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Article

Drinks and food caffeine consumption and factors associated with higher intakes. A cohort study in pregnant women.

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Abstract: We aimed to assess the caffeine intake before and during pregnancy, compliance with caffeine recommendations during pregnancy (<200 mg/day) and factors associated with higher intakes before and in first trimester of pregnancy. Caffeine consumption was collected in a Spanish cohort of pregnant women through a validated food questionnaire, before and in each trimester of gestation (T1, T2 and T3). 463 pregnant women were recruited and follow-up through pregnancy. Compliance with caffeine intake recommendations during pregnancy and quintiles of mg/day of caffeine before and in T1 of pregnancy were calculated. A multivariate logistic regression, comparing extreme quintiles of consumption (Q1 vs Q5) was used. Mean caffeine intake before pregnancy was 120.05 mg/day (SD 117.85), 42.76 mg/day (SD 63.90) at 12th GW, 42.00 mg/day (SD 59.76) at 24th GW and 39.34 mg/day (SD 50.9) at 32nd GW (p<0.001). 86% of women complied with caffeine recommendations during pregnancy. At pregnancy (T1), being an active smoker was associated with Q5 > 100.1 mg/day, aOR = 22.69; 95% CI 4.67- 110.26. igh diet quality, aOR = 0.30; 95% CI, 0.13- 0.68, and moderate physical activity level, aOR= 0.44; 95% CI, 0.19-1.00, were inversely associated with Q5 > 100.1 mg/day. Pregnant women are mostly adhering to current caffeine intake guidelines. Higher caffeine intake at pregnancy is associated with other unhealthy habits during pregnancy.

Keywords: caffeine, pre-pregnancy, pregnancy, intake, quintiles

1. Introduction

Caffeine is the world´s most widely used and accepted psychoactive substance, an alkaloid from the methylxanthines family, which freely cross the placenta barrier, so the fetal plasma concentration is similar to the maternal plasma concentration [1]. Cytochrome P450 1A2 (CYP1A2) enzyme is responsible of 90% of the caffeine metabolism and it is in the maternal liver but absent in the fetal liver and placenta [1-3]. The average half-life of caffeine increase in pregnancy, reaching 9-11 hours in the third trimester. [3].

Caffeine is the only psychoactive substance that is sold as a nutritional food supplement in a variety of products, including food, dietary supplements and medications [4], which make its consumption habitual also among pregnant population [5-7]. During pregnancy, the maximum limit of caffeine intake recommended should be 200 mg/day [8, 9].

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Findings from observational studies and meta-analyses indicate that maternal caffeine consumption is reliably associated with miscarriage, stillbirth, low birth weight and/or small for gestational age, childhood acute leukemia and childhood overweight and obesity [10, 11]. Recently, it has been associated in Korean pregnant women a higher risk of bleeding in early pregnancy among those with heavy coffee consumption (≥2 cups of coffee/day) before pregnancy [12].

Mean daily caffeine intake in European pregnant women reveals a median value of 58 mg of caffeine at 22 GW, in Norwegian women [13] and 59.2 mg/day during the first trimester in French women [14]. Nevertheless, knowledge about the adequacy of caffeine intake recommendations during pregnancy is rather low [15]. In order to promote healthy lifestyles according to caffeine intake during pregnancy and given the few publications about caffeine consumption in pregnant women in our setting [16] it is necessary to conduct studies to reveal the habits of caffeine intake in women of childbearing age and to analyzed its association with sociodemographic and other lifestyles, such us tobacco use, physical activity or adherence to the Mediterranean diet (AMD). The aim of this study was to evaluate the intake of caffeine before and through pregnancy, the compliance with caffeine intake recommendations during pregnancy, and to estimate factors associated with higher caffeine consumption before and during the first trimester of pregnancy.

2. Materials and Methods

2.1 Design

It was carried out a prospective cohort study: 'Lifestyles in Andalusian pregnant women' in which besides caffeine other habits were measured: smoking, alcohol, drugs, sleep habits, physical activity, and Adherence to the Mediterranean Diet (AMD).

2.2 Participants

The reference population included all those pregnant women controlled in health centers of the Andalusian Health Service from Seville, Huelva, Granada, and Jaen (south of Spain), who met the following selection criteria: healthy pregnant woman, with an appointment in the clinic before 14 weeks of gestation, and without any language, cognitive or understanding barriers and accepting to participate in the study. We excluded pregnant women with chronic disease, that alter diet or physical activity, such as diabetes, gestational diabetes, hypertension or gestational hypertension, heart failure, respiratory, moderate, or severe renal or hepatic disease, or neurological or musculoskeletal diseases that influence mobility, in absolute rest or with multiple gestations.

Volunteer midwifes from the Health Centers selected women from February 2013 to February 2016. In March 2013, the Provincial Ethics Committee of Granada approved the study (C-24-2013). Database is fully anonymized, by identifying each participant with a numeric code according to the Organic Law of Protection of Personal Data. All women included in this study provided informed consent. The study follows the rules of the Declaration of Helsinki of 1975, revised in 2013.

2.3 Sample size estimation

Considering an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, 333 subjects were necessary to recognize as statistically significant a minimum difference greater than or equal to 5 mg/day of caffeine among different measures. It has been anticipated a dropout rate of 15%.

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2.4 Information sources

Throughout pregnancy, a trained interviewer conducted three structured personal (T1) or telephone interviews (T2 and T3). The first interview (T1) was at 12th gestational week (GW). At this moment we collected information about first trimester of pregnancy and from the 2-3 pre-pregnancy months. Follow-up appointments were in two subsequent interviews, in the 24 GW, ± 2 weeks (T2), and in the 32 GW (T3), respectively.

In T1 data collected were: *sociodemographic variables:* age, nationality, education level, paid work, parity, and social class (I high, II medium-high, III medium, IV medium-low, V low), taking into account the higher social class, either the woman's or her partner's occupation [17]; pre-pregnancy *anthropometrics data* (weight, height and BMI). In T1, T2 and T3 we evaluated *intake variables* (caffeine, smoking and alcohol), and other lifestyles such as *insomnia* (by EAI) [18], *physical activity* (short-IPAQ) [19] and *AMD,* using the 13-point MDA-score categorized as low adherence (<8) and high adherence to Mediterranean diet (≥8) [20, 21].

2.5 Caffeine measurement

The intake of caffeine was collected from drinks and foods through questions from a validated food questionnaire [22] pre-pregnancy, in T1, T2 and T3. The daily, weekly, or monthly caffeine intake was collected. We obtained number of cups of 150 milliliters (ml) of coffee, decaffeinated coffee, and tea per day; bottles of 200 ml for Coke and energy drinks, respectively, and number of squares (28 mg) a day of milk chocolate and chocolate without milk.

Transformation in mg/day of caffeine from each source were calculated according to the literature (Supplementary Table S1) [23, 24]: 100 mg per cup of caffeinated coffee, 2 mg per cup of decaffeinated coffee, 39 mg per cup of tea, 20 mg per bottle of 200 ml of Coke, 64 mg per 200 ml of energy drink, 6 mg per square of milk chocolate and 23 mg per square of dark chocolate. Caffeine recommendation during pregnancy was achieved if caffeine consumption was lower than 200 mg/day [8, 9].

2.6 Statistical analysis

Categorical variables required absolute and relative frequency and 95% CI, whereas for quantitative variables average, standard deviations and quintiles were calculated. One way ANOVA or Chi square test were used to compare the independent variables between quintiles of caffeine intake pre-pregnancy and in T1. Repeated measures ANOVA was applied to compare mean caffeine intake and mg/day of caffeine from different drinks and foods across pregnancy, from pre-pregnancy to T3. To assess the factors associated with a higher consumption of caffeine before pregnancy and in the first trimester of pregnancy (Q5), we used a multiple logistic regression comparing extreme quintiles of consumption (Q1 vs Q5).

A priori, those factors related to caffeine intake - tobacco, pre-pregnancy BMI, maternal educational level, paid work, and social class were considered as potential confounders. To control for confounding variables, those variables that changed the caffeine intake coefficient by >10% were retained in the logistic models. Finally, the models were adjusted by age (18-25; 26-30; 31-35; >35), social class (I-II; III; IV-V), parity (0,1, ≥2), paid work (yes, no), Body Mass Index (normal, overweight and obesity), and IPAQ physical activity level (light, moderate and vigorous). First model, about higher intake of caffeine before pregnancy, was also adjusted for Adherence to the Mediterranean diet (AMD) (low<8; high≥8) and active smokers (no, yes) before pregnancy. Second model, about higher intakes of caffeine in T1, was also adjusted for AMD and active smokers during pregnancy. We considered statistically significant a p value below 0.05 and a confidence

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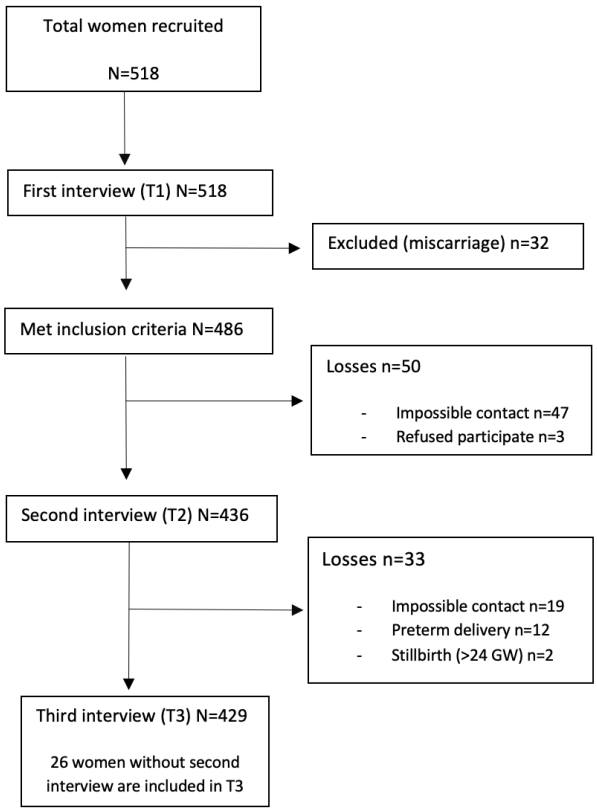
level of 95%. We used STATA 14 College Station, TX, USA statistical packages for the analysis.

3. Results

A total of 518 pregnant women were recruited and 89.3% of them (N= 463) had some follow-up through pregnancy. 55 women were lost because of miscarriage, refusing to participate, stillbirth < 24 GW, preterm birth and because they were unable to contact with, Figure 1.

Figure 1. Cohort flow chart



The average age of pregnant women was 31.2 years (SD 4.87). Mostly all of them had Spanish nationality (94%), 42.5% had university studies and 53.3% were at moderate-high social class (I to III). Pre-pregnancy, a 70.6% of the sample had paid work. Around half of pregnant women (51.6%) were primiparous (data not shown in tables).

3.1 Caffeine intake, compliance with recommendations and source of caffeine intake

The mean caffeine intake before pregnancy was 120.05 mg/day (SD 117.85), 42.76 mg/day (SD 63.90) at 12th GW, 42.00 mg/day (SD 59.76) at 24th GW and 39.34 mg/day (SD 50.9) after 32nd GW ($p<0.001$). Caffeine intake, in mg/day, before and during pregnancy according to sociodemographic and lifestyles variables is shown in Table 1. Before pregnancy the mean caffeine intake was higher in women with a previous child ($p< 0.001$), paid work ($p= 0.005$), active smokers ($p<0.001$) and obese ($p<0.002$). In T1, women over 35 years old ($p=0.015$), active smokers ($p< 0.001$), overweigh ($p<0.001$), and with low AMD ($p<0.001$) had a higher average intake of caffeine. And in T2 and T3 those with > 1 child, overweight and active smokers.

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Table 1. *Mg/day of caffeine intake before and during pregnancy according to sociodemographic and lifestyles variables.*

		Pre-pregnancy	**First Trimester (T1)**	**Second Trimester (T2)**	**Third Trimester (T3)**
		N= 462	N= 462	N= 428	N= 423
ẋ: mg/day of caffeine (SD)		ẋ=120.05 (117.85)	ẋ=42.76 (63.90)	ẋ=42.00 (59.76)	ẋ=39.30 (0.99)
Age		*0.463*	***0.015****	*0.421*	*0.313*
	18-25	53	49	48	49
		119.79 (123.36)	47.36 (81.88)	41.87 (58.05)	39.21 (59.48)
	26-30	135	127	129	125
		114.08 (116.64)	35.86 (59.58)	34.38 (57.61)	35.35 (49.21)
	31-35	184	159	167	168
		121.79 (124.02)	39.53 (58.78)	41.93 (63.60)	38.63 (48.88)
	>35	88	81	84	81
		125.87 (108.93)	**57.13 (66.51)**	53.92 (55.01)	46.82 (52.62)
Social Class		*0.080*	*0.187*	*0.755*	*0.086*
	I -II	157	140	149	148
		119.05 (108.85)	43.08 (58.69)	45.51 (60.57)	43.37 (52.14)
	III	89	84	85	83
		125.87 (134.10)	38.55 (63.38)	40.94 (62.14)	43.43 (57.17)
	IV - V	216	192	194	192
		118.38 (117.51)	44.37 (67.88)	39.77 (58.25)	34.36 (46.95)
Parity		***0.001****	***0.019****	***0.013****	***0.002****
	0	239	217	222	219
		119.98 (107.96)	38.64 (58.00)	38.19 (53.84)	35.73 (44.51)
	1	196	174	181	180
		120.45 (133.12)	45.81 (70.94)	44.40 (66.31)	**44.02 (57.41)**
	≥2	27	25	25	24
		117.86 (81.71)	**57.35 (60.06)**	**58.48 (58.51)**	36.40 (54.51)
Paid work (yes)		***0.005****	*0.058*	***0.021****	*0.081*
		326	298	298	301
		127.16 (123.87)	45.03 (66.10)	**44.85 (62.57)**	42.20 (52.68)
AMD (high)		*0.127*	***0.001****	*0.994*	***0.010****
		218	239	257	257
		112.58 (111.36)	35.43 (56.51)	40.08 (59.80)	33.40 (46.18)
Active smokers (yes)		***<0.001****	***<0.001****	***<0.001****	***<0.001****
		167	59	53	51
		161.28 (135.28)	77.89 (85.69)	89.75 (98.40)	69.43 (73.31)
BMI		***0.002****	***<0.001****	***<0.001****	***0.001****
	Normal	286	260	268	265
		113.87 (107.11)	38.09 (57.57)	40.10 (55.46)	37.89 (48.56)
	Overweight	128	117	116	114

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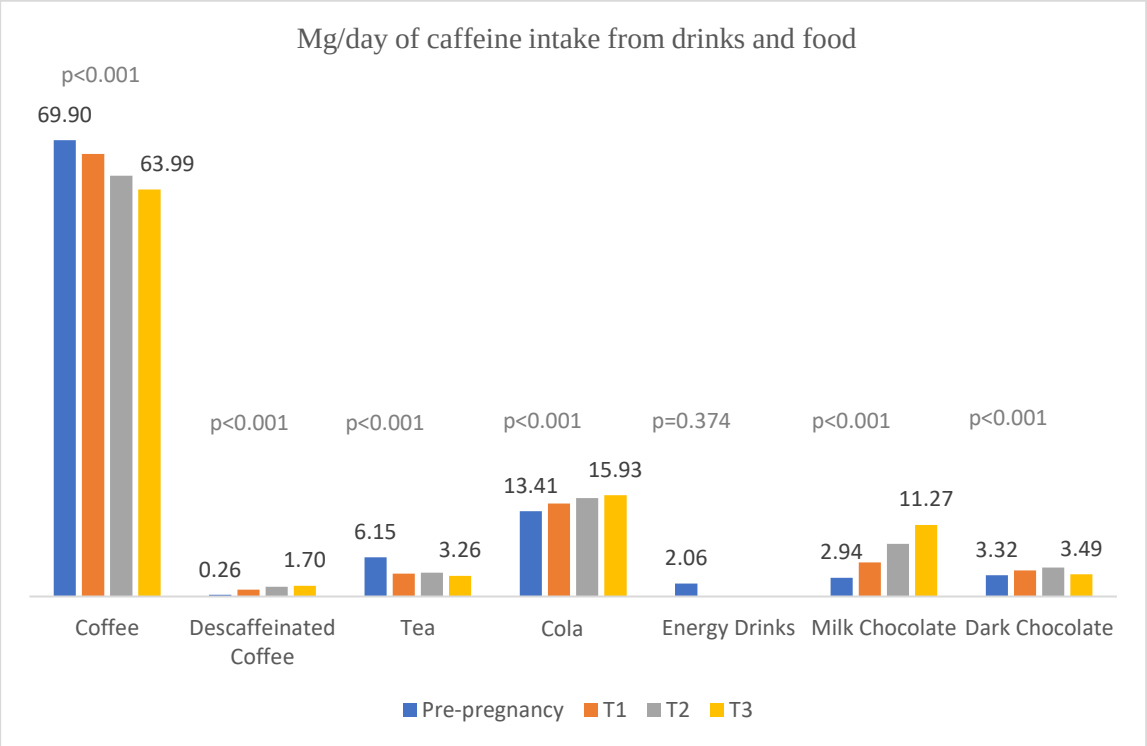
		127.51 (138.97)	**53.93 (78.17)**	**50.95 (72.84)**	**44.89 (59.96)**
	Obesity	45	36	42	41
		134.62 (118.24)	38.06 (52.91)	28.90 (41.65)	33.03 (37.44)
IPAQ		*0.074*	*0.269*	*0.207*	*0.850*
	Light	181	213	214	215
		113.15 (106.77)	42.57 (60.47)	40 (56.81)	36.65 (50.49)
	Moderate	239	182	207	204
		121.52 (125.48)	42.10 (67.21)	42.96 (62.94)	41.61 (51.65)
	Vigorous	42	21	6	4
		141.45 (118.47)	50.36 (70.82)	85.14 (41.49)	63.74 (41.28)

Anova p <0.05; Anova p value <0.001; **BMI**, Body Mass Index; **IPAQ**, International Physical Activity Questionnaire; **AMD**, Adherence to the Mediterranean Diet; **mg**, milligrams

According to the compliance with caffeine intake during pregnancy (<200 mg/day), 13.8% of women (n=64) exceed the recommendations in T1, 3.9% (n=17) in T2 and 2.3% (n=10) in T3 (data not shown in tables).

Mg/day of caffeine from drinks and foods before pregnancy and through pregnancy is shown in Figure 2. Coffee decreased and decaffeinated coffee, coke and chocolate increased during pregnancy (p<0.001).

Figure 2. Mg/day of caffeine intake from drinks and food.



P value: ANOVA repeated measure

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3.2 Factors associated with a higher caffeine consumption (Q5 versus Q1).

Before pregnancy an association was observed between a higher caffeine consumption (Q5>214.2 mg/day) and active smokers (p<0.001) or employed women (p=0.012), Table 2.

Table 2. *Sociodemographics, anthropometrics and lifestyles in quintiles of caffeine intake before pregnancy (N=462)*

Before pregnancy	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	
	n=93 (20.2%)	**n=95 (20.5%)**	**n=99 (21.4%)**	**n=86 (18.6.4%)**	**n=89 (19.2%)**	
	< 12.78mg/day	**12.79-54.07mg/day**	**54.08-**	**116.15-**	**>214.2 mg/day**	**P value[1]**
			116.14mg/day	**214.14 mg/day**		
Age	ẋ=32.48 (SD=4.11)	ẋ= 29.90 (SD=4.5)	ẋ= 30.42	ẋ= 31.60	ẋ=31.89	0.002*
			(SD= 5.89)	(SD= 4.96)	(SD= 4.27)	
Social Class						0.705
I -II	36.6%	27.5%	33.7%	36.2%	35.6%	
III	23.7%	19.8%	14.1%	19.1%	20%	
IV - V	39.8%	52.7%	52.2%	44.7%	44.4%	
Parity						0.067
0	47.31%	50.5%	52.2%	60.6%	48.9%	
1	48.39%	47.3%	40.2%	29.8%	46.7%	
≥2	4.3%	2.2%	7.6%	9.6%	4.4%	
Paid work						0.012*
Yes	75.2%	62.1%	61.6%	80.2%	75.3%	
AMD before pregnancy						0.713
Yes (high)	46.24%	51.6%	49.5%	46.5%	41.5%	
Active smokers before pregnancy						<0.001**
Yes	20.4%	28.4%	37.4%	37.2%	58.4%	
BMI						0.772
Normal	65.6%	58.9%	63.9%	62.8%	60.2%	
Overweight	27.9%	29.4%	28.8%	23.3%	29.5%	
Obesity	6.4%	11.6%	7.2%	13.9%	10.2%	
IPAQ						0.857
Light	38.7%	38.9%	40.4%	38.3%	39.3%	
Moderate	54.8%	51.6%	53.5%	48.8%	49.4%	
Vigorous	6.4%	9.5%	6.0%	12.8%	11.2%	

[1]Anova or Chi Square p value; * p<0.05; **p<0.001. Abbreviations: **BMI**, Body Mass Index; **IPAQ**, International Physical Activity Questionnaire; **AMD**, Adherence to the Mediterranean Diet.

During T1, active smokers (<0.001), and paid work women (p=0.034) were associated with Q5 caffeine intake (>100.1 mg/day), and high AMD was associated to Q1 caffeine intake (<0.39 mg/day) (p=0.017), Table 3.

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Table 3. *Sociodemographics, anthropometrics and lifestyles in quintiles of caffeine intake in first trimester (N=459)*

T1		**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**P value**[1]
		n=92	n=94	n=90	n=92	n=91	
		< 0.39mg/day	0.40- 5.11mg/day	5.12-23.19mg/day	23.20- 100.39mg/day	>100.4 mg/day	
Age		ẋ=31.5 (DS=4.6)	ẋ= 30.5 (DS=5.3)	ẋ= 30.7 (DS= 4.7)	ẋ= 30.5 (DS=4.9)	ẋ=32.6 (DS=4.8)	0.710
Social Class							0.013*
	I -II	42.1%	36.6%	21.4%	25.6%	43.2%	
	III	22.9%	17.1%	26.2%	16.3%	18.5%	
	IV - V	34.9%	46.3%	52.4%	58.1%	38.3%	
Parity							0.082
	0	63.8%	54.8%	45.2%	43.0%	54.3%	
	1	32.5%	40.2%	50.0%	45.3%	40.7%	
	≥2	3.6%	4.9%	4.7%	11.6%	4.9%	
Paid work							0.034*
	Yes	80.7%	62.2%	70.2.7%	66.3%	79.0%	
AMD (in T1)							0.017*
	Yes (high)	72.2%	53.7%	60.7%	52.3%	48.1%	
Active smokers (in T1)							<0.001**
	Yes	2.4%	9.7%	14.3%	16.3%	28.4%	
BMI							0.420
	Normal	68.7%	65.4%	64.3%	59.5%	56.8%	
	Overweight	26.5%	24.7%	22.6%	33.3%	34.6%	
	Obesity	4.9%	9.9%	13.1%	7.1%	8.6%	
IPAQ (in T1)							0.591
	Light	43.4%	53.7%	58.3%	47.7%	53.1%	
	Moderate	51.8%	43.9%	36.9%	45.3%	40.7%	
	Vigorous	4.8%	2.4%	4.7%	6.9%	6.2%	

[1]Anova or Chi Square p value; * p<0.05; **p<0.001. Abbreviations: **BMI**, Body Mass Index; **IPAQ**, International Physical Activity Questionnaire; **AMD**, Adherence to the Mediterranean Diet; T1: First trimester

Table 4 shows the logistic regression of factors associated with a higher caffeine intake before and in the first trimester of pregnancy, comparing Q5 with Q1. Smoking before pregnancy was associated with higher caffeine intake (Q5 > 214.2 mg/day) before pregnancy aOR =7.12; 95% CI, 3.40-14.92. During T1, being an active smoker was a risk factor of a higher caffeine intake (Q5 > 100.1 mg/day), aOR = 22.69; 95% CI 4.67- 110.26. Women with high AMD in T1, aOR = 0.30; 95% CI, 0.13- 0.68, and those with moderate physical activity level, aOR= 0.44; 95% CI, 0.19-1.00, were inversely associated with a higher consumption of caffeine.

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Table 4. *Logistic regression of factors associated with a higher caffeine intake before and in the first trimester of pregnancy*

	Model 1. Pre-pregnancy higher caffeine intake n=89 (Q5[1]; > 214.2 mg/day)				Model 2. First trimester higher caffeine intake n= 91 (Q5[2]; > 100.1 mg/day)			
	cOR	**CI 95%**	**aOR[a]**	**CI 95%**	**cOR**	**CI 95%**	**aOR[a]**	**CI 95%**
Age								
18-25	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**
26-30	1.04	0.30-3.61	1.20	0.29-5.01	0.56	0.16- 1.86	0.55	0.11- 2.67
31-35	0.71	0.22-2.30	1.24	0.32- 4.83	0.53	0.17- 1.71	0.74	0.16- 3.43
>35	0.81	0.22-2.88	1.36	0.30- 6.03	1.62	0.46- 3.84	2.67	0.53- 13.55
Social Class								
I -II	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**
III	0.86	0.39- 1.91	0.67	0.27- 1.69	0.78	0.35- 1.79	0.69	0.25- 1.90
IV-V	1.11	0.57- 2.16	0.73	0.30- 1.77	1.06	0.54- 2.13	0.55	0.20- 1.48
Parity								
0	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**
1	0.95	0.53- 1.73	0.90	0.45- 1.80	1.47	0.77- 2.81	0.94	0.42- 2.14
≥2	1.02	0.24- 4.35	1.39	0.27-7.05	1.60	0.34-7.56	1.50	0.25-9.02
Paid Work								
Yes	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**
No	0.99	0.51- 1.96	0.80	0.34- 1.87	1.11	0.51- 2.38	0.86	0.31- 2.39
AMD								
Low (<8)	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**
High (≥8)	0.82	0.46-1.48	0.63	0.31- 1.28	0.35	0.18- 0.68	0.30	0.13- 0.68
Active								
smokers	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**
No	5.47	2.83-10.55	7.12	3.40-14.92	16.06	3.64-70.81	22.69	4.67-110.26
Yes								
BMI								
Normal	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**
Overweight	1.15	0.60- 2.22	1.35	0.62- 2.98	1.58	0.80- 3.11	1.15	0.49- 2.70
Obesity	1.72	0.57- 5.16	2.76	0.76-10.06	2.16	0.60- 7.86	3.37	0.70- 16.35
IPAQ								
Light	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**	**1**	**Ref.**
Moderate	0.89	0.48-1.64	1.00	0.48- 2.09	0.64	0.34- 1.21	0.44	0.19- 1.00
Vigorous	1.71	0.56- 5.22	1.56	0.41- 5.97	1.04	0.26- 4.19	1.04	0.18- 6.03

[a]Adjusted for age, social class, parity, paid work, Adherence to the Mediterranean Diet before (model 1) or during pregnancy (model 2), active smokers before (model 1) or during pregnancy (model 2), BMI, IPAQ. Abbreviations: **AMD**, Adherence to the Mediterranean Diet; **BMI**, Body Mass Index; **IPAQ**, International Physical Activity Questionnaire; [1] Compared to Q1 (n=93), <12.78mg/day; [2] Compared to Q1 (n= 92), <0.39mg/day.

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4. Discussion

The present study shows that caffeine intake in pregnant women decrease throughout pregnancy. During pregnancy, the average consumption of caffeine decreases below half compared to pre-pregnancy. Throughout the entire pregnancy, more than 86% of women have less than 200 mg/day caffeine intake, as it is recommended. Active smoker women had higher caffeine intake before and during pregnancy. A lower consumption of total caffeine intake per day during the first half of pregnancy was observed in those who performed moderate physical activity and had higher Adherence to the Mediterranean Diet.

4.1 Limitations and strengths

Selection of health centers was done by convenience, so the sample was representative of healthy pregnant women from the south of Spain. They represent healthy women from developed countries but no other low sociodemographic populations. Hindsight of caffeine intake before pregnancy, after being already pregnant, may be a potential risk of memory bias. Medications and dietary supplements were not considered in the caffeine measurement. We considered exclusively drinks and food containing caffeine. Because caffeine intake in our sample was rather low, there was a limitation to achieve risk factors involved in >400 mg/day of caffeine intake before pregnancy and > 200 mg/day during pregnancy. Only 2.16% of women did not achieve the caffeine recommendations before pregnancy and 6.7% during the entire pregnancy.

The strength of our study is mostly its design, a prospective cohort study and the first carried out in pregnant Spanish population. It also allows a comparison of multiple sources of caffeine consumption between different trimesters of pregnancy and the pregestational stage. The same researcher collected the data, giving uniform information and consistency to the recorded data. We used questions from a validated food frequency questionnaire, specifically to collect caffeine intake, like others previously used in pregnancy [16]. Women who dropped out of the study or follow up were similar in demographics variables from those who finished the study.

4.2 Comparison with other studies

Previous studies conducted in New York [25] and United Kingdom [26] also used questionnaires to collect caffeine intake –Food Frequency Questionnaire and CAT Questionnaire. In the assessment of caffeine intake, other authors have considered, as we did, cola products and tea [27] or energy drinks and chocolate [2, 24, 28].

Mean daily caffeine intake in European pregnant women reveals an intake lower than the recommendations; for example, 44 mg/day at 17 gestational week (GW) in Norwegian women [28], or a median value of 58 mg at 22 GW, also in Norwegian women [13]. In English population, average caffeine intake during pregnancy (mostly from tea) was 128.6 mg/day. [26]

According to the adherence to the caffeine intake guideline during pregnancy, 70% of Australian pregnant women seems to comply [15]. In our study, we found a better adherence to the guidelines, with more than 80% of pregnant women consuming bellow 200 mg/day of caffeine. On the contrary, more than 40% of pregnant women in Finland reported consuming more than the recommended maximum of 200 mg of caffeine per day. [29]

In this study and in the American one, coffee is the main source of caffeine, assuming over 60% of total consumption [30]. This also happens in Asian pregnant women. Data from the Korean pregnant outcome study (KPOS) shows that before conception, 17% of

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women were moderate coffee drinkers (1cup/day) and 18% were heavy coffee drinkers (≥ 2 cups/day) [12]. It should be noted in our study that, from conception, chocolate is more consumed than tea, which was not happening in the preconception stage, and differs from the results of other European studies [7, 28] where chocolate is slightly consumed during pregnancy.

Accordingly with other studies [14, 16, 25-28], the average consumption of caffeine decreased through pregnancy compared to pre-pregnancy. Also, in line with other studies [12, 15, 30], smoking before pregnancy was associated with higher caffeine consumption during pregnancy. We found that also in smoking during pregnancy. Smokers may drink more caffeine because smoking increases the rate of caffeine metabolism (upregulates CYP1A2), which means that smokers may need to drink more caffeine to experience the same effects as non-smokers.

Additionally, prenatal caffeinated drinks, not including coffee, such as soft drinks/soda/pop/sugary drinks/fizzy drinks and energy drinks have been related to non-Adherence to the Mediterranean Diet [31]. In our study, we found a higher caffeine intake, during first trimester of pregnancy in those women with non-Adherence to the Mediterranean Diet. Furthermore, we found that moderate physical activity in the first trimester of pregnancy seems to be associated with lower mg/day of caffeine intake.

4.3 Implications for research and practice

Accumulating scientific evidence advises pregnant women and women contemplating pregnancy to avoid caffeine. Health promotion by informing about adequate caffeine intake should focus on all pregnant women. Because there seems to be a general aggrupation of unhealthy lifestyles during pregnancy, health educators must be alert and pay special attention to women who add unhealthy lifestyles from before conception, such as active smokers, overweight and those with poor quality diet. Future research should be focused on the influence of insomnia, depression, or anxiety on caffeine consumption in pregnancy, as well as the caffeine intake patterns of pregnant women's partners and their influence on them.

5. Conclusions

Caffeine intake by pregnant women may be considered low. Pregnant women are mostly adhering to current caffeine intake guidelines. Higher caffeine intake at pregnancy is associated with other unhealthy habits during pregnancy, such as smoking and non-Adherence to the Mediterranean Diet.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Table S1: Transformation of mg of caffeine.

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