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Nutritional status and food intake in women with human papillomavirus

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ABSTRACT

Introduction: Human papilloma virus (HPV) is the mainly cause of cervical cancer. Nutritional management considerations with antioxidant rich diet, an adequate BMI range are protective factors that can modify the disease natural progression.

Objective: To evaluate the nutritional status and food intake in women with HPV.

Methods: A cross-sectional study in 75 women of 18 to 35 years old, selected by simple availability. A frequency food intake was applied and analyzed with adequacy percentage. Nutritional status and risk factors as tobacco smoke were assessed.

Results: A 66% of women were obese or overweight. Tobacco was positive in 36%. The energy intake was covered in 73%, 84% for lipid, 52% for protein and 66% for carbohydrates. Micronutrient intake was according recommendations. Marital Status, Smoking, Firs sexual intercourse age <18, obesity or overweight, Waist circumference >80cm were risk factors associated between group 18 to 28 years vs 29 to 35 years old. Frecuency food intake were low for foods rich in acid folic, carotenoids, vitamin C mainly.

Conclusions: This evidence showed the poor nutriments intake in the participants related with antioxidant function, that is important for treatment in premalignant lesion for HPV. These results highlight the importance of nutritional management considerations in prevention for resolution of human papillomavirus premalignant lesions.

KEYWORDS

Human papilloma virus; antioxidants, obesity, nutritional management, diet.

LIST OF ABBREVIATIONS

RDA: Recommended daily average.

HPV: Human papillomavirus.

OC: Oral contraceptives.

SNUT: Nutritional habits and nutrient consumption evaluation system.

INTRODUCTION

Cervical cancer (CEC) is prevalent in Mexico with a second place in morbidity and mortality in women[1]. In 2018 the mortality rate was found in a 11 women per every 100,000. The same rate was found in Guanajuato, Mexico where this pathology is still prevalent. A 30% of the state population is from Leon. Annually, the public Hospital of Ministry of Health attended an average of 900 patients with cervical dysplasia (75 patients per month and 2 per day). This diagnosis is more prevalent in young women (reproductive age). Once the diagnosis has been established the surveillance for these patients is approximately for 3 months. It is important to mention that the dysplasia clinic in public and private hospital there are not service of nutritional counseling[2].

Several risk factors are identified for acquire cervical dysplasia: early sexual intercourse (RR: 1.2, CI: 0.69 to 2.1),

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number of sexual partners (RR=1.082, CI=1.015 to 1.154)[2], viral and bacterial infections, pregnancy (RR=4.6, CI=1.1 to 20) contraceptive use (RR=4.0, CI=1.5 to 10), obesity (1.40 (95% CI: 1.08, 1.71), smoking habit (OR=3.23; CI95%= 1.33 to 7.69)[3-5]. The main causal factor is the presence of HPV. The evidence is enough to integrate the medical treatment to the nutritional and dietetics teraphy for preventing pre-cancerous lesions. In patients with recurrent infections, 4 or more positive tests for HPV are important indicators to increase the risk for developing cervical cancer. Above 100 variants of HPV are known to cause epithelial and mucose lesions, with variable oncogenic potential. Strains 16 and 18 are associated to cervical cancer in 70 to 76%[6].

Lesions and warts caused by HPV infection just to remit with the time but only in patients without recurrent infections. Patients with immunosuppression have a higher risk of developing oncogenic lesions and the risk of infections increases with the use of contraceptives with a duration more than 5 years[7]. The immune system can suppress when macronutrients (protein, carbohydrates, lipids) and micro-nutrients (zinc, folic acid and vitamin A and C) are not enough in the diet of women exposed to some risk factor mentioned as well as for inadequate nutritional status derived of poor healthy habits as the obesity[8]. The evidence shows that the obesity (BMI>30) and overweight (BMI>25 to 29.9) is associated directly with risk of developing cervical cancer. This association can be explained via metabolic alterations in endogenous hormones where the adipose tissue is related with production of proinflammatory cytokines[9]. As mentioned and due to the lack of a well-established nutritional therapy in the public hospitals in Leon Guanajuato, the main objective of this study was to analyzing nutritional status and food intake with emphasis in carotenoids, folic acid, vitamin A and C, which are considered protective factors for prevention and remission the premalignant HPV lesions in women[9].

METHOD

Study area

The study was conducted in a public hospital of Ministry of Health of Guanajuato State. Guanajuato is a Mexican state located in the middle area of the country and according to the 2015 intercensal National representing the 4.9% of the total of the country. Guanajuato is divided into 6 socioeconomic and geographic regions[10] with 46 municipalities.

Study design and participants

From August 2006 to May 2007, 75 women with confirmed diagnosis of HPV infection were admitted to the dysplasia clinic in a public hospital from Leon, Guanajuato. The infection was confirmed through a histopathological report. The sample was for convenience in this period. Exclusion criteria were anemia, gastritis, hepatic and renal disease, immunological and psychological pathologies. Once the patient signed an informed consent, a questionnaire was applied to collect the demographic data as well as risk factors: education, contraceptives, smoking habit, marital status, sexual partners, nutritional status, waist circumference >80 cm and dietetic factors (food frequency consumption).

Dietary Assessment

A food frequency questionnaire (FFQ) was carried out and the quantification of the average energy consumption (kcal), proteins (g), carbohydrates (g), fats (g) and the main micronutrients were calculated according to Evaluation System program of nutrition habits and nutrients consumption (SNUT for its acronym in Spanish)[11]. The register was made by a nutritionist. The analysis and measurements of carotenoids were done separately, through a frequency food intake survey of carotenoid rich food. In the SNUT were included 104 food types and divided by groups. For accuracy, plates and cutlery with known measurements were used. SNUT results were compared against Dietary Reference Intake (DRI) for Mexican population[12], analyzing dietary adequacy when the range was among 90% to 100%. Dietary analysis was based in energy intake (total kilocalories), proteins (expressed in grams), lipids (expressed in grams) and carbohydrates (grams). A valid survey tool was applied to determine intake of Vitamin A, carotenoids, folic acid and vitamin C. Vitamin A intake was expressed in retinol units, whereas carotenoids in IU/day and folic acid in µg/day.

Anthropometric assessment

The nutritional status was evaluated using a Torino® scale with a maximum capacity of 120 kg, a stadiometer (Torino®) with 195 cm of capacity. With the weight and height, the body mass index (BMI) was calculated in order to establish a nutritional diagnosis; WHO criteria were used to determine healthy weight (18.5-24.9) overweight (25 and 29.9) and obesity (30 and 39.9).

Waist and hip circumference were measured to complement diagnosis. The following thresholds for waist-hip ratio were considered: gynecoid < 0.7 and android > 0.8. It is noteworthy that variables such as obesity, overweight, obesity and tobacco habit were considered as control variables.

Statistical analyses

Database was managed in Excel office® 2013, were descriptive statistics (standard deviation, media, percentages) were obtained for anthropometric, dietetic, and socio-demographic variables. Non-parametric tests as Ji^2 were obtained for inferential statistics with the software IBM SPSS® Non-parametric tests as Ji^2 were obtained for inferential statistics with the software IBM SPSS® to find any association between risk factors and age group. To know how risk age can be associated to risk factor, a risk assessment was conducted,

and the outcome was reported in Odds ratio with confidence interval 95%.

RESULTS

The mean age of participants was 25 ± 6 (range 18 to 35) years old. Respect to the risk factors a 40% of participants referred use of oral contraceptives (OC) sometime and 26% currently use them. A 36% were smokers which 13% mentioned smoking every day. Tobacco use was higher for age 21 to 30 years ($p<0.05$), as well as frequency (19% of women in this group used tobacco daily, $p<0.05$). The marital status more prevalent in women was married (43%); 31-35 years age group had a higher number of married women (68%). Respect to number of sexual partners the age group 18 to 20 years had a higher proportion (>2). (Table 1).

Average weight in participants was 61 ± 11.4 kg, a mean height of 155 ± 6 cm and 80 ±10.6 cm of waist circumference. A 27% had overweight and a 30% obesity. A 51% had hip circumference > 80 cm. Respect the age ranges the age group of 31 to 35 years had the higher percentage of overweight

Table 1. Sociodemographic chacarteristics.

Risk factor		Age (years)				*P value**
		Total	18-20	21-29	30-35	
		n=75 (%)	n=11 (%)	n=36 (%)	n=28 (%)	
Education	None	5(7)	0(0)	1(3)	4(14)	*0.505*
	Primary	31(41)	6(54.4)	12(33)	13(46)	
	Secundary	22(29)	3(27)	11(31)	8(29)	
	High school	12(16)	2(18.5)	8(22)	2(7)	
	University	5(7)	0(0)	4(11)	1(4)	
Contraceptives	Never	45 (60)	10 (90.9)	18(50)	17(60.7)	*0.520*
	Before	30(40)	1(9.09)	12(33.3)	8(28.5)	
	At present	20(26)	0 (0)	6(16.6)	3(10.7)	
Smoking habit		27(36)	5(45.4)	18(50)	4(14.2)	*0.009*
	Daily	13(17)	3(27.2)	7(19.4)	3(10.7)	*0.003*
	Weekly	8(10)	2(18.2)	6(16.6)	0(0)	
	Infrequent	6(8)	0(0)	5(13.8)	1(3.5)	
	Never	48(65)	6(54.5)	18(50)	24(85.7)	
Marital status	Single	24(32)	7(64)	14(39)	3(11)	*0.008*
	Married	43(57)	4(36)	20(55)	19(68)	
	Divorced	8(11)	0(0)	2(6)	6(21)	
Sexual partners**		2(1-20)	2(1-20)	2(1-8)	1(1-4)	*0.042*
Nutritional status	Overweight	20(27)	2(18)	7(19)	11(39)	*0.003*
	Obesity	23(30)	1(9)	9(25)	13(47)	
Waist circunference >80 cm		38(51)	3(27)	14(39)	21(75)	*0.004*

*Chi square test. **Mean (Rank).

(39%), obesity (47%) and waist circumference > 80 cm (75%) (Table 1).

Regarding food and nutritional intake, carotenoid rich foods were consumed less often, spinach, broccoli, carrot, and papaya were consumed less than once per week (70%, 54%, 68%, 37% and 48%, respectively). Nutritional intake was similar among age group and range. Broccoli and carrot consumption were significantly reduced in age group 21 to 31 years, (58% and 30% respectively reported a consumption fewer than 1 portion per week).

Mean energy intake was 2145 kcal (911 to 4758 kcal) with a dietary adequacy >110% in 73% of participants. Median lipid consumption was 91g (27 to 254g) where 84% of participants had an intake >110% in relation to adequacy ratio. Protein and carbohydrates consumption median were 68g (31-143g) and 280g (95-620g). 52% and 66% of participants had an over the limit intake of carbohydrates and proteins, respectively ((>110%). Carbohydrates and dietetic fiber consumption were significantly higher in participants 18 to 20 years old (Table 2).

Frequency consumption of food rich in vitamin A, vitamin C, folic acid and carotene were not statistically significant between groups. Nonetheless, tomato (60% consumed tomato everyday) and milk (39% consumed milk everyday) were consumed more frequently than the other foods (Table 3).

To calculate the risk factors between older and younger women, we decided to analyze Odds ratio and to compare

Table 2. Nutrimental consumption per age group.

	DRI*	***18-20***	***21-30***	***31-35***	***P value*** **
	Mean (±SD)	***Mean (±SD)***	***Mean (±SD)***	***Mean (±SD)***	
Energy (Kcal)	1300-1900	2592.9±907.6	2274.1±861.4	1894.7±561.9	*0.056*
Proteins (g)	48-76	84.3±26.8	71.9±30.9	66.5±19.0	*0.259*
Carbohydrates (g)	161-258	357.6±141.3	298.9±116.6	238.6±83.9	*0.021*
Lipids (g)	40-64	100.6±34.8	93.2±43.4	81.5±25.3	*0.410*
Dietetic fiber (g)	24	39.5±14.7	30.7±12.2	26.1±10.2	*0.028*
Vitamin C (mg)	60	250.7±155.6	174.0±92.8	163.8±77.3	*0.211*
Vitamin A (µg)	800	5464.2±4385.4	4129.1±4481.8	3835.1±3317.4	*0.432*
Folic acid (µg)	200	611.7±617.1	547.4±537.3	452.4±286.6	*0.664*
Carotenoid* **	-	6385.5±3748.8	5444.4±3651.6	5977.0±5998.3	*0.550*
Dietary adequacy					
Energy (kcal)		165.4±56.6	153.8±54.4	127.1±40.2	0.066
Proteins (g)		134.1±41.1	121.3±49.1	111.5±33.3	0.332
Carbohydrates (g)		192.4±64.5	188.0±78.2	164.8±56.2	0.446
Lipids (g)		169.2±65.7	150.2±56.9	118.3±42.8	0.029
Fiber (g)		164.9±61.4	127.9±50.8	108.7±42.5	0.028
Vitamin C (mg)		417.9±259.4	290.1±154.7	273.0±128.9	0.211
Vitamin A (µg)		683.0±548.1	516.1±560.2	479.3±414.6	0.432
Folic acid (µg)		305.8±308.5	273.7±268.6	226.2±143.3	0.664

*DRI: Daily Reference Intake. Kilocalories, carbohydrates, lipids and proteins were calculated individually, the remaining nutriments were compared to the DRI for mexican population. **Kruskall-Wallis test. *** A DRI for Carotenoids has not been established.
Overweight participants ingested a significantly higher quantity of vitamin A when compared to the other groups (Table 3).

Table 3. Frequency consumption of food rich in Vitamin A, Vitamin C, Folic acid and carotens.

Food	Frequency	Age (years)				*p value*
		Total	18-20	21-29	30-35	
		n=75(%)	n=11 (%)	n=36 (%)	n=28 (%)	
Spinach	Never	30(40)	6(54)	16(44)	9(32)	*0.849*
	Daily	3(4)	0(0)	3(8)	0(0)	
	1 to 3 times per week	19(26)	3(27)	10(28)	8(29)	
Broccoli	Ocassionaly*	23(30)	2(19)	13(36)	11(39)	*0.257*
	Never	24(32)	7(67)	9(25)	8(29)	
	Daily	1(1.3)	0(0)	1(3)	0(0)	
	1 to 3 times per week	23(30.6)	1(9)	14(39)	8(29)	
Carrot	Ocassionaly*	27(36)	3(27)	12(33)	12(43)	*0.794*
	Never	14(18.6)	3(27)	7(19)	4(14)	
	Daily	3(4)	0(0)	3(8)	0(0)	
	1 to 3 times per week	45(60)	6(54)	22(61)	17(61)	
Tomato	Ocassionaly*	13(17.3)	2(19)	4(11)	7(25)	*0.262*
	Never	2(2.6)	1(9)	1(3)	0(0)	
	Daily	45(60)	6(54)	24(67)	16(57)	
	1 to 3 times per week	27(36)	3(27)	11(30)	12(43)	
Papaya	Ocassionaly*	1(1.3)	1(9)	0(0)	0(0)	*0.547*
	Never	21(28)	5(45)	7(19)	9(32)	
	Daily	4(5.3)	1(9)	1(3)	2(7)	
	1 to 3 times per week	35(46.6)	3(27)	20(55)	12(43)	
Milk	Ocassionaly*	15(20)	2(19)	8(22)	5(18)	0.765
	Never	6(8)	1(9)	2(6)	3(11)	
	Daily	29(39)	2(19)	16(44)	11(39)	
	1 to 3 times per week	26(35)	5(45)	11(30)	10(36)	
Liver	Ocassionaly*	14(18)	3(27)	7(19)	4(14)	0.887
	Never	31(41)	5(45)	14(39)	12(43)	
	Daily	0(0)	0(0)	0(0)	0(0)	
	1 to 3 times per week	21(27.6)	4(36)	10(28)	7(25)	
	Ocassionaly*	22(29)	2(19)	12(33)	9(32)	

*Less than once a week.

risk factors in women of 18 to 28 years old vs women of 29 to 35 years old. We found higher risk of smoking, overweight or obesity, and higher waist circumference in women with VPH of 29 to 35 years than in women of 18 to 28 years. Older women were more exposed to being married or divorced and had an earlier sexual intercourse. There were no association between age and education (High scholl or college career), use of contraceptives and number of sexual partners (Table 4).

Table 4. Risk factors associated with women of 18 to 28 years old vs women of 29 to 35 years old.

Risk Factor	OR	CI95%	*P value**
Highschool or lower	0.330	0.096-1.132	*0.070*
College career	0.315	0.033-2.959	*0.289***
Use of contraceptives	1.313	0.516-3.336	*0.567*
Smoking	4.136	1.418-12.063	*0.007*
Marital Status	4.275	1.383-13.210	*0.009*
First sexual intercourse age <18	3.740	1.388-10.078	*0.008*
Sex partners >2	0.635	0.253-1.597	*0.333*
Nutritional status (overweight or obesity)	5.600	2.026-15.478	*0.001*
Waist circumference >80cm	3.713	1.407-9.795	*0.007*

*Chi square test, **Fisher´s exact test.
Odds ratio of the group divided between older and younger women.

DISCUSSION

In Mexico, prevention of Cervical Cancer is a priority. There was a decrease in HPV in women older than 20 years old because they had a test for Papanicolaou in 2018 (42.8%) when compared with 2012 (42.8%)[13], as a direct result of incentives given to early screening detection programs. An adequate nutritional status includes intake of foods rich in antioxidants is considered a crucial element to prevent cervical cancer. To assess food habits was the main objective of this study in women.

Different risk factors have been considered to promote HPV[14], a 2011 study reported a relative risk (RR) of 1.13 (CI95%,1.02-1.26) for women who used contraceptives before age 20, in comparison to those who used contraceptives after this age[15]. In the present study, 46% admitted previous use of OC, while 26% were still using OC. Concerning age groups, there was no statistically significant difference in oral contraceptive use between those who were above 20 years old (more than 40%) and those below 20 years old, where only one participant admitted use of OC (9%).

For women with history of tobacco use for more than 16 years, it is more likely to develop cervical cancer in presence of HPV infection (OR=3.23; CI95%= 1.33–7.69). These OR are still valid for women who smoke 20 or more cigarettes per day (OR=2.57; CI95%= 1.49–4.45). This risk persists even in patients who have abandoned the habit of smoking (RR=1.6, CI95%= 1.0–2.7)[3]. Age related analysis revealed that tobacco use is higher in women 18 to 30 years, when we compare it to age group 31 to 35 years ($p<0.05$). Thus, the reproductive age group could be at higher risk.

We found that 64% of patients in age group 18 to 20 years old had two or more sexual partners, thus, this age group could have a higher risk of being infected with HPV, given the fact that a relationship is well established for a higher number sexual partners and first sexual activity and HPV infection. On the other hand, a 2016 study showed that women who declare having multiple male sexual partners or casual sexual partners, are often detected in higher numbers 2.81 (CI95%, 1.38–5.69), in our study the women denied having had sexual intercourse in the last six months[16].

Obesity and overweight percentage found in this study reflect an inflammatory process and a higher immunosuppression. Moreover, waist circumference greater than 80 cm could be another risk factor to focus on since it reflects the level of central adiposity. An inadequate nutritional status increases the risk of an HPV infection progression to Cervical cancer, this could partly be explained due to a higher oxidative stress that suppresses the immune system. A body mass index (BMI) higher than 29, lack of screening via Papanicolaou test and other factors increase the risk of developing cervical cancer[17].

From 30% to 40% of cancer types are preventable. An adequate, healthy diet is associated to an ideal nutritional status, including physical activity[18]. Evidence has showed a link between cervical cancer and food habits. Concerning carotenoids and vitamin C, it has been established that consumption of these nutriments stops oxygen reactions, increase cellular, and humoral immunity response[19-20]. Additionally, oxidant-antioxidant balance, cellular reactions and transmissions are fundamental to cellular immunity. These events are crucial to reduce HPV infection, which in time could lead to cervical cancer[21].

Folic acid[22,23], betacarotene[24,25] and vitamin A, C, and E intake are a protective factor against cervical cancer. There is no evidence of vitamin B6 and B12 as protective factors against HPV[26]. Lycopene, lutein, and xanthine may reduce risk of cervical pre-malign lesions. Based on this, a reduced intake of these carotene rich foods may contribute to a pathologic state.

Additionally, studies that included dietary analysis have detected an inverse proportion between green and yellow vegetables consumption (rich in carotene and vitamins C and E) and pre-cancer lesions of high and low risk. High vitamin A-rich and carotenoid foods intake have been associated with a risk reduction for HPV[19]. Such mechanism is still not clear, but antioxidants may play a part. Folic acid, vitamins B12, B6 and methionine may act as protective factors in preventing cervical cancer, due to its involvement in DNA methylation[27].

It is worth mentioning that results are not very consistent, and evidence points toward promotion of fruit and vegetables consumption, to prevent progression of premalignant lesions to cervical cancer. Thus, it is required to focus on dietary consumption research in patients infected with HPV, to develop better ways to scrutinize, prevent and intervene from a nutritional point of view and to evaluate the antropomethric component as it may seem to associate with sarpenia and other risk factors which may diminish the quality of life of the patient[28]. Micronutrients were also evaluated in the present study, showing that Vitamin A, C and carotenoids consumption is a protective factor, Although an adequate or high intake was found in 70% of the cases, this information is not congruent with food frequency consumption surveys, where consumption of foods rich in these nutriments was lower than once per week in 54% of participants.

Cervical cancer is included in health institutions and given priority in healthcare programs because of its causal factors, numbers remain high considering adjustments in healthcare programs in Mexico[29]. As science continues to stride forward, we have evolved from a clinical and pharmacologic treatment to a multidisciplinary approach (dietitians, physicians, nurses, and health professionals) in which nutrition is not only considered prophylactic, but a therapeutic intervention on itself.

It is necessary to address the weaknesses in the present study; a descriptive design means there are no groups to compare or demonstrate that dietary patterns directly cause cervical cancer. Nonetheless, it adds evidence on important environmental risk factors, focusing mostly on diet. It is necessary to mention that quantitative inconsistencies shown in the SNUT survey concerning food intake referred by participants, would not allow us to observe a conclusion or generate definitive associations. Even so, it is possible to assess the importance of an adequate and healthy diet.

Food intake was high in carbohydrates, which are considered a risk factor. This is a weakness in the present study, e.g.: soda consumption occupied 11th place in 2007 as part of our country's list of basic foods, costing 2.5 times more than consuming a daily fruit on average, on the other hand, in 2018, 85% of population up to 20 years old in México consume sweetened drinks frequently[30]. This study contributes to emphasize the importance of integrating nutritional counseling and patient care.

CONCLUSION

Carotenoid, folic acid, and vitamin A and C consumption were sufficient to cover daily requirements in Mexican population, moreover, consumption in some cases was above daily requirement (>100%) nonetheless, intake frequency for these foods was low. Carrot (48%), milk (40%) and tomato (11%) were consumed more than once a week, and ≥2 times per week.

A 57% were overweight or obese, abdominal fat storage was present as indicator in 51%. The group with the highest risk factor was patients 31 to 35 years old, except for number of sexual partners and smoking, which was present in the age group of 18 to 21 years old.

No association was found between nutritional status and food intake, however, a caloric intake higher than 110% was found in 73% of participants. An inadequate macronutrients ingestion was also found. Carbohydrates shown a tendency to be consumed in higher quantities.

Even though the present study identified an adequate exposure to key nutrients, inadequate intake of macro-nutrients, pre-obesity and obesity, as well as risk factors already mentioned, allow us to define a hypothesis to identify and determine a study design with longer following times and shorter lapses to correct and modify lifestyles. This study showed the deficiency in the consumption of nutrients, the presence of obesity, waist circunference >80 cm, sexual partners, and smoking. Therefore, it is important to consider and implement nutritional management as part of medical treatment in clinics for dysplasias or premalignant lesions due to human papillomavirus.

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