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Original Research

Cancer risk assessment and dietary flavonoid intake following dietary counseling in high risk groups for ovarian and cervical cancer- A fact finding study in Chennai City, India

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ABSTRACT:

Background: Gynaecological cancers are a major health concern for women, especially in India, where late diagnoses due to low awareness and limited screening impact outcomes. This study aims to evaluate the dietary intake of flavonoid-rich foods among women at risk of ovarian and cervical cancer, analysing changes in consumption patterns following dietary counseling among different classes of body mass index (BMI). **Materials and Methods:** Risk factors associated with ovarian & Cervical cancer were evaluated among the participants attending Primary Health Centre in Kovur, Chennai, India. Participants who showed assertive responses to at least 50% of the questions related to ovarian & cervical cancer risk factors were included in the study. Flavonoid intake was assessed through a 7-day dietary recall, recorded at baseline, Day 14, and Day 21 and dietary counseling aimed at increasing the consumption of flavonoid-rich foods was implemented. **Results:** No overall association was found between BMI and the consumption of flavonoid-rich foods, except for berries. Significant differences in berry intake were observed across BMI categories on both the 14th day ($p < 0.001$) and 21st day ($p < 0.001$). Post-hoc analysis revealed that the 'Obese Class I' group consumed significantly more berries than the 'Normal' group at baseline ($p < 0.001$). By the 21st day, the 'Obese Class II' group consumed higher berry intake compared to the 'Obese Class I' ($p < 0.05$), 'Normal' ($p < 0.05$), and 'Overweight' groups ($p < 0.01$). No significant associations were found between BMI and fruit, vegetable, or legume intake. **Conclusion:** This study highlights disparities in flavonoid-rich food intake, particularly berries, across BMI categories in women at risk for ovarian and cervical cancer. The findings emphasize the need for targeted nutritional interventions to improve dietary habits and promote flavonoid consumption as a potential preventive strategy against gynaecological cancers.

Keywords: Flavonoids, Dietary counseling , Ovarian cancer , Cervical cancer.

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INTRODUCTION

Ovarian and cervical cancers are among the most common gynaecological cancers affecting women globally, including in India. Each year, 122,844 women in India are diagnosed with cervical cancer, and 67,477 die from it (1) Although cervical cancer rates are declining, it remains the second most common cancer in India. According to the GLOBACAN 2022 report, both ovarian and cervical cancers remain significant health concerns worldwide (2) Unhealthy Dietary and lifestyle habits are linked to an increased risk of cancer on their own next only to prominent risk factors like alcohol and smoking. On the contrary, a healthy diet that includes whole grains, fiber, and healthy gut bacterial environment seems to reduce risk (3) Current Treatment Strategies for ovarian & cervical cancer includes surgery , chemotherapy which can cause vomiting, hair loss, fatigue, increased susceptibility to infections, and potential long-term effects on fertility and organ function . These side effects and treatment limitations highlight the need for innovative, personalized, and less toxic approaches to enhance outcomes

Chemoprevention is an emerging and promising strategy to prevent cancer by using dietary or pharmaceutical interventions to halt or reverse the progression of premalignant conditions to invasive cancer (4) Dietary habits, particularly consumption of flavonoid-rich foods, are gaining attention for their positive role in cancer prevention (5) Flavonoids are a group of potentially chemoprotective compounds widely distributed in fruit, vegetables, and beverages of plant origin (5) Key flavonoids that have demonstrated potential in ovarian & cervical cancer include: Anthocyanin, quercetin, genistein, apigenin (6) Quercetin the most abundant flavonoids in plant foods are mainly present in leafy vegetables, apples, onions, broccoli, and berries.Apigenin and anthocyanidins are present in relatively small quantities in grains, leafy vegetables, and herbs.Genistein are mainly found in soybeans and soy-based products (5) These flavonoids may be promising candidates for use as anticancer agents in ovarian & cervical cancer due to their wide availability,effective cancer-fighting properties & minimal toxicity

Recent study have found that higher intake of certain types of flavonoids, particularly those from fruits and vegetables, was associated with a reduced risk of ovarian cancer. Specifically, increased intake of flavonoids such as quercetin, showed a potential protective effect against ovarian cancer.(7) Another study found that apigenin, demonstrated significant anticancer effect (8) These results imply that higher flavonoid intake may be linked to a lower risk of cancer, although this relationship may not be consistently observed across all studies.

The objective of this study was to assess the intake of flavonoid-rich foods related to prevention of ovarian & cervical cancer by tracking dietary history at the end of 7th and 14th day and 21st day following dietary counselling. We hypothesized that flavonoid intake varies among women across different categories of BMI

METHODOLOGY

Study Design and Population: This longitudinal study aimed to evaluate changes in flavonoid intake following dietary counseling. Participants' dietary habits were recorded over 7 days at three follow up periods: baseline, 14th day, and 21st day, to observe any alterations in consumption post-intervention. The study took place at Primary Health Centre, Kovur, Chennai, India between January 2024 and May 2024. Participants were women, predominantly middle-aged or older women.

Data Collection: Data were gathered from participants using an interviewer-led questionnaire which contained demographic information and risk factors for ovarian and cervical cancer, as given by CDC (9) Key risk factors included being middle-aged or older, having a family history of ovarian cancer, a personal history of breast, uterine, or colon cancer, diagnosis of endometriosis, difficulties with fertility or never given birth, and long-term use of estrogen-only hormone therapy for 10 years or more. Participants showing over 50% of these risk factors were included in the study, while those with fewer than 50% of the identified risk factors were excluded. The dietary history of the participants was documented over a period of 7 days at three intervals: baseline, the 14th day, and the 21st day, to evaluate their intake of flavonoid rich food .Participants were instructed to record the type, timing, and amount of food consumed. Upon reviewing the 7-day dietary history, dietary counseling was provided to promote the consumption of flavonoid rich foods in quercetin, genistein, apigenin, and anthocyanins as these compounds are known for their potential benefits in reducing the risk of ovarian and cervical cancers.

Sample size estimation: With the reported prevalence of ovarian cancer of 6.1% in Chennai, the sample size was calculated to be 92 using the formula: $4 \times p \times q / L^2$, where p represents the prevalence of ovarian cancer, q is (1 - p), and L is the precision set at 5%. To account for a potential 10% attrition rate, the sample size was increased to 102.

Statistical analysis: Analyses were carried out using IBM SPSS Statistics software (version 24). The data were tested for normality using the Kolmogorov-Smirnov test, which showed that the data did not follow a normal distribution. Therefore, non-parametric tests were used to determine significance. Descriptive statistical analyses were conducted to characterize the study sample. To compare mean values and investigate association between flavonoid-rich food consumption and body mass index (BMI),

the Kruskal-Wallis non-parametric test was employed, with a predetermined significance level of $\alpha = 0.05$.

RESULTS

This longitudinal study employed a follow-up design to assess and compare the consumption of flavonoid-rich foods among women attending Primary Health Centre in Kovur , Chennai ,India . The study consisted of three assessment periods: 7 days, 14 days, and 21 days post-intervention, following dietary counseling. A total of 176 participants were deemed eligible for the study. However, 31 participants did not satisfy the inclusion criteria, and an additional 42 participants declined to participate, resulting in a total of 73 exclusions. A total of 5 participants (5.1% of the initial sample) were lost to follow-up, yielding a final sample of 98 participants. To facilitate data analysis and interpretation, flavonoid-rich food intake was stratified into four distinct categories: (1) Berries, comprising blueberry, cranberry, and raspberry; (2) Fruits, including pomegranate, guava, apple, and grapes; (3) Legumes, solely consisting of soybeans; and (4) Vegetables, encompassing a range of varieties such as snake gourd, bell pepper, broccoli, carrot, radish, drumstick leaf, lady's finger, and cauliflower.

Table 1: Demographic characteristics of study participants

Groups		Frequency (n)	Percentage %
Age (in years)	<15 years	-	-
	15-39	33	33.7
	40-64	59	60.2
	>65	6	6.1
Religion	Hindu	67	68.4
	Christian	15	15.3
	Muslim	16	16.3
Educational qualification	Illiterate	4	4.1
	Primary school	5	5.1
	Middle school	16	16.3
	High school	12	12.2
	Intermediate / diploma	27	27.6
	Graduate	23	23.5
	Professional	11	11.2
Occupation	Unemployed	8	8.2
	Elementary occupation	14	14.3
	Plant and machine operators and assemblers	11	11.2
	Craft and related trade workers	12	12.2
	Skilled agricultural and fishery workers	11	11.2
	Skilled workers, shop and market sales	8	8.2
	Clerk	10	10.2
	Technician /Associate professors	11	11.2
	Professional	9	9.2
	Legislatures, senior officials, Manager	4	4.1
Body Mass Index (BMI)	Normal weight: 18.5-24.9	34	34.7
	Overweight: 25-29.9	42	42.9
	Obese class I: 30-34.9	17	17.3
	Obese class II: 35-39.9	5	5.1

The predominant age group among study participants was 40-56 years, accounting for more than half of the sample. Analysis of religious affiliation revealed that 68.4% (n = 67) of the study population identified as Hindu, making it the predominant religion among participants. To assess socio-economic status, participants were categorized according to their educational qualification and occupation using the Modified Kuppuswamy scale. The study population's educational background was as follows: 23.5% (n = 23) were graduates, while 4.1% (n = 4) were illiterate. Employment status revealed that 8.2% (n = 8) were unemployed and 4.1% (n = 4) held senior leadership positions. Furthermore, 42.9% (n = 42) of participants were classified as overweight (Table 1).

Table 2: Distribution of exposure to risk factor: Chi-Square Goodness-of-Fit test

Exposure to risk factor		N (%)	χ^2	*p*-value
Age: Middle aged or older	Yes	59 (60.2)	4.08	<0.05*
	No	39 (39.8)		
Familial history of ovarian cancer	Yes	8 (8.2)	68.61	<0.001**
	No	90 (91.8)		

Had history of breast, uterine or colorectal (colon) cancer	Yes	3 (3.1)	86.36	<0.001**
	No	95 (96.9)		
Had been diagnosed with endometriosis	Yes	12 (12.2)	55.87	<0.001**
	No	86 (87.8)		
Never given birth or have had trouble getting pregnant	Yes	19 (19.4)	36.73	<0.001**
	No	79 (80.6)		
Women who take estrogen by itself or (without progesterone) for 10 or more years	Yes	13 (13.3)	52.89	<0.001**
	No	85 (86.7)		
History of HPV infection	Yes	2 (2)	178.42	<0.001**
	No	95 (98)		

-N= number of study participants; χ^2=chi square with a df (degree of freedom)1
-**p<0.001, *p<0.05 is considered as statistically significant

The results of the Chi-Square Goodness-of-Fit test indicated a statistically significant difference ($p < 0.001$) between the observed and expected distributions of participants exhibiting specific risk factors, including: age ≥ 40 years, familial history of ovarian cancer, personal history of breast, uterine, or colorectal cancer, endometriosis, nulliparity or difficulty conceiving, prolonged use of estrogen-only therapy (≥ 10 years), and history of human papillomavirus (HPV) infection. The sample's risk factor distribution matched expected proportions (Table 2), suggesting a representative sample.

Table 3: Kruskal-Wallis test for intake of flavonoid rich food among different categories of BMI

Groups	Subgroups	BMI	N	Mean Rank	χ^2	*p* value
Berries	**Baseline**	Normal weight	34	49.69	3.06	0.38
		Overweight	42	45.79		
		Obese class I	17	56.47		
		Obese class II	5	55.70		
	14th day of follow-up	Normal weight	34	60.09	20.66	**<0.001****
		Overweight	42	52.00		
		Obese class I	17	29.21		
		Obese class II	5	25.50		
	21st day of follow-up	Normal weight	34	44.53	14.27	**<0.001****
		Overweight	42	51.81		
		Obese class I	17	43.38		
		Obese class II	5	84.70		
Fruits	**Baseline**	Normal weight	34	49.21	0.70	0.87
		Overweight	42	51.69		
		Obese class I	17	45.68		
		Obese class II	5	46.10		
	14th day of follow-up	Normal weight	34	47.53	0.88	0.83
		Overweight	42	52.44		
		Obese class I	17	47.71		
		Obese class II	5	44.30		
	21st day of follow-up	Normal weight	34	48.57	0.25	0.96
		Overweight	42	51.11		
		Obese class I	17	47.85		
		Obese class II	5	47.90		
Vegetables	**Baseline**	Normal weight	34	49.12	1.94	0.58
		Overweight	42	47.11		
		Obese class I	17	57.65		
		Obese class II	5	44.50		
	14th day of follow-up	Normal weight	34	50.62	3.00	0.39
		Overweight	42	48.85		
		Obese class I	17	54.56		
		Obese class II	5	30.20		
	21st day of follow-up	Normal weight	34	52.21	1.19	0.75
		Overweight	42	49.24		
		Obese class I	17	48.00		
		Obese class II	5	38.40		

Legumes	**Baseline**	Normal weight	34	52.10	3.89	0.27
		Overweight	42	50.18		
		Obese class I	17	42.00		
		Obese class II	5	51.60		
	14th day of follow-up	Normal weight	34	53.38	2.53	0.46
		Overweight	42	47.23		
		Obese class I	17	46.97		
		Obese class II	5	50.80		
	21st day of follow-up	Normal weight	34	47.82	3.73	0.29
		Overweight	42	49.29		
		Obese class I	17	57.91		
		Obese class II	5	34.10		

-N= number of study participants; χ^2=chi square; df=degree of freedom
-*p<0.05, **p<0.001 is considered as statistically significant

Kruskal-Wallis test results indicated no significant association between BMI categories and the consumption of vegetables, fruits, and legumes.The intake of flavonoid-rich berries varied significantly across different BMI categories on both the 14th day ($p < 0.001$) and 21st day ($p < 0.001$) of follow-up, indicating a relationship between BMI and flavonoid-rich berry consumption (Table 3).

Table 4: Post-hoc analysis of Kruskal-Wallis test: Pairwise comparisons of intake of flavonoid rich food across different categories of BMI

		Reference group	Comparison group	Mean difference	p-value
Berries consumption	**14th day of follow-up**	Obese Class II	Normal	34.58	<0.05
		Obese Class I	Overweight	22.79	<0.01
		Obese class I	Normal	30.88	<0.001
	21st day of follow-up	Obese class I	Obese Class II	-41.31	<0.05
		Normal	Obese Class II	-40.17	<0.05
		Overweight	Obese Class II	-32.89	<0.01

Post-hoc analysis revealed significantly higher berry intake in the 'Obese class I' group compared to the 'Normal' group at baseline ($p < 0.001$).By the 21-day follow-up, individuals in the 'Obese Class II' group were consuming more berries than those in the 'Obese Class I', 'Normal', and 'Overweight' groups ($p < 0.05$, $p < 0.05$, and $p < 0.01$, respectively).

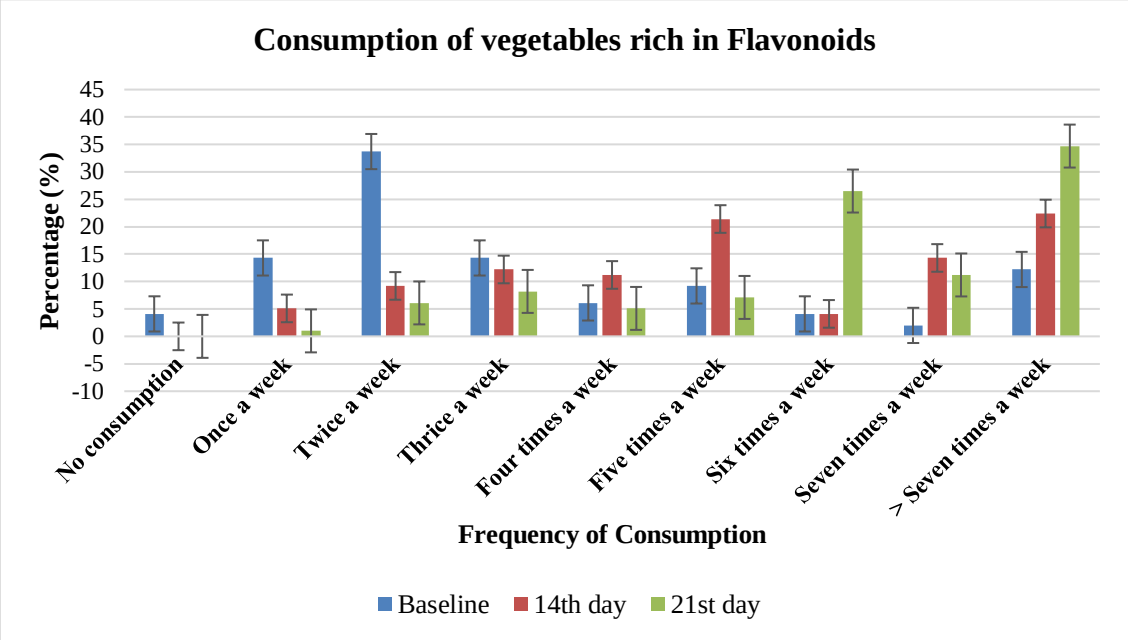

Figure 1: Distribution of vegetable consumption across three-time intervals (baseline, 14th day of follow-up and 21st day of follow-up) and different frequencies per week

Before the study started, nearly all participants (95.9%) reported eating vegetables, showing that vegetable consumption was a widespread and established habit. After receiving diet counseling, nearly a third of participants (34.7%) reported consuming vegetables more than 7 times per week, indicating a positive change in dietary behaviour [Figure 1].

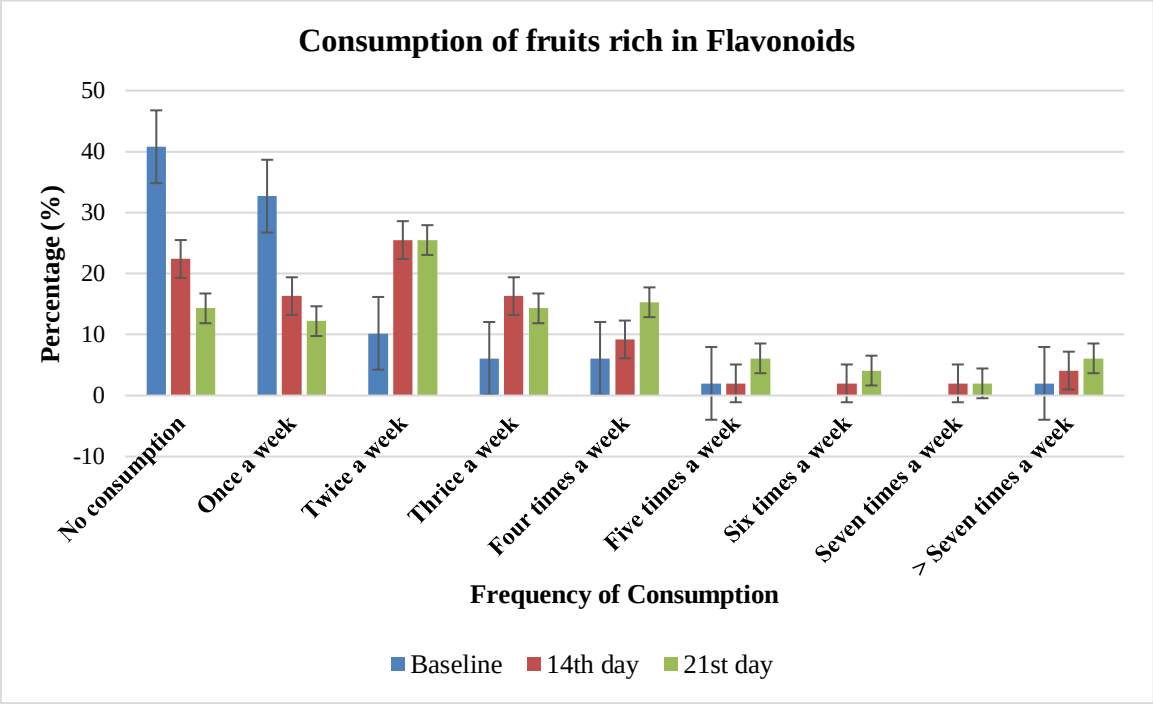

Figure 2: Distribution of fruits consumption across three-time intervals (baseline, 14th day of follow-up and 21st day of follow-up) and different frequencies per week

The study observed a notable increase in fruit consumption, with a significant reduction in the number of participants who reported not eating fruits at all, from 40.8% at the start to 4.3% by the end of the study.Analysis of fruit consumption patterns revealed that by day 21, a notable proportion of participants (18.5%) reported consuming fruits four times a week, indicating the formation of a stable and consistent habit [Figure 2].

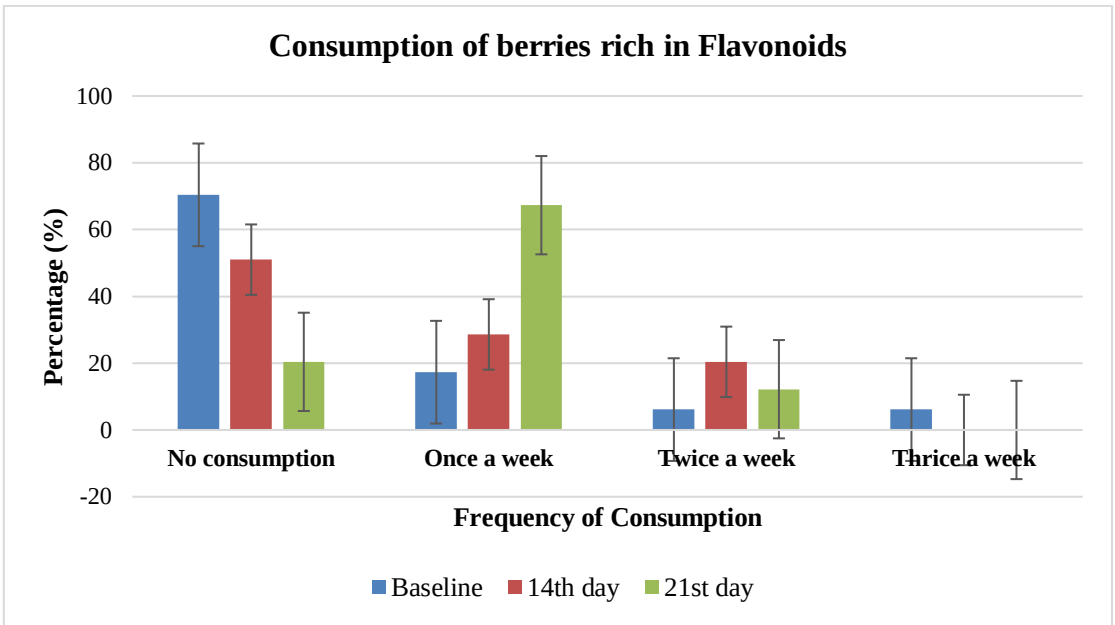

Figure 3: Distribution of berries consumption across three-time intervals (baseline, 14th day of follow-up and 21st day of follow-up) and different frequencies per week

Dietary counseling led to a significant increase in berry consumption, with the proportion of participants reporting no consumption decreasing from 70.4% at baseline to 20.4% at study completion [Figure 3].

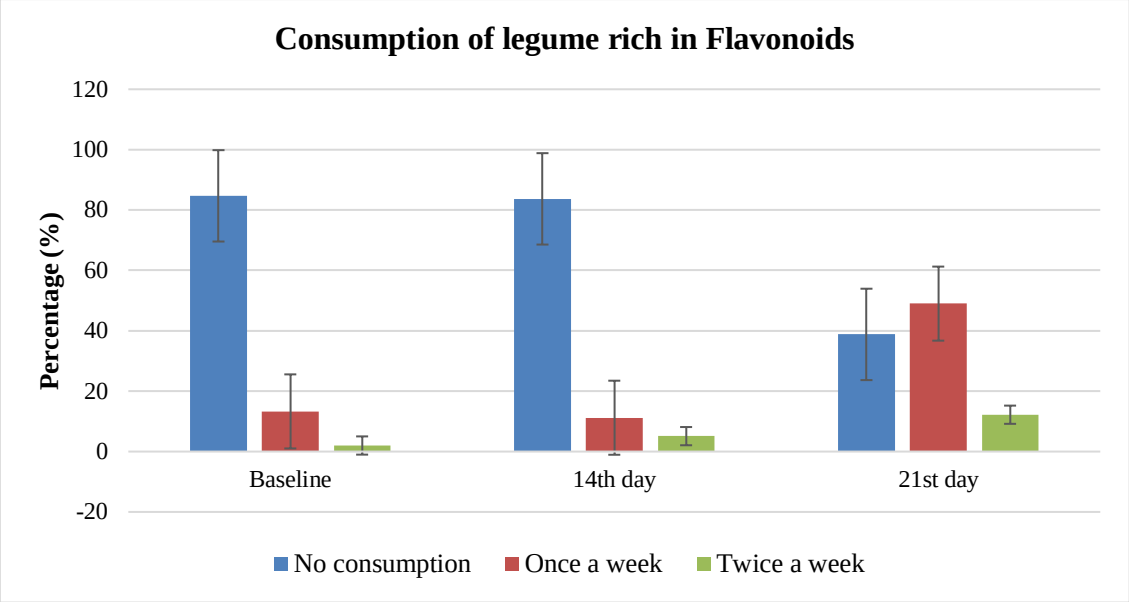

Figure 4: Distribution of legume consumption across three-time intervals (baseline, 14th day of follow-up and 21st day of follow-up) and different frequencies per week

Dietary counseling increased weekly legume consumption, with the percentage of participants reporting no consumption decreasing from 84.7% to 38.8% over the course of the study [Figure 4]

DISCUSSION

This longitudinal study investigated dietary patterns among women through repeated assessments, focusing on the relationship between flavonoid-rich food consumption and BMI. The results revealed no significant correlation between BMI and the intake of vegetables or legumes. However, noteworthy associations were identified between BMI and the consumption of specific food items, particularly berries, at various time periods. Berry intake varied significantly across BMI categories, with participants in the Obese Class I group reporting higher consumption on the 14th day, while Obese Class II participants recorded the highest intake by the 21st day. These findings suggest that BMI may play a role in shaping dietary habits related to certain flavonoid-rich foods, especially berries, over the study period. Regular intake of fresh fruits like apples, papaya, citrus fruits, pomegranates, amla, berries, watermelon, and kiwi has been found to be protective. These fruits contribute to increased dietary fiber intake, provide essential micronutrients, and support gut health. Additionally, compounds like quercetin in onions, ellagic acid in green tea, and apples have been found to be effective in preventing the recurrence of polyps, which are precursors to cancer. Higher intake of dietary fiber, calcium, and yogurt has also been associated with a lower risk of cancer (10)

A study by Larsson et al. demonstrated that for each additional daily serving of vegetables, the risk of ovarian cancer decreased by 10%. However, there was no evidence linking high fruit consumption with a reduced risk of ovarian cancer (11) . Similarly, a study by Leitzmann et al. highlights a moderate link between BMI and ovarian cancer risk, especially in women with low exogenous estrogen exposure.Findings of this study emphasize the need for obesity-focused public health strategies to reduce ovarian cancer risk (12), underscoring the importance of addressing obesity and promoting healthier dietary patterns to potentially reduce ovarian cancer risk. Additionally, a study by Lee et al. indicated that higher soy food consumption, rich in isoflavones, is associated with a lower risk of ovarian cancer (13). Another study by Lee et al. demonstrated that the antioxidant and anticancer properties of berry extracts exhibited strong cytotoxic effects on ovarian cancer cells (14), signifying the impact of flavonoid-rich foods, such as berries, on ovarian cancer risk, particularly in relation to BMI and dietary habits. Based on our findings, variations in the consumption of flavonoid-rich foods, particularly berries, fruits, and legumes, were observed among the study participants. While some participants showed minimal intake of these foods, others consumed them regularly, indicating the potential health benefits of moderate to high intake. Despite pre-existing high vegetable consumption, no significant association was found between very low consumption of flavonoid-rich foods and ovarian cancer risk.

A study by J.K. Chan et al. found that middle-aged and older women with ovarian cancer tend to present with higher-stage, poorly differentiated tumors and have lower survival rates than younger patients(15) .

In our study, 60.2% of participants were middle-aged or older. Additionally, a study by Brinton et al. (2004) found that women evaluated for infertility had a nearly doubled risk of ovarian cancer compared to the general population. The risk was higher for those with primary infertility and particularly elevated for women who never conceived. These findings suggest that the type and cause of infertility are important factors in assessing ovarian cancer risk. In our study, 19% of participants had never given birth or experienced difficulty conceiving. (16) Furthermore, a study by Milena et al suggests that endometriosis significantly increases the risk of ovarian cancer, particularly endometriosis-associated ovarian carcinoma (EAOC), with a higher prevalence in clear cell and endometrioid subtypes. In our study, 12.2% of participants were diagnosed with endometriosis, further highlighting its association with ovarian cancer risk (17). Another study showed that hormone therapy, particularly prolonged estrogen use, may further elevate ovarian cancer risk. Studies indicate that women with infertility, especially those with primary infertility and endometriosis, face a higher risk than the general population, with the highest risk observed in those who never conceive. In our study, about 13% of women used estrogen (without progesterone) for 10 or more years (18). Finally, a study by Cherif et al, demonstrated that a meta-analysis of 29 studies (2,280 ovarian cancer cases) found an overall HPV prevalence of 15.9%, with the highest rates in Asia (30.9%) and Eastern Europe (29.3%). HPV16 was the most common genotype (54%), though significant study variations suggest the need for further research on its link to ovarian cancer. In our study, 2% of participants had a history of HPV infection (19).

Few limitations are inherent in our study. First, the follow-up period of 21 days, with evaluations conducted at the baseline, 14th, and 21st days, was relatively brief. This timeframe may have limited our ability to assess the long-term maintenance of dietary changes and their broader effects on health outcomes. Second, the study did not incorporate a quantitative assessment of food intake, which could have offered more precise insights into the scale of dietary changes and their connection to health indicators, such as cancer risk. Lastly, the applicability of the findings is constrained by the demographic and cultural characteristics of the study population in Chennai. Participants' dietary behaviors were shaped by the availability of local foods and cultural norms, which may not reflect those of populations with different dietary practices or cultural settings. As such, caution is necessary when attempting to generalize these results to other groups or contexts.

CONCLUSION

Dietary counseling to enhance flavonoid intake may be a valuable strategy for lowering the incidence of ovarian and cervical cancer. Tailored dietary interventions in cancer prevention is the need of the hour, further studies are needed to confirm the long term impact of these dietary changes on health outcomes

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