



The impact of lactose intolerance diagnosis: costs, timing, and quality-of-life

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Abstract

Lactose intolerance (LI) is a very common condition but, despite many efforts of the Italian National Health Service to reduce diagnostic delay of chronic disorders and provide prompt treatments, its early diagnosis remains an unmet need. In addition, the COVID-19 pandemic has exacerbated this problem, due to the conversion of many public health services to COVID centers. This study aims to analyze the diagnostic journey of patients suffering from LI, taking into account the duration of the process, associated costs, and impact on quality of life. Anonymous surveys were designed and distributed to patients with LI as well as physicians involved in LI management. The data were analyzed to determine the time required for a reliable LI diagnosis and average costs. Diagnostic delay of LI proved to be longer than 2 years, its impact on quality of life proved to be moderate to high in most of participants, especially in their psychosocial domain, and average costs proved to be high. Further investigations are needed to determine the economic burden of maintaining an asymptomatic status in patients with LI.

Keywords Lactose intolerance · Quality of life · Diagnosis cost · Diagnosis delay · Public healthcare · Disease burden

Introduction

Lactose intolerance (LI) is a clinical condition characterized by predominantly gastrointestinal symptoms evoked by lactose ingestion in people with lactose malabsorption. Lactose malabsorption is caused by an insufficient digestion of lactose due to a partial or complete deficiency of the intestinal enzyme lactase, responsible for its physiological break down into glucose and galactose, the two monosaccharides which form lactose [1–3]. LI is the most frequent enzyme intolerance and it was acknowledged by the World Health Organization (WHO) as a food intolerance. It is estimated that lactose malabsorption afflicts around 70% of the worldwide population, although the number of individuals diagnosed with LI is still low [4, 5].

Currently, the H₂-Lactose Breath Test (H₂-LBT) represents the gold standard to diagnose lactose malabsorption. The test detects the peak of hydrogen excretion in breath during a period up to 7 h after oral administration of a water solution containing lactose, indicating the fermentation of malabsorbed lactose by the colonic microbiota [6].

The LCT C/T-13910 genetic test discriminates between the primary and the secondary form of lactose malabsorption. It is a rapid test detecting the presence of the C/T-13910

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polymorphism located 14 kb upstream of the LCT gene, which has a genetic tendency towards lactase-non-persistence in Caucasian population [7–10].

The management of LI patients, from diagnosis to treatment, involves several professional figures, such as gastroenterologists, dietitians, nutritionists, allergologists, and the duration of diagnostic approach may be prolonged due to the need of multiple consultations and diagnostic tests. Moreover, due to the overlap of LI symptoms with other conditions, such as celiac disease or irritable bowel syndrome, the diagnosis of LI represents a clinical challenge, causing also an increase of costs. Generally, patients undergo a long and non-linear diagnostic process to identify the presence of this condition [11, 12].

Commonly, hospital availability of H₂-LBT is limited, resulting in both patients inconvenience, extension of waiting lists and delayed diagnosis. During the COVID-19 health emergency, breath tests were suspended due to the high risk of viral transmission raising from both the aerosol-generating procedures and the long stay of patients in the outpatient clinic [13]. Moreover, during the pandemic, oral swabs were mainly used for SARS-Cov-2 diagnosis and they were not available for LCT C/T-13910 genetic testing [14].

Finally, the reconversion of public health services to center for the diagnosis and treatment of SARS-Cov-2 infection slowed considerably down the rhythm of both screening programs and routine medical activities. Consequently, overcrowded waiting lists resulted in a worsening of the diagnostic delay of all chronic conditions.

The 2021 report from the Italian National Statistical Institute (ISTAT) indicates an increase of people who had to forego specialist consultations and diagnostic screenings compared to 2019 [15]. This critical scenario becomes even more impressive if we consider that, in 2019, before the COVID-19 pandemic, the IX Rbm-Censis Report published by the Italian Centre for Social Investment Studies (Censis) already showed that the extended waiting lists of the Italian National Health Service forced 19.6 million Italians to consult private healthcare [16].

The main reason for giving up public medical services is the excessive length of the waiting lists, hindering visit schedule. This problem concerns first specialistic visits (25.3%), diagnostic exams (19.2%), surgical procedures (13.3%), and check-ups/follow-ups (8.3%). For instance, scheduling the first outpatient gastroenterological visit might be characterized by a wait time of up to 300 days or arranging a check-up appointment can take up to 100 days [17]. Consequently, patients frequently switch to private health care services. Unfortunately, private services are much more expensive than public hospitals resulting in an increase of costs. The Pit Salute 2023 Report states that among Italian patients who use private healthcare services, 33.3% incur costs for specialist visits, 17.9% incur costs for diagnostic

exams, and 9.4% for drugs not freely distributed by Italian National Health Service [17].

Based on these considerations, Italian lactose-intolerant patients' association (AILI, Associazione Italiana Latto-Intolleranti Aps) has brought attention to the discomfort experienced by patients with suspected LI, running the risk for an increase of both inappropriate self-diagnosis and dangerous self-prescribed diets. Accordingly, AILI promoted this survey to analyze the diagnostic path of patients with suspected lactose malabsorption, considering both the length of the entire process and its costs. Moreover, it was analyzed how LI impacts quality of life.

Materials and methods

To obtain an overview of the current Italian diagnostic scenario of intolerant patients, two anonymous surveys were designed. The questionnaires were developed in partnership between AILI and Faculty of Human Nutrition Sciences, Department of Pharmacy, University of Pisa and were developed using Google Forms.

The first survey consisted of 24 anonymous questions to patients with known lactose intolerance to understand patients' diagnostic journey and to estimate both the related costs and the impact on the quality of life. All the questions are listed in the Supplementary Material (Table S1). The survey was distributed through the AILI's website and through its official social channels (Facebook and Instagram) and it was made available to responders with a dedicated link for the period from 17th October 2022 to 31st January 2023.

The questionnaire reached a total of 2233 participants. In 2185 of these participants, a diagnosis of lactose malabsorption was established.

Some questions were multiple-choice questions, allowing the selection of more than one answer from the different available options, while others were single-choice questions allowing the selection of a single answer.

The second survey was directed to a wide range of healthcare figures involved in the management of LI such as general practitioners, gastroenterologists, allergologists, and nutritionists. This questionnaire, another anonymous Google Forms module, was distributed by AILI through all the Provincial Medical Professional Boards, directly contacted by mail, to reach general practitioners, gastroenterologists, and allergologists. A similar process was implemented to distribute the questionnaire to dietitians and nutritionists as well, involving Biologists and Nutritionists Professional Boards.

The questionnaire consisted in 17 questions and it was completed by 97 participants. All the questions are listed in the Supplementary Material (Table S2).

In order to estimate the average cost of healthcare services offered through public healthcare, the price list edited

by Italian Regions including the full range of outpatient diagnostic and therapeutic procedures, were consulted. The documents edited by the local Lombardia, Toscana, and Puglia regional authorities, which were taken as a reference for the North, Centre and South of Italy, respectively, were also used. These documents are accessible on the websites of the respective Italian Regions. An average cost representative of the entire nation was estimated.

For the evaluation of the mean cost of private healthcare, CupSolidale, was consulted [18]: it is an independent, online, real-time aggregator, and comparator of healthcare services that monitors the availability of private facilities across the country.

The aim of the CupSolidale platform is to facilitate access to health services for users through a simplified procedure that reduces time and facilitates the doctor–patient relationship. CupSolidale Srl is not owned by doctors or medical companies, pharmaceutical companies, government agencies, neither any private healthcare facilities. The site is financed by fees paid by medical institutions, analytical laboratories, or healthcare facilities for the online booking services, banner ads, and site sponsors [18].

Furthermore, the costs of medications and food supplements commonly used by intolerant patients to alleviate symptoms were also calculated. Drugs and food supplements, along with their prices, were selected based on the most recommended category by physicians.

Descriptive statistics were used to report participant demographics and characteristics regarding the impact of LI on quality of life. The same procedure was carried out for the questionnaires directed to medical personnel. Frequencies and percentages were used for categorical data.

Results

The demographic characteristics of LI patients are shown in Table 1.

The average age (\pm SD) of the sample was 35 ± 12.2 years. The large majority of the sample was represented by female subjects below 45 years of age. Geographic distribution was balanced among the Italian macroregions.

Table 2 shows the main symptoms of patients at the diagnosis time and the relative diagnostic approach. More than 80% of the participants were diagnosed with validated tests (82.7%), while one out of five was diagnosed without tests.

In patients diagnosed with tests, the prevalence of bloating and abdominal pain, abdominal cramps, diarrhea, and flatulence was similar to patients diagnosed without test. Among patients diagnosed without tests, those who self-diagnosed their intolerance mainly reported abdominal bloating and/or pain (22.3%), while only 1.5% reported diarrhea. On the contrary, in patients diagnosed by their general

Table 1 Demographic characteristics of patients with lactose malabsorption (n = 2185)

Gender	%
Females	91.7
Males	8.3
Age (years)	
< 18	3.5
18–24	16.4
25–34	37.2
35–44	22.4
45–54	12.6
55–64	6.1
> 65	1.8
Region of origin	
North-West	27.1
North-East	14.3
Centre	19.4
South	25.9
Islands	13.3
Profession	
Employee	50.5
Freelancer/Entrepreneur	10.5
Homemaker	7.9
Retired	2.3
Student	21.0
Unemployed	7.8

practitioner on the basis of anamnestic evaluation, diarrhea was the most commonly reported symptom (25.1%).

As far as diagnostic tests are concerned, the majority of patients underwent LBT while in patients diagnosed without tests, roughly half self-reported diagnosis and the other half were diagnosed on the basis of anamnestic data by general practitioners (Table 2).

The vast majority of patients who underwent diagnostic testing were diagnosed more than 3 years ago (54.9%).

As expected, the main reason guiding the choice of performing diagnostic tests in public hospitals or private setting relates to costs and length of waiting lists. In particular, people affirm a preference for the SSN to reduce costs (74.5%) and for private facilities to drastically reduce waiting lists (62.9%). People from the three geographic areas provided similar answers.

Figure 1 shows the physician consulted to diagnose lactose intolerance and the management of this condition. Half of the patients diagnosed without tests are managed by their general practitioner (48.1%) (Fig. 1a), who mainly associated symptoms to lactose ingestion and recommended the exclusion of milk and dairy products from the diet (72.6%) (Fig. 1b). In 21.8% of individuals diagnosed without tests, no examinations were scheduled, including

Table 2 Distribution of subjects between test- and no test-based diagnoses

	Test-based diagnosis <i>n</i> = 1807 (82.7%)	Not tested-based diagnosis <i>n</i> = 378 (17.3%)
	N (%)	N (%)
Main symptoms		
Bloating and/or abdominal pain	322 (17.8%)	51 (18.1%)
Abdominal cramps	264 (14.6%)	43 (14.8%)
Diarrhea	241 (14.1%)	47 (16.4%)
Meteorism and/or flatulence	239 (13.2%)	41 (14.2%)
Test performed		
LBT	1312 (77.2%)	
LCT C/T-13910 genetic test	135 (7.5%)	
LBT and LCT C/T-13910 genetic test	99 (5.5%)	
Food intolerance tests*	261 (14.4%)	
Self-reported diagnosis		172 (45.5%)
Anamnestic diagnosis by general practitioner		206 (54.5%)
Time elapsed since diagnosis		
Less than 1 year	315 (17.5%)	
From 1 to 3 years	402 (22.2%)	
More than 3 years	1041 (54.9%)	
From the birth	49 (2.7%)	

*Food intolerance tests were included among the group of diagnostic tests because patients frequently undergo these tests, despite the limited scientific evidence supporting their accuracy

routine blood tests, coeliac disease serology, or screening for thyroid disease.

Patients with test-based diagnosis were mainly managed by general practitioners (59.7%) and in a minority of cases by gastroenterologists (21.3%) (Fig. 1c). In this context, general practitioners are accustomed to prescribing diagnostic tests (37.8%), with 23.2% of GPs attributing the symptoms to stress, 22.8% referring patients to another specialist, and 16.2% recommending the elimination of milk and dairy products from the diet, as reported by the surveyed patients (Fig. 1d).

To diagnose LI, LBT or genetic test were mainly performed and, in a minority of case, allergy tests (7.7%), stool cultures (10%) and fecal calprotectin tests (5.7%) were also conducted.

As far as diagnostic delay is concerned, in 40.6% of the cases, there was a time lapse of more than 2 years between the appearance of the first symptoms and the reliable diagnosis (the day the test was performed). In 15.6% of cases, this time lapse was between 1 and 2 years (Fig. 2).

Considering drug treatments and dietary modifications, the drugs most frequently used were antidiarrhoeics (15.5%), anti-reflux (12.9%), and symptomatic drugs for abdominal pain (16%). In contrast, patients who self-diagnosed or received a diagnosis without tests did not report the use of drugs (33.5%) and mainly relied on dietary supplements (21.6%).

Both groups of participants agreed that LI has a considerable negative impact on quality of life, as expressed in Fig. 3. Moreover, 68.9% of participants reported a medium-to-strong impact on their psycho-social well-being (Fig. 3b), and 59.7% reported a significant impact on work due to their intolerance (Fig. 3c).

Considering the whole group of participants, it emerges that specific symptoms do not represent drivers to seek medical care. The majority of participants first turn to general practitioners (57.7%) or gastroenterologists (20.1%), and in both cases for gastrointestinal symptoms (68.2%), such as diarrhea or constipation and bloating and/or abdominal pain. On the contrary, when skin rashes are present, patients turn to allergologists (8.9%).

According to CupSolidale and regional price lists, the average healthcare cost is estimated to be €495 in the private health system and €262 in public hospitals. It is important to note that these estimates represent a mean value of costs, as the cost of a LBT performed in public hospitals is €28, while in private healthcare services it ranges from €35 to €180. Similarly, the LCT C/T-13910 genetic test is generally not available in public hospitals, and private services offer this test with costs ranging from €50 to €170 [18].

The second survey investigated the attitudes of general practitioners and specialists (*n* = 97), including gastroenterologists, allergologists, and nutritionists.

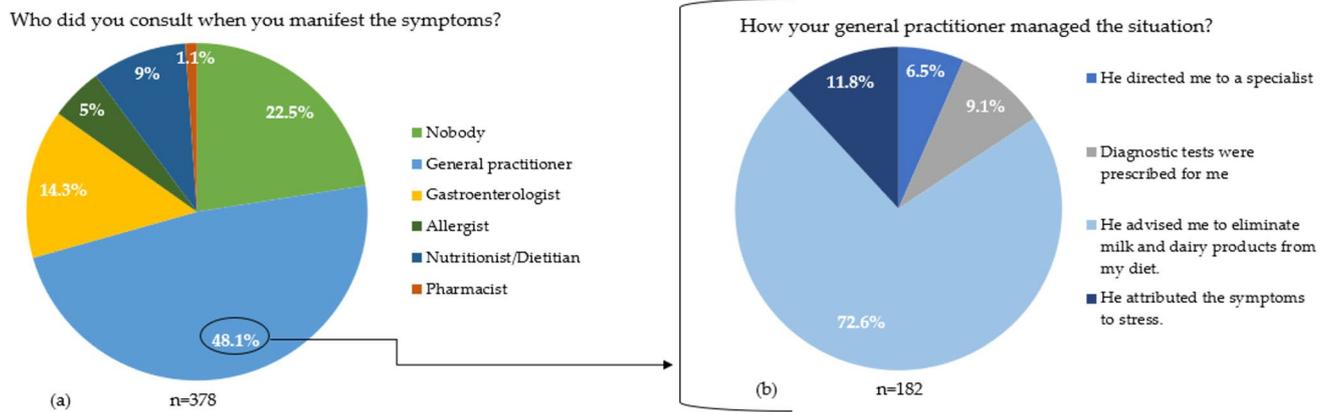
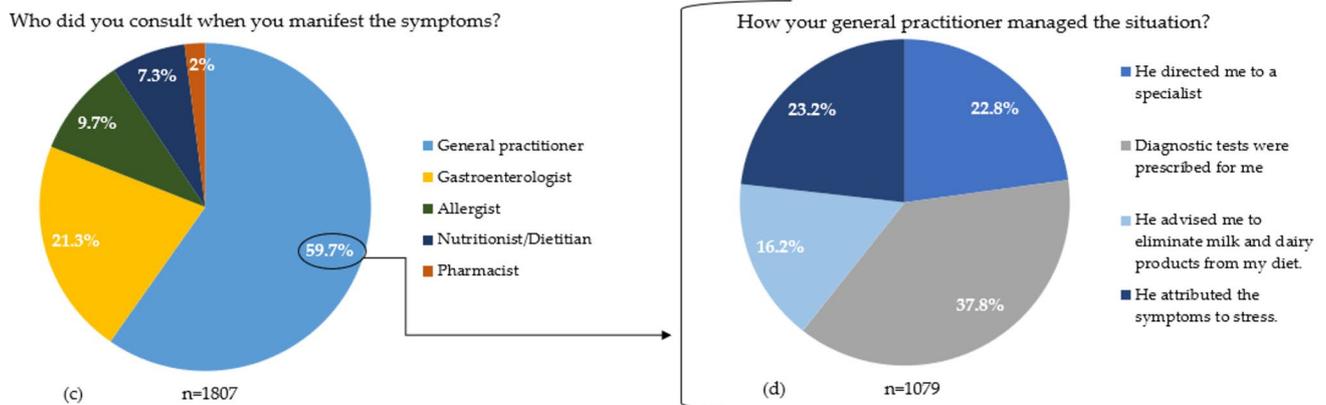
Patients with a not test-based diagnosisPatients with a test-based diagnosis

Fig. 1 Responses to the questionnaires administered to patients with LI, according to their diagnostic approach. **a** Physician consulted by patients diagnoses without tests **b** Diagnostic suggestions by the general practitioner to patients diagnosed without tests to manage the

condition. **c** Physician consulted by patients diagnosed with tests **d** Diagnostic suggestions by the general practitioner to patients diagnosed with tests to manage the condition

This survey showed that 71.1% of general practitioners suggested to patients with typical gastrointestinal symptoms to avoid milk and dairy products from their diet, while only 18.4% of them prescribed tests. In particular, in 33.3% of the cases they suggested LBT and in 26.7% celiac disease serology.

According to gastroenterologists and allergologists, 41.7% of patients spontaneously decided to consult a specialist, as it was not suggested by other physicians.

It is noteworthy that the frequency with which individuals consult a general practitioner, a gastroenterologist, an allergist or a nutritionist for gastrointestinal symptoms after consumption of lactose is relatively high. In particular, as illustrated in Fig. 4, general practitioners receive patients

complaining of gastrointestinal symptoms at least once a week or once a month (52.6%), gastroenterologists and allergists report that they receive these patients at least once a day or once a week (66.6%), and nutritionists at least once a week or once a month (78.7%).

Discussion

To our knowledge, this is the first survey investigating diagnostic delay and costs of LI. The analysis of the first questionnaire suggests that the diagnostic delay of LI is significant. More than 40% of patients reported a diagnostic delay longer than 2 years. Therefore, for a 2-year period,

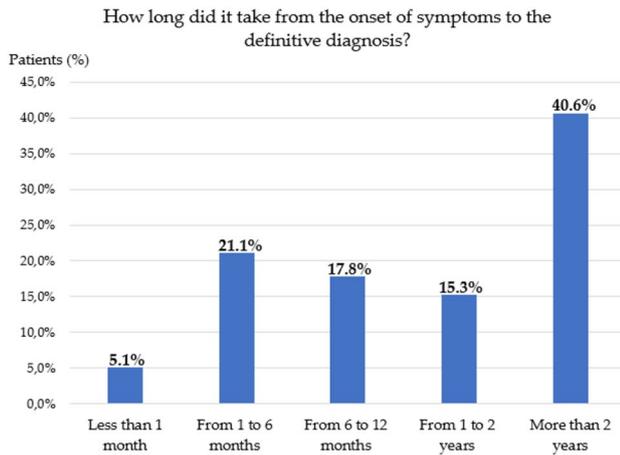


Fig. 2 Diagnostic delay time from onset of symptoms to definitive diagnosis

patients with LI seek medical care, undergo diagnostic tests and follow treatments without a definitive diagnosis. Unfortunately, our questionnaire's design did not allow for a more precise quantification of this period, but we can analyze at least three main reasons for this delay.

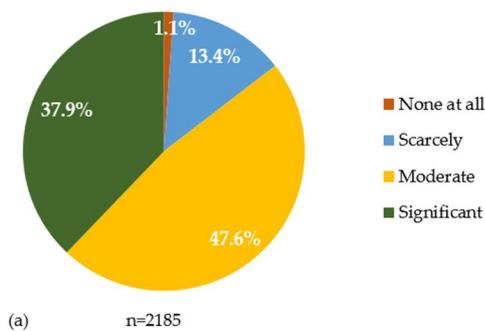
First of all, a frequent underestimation of this condition is detectable in clinical practice of both general practitioners

and specialists. A still too high portion of patients were diagnosed on an anamnestic basis, without the support of diagnostic tests, beside previous results unequivocally showed that patients' judgement of the relationship between lactose intake and symptom onset is largely inaccurate [19]. Hydrogen breath test is very accurate to diagnose lactose malabsorption but an accurate test to diagnose lactose intolerance is not yet available: it was recently demonstrated the inaccuracy of the monitoring of symptom onset after lactose oral load [20, 21]. However, results of H₂-LBT, integrated by the information provided by genetic test, allow to discriminate between patients with a high risk and low risk of suffering from lactose intolerance [22].

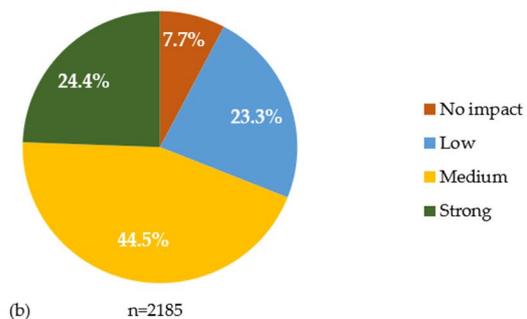
Secondly, the length of waiting lists for reliable diagnostic tests at a reasonable cost, accessible to everyone through the public health service, represents a main factor for diagnostic delay. Under this light, the recent impact of COVID-19 pandemic on Italian health service worsened this problem. The conversion of many public hospitals to COVID centers limited the possibility to undergo many ambulatory diagnostic tests, inducing an enormous lengthening of waiting lists.

Still today, up to 4 years after the first disease wave, the elongation of waiting lists for common diagnostic tests represents an important problem for public health services. Unfortunately, the unavailability of data on the diagnostic

How much do you think intolerance affects your quality of life?



What is the impact of LI on the psychological and social spheres?



How frequently have you missed work or study days due to LI-related reasons?

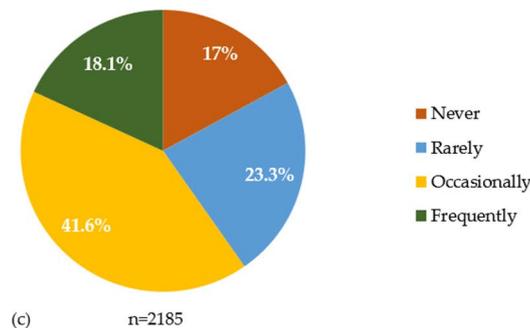


Fig. 3 Impact of LI on quality of life

How frequently do you visit patients with gastrointestinal symptoms after consuming milk and dairy products?

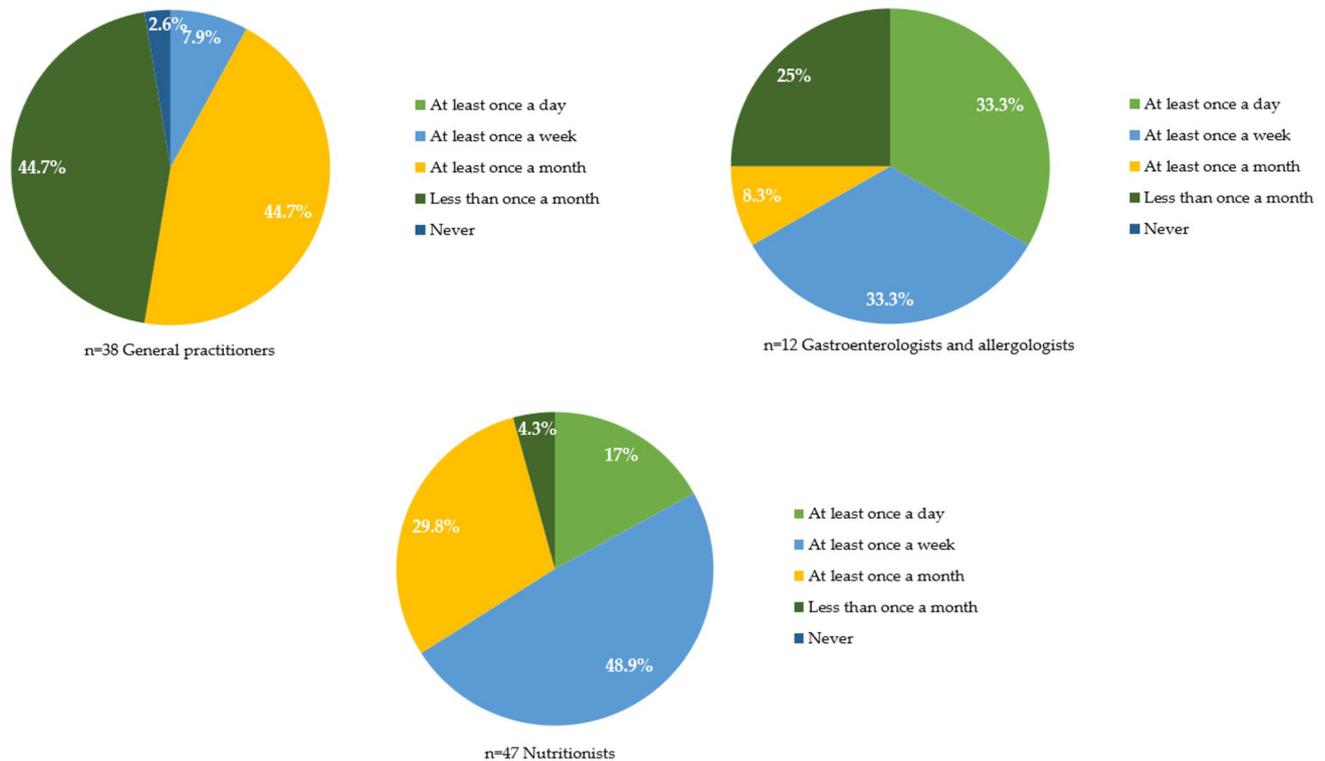


Fig. 4 The frequency with which professionals receive patients complaining of gastrointestinal symptoms after milk and dairy products consume

delay and costs before COVID-19 pandemic makes impossible the comparison with our results.

Finally, the need to seek care in private centers to undergo both visits and diagnostic tests increases the burden of the disease and limits patients request for medical care. The prevision of supporting high costs represents also a brake of patients' journey and increases diagnostic delay.

Accordingly, it was not a surprise that lactose intolerance negatively impacts on patients' quality of life, in particular their psycho-social well-being.

Our results emphasize the need for an increased awareness of the impact lactose intolerance has on the general well-being of patients. Food intolerances suffer from the skepticism of many physicians, underestimating this condition. Very frequently, a simple but shallow recommendation to avoid dairy products is the unique therapeutic measure prescribed, forgetting clinical consequences of this restrictive diet on bone mass and mineral metabolism [23], in particular in female patients, heavily exposed to bone derangement in peri-menopausal and post-menopausal periods. Moreover, this diet modification could lead to nutritional deficiencies, particularly in vitamin D and calcium. Therefore, it is not advisable to exclude milk

and dairy products from the diet [24–26]. In addition, in our study, the number of female participants was higher than male, reaching a rate of 9:1. A similarly large difference was observed also in previous studies suggesting that women tend to search for the causes of their symptoms, more frequently than males, even when they are mild [27–29].

It is also crucial to increase the awareness of the general population on the inaccuracy of several tests, available in private setting but not in public hospitals, claiming to detect food intolerances. Scientific validation of these tests is lacking and their reproducibility was never tested. Due to incorrect indications and a lack of attention by physicians, many people spontaneously undergo these tests in private settings, without the awareness of their inaccuracy [30]. Accordingly, in 2018, the Italian Ministry of Health approved a document depicting the approach strategy needed for food intolerance and debunking unhelpful self-diagnosis. It should be underlined that relying on unvalidated tests frequently causes a wrong diagnosis with at least two main consequences: first of all, a wrong diagnosis causes a wrong treatment, secondly, a wrong diagnosis causes a further delay of the correct one [31].

Moreover, it should be emphasized that also diagnostic delay causes a reduction of quality of life, due to the need to consult multiple healthcare services and specialists. After each medical consultation, further diagnostic tests and treatments are prescribed causing both further psychological distress and negative patients' expectation.

The impact of diagnostic delay on patients' quality of life proved to be significant. Performing targeted clinical tests in a timely manner could mitigate these uncomfortable situations, as while waiting for a diagnosis, patients continue to experience symptoms causing loss of work days and reduced productivity. Among patient-related causes for diagnostic delay, it should be also underlined that the difficulty of patients with gastrointestinal symptoms to define the correct relationship between symptoms and food intake. Accordingly, our results agree with previous findings that reported the negative impact of LI on the daily life and psychological well-being of affected individuals [28, 29]. This negative impact on quality of life is present also in other gastrointestinal diseases, also exacerbated by the COVID-19 pandemic, as recently reported, for instance, in patients with celiac disease [32–34] and IBS. Furthermore, due to their overlapping clinical presentation, LI is frequently misdiagnosed and a wrong diagnosis of IBS is done, in particular when diarrhea is present. Consequently, both diagnostic delay and patient quality of life worsen [35, 36].

Conclusions

In conclusion, we showed that LI is characterized by a significant diagnostic delay due to underestimation of the disease, length of waiting lists, and remarkable costs. Both disease and difficulties in patients' journey cause a reduction of quality of life. Moreover, an improvement of physician awareness of the burden of the disease could be useful to reduce the impact of the disease on both quality of life and diagnostic delay. Accordingly, it seems appropriate the planning of information campaigns to improve the knowledge of the disease and the correlated unmet needs.

Further studies are needed to investigate the costs required to maintain an asymptomatic status in these patients, considering the follow-up visits, nutritional consultations, and drugs.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11739-024-03787-1>.

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Stefano M.; project administration, Facioni M.S. All authors have read and agreed to the published version of the manuscript.

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Data availability Data available on request from the authors.

Declarations

Conflict of interest Maria Sole Facioni is president of AILI (Associazione Italiana Latto-Intolleranti Aps) the only association for lactose-intolerant patients in Italy. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be constructed as a potential conflict of interest.

Human and animal rights This study does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent is not required for this study (as all the participants gave implicit consent by filling in the survey). Participation in the survey was anonymous and it is not possible to trace the identity of the respondents in any way. The questions do not contain any personally identifiable information linking them to the respondents. Therefore, approval by a bioethics committee is not necessary.

References

- Misselwitz B, Butter M, Verbeke K, Fox MR (2019) Update on lactose malabsorption and intolerance: pathogenesis, diagnosis and clinical management. *Gut* 68(11):2080–2091. <https://doi.org/10.1136/gutjnl-2019-318404>
- Fassio F, Facioni MS, Guagnini F (2018) Lactose maldigestion, malabsorption, and intolerance: a comprehensive review with a focus on current management and future perspectives. *Nutrients* 10:1599. <https://doi.org/10.3390/nu10111599>
- Dominici S, Marescotti F, Sanmartin C, Macaluso M, Taglieri I, Venturi F, Zinnai A, Facioni MS (2022) Lactose: characteristics, food and drug-related applications, and its possible substitutions in meeting the needs of people with lactose intolerance. *Foods* 11(10):1486. <https://doi.org/10.3390/foods11101486>
- EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (2010) Scientific opinion on lactose thresholds in lactose intolerance and galactosaemia. *EFSA J* 8:1777
- Storhaug CL, Fosse SK, Fadnes LT (2017) Country, regional, and global estimates for lactose malabsorption in adults: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2:738–746. [https://doi.org/10.1016/S2468-1253\(17\)30154-1](https://doi.org/10.1016/S2468-1253(17)30154-1)
- Gasbarrini A, Corazza GR, Gasbarrini G, Montalto M, Di Stefano M, Basilisco G, Parodi A, Usai-Satta P, Vernia P, Anania C, Astegiano M, Barbara G, Benini L, Bonazzi P, Capurso G, Certo M, Colecchia A, Cuoco L, Di Sario A, Festi D, Lauritano C, Miceli E, Nardone G, Perri F, Portincasa P, Riscicato R, Sorge M, Tursi A (2009) 1st rome H2-breath testing consensus conference working group. Methodology and indications of H2-breath testing in gastrointestinal diseases: the Rome consensus conference. *Aliment Pharmacol Ther*. <https://doi.org/10.1111/j.1365-2036.2009.03951.x>
- Büning C, Genschel J, Jurga J, Fiedler T, Voderholzer W, Fiedler EM, Ockenga J (2005) Introducing genetic testing for adult-type hypolactasia. *Digestion* 71(4):245–250. <https://doi.org/10.1159/000087050>

8. Anguita-Ruiz A, Aguilera CM, Gil A (2020) Genetics of lactose intolerance: an updated review and online interactive world maps of phenotype and genotype frequencies. *Nutrients* 12(9):2689. <https://doi.org/10.3390/nu12092689>
9. Usai-Satta P, Scarpa M, Oppia F, Cabras F (2012) Lactose malabsorption and intolerance: What should be the best clinical management? *World J Gastrointest Pharmacol Ther* 3(3):29–33. <https://doi.org/10.4292/wjgpt.v3.i3.29>
10. Enattah NS, Sahi T, Savilahti E, Terwilliger JD, Peltonen L, Jarvela I (2002) Identification of a variant associated with adult-type hypolactasia. *Nat Genet* 30:233–237. <https://doi.org/10.1038/ng826>
11. Celi A, Trelis Villanueva M, Tena B, Taroncher S, Soriano JM, Merino Torres JF (2023) Benefits of using a recommended testing algorithm for the diagnosis and dietary-nutritional management of patients with chronic gastrointestinal disorders. *Nutr Hosp* 40(5):1017–1024. <https://doi.org/10.20960/nh.04518>
12. Jansson-Knodell CL, White M, Lockett C, Xu H, Shin A (2022) Associations of food intolerance with irritable bowel syndrome, psychological symptoms, and quality of life. *Clin Gastroenterol Hepatol* 20(9):2121–2131.e3. <https://doi.org/10.1016/j.cgh.2021.12.021>
13. Ahmed J, Padam P, Ruban A (2021) A retrospective analysis of patients on a waiting list for small intestinal bacterial overgrowth (SIBO) breath testing during the COVID-19 pandemic and introduction of a home testing pathway. *United Euro Gastroenterol J* 9(SUPPL 8):342
14. Willemsen M, Van De Maele K, Vandenplas Y (2022) Delayed analysis of hydrogen-methane breath samples. *Pediatr Gastroenterol Hepatol Nutr* 25(1):13–20. <https://doi.org/10.5223/pghn.2022.25.1.13>
15. Istat–Istituto nazionale di statistica. Available online: www.istat.it. Accessed 20 Mar 2023
16. Censis–Centro Studi Investimenti Sociali. Available online: www.censis.it. Accessed 12 Dec 2023
17. Rapporto Pit Salute 2023–Elaborazione Agenzia Valutazione Civica–Cittadinanzattiva
18. CupSolidale. Available online: <https://www.cupsolidale.it/>. Accessed 14 Dec 2023
19. Suarez FL, Savaiano DA, Levitt MD (1995) A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med* 333(1):1–4. <https://doi.org/10.1056/NEJM199507063330101>
20. Vernia P, Di Camillo M, Foglietta T, Avallone VE, De Carolis A (2010) Diagnosis of lactose intolerance and the “nocebo” effect: the role of negative expectations. *Dig Liver Dis* 42:616–619. <https://doi.org/10.3390/nu13051653>
21. Di Stefano M, Brondino N, Bonaso V, Miceli E, Lapia F, Grandi G, Pagani E, Corazza GR, Di Sabatino A (2022) The perception of lactose-related symptoms of patients with lactose malabsorption. *Int J Environ Res Public Health* 19(16):10234. <https://doi.org/10.3390/ijerph191610234>
22. Di Stefano M, Terulla V, Tana P, Mazzocchi S, Romero E, Corazza GR (2009) Genetic test for lactase non-persistence and hydrogen breath test: is genotype better than phenotype to diagnose lactose malabsorption? *Dig Liver Dis* 41(7):474–479. <https://doi.org/10.1016/j.dld.2008.09.020>
23. Di Stefano M, Veneto G, Malservisi S, Cecchetti L, Minguzzi L, Strocchi A, Corazza GR (2002) Lactose malabsorption and intolerance and peak bone mass. *Gastroenterology* 122(7):1793–1799. <https://doi.org/10.1053/gast.2002.33600>
24. Perino A, Cabras S, Obinu D, Cavalli Sforza L (2009) Lactose intolerance: a non-allergic disorder often managed by allergologists. *Eur Ann Allergy Clin Immunol* 41(1):3–16
25. Facioni MS, Raspini B, Pivari F, Dogliotti E, Cena H (2020) Nutritional management of lactose intolerance: the importance of diet and food labelling. *J Transl Med* 18:260. <https://doi.org/10.1186/s12967-020-02429-2>
26. Facioni MS, Dominici S, Marescotti F, Covucci R, Taglieri I, Venturi F, Zinnai A (2021) Lactose residual content in PDO cheeses: novel inclusions for consumers with lactose intolerance. *Foods* 10:2236. <https://doi.org/10.3390/foods10092236>
27. Casellas F, Varela E, Aparici A, Casaus M, Rodríguez P (2009) Development, validation, and applicability of a symptoms questionnaire for lactose malabsorption screening. *Dig Dis Sci* 54(5):1059–1065. <https://doi.org/10.1007/s10620-008-0443-3>
28. Casellas F, Aparici A, Pérez MJ, Rodríguez P (2016) Perception of lactose intolerance impairs health-related quality of life. *Eur J Clin Nutr* 70(9):1068–1072. <https://doi.org/10.1038/ejcn.2016.80>
29. Facioni MS, Dominici S, Farace B, Apicella A, Romano MF, Tarabella A (2022) A survey on consumers with lactose intolerance in Italy: their perception, habits and needs when shopping for groceries. *EC Nutrition* 17(9):28–42
30. 'Ten rules for the management of food intolerances'. Available online: <https://www.adiitalia.org/2011-08-09-02-47-49/dalla-letta-ratura-2.html?download=459:dieci-regole-per-gestire-le-intolleranze-alimentari>. Accessed 12 Mar 2024
31. Wróblewska B, Szyk AM, Markiewicz LH, Zakrzewska M, Romaszko E (2018) Increased prevalence of eating disorders as a biopsychosocial implication of food allergy. *PLoS ONE* 13(6):e0198607. <https://doi.org/10.1371/journal.pone.0198607>
32. Amirian P, Zarpoosh M, Moradi S, Jalili C (2023) Celiac disease and COVID-19 in adults: a systematic review. *PLoS ONE* 18(5):e0285880. <https://doi.org/10.1371/journal.pone.0285880>
33. Möller SP, Apputhurai P, Tye-Din JA, Knowles SR (2021) Quality of life in coeliac disease: relationship between psychosocial processes and quality of life in a sample of 1697 adults living with coeliac disease. *J Psychosom Res* 151:110652. <https://doi.org/10.1016/j.jpsychores.2021.110652>
34. Silva JTC, Fonseca Neto OCLD (2023) Post-COVID-19 irritable bowel syndrome: an integrative review. *Rev Col Bras Cir* 50:e20233618. <https://doi.org/10.1590/0100-6991e-20233618-en>
35. Sciumè GD, Berti G, Lambiase C, Paglianiti I, Villanacci V, Rettura F, Grosso A, Ricchiuti A, Bortoli Nd, Usai Satta P, Bassotti G, Bellini M (2023) Misinterpreting diarrhea-predominant irritable bowel syndrome and functional diarrhea: pathophysiological highlights. *J Clin Med* 12(18):5787. <https://doi.org/10.3390/jcm12185787>
36. Pop A, Popa SL, Pop DD, Ismaiel A, Nechita VI, Dumitrascu DL (2024) Self-perceived lactose intolerance versus confirmed lactose intolerance in irritable bowel syndrome: a systematic review. *J Gastrointest Liver Dis*. <https://doi.org/10.15403/jgld-5836>

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