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Relationship between shift work and the risk of colorectal cancer among Moroccan women

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ABSTRACT

Colorectal cancer (CRC) is a public health problem worldwide, and also in Morocco, with 7.9% of new cancer cases. Dietary factors have been linked to CRC risk; however, several modifiable risk factors have not been studied in Morocco. This study aimed to explore the association between shift work and the risk of colorectal cancer among Moroccan women. A case-control study was conducted at CHU Mohamed VI Marrakech, involving 165 cases and 165 controls. Data were collected using a self-administered questionnaire. For general characteristics, we used the Chi-square test for categorical variables and student's t-test or Mann-Whitney U for continuous variables to select confounding factors, we ran logistic regression analysis to estimate odds ratios and 95% confidence intervals. Findings from our study show an increased risk of CRC for rotating shift workers ORb:1.74 (95% CI:1.05-2.91) (p-value = 0.01). When stratified by tumor location, night shift work was correlated with an increased risk of rectal cancer, while stratified by age, rotating shift work was also correlated with an increased risk of CRC among those aged 45 to 65 years ORb: 2.18 (95% CI:1.03-4.79) (p-value = 0.048). Findings from this study may be helpful for future research in Morocco and North African countries.

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1. INTRODUCTION

Colorectal cancer (CRC) is defined as a cancer that affects either the colon or rectum. Based on the cancer site, 49.09% of cases are classified as colon cancer and 49.66% as rectal cancer, while 1.25% are classified as colorectal cancers [1]. CRC is known to be multifactorial, involving both environmental and genetic factors [2]. Among the genetic factors, which are non-modifiable, approximately 20% of CRC cases are linked to 2 genetic factors: familial adenomatous polyposis (FAP) and mismatch repair gene (MMR). Age is another non-modifiable risk factor for CRC, with a lower incidence and mortality for individuals under 45 years. However, recent trends have shown an increasing incidence of CRC among younger populations [3]. Sex is also a non-modifiable risk factor for CRC, with a higher incidence among men than women [4]. On the other hand, numerous modifiable risk factors have been recognized. The World Cancer Research Fund (WCRF) has established strong links between these modifiable risk factors and increased or decreased risk of CRC. Diet has been recognized as an important modifiable risk factor for CRC, such as, excessive consumption of red and processed meats has been shown to increase the risk of CRC, while cereals containing dietary fiber offer a protective effect against CRC. Likewise, vegetables and fruits, abundant in

antioxidants and anti-inflammatory compounds, contribute to lowering CRC risk [5], [6]. Additionally, an elevated body mass index (BMI) is linked to an augmented risk of CRC, whereas higher physical activity is correlated with a decreased risk of CRC. However, many other modifiable risk factors have not yet been explored with sufficient supporting evidence [7].

In recent years, CRC has become a significant public health problem. In 2020, CRC ranked third among the most common cancers, with nearly 2 million new cases reported worldwide for both sexes combined. In addition, CRC is the second deadliest cancer after breast cancer, causing 935,173 (9.4%) deaths, with an incidence rate of 23.4 and 16.2 per 100,000 for men and women, respectively [8]. The incidence of CRC varies significantly across different geographic regions, developed or high-income countries tend to have a higher incidence compared to developing or middle- and low-income countries [9]. Over the past decade, Morocco has undergone an important industrial transition, leading to fundamental changes in the lifestyle of its population. Many industrial workers are now engaged in shift work, including night shift and rotating shifts [10]. These lifestyle changes, along with dietary factors, have played a role in the rise of various diseases and cancers within the Moroccan population. In 2020, CRC once again ranked third among the most frequently diagnosed cancers in Morocco, representing 7.5% of all cancer cases, with an incidence of 11.3 per 100,000 for both sexes combined [11]. Unfortunately, Morocco lacks a national cancer registry, relying instead on two regional registries: the Grand Casablanca region, where CRC represented 7.7% of cases between 2013 and 2017, with an incidence of 9 per 100,000 for both sexes combined. Similarly, in the region of Rabat, CRC ranked third with 8.3% of cancer cases for men and 7.8% for women between 2009 and 2012, with an incidence of 7.02 per 100,000 for men and 5.86 per 100,000 for women [12], [13].

The International Agency for Research on Cancer (IARC) has categorized shift work that disrupts the circadian cycle as a "probable human carcinogen" (group 2A) [14]. Some epidemiological studies have already established evidence of an association between shift work and breast cancer [15] only a few epidemiological studies in high-income countries have examined the association between shift work and CRC, Papantoniou *et al.* [16] showed an increased risk of CRC on shift workers reporting an OR of 1.22 (95% CI: 1.04-1.43). However, other studies have suggested no correlation between shift work and CRC risk, such as an Australian case-control study where no correlation was found between shift work and a higher risk of CRC with OR: 0.95 (95% CI: 0.57-1.58) [17]. In contrast, in developing countries such as Morocco, the majority of the studies mainly focus on diet, physical activity, tobacco and alcohol consumption, limited data on the other modifiable risk factors [18], [19]. To date, no previous study in Morocco has evaluated the effect of shift work on CRC risk. The potential carcinogenic effect of circadian disruption seems biologically plausible, since the circadian cycle controls several biological processes and mechanisms within our body including its capacity for periodic transcription, and the regulation of deoxyribonucleic acid (DNA) damage and repair [20].

The state of the art for this research highlights that several risk factors such as diet, BMI, tobacco, and alcohol have an influence on CRC risk, supported by strong evidence. However, other potential modifiable risk factors like shift work have not been fully established as linked to CRC risk. Nevertheless, all the studies investigating the link between shift work and CRC risk have been conducted in developed countries with inconclusive and conflicting results that still to need be studied further. No research of this kind has been conducted in Morocco. To build upon and enhance previous research also to strengthen and guide future studies, the aim of our study was to examine the potential relationship between shift work and colorectal cancer risk, while accounting for all possible confounding factors of CRC for different professions among Moroccan women according to tumor location, age categories, and duration of shift work in Marrakech, Morocco, to provide novel insights and contribute to both local and global knowledge on the subject.

2. METHOD

We conducted a case-control study from November 2022 to February 2024 at the University Hospital Center Mohamed VI in Marrakech, Morocco. The participants of the study were recruited according to several eligibility criteria. For cases, adult women aged between 25 and 85 years who were professionally active or have at least 5 years of professional experience, with a confirmed histopathological CRC diagnosis made within the past 3 months. Absence of cognitive or eating disorders, who were admitted to the oncology and hematology center during the recruitment period in the order of admission. Controls were recruited from the same hospital but from traumatology department, controls were women aged between 25 and 85 years, with no prior diagnosis of any cancer or gastrointestinal disease, who were professionally active or had at least 5 years of work experience, had no cognitive or eating disorders, also no disease requiring a specific diet, and no family history of CRC cases in first-degree relatives, who attended the hospital during the same

period as cases. Cases and controls were matched according to age (±3 years) for cases was the age at diagnosis and controls age at the interview, with a ratio of 1 case to 1 control. Prior to the recruitment process, the sample size was calculated using the appropriate case-control study formula [21], the minimum required sample size was 150 cases and 150 controls, to detect an odds ratio (OR) of 2 for 25% of exposed controls, with a power of 80% and 5% type I error. The study protocol was approved by research ethics committee of the Moroccan association for research and ethics under the identifier 12-REC-2022. A pilot test of the questionnaire was conducted on a sample of 30 participants before the study to evaluate and make appropriate modifications to the questionnaire.

Each participant was first approached to evaluate their eligibility. The investigator explained the aim and purpose of the study to each participant. When the investigator obtained the written and informed consent of the participant, we proceeded to a face-to-face interview of an average duration of 25 minutes. Data were collected using a questionnaire divided into 3 sections. The first section concerned the general characteristics of the participants: age as a continuous variable, weight as a continuous variable, for cases, the weight recorded prior to CRC symptoms, while for controls, weight was measured on the day of the interview, recorded to the nearest 100 g using an electronic Seca 803 scale. Height was treated as a continuous variable and was measured during the interview to the nearest 0.1 cm using a Comed tape measure. BMI was calculated using the appropriate formula based on height and weight (kg/m^2) categorized into 4 groups in line with the WHO classification [22] underweight for an BMI <18.5, normal BMI between 18.5-24.9, overweight BMI: 25-29.9, and finally obesity for an BMI ≥30. Educational level was divided into 4 categorical variables: illiterate, primary, secondary, and university. Residency was categorized as urban or rural. Physical activity was assessed based on the global physical activity questionnaire (GPAQ) [23], and classified into three groups: low <600 MET-min/week, moderate 600–3,000 MET-min/week, and high ≥3,000 MET-min/week, family history of colorectal cancer was recorded as either 'yes' or 'no'. The second section of the questionnaire was a validated semi quantitative food frequency questionnaire (SQ-FFQ) for Moroccan adult population [24]. Using the Moroccan table of food composition [25], We estimated the daily quantity of food consumed by each participant by multiplying the frequency of consumption by the portion sizes. We also converted the consumed foods into nutrient intakes by multiplying the quantity of each food by its nutrient content (per 100 g). To calculate energy intake, we multiplied the daily intake of each food item by its caloric content. The third section of the questionnaire was to assess shift work retrospectively for every job held for a minimum of one year, including details on the type of shift, duration, and number of hours worked. The investigators defined 3 categories of shift work based on the common shift schedules in Moroccan factories: day shift work, night shift work, and rotating shift work:

- Day shift work was determined as working ≥4 hours between 6:00 and 20:00 for at least 15 days per month;
- Night shift work was determined as working ≥4 hours between 22:00 and 5:00 for at least 15 days a month;
- Finally, rotating work referred to any shift that alternates between the two shifts of day and night.

For each participant, we assessed: Shift of work: day shift work, rotating shift work, night shift work, and the duration of each work held. Cumulative years of rotating and night shift work were categorized into quartiles based on the distribution among controls. For rotating shift work the quartiles were: Q1(<8) Q2(≤8-13<), Q3 (≤13-17<), and Q4 (≥17). While for cumulative years of night shift work the quartiles were: Q1(<2), Q2(≤2-5 <), Q3(≤5-8<), and Q4(≥8).

The general characteristics of the population included categorical variables illustrated as frequencies and continuous variables illustrated as means (±SD). We performed a bivariate analysis to assess the differences between cases and controls, for categorical variables, we used the Chi-square test, and for continuous variables, we used Student's t-test or Mann-Whitney U (depending on the normality of the distribution). To examine the correlation between shift work and CRC risk, we performed logistic regression analysis to estimate Odds Ratios and 95% confidence intervals (CI). Two models were considered: the first crude model (ORa) adjusted only for age (±3 years), and a second model adjusted for confounding factors based on the general characteristics of the population (ORb) adjusted for: educational level (illiterate, primary, secondary, university); marital status (never married, married, divorced, widowed); residency (urban, rural); BMI (underweight, normal, overweight, obesity); physical activity (low, moderate, high); total energy intake (kcal) as continuous variable; fiber Intake (g/day) as continuous variable; calcium Intake (mg/day) as continuous variable; red meat intake (g/week) as continuous variable. All groups of shift work and cumulative years of shift work were compared to day shift workers, who served as the reference group, the significance level was established at p-value <0.05. Participants with missing data were excluded from the study prior to the statistical analysis. we used SPSS v23 software to enter and analyze data.

3. RESULTS AND DISCUSSION

3.1. General characteristics of the participants

Our study included 330 participants, divided into 165 cases and 165 controls. Our investigators approached 174 eligible cases, 168 of whom accepted to participate, with 96.55% of participation rate. Three cases were excluded before statistical analysis due to incomplete or invalidated data. A total of 180 eligible controls were approached 170 of them accepted to participate (94.44%), 2 controls were excluded from the study for incomplete or invalidated data and 3 additional were excluded to match case participants according to matching parameters. The mean age of cases was 49±6.13 years and 50±4.25 years for controls (p-value = 0.86), regarding educational level nearly the half of cases (47.27%) were illiterate, compared to only 31.51% of controls. For marital status, 26.06% of cases had never been married versus 16.36% for controls, married women represented 52.12% of cases and 71.51% of controls, resulting in a significant difference (p-value = 0.002) for marital status. The majority of controls lived in urban areas (86.66%) against 53.33% of cases, showing a significant difference (p-value <0.001). More than half of controls (63.03%) had a normal BMI, while half of the cases (50.29%) were above the normal range (overweight and obese) (p-value <0.001). Additionally, 75.15% of cases had low physical activity, compared to 51.82% of controls, also only 22.42% of cases had moderate physical activity versus 37.57% of controls (p-value <0.001). No significant difference (p-value= 0.251) was observed concerning family history of CRC. The total energy intake consumed by cases was higher than controls, with a significant difference (p-value <0.001). In contrast, fiber intake was higher among controls than cases (p-value <0.001) as shown in Table 1. Our findings are consistent with another Moroccan case-control study conducted by Kinany *et al.* [26] which reported that over 50% of both cases and controls were married, and over 30 % of cases lived in rural areas, similarly to our study nearly the half of cases were illeterate and only 38% of cases had normal BMI. However, in contrast with our study, Deoula *et al.* [27] reported that more than 80% of cases were illiterate, only 1.2% of cases had a normal BMI, and over 80% were married.

Table 1. Overview of participant general characteristics in a Moroccan women case control study

Characteristics	Cases (%)	Controls (%)	p-value
# Educational level			0.002
Illiterate	78 (47.27)	52 (31.51)	
Primary	47 (28.48)	39 (23.63)	
Secondary	35 (21.21)	61 (36.96)	
University	5 (3.04)	13 (7.87)	
# Marital status			0.002
Never married	43 (26.06)	27 (16.36)	
Married	86 (52.12)	118 (71.51)	
Divorced	11 (6.66)	3 (1.81)	
Widowed	25 (15.15)	17 (10.30)	
# Residency			<0.001
Urban	88 (53.33)	143 (86.66)	
Rural	77 (46.67)	22 (13.34)	
# BMI			<0.001
Underweight	15 (9.09)	24 (14.54)	
Normal	67 (40.60)	104 (63.03)	
Overweight	65 (39.39)	21 (12.72)	
Obesity	18 (10.90)	16 (9.69)	
# Physical activity			<0.001
Low	124 (75.15)	85 (51.82)	
Moderate	37 (22.42)	62 (37.57)	
High	4 (2.42)	18 (10.90)	
# Family history of CRC			0.251
No	160 (96.96)	163 (98.78)	
Yes	5 (3.04)	2 (1.22)	
	Cases mean±SD	Control mean±SD	
# Age	49 ± 6.13	50±4.25	0.86
Total energy intake (Kcal/day)	2479.31±84.13	2130.15±20.92	<0.001
Fiber intake (g/day)	18.04±3.21	24.13±2.64	<0.001
Calcium intake (mg/day)	764.12±4.22	758.81±3.40	<0.001
Folate intake (mcg/day)	120.14±10.26	122.03±9.18	0.078
Vitamin D intake (mcg/day)	1.8±1.02	1.9±1.07	0.385
Red meat intake (g/week)	287.72±119.12	253.95±123.65	0.012

While no age difference was detected due to the matching parameters, educational level was significantly lower among cases. It has been demonstrated that a higher education level is correlated with a better access to information and greater awareness of risk factors, furthermore, a higher educational level is

associated with greater acceptance of colonoscopy as a preventive measure [28]. In line with our findings, marital status is associated with risk of CRC, due to reproductive and sex hormones such as estrogen, which may have a protective effect against CRC by regulating bile acids [29]. For residency area, CRC is typically considered as an urban cancer, often linked to an urban lifestyle, paradoxically, in our study nearly the half of cases were from rural areas. In Morocco, living in rural areas is often associated with a limited access to healthcare services, as well as higher levels of pollution and contamination due to weak sanitation infrastructure. Moreover, people in rural areas tend to have a lower educational level. As mentioned earlier, BMI and physical activity are strongly related to CRC risk, with substantial evidence supporting this relationship [5].

3.2. Shift work and colorectal cancer risk according to location and age categories

Table 2 presents the crude and adjusted OR and 95% CI for all types of shift work in relation to CRC risk, with significant general characteristics considered as confounding factors. Rotating shift work showed a significant increase in CRC risk in the crude model (OR^a: 1.76; 95% CI: 1.06-2.93), after adjusting for confounding factors the risk was slightly attenuated but remained statistically significant (OR^b: 1.74; 95% CI: 1.05-2.91), with respectively p-value = 0.029 for the crude model and p-value = 0.01 for the adjusted model. Night shift work was correlated with a slight increase of CRC risk but this was not statistically significant OR^b: 1.08; 95% CI: 0.62-1.92 (p-value = 0.75). During our study, we also examined the cumulative effect of shift work, evaluated by quartiles, for cumulative years of rotating shift work, only the second quartile (≤8-13<) was associated significantly with a higher risk of CRC in both crude OR^a: 2.23; 95% CI: 1.11-4.47 (p-value = 0.022) and adjusted models OR^b: 2.23; 95% CI: 1.09-4.47 (p-value= 0.012) when compared to day shift workers, other quartiles did not show a significant correlation with CRC risk. Similarly, no significant association was found between cumulative years of night shift work and CRC risk across all quartiles.

Table 2. The estimated OR and CI95% for different shift works with colorectal cancer risk

Years of work	Cases N (%)	Controls N (%)	OR^a (CI95%)	OR^b (CI95%)
Day shift work (Ref)	78 (47.2)	93 (56.3)	1.00	1.00
Rotating shift work	56 (33.9)	38 (23)	1.76 (1.06-2.93)	1.74 (1.05-2.91)
p-value			0.029	0.01
Night shift work	31 (18.7)	34 (20.6)	1.09 (0.62-1.93)	1.08 (0.62-1.92)
P-value			0.774	0.75
Cumulative rotating shift work (year)				
<8	14 (25)	11 (28.9)	1.52 (0.65-3.54)	1.50 (0.65-3.43)
p-value			0.331	0.25
≤8-<13	28 (50)	15 (39.4)	2.23 (1.11-4.47)	2.23 (1.09-4.47)
P-value			0.022	0.012
≤13-<17	4 (7.1)	7 (18.4)	0.68 (0.19-2.41)	0.67 (0.17-2.40)
p-value			0.55	0.55
≥17	10 (17.8)	5 (8.9)	2.38 (0.78-7.26)	2.35 (0.77-7.24)
P-value			0.117	0.128
Cumulative night shift work (year)				
<2	7 (22.5)	11 (32.3)	0.76 (0.28-2.05)	0.75 (0.26-2.02)
p-value			0.585	0.557
≤2-<5	10 (32.2)	9 (26.4)	1.32 (0.51-3.41)	1.29 (0.51-3.40)
P-value			0.56	0.42
≤5-<8	6 (19.3)	10 (29.4)	0.72 (0.25-2.07)	0.71 (0.24-2.07)
p-value			0.532	0.5
≥8	8 (25.8)	4 (11.7)	2.38 (0.69-8.20)	2.36 (0.67-8.19)
p-value			0.157	0.1

OR^a: Crude odds ratio adjusted only for age (±3 years), OR^b: Adjusted for: Educational level (illiterate, primary, secondary, university); Residency (urban, rural); Martial status (never married, married, divorced, widowed); BMI (underweight, normal, overweight, obesity); Physical activity (low, moderate, high); Total energy intake (Kcal) continuous variable; Fiber Intake (g/day) continuous variable; Calcium Intake (mg/day) continuous variable; Red meat intake (g/week) continuous variable.

In respect with our findings, a Spanish population-based study, indicates that rotating shift work was positively correlated with CRC risk OR: 1.22; 95% CI: 1.04-1.43 compared to day shift workers, while night shift work was not found to be correlated with CRC risk OR:0.79; 95% CI: 0.62-1.00. Moreover, 20 to 34 years of cumulative rotating shift work were correlated with an increased risk of CRC, although, in our study only 8 to 13 years of cumulative rotating shift work showed this association [16]. In contrast to our study, a black women's cohort study found a higher risk of CRC among night shift workers with over 10 years of exposure, with HR: 1.64; 95% CI: 1.01-2.66, while our study showed no correlation between cumulative years of night shift work and the risk of CRC overall [30]. When stratified by tumor location, night shift work was positively correlated with the risk of rectal cancer in the adjusted model OR^b: 2.14; 95% CI: 1.04-4.42 (p-value = 0.048). However, for colon cancer rotating shift workers showed a borderline

non-significant increase in CRC risk OR[b]: 1.62; 95% CI: 0.96-2.68 as shown in Table 3. Similarly, a Canadian case-control study focusing on men showed that permanent night shift workers had twice the risk than day shift workers for colon cancer OR: 2.03; 95% CI: 1.43-2.89 and rectal cancer OR: 2.09; 95% CI: 1.40-3.14 [31]. Meanwhile, a case-control study of Australian women found no correlation between rotating shift work and the risk of colon and rectal cancer [17]. Moreover, a recent meta-analysis showed a borderline risk of CRC on night shift workers but non-significative OR: 1.01; 95% CI: 0.96-1.06 [32]. When stratified by age groups, rotating shift work showed a positive non-significant correlation with CRC risk for people aged between 45-65 OR[a]: 2.12; 95% CI: 0.95-4.75, after adjusting for confounding factors, the risk of CRC became significant OR[b]:2.18 CI95%: 1.03-4.49 (p-value = 0.042). While no association was observed across the other age categories as shown in Table 4. In contrast, other studies have suggested that the risk of these modifiable risk factors decreases after retirement, when shift workers resume a normal lifestyle with regular meal and sleep schedule [17], [33]. In a Swedish cohort study of approximately 3.5 million participants and 19 years follow-up, showed no association between shift work and the risk of CRC for both men and women, moreover, another cohort study also found no correlation between shift work and CRC in Japan [2], [34].

Table 3. The estimated OR and CI95% for different shift works with colorectal cancer risk by tumor location

Location	Colon		Rectal		Colorectal overall	
	OR[a] (CI95%)	OR[b] (CI95%)	OR[a] (CI95%)	OR[b] (CI95%)	OR[a] (CI95%)	OR[b] (CI95%)
Cases/controls	46/93		25/93		78/93	
Day S. W.	1.00	1.00	1.00	1.00	1.00	1.00
Cases/controls	31/38		17/38		56/38	
Rotating S. W.	1.65 (0.91-2.98)	1.69 (0.96-2.98)	1.66 (0.81-3.42)	1.62 (0.75-3.39)	1.76 (1.06-2.93)	1.74 (1.05-2.91)
Cases/controls	10/34		20/34		31/34	
Night S. W.	0.59 (0.27-1.3)	0.65 (0.34-1.34)	2.19 (1.08-4.44)	2.14 (1.04-4.42)	1.09 (0.62-1.93)	1.08 (0.62-1.92)
P-value	0.046	0.058	0.075	0.048	0.062	0.044

OR[a]: Crude odds ratio adjusted only for age (±3 years), OR[b]: Adjusted for: Educational level (illiterate, primary, secondary, university); Residency (urban, rural); Martial status (never married, married, divorced, widowed); BMI (underweight, normal, overweight, obesity); Physical activity (low, moderate, high); Total energy intake (Kcal) continuous variable; Fiber Intake (g/day) continuous variable; Calcium Intake (mg/day) continuous variable; Red meat intake (g/week) continuous variable. 87 colon cancer cases and 62 rectal cancer cases are less than 165 due to unknown location (n=16). S.W: Shift work.

Table 4. The estimated OR and CI95% for different shift works with colorectal cancer risk by age categories

Age Category	From 25 to less than 45		From 45 to less than 65		From 65 to 85	
	OR[a] (CI95%)	OR[b] (CI95%)	OR[a] (CI95%)	OR[b] (CI95%)	OR[a] (CI95%)	OR[b] (CI95%)
Cases/controls	19/22		25/43		34/28	
Day S. W.	1.00	1.00	1.00	1.00	1.00	1.00
Cases/controls	16/9		21/17		19/12	
Rotating S. W.	2.06 (0.74-5.72)	2.13 (0.85-5.83)	2.12 (0.95-4.75)	2.18 (1.03-4.79)	1.3 (0.54-3.13)	1.27 (0.49-3.11)
Cases/controls	14/11		11/15		6/8	
Night S. W.	1.47 (0.54-4)	1.42 (0.59-4.05)	1.26 (0.5-3.17)	1.3 (0.54-3.21)	0.62 (0.19-2)	0.59 (0.17-1.98)
P-value	0.365	0.382	0.033	0.042	0.513	0.502

OR[a]: Crude odds ratio adjusted only for age (±3 years), OR[b]: Adjusted for: Educational level (illiterate, primary, secondary, university); Residency (urban, rural); Martial status (never married, married, divorced, widowed); BMI (underweight, normal, overweight, obesity); Physical activity (low, moderate, high); Total energy intake (Kcal) continuous variable; Fiber Intake (g/day) continuous variable; Calcium Intake (mg/day) continuous variable; Red meat intake (g/week) continuous variable. S.W: Shift work.

3.3. Carcinogenesis of rotational and night shift of work

Several hypotheses have been advanced to explain the carcinogenic potential of rotating and night shift work. Two of these remain the strongest, the first suggests that rotating and night shift workers adhere more to an unhealthy lifestyle, consuming mainly fast food and energy-dense foods due to the challenges of maintaining a healthy diet with their work schedules [35]. Shift workers also have less recreational physical activity than the general population [36], which places shift workers at an elevated risk for both type II diabetes and obesity [37], both of which recognized risk factors for CRC [38]. In a women's cohort study, rotating and night shift workers were more likely to be smokers and exhibited a higher risk of CRC compared to day shift workers, with higher expression of insulin receptor substrate 1 (IRS1) and IRS 2, which promote cell proliferation and insulin resistance [39]. In our study, cigarette smoking and alcohol consumption were not considered due to the sociocultural context of Morocco, where their prevalence among women is low.

The second mechanism is circadian rhythm disruption. Melatonin, a hormone that follows a fluctuating pattern within individuals over a 24-h cycle, reaches the highest levels in the absence of light at

night. However, it has been shown that rotating and night shift workers have lower level of melatonin, due to the disruption of its production by artificial light during night shifts [40], [41]. Furthermore, night shift workers suffer from significant sleep deprivation with an average of 8.3h of sleep for day shift workers versus only 4.8h for night shift workers, which may result in a low level of melatonin production [42]. A previous review reported that 75% of night shift workers have irregular melatonin rhythms [43]. Melatonin exerts anticarcinogenic effects in CRC tumor growth by regulating tumor development, a regular level of melatonin maintains homeostasis in colorectal tissues [44]. Moreover, the circadian cycle controls metabolic processes in our body, a cohort study showed that circadian rhythm disruption could be a risk factor for colorectal cancer [45]. A metabolic study of circadian clock pathway genes identified that the SNP rs37436997 in RORA may elevate the risk of developing colorectal cancer [46]. Several circadian genes may be deregulated in colon cancer cell lines, which may promote cell proliferation in animal studies [47]. It is likely that shift work acts more as a cancer promoter than a cancer initiator [48].

In this study, workers were deprived of healthy nocturnal sleep, in addition reduction of melatonin level due to exposure to artificial light in factories. Rotational shift workers also suffered from the disruptions of the circadian rhythm caused by alternating between the day and night shifts. Although our study focused only on women, who are known to maintain a healthier lifestyle, 75% of shift workers in our study reported irregular eating schedules, with some even skipping meals, and avoiding physical activity. Our study has some limitations that must be acknowledged, the study was retrospective relying on the memory of the participants, despite the assistance of trained investigators, participants may have misclassified themselves. In addition, the classification of shift work varies between countries, making direct comparisons with other studies challenging. As for the main strengths of this study, as far as we know, this is the first Moroccan study to assess shift work in relation to colorectal cancer risk. The study was conducted at CHU Mohamed VI, ranked as the second largest hospital in Morocco which provides the study with a large ethnic and socio-economic diversity. Moreover, shift work was evaluated in different jobs from various fields. Training sessions were provided to investigators prior to the study to enhance quality of generated data, and minimize recall bias, with a pilot test to evaluate the questionnaire and make necessary adjustments.

4. CONCLUSION

The findings from this study emphasize the potential influence of rotating shift work in increasing the risk of colorectal cancer among Moroccan women, affected by the duration of shift work. These findings are consistent with observations from developed countries. Gaining a comprehensive understanding of both modifiable and non-modifiable risk factors of colorectal cancer will be valuable for future studies in Morocco and North African countries, given their socio-demographic similarities. Additionally, shift work should be considered as a confounding factor in future studies. Moreover, the development of better preventive strategies for shift workers, such as promoting a healthier diet, lifestyle and sleep patterns, as they are at an elevated risk for colorectal cancer.

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AUTHOR CONTRIBUTIONS STATEMENT

This journal uses the Contributor Roles Taxonomy (CRediT) to recognize individual author contributions, reduce authorship disputes, and facilitate collaboration.

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
Hamze Elbaylek	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			
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C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known financial, personal, professional, or non-financial competing interests that could have influenced the work presented in this paper. There are no external funding sources, affiliations, or relationships that could be perceived as a conflict of interest. Furthermore, the authors affirm that there are no political, religious, ideological, academic, or intellectual interests that could have affected the objectivity or integrity of the research. The research was conducted independently, without any bias or external influence, ensuring fair and objective decision-making throughout the study.

INFORMED CONSENT

The we have obtained informed consent from all individuals included in this study. Each participant was fully informed about the purpose, procedures, and potential risks of the research. Written permission was obtained prior to their inclusion, ensuring their voluntary participation and understanding of the study with respect of privacy.

ETHICAL APPROVAL

This study involving human participants was conducted in compliance with all relevant national regulations and institutional policies, following the ethical principles outlined in the Helsinki Declaration. The research protocol was reviewed and approved by research ethics committee of the Moroccan association for research and ethics under the identifier, under approval number 12-REC-2022.

DATA AVAILABILITY

The data that support the findings of this study are available on request from the corresponding author, [HE]. The data, which contain information that could compromise the privacy of research participants, are not publicly available due to ethical and privacy restrictions.

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