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Is dairy foods restriction mandatory for inflammatory bowel disease patients: a multinational cross-sectional study

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ABSTRACT – Background – The role of dairy foods in inflammatory bowel disease (IBD) has been controversial and it is debatable if patients with IBD should avoid milk and dairy products or not, as well as the relationship between these foods and symptoms among those population. **Objective –** This multi centric cross-sectional study designed to evaluate if it is really necessary to deprive IBD patients from consumption of dairy foods. **Methods –** A multicenter study with 12 gastroenterology referral centers in four countries was designed to evaluate gastrointestinal (GI) symptoms after consumption of dairy foods from all outpatients with IBD during 6 months and to compare patients treated at the same centers without IBD (non IBD cases). **Results –** Overall 1888 cases included (872 IBD patients and 1016 non IBD cases). 56.6% of participants were female with average age of 40.1 years. Racially 79.8% participants were Caucasians and originally they were citizens of 10 countries. Relative prevalence of IBD was higher in Africans and Indians and the most frequent prevalence of dairy foods intolerance was seen in Asians. Among IBD patients, 571 cases diagnosed as ulcerative colitis and 189 participants as Crohn's disease. Average duration of diagnosis as IBD was 6.8 years (from 2 months to 35 years). The most prevalent GI symptoms after consumption of all the dairy foods were bloating and abdominal pain. Totally, intolerance of dairy foods and lactase deficiency was more prevalent among IBD patients in comparison with non IBD cases (65.5% vs 46.1%, *P*=0.0001). But the rate of GI complains among IBD patients who had not any family history of lactase deficiency, history of food sensitivity or both were 59.91%, 52.87% & 50.33% respectively and similar to non IBD cases (*P*=0.68, 0.98 & 0.99 respectively). **Conclusion –** The rate of dairy foods intolerance among IBD patients without family history of lactase deficiency or history of food sensitivity is similar to non IBD cases and probably there is no reason to deprive them from this important source of dietary calcium, vitamin D and other nutrients.

Keywords – Inflammatory bowel disease; lactase deficiency; dairy foods; bloating; abdominal pain.

INTRODUCTION

Inflammatory bowel disease (IBD) is a spectrum of inflammatory disorders which are characterized by chronic inflammation of the gastrointestinal tract in genetically susceptible individuals upon exposure to environmental risk factors[1,2]. The disease pathogenesis is not fully understood and considerable variation in the epidemiology of IBD has been observed around the world, with a wide range of estimates both within and between geographic regions[3]. Regardless of etiology, IBD is associated with bone loss and these patients are prone to osteoporosis not only because of chronic inflammation but also due to frequent use of corticosteroids, which stimulates osteoclastogenesis. IBD is also associated with vitamin D deficiency, which further contributes to bone loss[4-6].

Abdominal pain, gas/bloating, diarrhea and bowel incontinence are among the most frequent symptoms of IBD patients with some degrees of overlap between IBD and irritable bowel syndrome[7,8]. In clinical practice, restricting dairy products is common among IBD patients, possibly due to fear of disease activity, presence of gastrointestinal (GI) symptoms and extension of the disease[9]. The prevalence of osteopenia and osteoporosis in the IBD patients is 48.1%[10]. At the same time, 87% of patients with IBD reported

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milk consumption and patients' consumption of milk and other dairy products decrease after diagnosis[10]. Although there was a suggestion that dairy foods may protect against IBD and nutritional consequences of dairy restrictions might impact adversely on bone and colonic complications[11]. Dairy products constitute an important source of fats, vitamin D, proteins, and dietary calcium, and could be implicated in the development of IBD by modulating effects on intestinal microbiota and immune responses[12]. Both molecular and clinical studies suggest that dairy nutrients are inversely associated with low-grade inflammation, and affect key cytokines such as tumor necrosis factor alpha in the pathogenesis of IBD[13, 14].

Despite controversies regarding links of dairy products to the development of IBD, there are few epidemiological studies which have examined the relationship between these foods and the development of either Crohn's disease (CD) or ulcerative colitis (UC)[15-17]. So this cross sectional study designed to evaluate if there is any difference between IBD and non IBD patients in sensitivity to dairy products and GI complains following consumption of dairy foods and is it really necessary to deprive these patients from consumption of dairy foods as an important source of calcium, vitamin D and other nutrients in human diet.

METHODS

During a 6 months period, all of the IBD cases who attend in outpatient GI clinics of 12 referral centers in four countries (Egypt, Iran, Saudi Arabia and Vietnam) included and evaluated about any GI complain after consuming dairy foods including milk, yoghourt and cheese, any history of food allergy or family history of lactase deficiency. Diagnosis of IBD confirmed based on clinical and endoscopic findings plus compatible pathology report. The control group was non IBD cases who simultaneously attend in the same centers because of any other GI diseases including functional GI disorders or irritable bowel syndrome. Inclusion criteria include attendance in outpatient GI clinic because of any GI complain and about IBD cases, confirmed diagnosis of IBD based on colonoscopy and pathology report. The exclusion criteria include unwilling or refuse to participate in the study and any major problem that necessitate admission in the hospital. The questionnaire designed by supervision of two academic nutritionists and translated to four languages (English, Arabic, Persian and Vietnamese). In this questionnaire, any GI complain after consumption of three most popular dairy products (milk, yoghurt and cheese) including abdominal pain, bloating, nausea, vomiting and diarrhea evaluated and scored from 0 (no complain) to 5 (the most sever) (supplementary file). Also the participants questioned about food allergy and family history of lactose intolerance. The IBD cases subgroups include UC, CD and indeterminate colitis (those who did not fill the full criteria to categorize as UC or CD).

This study approved by Ethic Committee of Ahvaz Jundishapur University of Medical sciences (IR.AJUMS.REC.1399.252). We used SPSS software version 16.0 for data analysis. Data was checked for normality using Kolmogorov–Smirnov and Shapiro–Wilk tests. Mann Whitney U test and independent two-sample *t*-test were employed for comparing two quantitative variables. Chi-square test was used to evaluate association between two qualitative variables. To control potential confounders, multiple logistic regression model was used. Crude and adjusted odds ratios with 95% confidence intervals (CI) were presented. Analyses were declared significant for *P*-value <0.05.

RESULTS

Overall 1888 cases included (872 IBD patients and 1016 non IBD cases). 56.6% of participant were female (1069 cases) with average age of 40.1 y (age range 4–91). The demographic characters of participant are shown in TABLE 1. Racially 79.8% of participant were Caucasian (TABLE 2) and originally they were citizens of 10 countries. Relative prevalence of IBD was higher in Africans and Indians and recruited Asians showed the highest dairy foods intolerance among the studied races with prevalence rate of 98.5%, as shown in TABLE 2.

TABLE 1. Demographic characters of participants.

Group	IBD	Non IBD	*P* value
Number	872	1016	
M/F ratio	378/494	441/575	0.98
Average Age y (range)	36.8 (5–80)	42.9 (4–91)	0.46
Average weight kg (range)	69.8 (12–168)	78.2 (40–172)	0.09
BMI (average)	25.03	28.06	0.631
History of food allergy	41.9%	22.2%	0.0001
Family history of lactase deficiency	19.5%	8.8%	0.0001

IBD: inflammatory bowel disease; BMI: body mass index.

TABLE 2. Relative prevalence of dairy intolerance between IBD and non IBD cases based on race.

Race	Dairy intolerance			
	Total number of participants	IBD	Non IBD	*P*
Caucasian	1508 (79.8%)	442/670 (66.0%)	373/838 (44.5%)	0.000
ARAB	174 (9.2%)	51/98 (52.0%)	37/76 (48.7%)	0.775
African	87 (4.6%)	41/54 (75.9%)	4/33 (12.1%)	0.000
Asian	67 (3.5%)	15/17 (88.2%)	50/50 (100%)	0.102
Turk	29 (1.5%)	11/16 (68.8%)	3/13 (23.1%)	0.038
Indian	18 (0.9%)	10/16 (62.5%)	0/2 (0.0%)	0.356
Afghan	5 (0.2%)	1/1 (100%)	1/4 (25%)	0.819

IBD: inflammatory bowel disease.

Disease characteristics

Among IBD patients, 571 (65.48%) cases diagnosed as ulcerative colitis (UC), 189 (21.67%) participants as CD and 112 (12.84%) as indeterminate colitis with average duration of 7.3, 6.9 and 3.3 years respectively. Average duration of diagnosis as IBD was 6.8 years (from 2 months to 35 years). Relative prevalence of GI problems and intolerance of dairy products based on diagnosis are illustrated in TABLE 3.

Dairy products and bowel

The most prevalent GI symptoms after consumption of all of the dairy products were bloating and abdominal pain (TABLE 4, FIGURE 1). When we ignored mild symptoms and considered moderate to severe complains for analysis, the most prevalent symptoms were different among different diagnostic subgroups (TABLE 5).

Totally, intolerance of dairy foods was more prevalent among IBD patients in comparison with non IBD cases (65.5% vs 46.1%, *P*=0.0001) (TABLE 3) except those with Arab descent (52% vs 48.7%, *P*=0.66, TABLE 2). On the other hand, the prevalence of food allergy and family history of lactose intolerance were higher

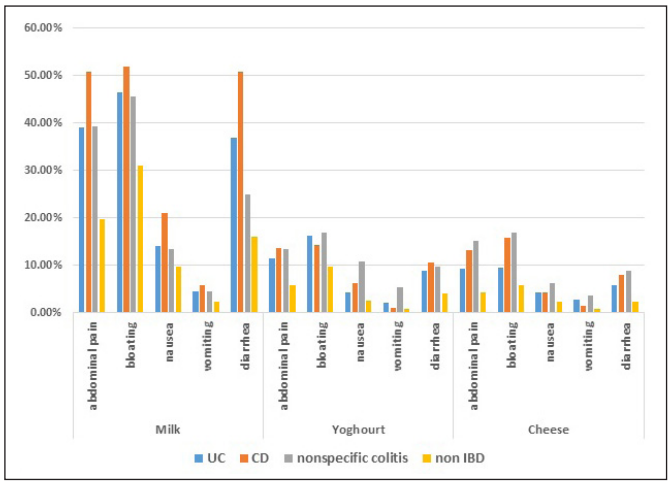

FIGURE 1. Prevalence of GI symptoms based on dairy product.
GI: gastrointestinal; UC: ulcerative colitis; CD: Crohn's disease; IBD: inflammatory bowel disease.

TABLE 3. Relative prevalence of GI problems after consumption of dairy products based on diagnosis (*P* value is comparison between IBD in total vs non IBD).

Dairy product	UC	CD	Indeterminate colitis	IBD total	non IBD	*P* value
Total	421 (73.7%)	135 (71.4%)	69 (61.6%)	571 (65.5%)	464 (46.1%)	0.000
Milk	351 (61.4%)	133 (70.3%)	67 (59.8%)	545 (62.5%)	438 (43.1%)	0.000
Yoghourt	136 (23.8%)	48 (25.3%)	32 (28.5%)	218 (25%)	145 (14.2%)	0.001
Cheese	91 (15.1%)	39 (20.6%)	28 (25%)	163 (18.69%)	95 (9.3%)	0.002

GI: gastrointestinal; UC: ulcerative colitis; CD: Crohn's disease; IBD: inflammatory bowel disease.

TABLE 4. Relative prevalence of GI symptoms based on different dairy products.

Dairy product	Symptom	UC	CD	Indeterminate colitis	non IBD	*P* value
Milk	abdominal pain	39.00%	50.70%	39.20%	19.70%	0.000
	bloating	46.50%	51.80%	45.50%	31%	0.000
	nausea	14%	21.10%	13.30%	9.80%	0.000
	vomiting	4.50%	5.80%	4.40%	2.26%	0.02
	diarrhea	36.90%	50.70%	25%	16.10%	0.000
Yoghourt	abdominal pain	11.50%	13.70%	13.30%	5.80%	0.000
	bloating	16.20%	14.20%	16.90%	9.64%	0.03
	nausea	4.20%	6.30%	10.70%	2.50%	0.017
	vomiting	2.10%	1%	5.30%	0.68%	0.013
	diarrhea	8.90%	10.50%	9.80%	4%	0.000
Cheese	abdominal pain	9.20%	13.20%	15.10%	4.20%	0.000
	bloating	9.40%	15.80%	16.90%	5.80%	0.02
	nausea	4.30%	4.20%	6.25%	2.40%	0.29
	vomiting	2.80%	1.50%	3.50%	0.88%	0.06
	diarrhea	5.70%	7.90%	8.90%	2.36%	0.000

GI: gastrointestinal; UC: ulcerative colitis; CD: Crohn's disease; IBD: inflammatory bowel disease.

TABLE 5. Prevalence of moderate to severe complains after consuming dairy products.

Dairy product	Symptom	UC	CD	indeterminate colitis	non IBD
Milk	abdominal pain	17.50%	19.57%	21.42%	5.70%
	bloating	23.80%	26.45%	25.89%	10.82%
	nausea	6.10%	4.76%	5.35%	2.36%
	vomiting	1.90%	2.11%	3.57%	0.98%
	diarrhea	21.30%	32.20%	14%	6.69%
Yoghourt	abdominal pain	3.67%	4.23%	8.03%	2.26%
	bloating	4.20%	4.76%	10.71%	3.54%
	nausea	1.92%	0.00%	3.57%	1.08%
	vomiting	0.70%	0%	1.78%	0.19%
	diarrhea	2.80%	3.17%	7.14%	1.37%
Cheese	abdominal pain	3.15%	4.23%	8.92%	1.47%
	bloating	2.80%	5.82%	5.35%	2.26%
	nausea	1.57%	0.52%	1.78%	1.08%
	vomiting	1.05%	0.52%	0.89%	0.39%
	diarrhea	1.75%	2.64%	5.35%	0.68%

UC: ulcerative colitis; CD: Crohn's disease; IBD: inflammatory bowel disease.

among IBD cases in comparison with non IBD patients (41.9% vs 22.2% and 19.5% vs 8.8% respectively, *P*=0.0001).

The rate of GI complains among IBD patients who had not any family history of lactase deficiency, history of food sensitivity or both were 59.91%, 52.87% & 50.33% respectively and similar to non IBD (46.1%) cases (*P*=0.68, 0.98 & 0.99 respectively, TABLE 6).

DISCUSSION

Lactase enzyme allows the intestines to absorb carbohydrates from the milk. The infant's gut has the highest lactase activity and deficiency of this enzyme occurs after weaning[18, 19]. This occurs to varying degrees across different populations, and can result in lactose malabsorption. Ethnic and geographical factors have an important role in this decline[20, 21]. Apart from some human populations in Northern Europeans, lactase deficiency with unknown mechanism occurs in all mammals, and consequently, intestinal bacteria carry on the task to metabolize lactose[22]. The activity of these bacteria leads to the production of hydrogen and other metabolites through anaerobic processes[23]. These metabolites cause abdominal and systemic symptoms, the most important of which are abdominal and joint pain, diarrhea, flatulence, headache, fatigue, and mouth ulcer[24].

In addition to genetic factors, the reduced activity of lactase-phlorizin hydrolase (LPH) can result from the over growth of bacteria in the small intestine, damage of the mucosa which occur in coeliac disease, CD, and infection[25, 26]. Moreover, the short contact time in the intestine and the inhibition of the sodium-dependent glucose transporter contributes to the incomplete absorption of carbohydrates in the intestine. Lactose intolerance can also originate from damage in the intestinal mucosa, like transient damage caused by the CD[27].

IBD is an increasing health-care problem over the world and both genetic and environmental factors have an important role in pathophysiology of these disorders[28-30]. Also, IBD occurs more commonly in countries of northern latitudes, which has been postulated to be related to vitamin D deficiency from less sun exposure[31]. The effect of dairy products on pathogenesis and the period of IBD is not known. Microbiome appears to play an important role in pathogenesis of IBD and diet may impact the composition and functionality of the microbiome[32, 33]. Previous studies showed that the consumption of dairy foods decreases the risk of CD and symptoms of UC. Intolerance symptoms depend on several parameters besides lactose maldigestion. Dairy foods may decrease risks of inflammatory bowel disease and dairy restrictions may adversely affect disease outcome[33].

TABLE 6. Relative prevalence of GI problems after consumption of dairy products among different sub groups of IBD patients.

Dairy product	IBD cases whit negative family history	IBD cases without food allergy	IBD cases without food allergy and negative family history	non IBD
Total	420 (59.91%)	267 (52.87%)	225 (50.33)	464 (46.1%)
Milk	416 (59.25%)	254 (50.29%)	215 (48.09%)	438 (43.1%)
Yoghourt	140 (19.94%)	86 (17.02%)	67 (14.98%)	145 (14.2%)
Cheese	104 (14.81%)	59 (11.68%)	46 (10.29%)	95 (9.3%)

GI: gastrointestinal; IBD: inflammatory bowel disease.

Patients with IBD may find that dairy products aggravate their symptoms, leading them and some professionals to recommend a reduced lactose diet[34]. Also the role dairy foods avoidance on nutritional effects among IBD patients remains unclear. Gupta et al. evaluated lactose and milk intolerance in Indian patients with IBD (n=45). They found that there is no significant difference in milk and lactose intolerance between patients with IBD and healthy subjects[35]. Another study from Spain reported non significant differences in the prevalence of lactose malabsorption between patients with ulcerative colitis and controls (25% vs 32%, *P*=0.45). They believe that systematic elimination of lactose from the diets of these patients is erroneous[36]. Cabrera-Acosta et al. reported Lactose digestion deficiency frequency similar in subjects with chronic idiopathic ulcerative colitis and in healthy individuals in Mexico[37]. These findings are in contrast to findings of current study. Based on our results, the rate of dairy products intolerance was overall more prevalent in IBD patients in comparison with non IBD cases (65.5% vs 46.1%, *P*=0.0001, TABLE 3). Although among those with Arab descent, the rate of sensitivity to dairy products was almost similar between IBD and non IBD patients (52% vs 48.7%, *P*=0.775, TABLE 2).

While the rate of food allergy and family history of lactose intolerance were higher among IBD patients in comparison with non IBD participants (41.9% vs 22.2% and 19.5% vs 8.8% respectively, *P*=0.0001), probably because of mucosal barrier dysfunction through which food antigens can cross and evoke further allergic reactions[38-39], there are some subgroups of IBD patients including those without any history of food sensitivity or family history of lactase deficiency (TABLE 6). The rate of dairy intolerance among these subgroups are also comparable to non IBD patients (59.91%, 52.87% & 50.33% vs 46.1%, *P*=0.68, 0.98 & 0.99 respectively, TABLE 6). These results are similar to a study which conclude that not all the patients with IBD are intolerant to the lactose and advise to avoid dairy foods must not be generalized in the diet of these patients. They reported, IBD patients to avoid lacteal products without evidence of lactose malabsorption, probably because of incorrect patient perceptions and arbitrary advice from physicians and diet books[40]. In addition, vitamin D deficiency seems to be inversely linked to disease activity, clinical relapse, frequent hospitalization, and poor quality of life in patients with IBD, then avoiding dairy foods (an import source of this vitamin) could have a significant impact[41].

Usually patients with IBD have lower body mass index than healthy controls. They consume fresh milk, cheese, canned and fresh vegetables and fruits less frequently[10, 42]. So in clinical practice, it is important to ask IBD cases about history of food allergy or sensitivity and family history of lactose intolerance in their routine visits and if IBD patients have no family history of lactase deficiency or food sensitivity, there is no reason to advise them to avoid dairy products consumption. This fact is also true about those IBD cases with Arab descent.

The advantage of current study is to be multi centric with considerable number of participants and inclusion of different races. As we performed this study during COVID 19 pandemic, there were some limitation in case collection. Another limitation is the lack of using diagnostic method such as lactose breathe test to confirm lactase deficiency.

CONCLUSION

The rate of dairy product intolerance among IBD patients without family history of lactase deficiency or history of food sensitivity is similar to non IBD cases and there is no reason to deprive them from this important source of dietary calcium, vitamin D and other nutrients.

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Authors' contribution

Alavinejad P: corresponding author. Nayebi M, Parsi A, Maghool F, Alipour Z, Alimadadi M, Ahmed MH, Hang DV, Shahrokh S, Emami MH, Dehnavi D, Seyedian SS, Emara MH, Shahinzadeh S, Tran QT and Daryani NE main colleague in data collection. Farsi F: clinical nutritionist. Cheraghian B: epidemiologist and statistician for data analysis. Hashemi SJ and Alboraie M: clinical supervisor. Riazi M: nutritionist. Lenz L: clinical consultant and supervisor. Hajiani E: supervisor and consultant. Moghaddam EK: cooperator in final draft writing. Shahi MM: clinical nutritionist and consultant. Rezvanifar M: data collector. Azimi T: statistician for data analysis.

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RESUMO – Contexto – O papel dos alimentos lácteos na doença inflamatória intestinal (DII) tem sido controverso e é discutível se os pacientes com DII devem ou não evitar leite e laticínios, bem como a relação entre esses alimentos e sintomas nesta população. **Objetivo –** Estudo transversal multicêntrico foi projetado para avaliar se é realmente necessário privar os pacientes com DII do consumo desta classe de alimentos. **Métodos –** Um estudo multicêntrico com 12 centros de referência em gastroenterologia de quatro países foi projetado para avaliar sintomas gastrointestinais após o consumo de alimentos lácteos em todos os ambulatórios de DII durante seis meses e comparar pacientes tratados nos mesmos centros sem DII. **Resultados –** No total, foram incluídos 1888 casos (872 pacientes com DII e 1016 casos sem DII. 56,6% dos participantes eram do sexo feminino com idade média de 40,1 anos. 79,8% dos participantes eram caucasianos e originalmente eram cidadãos de 10 países. A prevalência relativa de DII foi maior em africanos e indianos e a prevalência mais frequente de intolerância a alimentos lácteos observada nos asiáticos. Entre os pacientes com DII, 571 casos foram diagnosticados como colite ulcerativa e 189 participantes como doença de Crohn. A duração média do diagnóstico como DII foi de 6,8 anos (de 2 meses a 35 anos). Os sintomas de gastrointestinais mais prevalentes após o consumo de todos os alimentos lácteos foram inchaço e dor abdominal. No total, a intolerância aos alimentos lácteos e a deficiência de lactase foi mais prevalente entre os pacientes com DII em comparação com os casos sem DII (65,5% vs 46,1%, *P*=0,0001). A taxa de queixas gastrointestinais entre os pacientes com DII que não tinham histórico familiar de deficiência de lactase, histórico de sensibilidade alimentar ou ambos foram de 59,91%, 52,87% e 50,33% respectivamente e semelhantes aos casos sem DII (*P*=0,68, 0,98 e 0,99, respectivamente). **Conclusão –** A taxa de intolerância de alimentos lácteos entre pacientes com DII sem histórico familiar de deficiência de lactase ou histórico de sensibilidade alimentar é semelhante aos casos sem DII e provavelmente não há razão para privá-los dessa importante fonte de cálcio dietético, vitamina D e outros nutrientes.

Palavras-chave – Doença inflamatória intestinal; deficiência de lactase; comida diária; inchaço, dor abdominal.

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