-1.2	0.118

** Significant at 0.05*

The researchers computed the odds ratio and the confidence interval of rotating shift workers with MetS, by comparing the measurement of each component of the MetS for the normal and the abnormal level table (4.7). In our study 70.6% of participants with high-level of FBS had MetS vs. 29.4% with normal FBS. This difference was found to be statistically significant, (*P*= 0.001, OR = 43.9, 95% CI= 12.9-149.1). For Bp, 76.5% of rotating shift workers who had high Bp had MetS vs. 23.5% with normal Bp had MetS. The difference was statistically significant, (*P*= 0.001, OR=59.5, 95% CI=16.4-215.8). Also, 64.7% of shift workers with BMI>30 had MetS vs. 35.3% with BMI<30 and the difference were statistically significant (*P*= 0.001, OR= 11.8, 95% CI= 4.0-34.6). Then the study showed that 94.1% of shift workers with high TG had MetS vs. only 5.9% with normal level of TG had MetS. Again, these differences were statistically significant where (*P*= 0.001, OR= 42.3, 95% CI=5.5-326.6). Moreover, 11.8% of rotating shift workers with low level of HDL cholesterol had MetS vs. 88.2% with normal level, and the difference didn't reach a statistically significant level. Finally, 58.8% of participant with elevated CRP had MetS vs. 41.2% with normal level but the difference didn't reach the statistically significant level (*P*= 0.118).

We concluded that the risk factors of MetS among rotating shift workers based on value of OR in our sample is in descending order were as follow: high BP, high FBS, high level of TG, elevated BMI >30, and low HDL cholesterol level. They were in the order of risk factors in daytime workers except for FBS and TG (Table 4.6& 4.7).

DISCUSSION

Metabolic syndrome (MetS) is multifaceted syndrome that usually occurs in general population, mainly in adults over 50 years of age [1] Patients with MetS have a twofold increased risk of mortality from coronary heart disease (CHD) [7]. In this study, we find out the prevalence of MetS among rotating shift workers and explore the association between shift work and MetS with further emphasizes on inflammation markers.

Our findings demonstrated that 8.4% of health personnel had MetS with higher prevalence among day worker 9.0% than rotating shift workers 8.1%, with no statistical relationship (P > 0.05) between MetS and shift category, which mean that daytime and rotating shift workers had the same opportunity to have MetS. The results for this study showed that according to NCEP-ATP III criteria, the prevalence of MetS among health personnel who work at ASH and ANPH in Gaza was 8.4% and the prevalence increases as age increases. Studies in Pakistan [18] and Lampang hospital [19] revealed higher rates of 14.95 and 9.5%, respectively than the prevalence of this study. In another study conducted in Ethiopia [20], using the NCEP-ATP III, the overall prevalence of MetS was 12.5 which is higher than our prevalence (8.4%) in this study.

In this study the researchers observed that there were no statistical differences between rotating shift work and the MetS when compared with current day workers. This finding was consistent with a study performed on male workers with rotating three shift works [21], and a study done by Shafei [22]. This could be explained by the positive values that the healthcare workers had such as more exercise, walking during the shift and outside the work as well as fast forward rotation shift schedule practice among rotating shift workers. Fast forward rotation is at this time considered the best in reducing sleep loss and fatigue among shift workers [23], thus reducing other health effects linked with circadian rhythm disruption, also daytime workers were not only involved with their job some of them had administrative job that increased the stress that may involve in the mechanism of MetS. In addition, environmental and genetic factors had been implicated in the development of this syndrome. Older age, sedentary lifestyle, and high-fat diet can increase the prevalence of MetS [24]. This study showed that 27.0% of daytime workers were obese (BMI > 30) vs. 17.6% of rotating shift workers, without

statistical relationship (P-value> 0.05). Our findings were consistent with a study that conducted in Korea on 9,989 female nurses, in which obesity for shift workers and non-shift workers were 5.8% and 9.1 respectively [25]. But it was not consistent with a cross-sectional study from Australia in which nurses who had shift work were 1.15 times more likely to be overweight or obese than day workers [26]. BMI in daytime workers was higher than that in shift workers, which might be influenced by relatively older age of daytime workers, as well as other potential confounding factors.

Also 16.0% of the daytime workers had elevated BP vs. 11.0% of rotating shift workers without statistical relationship (P-value > 0.05). Regarding to elevate BP, our findings were in accordance with cross-sectional survey of a representative sample of 493 nursing staff of a large general hospital in (Hospital São Vicente de Paulo). Passo Fundo, Brazil [27]. Their results showed that 17.7% of the day workers had HTN, while 13.9 and 17% of morning and evening night shift workers had HTN respectively. Their findings indicated that there was no association between shift work and HTN. Some studies identified a trend towards higher BP among shift workers. Ye [28] showed that shift worker had elevated HTN than day workers (50.3%, 28.2 %) respectively. The researchers clarified this by the old age. 32.2% of shift workers in this study were above 50 years and only 11.3% of day workers were above 50 years.

For FBS, 17.0% of the daytime workers had elevated FBS vs. 10.5% in rotating shift workers with no statistical relationship (P-value>0.05). Similar results were found in a study performed in Brazil by Canuto [29] in which their results revealed that elevated FBS was more in day workers than night shift workers (4.9%, 3.8%) respectively. However, a study by Ye [28] found that FBS was more among shift workers (24.6%) than day workers (4.2%) ($P < 0.001$). This can be explained by that most shift workers were aged between 40-49 years (55%) while most day workers were aged between 18-39 years (64.8%).

Our results showed a significant difference in cholesterol, HDL-C, and LDL-C between shift workers and day workers where day workers had increased results ($P <0.05$), but no such difference was observed for TG ($P > 0.05$). A study that conducted by Nazri [22] for estimation of HDL- C in day and shift workers showed a consistent result that the day workers had hypo- HDL-C more than shift workers (13.89%, 9.21% respectively). Meanwhile, their result showed no statistically difference relationship between the two groups, our findings were in contrast where we found a significant different between HDL-C level of daytime and shift workers. In this study the result of HDL-C was statistically significant between the two groups refer to that most daytime workers were older and traditionally HDL levels below the reference value have been associated with increasing age, especially among women [30]. The result regarding TG that obtained in this study was similar to a cross sectional study on 12 shift workers and 13-day workers using pre and posttest, during a six-month period, that demonstrated the prevalence of TG among day workers and shift workers was (28%, 25% respectively) with no significant difference between the two groups ($P>0.05$) [31].

According to Sookoian [32] leukocyte count was significantly higher in shift workers than in daytime workers (6530 ± 1,216 , 5556 ± 1,123, cells/μL, respectively, *P*= <0.001), Puttonen [33] also reported an increase in hs-CRP in 3-shift workers and an increase in leukocyte count in 2-shift and 3-shift workers, additionally a study done by Lu [34] showed that increased total and differential leukocyte counts (neutrophil, monocyte, and lymphocyte) were associated with shift work ($P < 0.05$), thus disagreeing with our findings. The researchers explained that may be due to the type of job and the age that most day workers were above 40 years and CRP level affected by age.

According to our results, in the daytime workers and shift workers, respectively, MetS increased from 0% and 5.9% within less than 30-year-old group to 66.7% and 47.1% in the participants of more than 41 years of age. There was a statistically significant relationship (*p*-value<0.05) between MetS and age (30 years & less, 31- 40 years, 41 years & above) among rotating shift workers. In addition, for rotating shift workers the result showed that the ratio of having MetS for 41 years and above equals 4.5 times of other age groups and their percent of susceptible ranging between 1.6 to 12.9 times. Our result come in agreement with two previous studies on shift workers where both studies also reported that age was directly associated with MetS [35-37].

The study showed that 66.7% of the daytime workers who have MetS had been exposed to night shifts previously for more than 5 years without statistically significant relationship vs. 82.4% in the rotating shift workers with statistical significant relationship (*P*-value= 0.026 OR= 3.9, 95% CI= 1.1-14), this mean that rotating shift workers who have night shifts more than 5 years have four times to have MetS than workers who had night shifts less than 5 years. Our results come in consistent with a study done by Guo [38] which suggested that the ORs for MetS increased with the extension of shift work duration. Every 10 years increase of shift work was related to 17% increase of OR in the unadjusted model. Also, another study that conducted by Shafei [22] supported our results and showed that nurses who worked 10 years more than others were two times more likely to have MetS.

5. LIMITATIONS

1- Lack of resources including budget and facilities.
2- Time limitation because of the nature of researchers work and life condition.
3- The study did not include the NGOs and the private sectors.
4- Matching was not possible due to the fact that the age of healthcare workers who work currently day shift is different from rotating shift.
5- Comparative group was not selected from other places in which we can exclude the fact that employee had work previously in rotating shift which in fact introduce bias to the study.

6. CONCLUSIONS

An important finding of this study was the overall prevalence of MetS among health personnel was 8.4% (9% among daytime workers was which was higher than among rotating shift workers 8.1%) without statistically significant difference between the two groups, and the prevalence increases as age increases. According to the results of the study, MetS was more prevalent among male daytime and rotating shift workers than females. There were 27.0% of daytime workers obese (BMI > 30) vs. 17.6% of rotating shift workers. For FBS, 17.0% of the daytime workers had elevated FBS vs. 10.5% in rotating shift workers, also 16.0% of the daytime workers had elevated BP vs. 11.0% of rotating shift workers without statistical relationship.

A statistically significant difference appeared between cholesterol level and shift category with higher prevalence among daytime workers. For TG, 41.0% of the daytime workers had elevated TG vs.32.9% of the rotating shift workers with no statistical relationship. Moreover, there is a statistical difference between low level of HDL and high level of LDL and the shift category. From our results, there were no statistical differences in the CBC results including WBC and its differential count, and the level of CRP between daytime and rotating shift workers. There were 52.0% of daytime workers had elevated level of CRP with higher percentage in males 53.8% than females 46.2%. Also, 41.0% of rotating shift workers had high level of CRP with higher in males 75.6% than females 24.4%. About 82.4% of rotating shift workers who have MetS had been exposed previously to night shifts for more than 5 years. Our results showed that most of daytime and rotating shift workers who had elevated CRP had been exposed to night shifts for more than 5 years (75.0%, and 59.3%) respectively. The current study also investigates the risk factors that define MetS among currently daytime workers which based on value of OR in descending order were as follow: high BP, high level of TG, high FBS, elevated BMI >30, and low HDL cholesterol level, while the risk factors that define MetS among rotating shift workers which based on value of OR in descending order were as follow: high BP, high FBS, high level of TG, elevated BMI >30, and low HDL cholesterol level. They were in the order of risk factors in daytime workers except for high FBS and elevated TG.

7. FUTURE CLINICAL IMPLICATIONS

1- A national prevention programs need to be implemented to combat hypertension, diabetes, obesity, dyslipidemia, and related co morbidity and change in lifestyle, especially with respect to physical activity and nutrition.

2- As blood pressure was the main risk factor of MetS, conducting regular check-up of BP health settings is very important.

3- As age was one of the main determinants of MetS, Ministry of Health need to develop policies to regulate the work schedule of employees, particularly of those who are over 40.

4- Future prospective longitudinal studies should be carried out for identifying the prevalence and the effect of shift work on biomarkers of MetS and inflammation on a large sample to include all healthcare workers in all governmental and private hospitals in the Gaza Strip.

5- It is recommended to conduct other studies that involve selection of comparative groups from places other than the hospitals.

8 CONSENT

Informed consent was taken from all participants who accepted to participate in the study after well explanation of the procedures and objectives and considerations beyond the study.

9 ETHICAL APPROVAL

An approval to perform the study was taken from the Palestinian Ethical Committee (Helsinki Ethics Committee) (PHRC/HC/154/16).

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