



FOGSI FOCUS

CONSTIPATION IN WOMEN

Insights into a Common Concern

CHIEF EDITOR

Dr. Suchitra N Pandit

CONTRIBUTORS

Dr. Arati Shah

Dr. Basab Mukherjee

Dr. Chandrakant Sankalecha

Dr. Charmila Ayyavoo

Dr. Girija Wagh

Dr. Gorakh G Mandrupkar

Dr. Parikshit Tank

Dr. Sanjay Gupte

Dr. Suchitra N Pandit

Dr. Ursula Pandit

This Project is supported financially from Abbott India Limited to Medicca Press Limited as a service to the medical profession

MEDICCA PRESS LIMITED™
A Medical Content Company

FOGSI TEAM 2024



Dr. Jaydeep D Tank
President, FOGSI



Dr. Hrishikesh D Pai
FOGSI President 2023



Dr. Sunita Tandulwadkar
FOGSI President 2025



Dr. Madhuri Patel
*FOGSI Secretary General,
Editor in Chief - JOGI*



Dr. Ajay Mane
Vice President, FOGSI



Dr. Charmila Ayyavoo
Vice President, FOGSI



Dr. Girija Wagh
Vice President, FOGSI



Dr. Janmejaya Mohapatra
Vice President, FOGSI



Dr. Neerja Bhatla
Vice President, FOGSI



Dr. Suvarna Khadilkar
Dy. Secretary General, FOGSI



Dr. Parikshit Tank
Treasurer, FOGSI



Dr. Niranjana Chavan
Joint Treasurer, FOGSI



Dr. Kunal Doshi
Joint Secretary 2024, FOGSI



Dr. Parul Kotdawala
Chair, ICOG



Dr. Sheela Mane
Vice Chair, ICOG



Dr. Sarita Bhalerao
Secretary, ICOG



Dr. Parag Biniwale
ICOG Chairman elect



Prof. Ashok Kumar
ICOG Vice Chairman elect



Dr. Sujata Dalvi
Jt Associate Editor, JOGI



Dr. Arun Nayak
Assistant Editor, JOGI



Dr. Anahita R Chauhan
First Jt Assistant Editor, JOGI



Dr. Ashwini Bhalerao Gandhi
Second Jt Assistant Editor, JOGI



Dr. Pradnya Changede
Secretary & Manager, JOGI

CONTRIBUTORS

Dr. Arati Shah

MS ObGyn

Director, Pulse hospital,
Consultant, Greenarray Genomics Research and
Solutions, Ahmedabad.

Dr. Gorakh G Mandrupkar

MBBS, DGO, FICOG

Consultant, Reproductive Medicine
Angel IVF, Pune.
Vice President, Gestosis India Association

Dr. Basab Mukherjee

MBBS (Vellore), MD (Vellore), FRCOG (London), FICOG

Director, Ankuran Fertility & Fetal Medicine Centre,
Kolkata.
President elect, Bengal Society of Obstetrics and
Gynecology

Dr. Parikshit Tank

MD, DNB, FCPS, DGO, DFP, MNAMS, FICOG, FRCOG

Consultant, Obstetrician and Gynaecologist
The Ashwini Clinic, Mumbai.
Treasurer, FOGSI

Dr. Chandrakant Sankalecha

MD, FICOG

Consultant, Sankalecha Hospital, Nashik.
Member Executive committee, Gestosis India
Association

Dr. Sanjay Gupte

MD, DGO, FICOG, FRCOG

Director, Gupte Hospital and Center for Research in
Reproduction
Director, Greenarray Genomic Research and Solutions,
Pune.
President, FOGSI (2010–11)

Dr. Charmila Ayyavoo

MD, DGO, DFP, FICOG, PGDCR

Director, Aditi Hospital & Parvathy Ayyavoo
Fertility Center, Trichy
Associate Professor, Dhanalakshmi Srinivasan
Medical College & Hospital, Perambalur.
Vice President, FOGSI (2024–25)

Dr. Suchitra N Pandit

MD, DNB, FRCOG, MRCOG, DFP, FICOG, MNAMS, B. Pharm

Senior Consultant, OBGYN
Surya Group of Hospitals, Mumbai.
President, FOGSI & ICOG (2014–15)

Dr. Girija Wagh

MBBS, MD, FICOG, FICS

Professor & HOD, Dept of OBGYN, Bharathi
Vidyapeeth Medical College Hospital, Pune
Senior Consultant, Cloud Nine & Apollo Hospitals,
Pune.
Vice President, FOGSI (2024–25)

Dr. Ursula Pandit

MD, ABIM Board certified in Internal Medicine

Consultant, Methodist Mansfield Medical Center Dallas,
Texas.

FOREWORD FROM THE PRESIDENT FOGSI



It gives me great pleasure to write a foreword for this excellent FOGSI FOCUS on “Constipation in Women: Insights into a Common Concern” which addresses a topic that is often overlooked yet significantly impacts many women. In this comprehensive FOGSI FOCUS, we embark to explore the multifaceted aspects of constipation in women.

Constipation in women presents unique challenges and considerations, often intertwined with hormonal changes, pregnancy, and various life stages. This comprehensive guide, authored by distinguished experts in the field, provides an in-depth exploration of the physiological, psychological, and lifestyle factors contributing to constipation in women.

FOGSI FOCUS is meticulously structured into eight chapters, each authored by leading clinicians and academicians, ensuring a thorough and multi-faceted approach to understanding and managing this condition. Each chapter is rich with clinical insights, making this FOGSI FOCUS an indispensable tool for practitioners seeking to enhance their understanding and management of constipation in women. The contributions from various experts provide a well-rounded perspective, ensuring that the content is both authoritative and relevant.

I sincerely thank Dr. Suchitra Pandit for her outstanding work as the chief editor of FOGSI FOCUS. I would also like to appreciate the contributing authors for their valuable work and dedication to advancing women’s health. This FOGSI FOCUS will serve as an indispensable reference for clinical practitioners.

Warm Regards

Dr. Jaydeep D Tank

MD, DNB, DGO, FCPS, FICOG, FRCOG (Honoraris Causa)

President FOGSI 2024-25

Chair - YGAA Committee Asia Oceana Federation of Obstetrics and Gynaecology (AOFOG)

Project Lead FOGSI - USAID Projects 2020-2024

Secretary General - FOGSI (2018-21)

Past President Mumbai Society of Obstetrics & Gynecology

Immediate past Chair of International Federation of Obstetrics and Gynecology (FIGO) committee for Safe Abortion

Obstetrician and Gynaecologist, IVF Consultant,
The Ashwini Clinic, Mumbai, India.

FOREWORD FROM THE SECRETARY GENERAL FOGSI



Constipation is a prevalent yet often underdiscussed issue in our field of Obstetrics and Gynaecology. Constipation can significantly impact the health and well-being of our patients particularly during pregnancy and postpartum.

Broadly, the issue of constipation can be due to one or more factors like hormonal changes, increase in progesterone level, reduction in physical activity and pressure of growing uterus on the intestine. During postpartum period, decreased physical activity and perineal pain may decrease the bowel movements which eventually leads to constipation. Pain relieving medication sometimes exaggerate this condition.

Chronic constipation may lead to the development of hemorrhoids, fissure and rectal prolapse which eventually affects the physical and emotional well-being of women.

As Obstetricians and Gynecologists, we play a very important role in addressing this issue. We can significantly improve the health and motility of the bowel of our patients by proactively discussing the bowel health and giving them appropriate advice.

I congratulate Dr. Jaydeep Tank, Dr. Suchitra Pandit and team for selecting this most relevant topic of Constipation in Women. I am sure this issue of FOGSI FOCUS on 'Constipation in Women: Insights into a Common Concern' will serve as a valuable resource providing practical solutions that we can incorporate into our clinical practice in the effective management of constipation.

Warm Regards

Dr. Madhuri Patel

MD, DGO, FICOG

Secretary General, FOGSI

Editor in Chief, Journal of Obstetrics and Gynecology of India (JOGI)

Joint Secretary, FOGSI-2009

Committee Member, International Federation of Obstetrics and Gynecology (FIGO) committee on Preterm Birth

Hon. Clinical Associate, N. Wadia Hospital, Parel, Mumbai

Hon, Consultant Police hospital, Mumbai and St. Elizabeth Hospital, Mumbai.

FROM THE EDITOR'S DESK



Constipation is fairly common problem. It generally means passing fewer than three stools a week or having a difficult time passing stool.

Studies from India have reported a prevalence of constipation ranging from 8.6% to 24.8%. The global prevalence of chronic constipation is around 14%.

According to the Indian consensus, chronic constipation is a common concern, with the National Health Portal of India reporting that 22% of Indian adults suffer from this condition.

Constipation was significantly more frequent in women than in men (20% vs. 13%) and in nonworking population than in working population (20% vs. 12%). A healthy gut is an important part of a woman's overall health. Poor dietary habits, lesser fluid intake per day, ignoring the urge to pass stools for various reasons like lack of clean toilets, anxiety, medications, and lesser physical activity were found to be significant factors leading to constipation. As compared to men, women are more likely to seek medical attention for it.

Constipation is uncomfortable, but consistent straining during bowel movements also increases the odds of developing unpleasant complications like hemorrhoids, anal fissures and pelvic floor dysfunction.

Understanding the importance of this subject we decided to bring out a simple attempt at understanding the pathophysiology, risk factors and discussing prevention through lifestyle changes and treatment.

I wish to thank Dr. Jaydeep Tank, President, FOGSI 2024 and Dr. Madhuri Patel, Secretary General, FOGSI for this FOGSI FOCUS.

Warm Regards

Dr. Suchitra N Pandit

MD, DNB, FRCOG, MRCOG, DFP, FICOG, MNAMS, B.Pharm

Senior Consultant, OBGYN Surya Group of Hospitals, Mumbai

FOGSI representative to SAFOG

Co-chair SAFOG NCD Committee

Associate Member of FIGO Ethics Committee

Past President FOGSI & ICOG

Past President ISOPARB, Gestosis India Association & AICC RCOG

PREFACE

Constipation, a common gastrointestinal disorder, affects around 10–15% of the population. Its chronic form presents a substantial burden on healthcare system and significantly impacts individuals' quality of life.¹

Constipation is a common health concern in Indian women due to various lifestyle considerations like unhealthy eating habits, low fluid intake, and sanitation challenges.²⁻⁵ In addition to this, anatomical, hormonal, and neurological factors variably contribute to constipation in women.⁶⁻⁸ Gut dysbiosis/imbalance in the gut microbiota can also result in constipation symptoms.⁹ Women with constipation face challenges affecting cognitive, physical, and self-care tasks, social participation, and overall quality of life, alongside issues like abdominal discomfort, insomnia, psychological disorders, and reproductive health problems.¹⁰

While lifestyle changes and other nonpharmacological interventions are effective first-line strategies for management of constipation in some cases, pharmacological approaches are often necessary in others.¹¹ The majority of patients with constipation ultimately need to use laxatives during their treatment.¹² Lactulose, a versatile osmotic laxative, demonstrates efficacy in constipation management through its osmotic, prebiotic, and detoxifying actions.¹³ Clinical evidence on lactulose supports its use during pregnancy and postpartum.¹⁴

FOGSI FOCUS aims to provide healthcare professionals with a comprehensive understanding of constipation in women across various life stages, including pregnancy, postpartum, and old age. It covers the underlying mechanisms of constipation and offers evidence-based management strategies tailored to each phase. We hope to empower healthcare providers in delivering optimal care to women facing with this prevalent condition.

References

1. Aziz I, Whitehead WE, Palsson OS, et al. An approach to the diagnosis and management of Rome IV functional disorders of chronic constipation. *Expert Rev Gastroenterol Hepatol.* 2020;14(1):39-46.
2. Ghoshal UC, Sachdeva S, Pratap N, et al. Indian consensus on chronic constipation in adults: A joint position statement of the Indian Motility and Functional Diseases Association and the Indian Society of Gastroenterology. *Indian J Gastroenterol.* 2018;37(6):526-44.
3. Kaur N, Kumar S, Agarwal S. Relationship between fast food consumption and health of late childhood. *Int J Res. – Granthaalayah.* 2016;4(6):72-81.
4. Chaudhari O. Impact of sanitation insecurity on women: A case from rural Odisha in India. *Sanitation.* 2023;7(2): 43-58.
5. Kumar R. For many Indian women lack of toilet access poses health risks. [Internet] [Cited 2024 Feb 23] Available from: <https://undark.org/2022/07/20/for-many-indian-women-lack-of-toilet-access-poses-health-risks/>
6. Andrews CN, Storr M. The pathophysiology of chronic constipation. *Can J Gastroenterol.* 2011;25(Suppl B):16B-21B.
7. Judkins TC, Dennis-Wall JC, Sims SM, et al. Stool frequency and form and gastrointestinal symptoms differ by day of the menstrual cycle in healthy adult women taking oral contraceptives: A prospective observational study. *BMC Womens Health.* 2020;20(1):136. Doi.org/10.1186/s12905-020-01000-x.
8. Callan NGL, Mitchell ES, Heitkemper MM, et al. Constipation and diarrhea during the menopause transition and early postmenopause: Observations from the Seattle Midlife Women's Health Study. *Menopause.* 2018;25(6):615-24.
9. Pan R, Wang L, Xu X, et al. Crosstalk between the gut microbiome and colonic motility in chronic constipation: Potential mechanisms and microbiota modulation. *Nutrients.* 2022;14(18):3704. Doi.org/10.3390/nu14183704
10. Dantas AAG, Pereira ARR, de Castro SS, et al. Is Constipation associated with worse functioning in adult women? A cross-sectional study. *Journal of Multidisciplinary Healthcare.* 2020;13:883-89.
11. Costilla VC, Foxx-Orenstein AE. Constipation: Understanding mechanisms and management. *Clin Geriatr Med.* 2014;30(1):107-15.
12. Jani B, Marsicano E. Constipation: Evaluation and management. *Mo Med.* 2018;115(3):236-40.
13. Pranami D, Sharma R, Pathak H. Lactulose: A prebiotic, laxative and detoxifying agent. *Drugs Ther Perspect* 2017;33:228-33.
14. Sokur TN, Dubrovina NN. Use of lactulose in the treatment of constipation during pregnancy and postpartum. *Obstetrics and Gynecology.* 2013;8:103-107.

TABLE OF CONTENTS

Epidemiological aspects	07
Dr. Parikshit Tank	
Pathophysiology of constipation	11
Dr. Chandrakant Sankalecha	
Clinical presentation, causes, and risk factors of constipation	16
Dr. Gorakh G Mandrupkar	
Clinical evaluation of constipation	19
Dr. Charmila Ayyavoo	
Alarm signs and symptoms in constipation	23
Dr. Basab Mukherjee	
Consequences of constipation on women's health	26
Dr. Ursula Pandit; Dr. Suchitra N Pandit	
Prevention and management of constipation	29
Dr. Girija Wagh	
New thoughts on treatment of gut dysbiosis leading to chronic constipation	37
Dr. Sanjay Gupte; Dr. Arati Shah	



Dr. Parikshit Tank

MD, DNB, FCPS, DGO, DFP, MNAMS, FICOG, FRCOG
Consultant, Obstetrician and Gynaecologist
The Ashwini Clinic, Mumbai
Treasurer, FOGSI

EPIDEMIOLOGICAL ASPECTS

The term constipation refers to the symptoms associated with challenges in the process of defecation. These symptoms comprise infrequent bowel movements, presence of hard or lumpy stools, excessive straining, a feeling of incomplete evacuation or blockage, and in certain cases, resorting to manual maneuvers to aid in the evacuation process.¹

In **acute constipation**, symptoms are typically short-lived, lasting less than a week, and are often triggered by changes in diet and/or lifestyle such as reduced fiber intake, decreased physical activity, stress, or toileting in unfamiliar surroundings.¹

On the other hand, **chronic constipation** is generally characterized by symptoms that persist for at least 3 months.¹

Constipation is characterized by persistent difficulties in initiating bowel movements, incomplete evacuation, and infrequent bowel movements occurring every 3 or 4 days, or even less frequently in the absence of alarming symptoms or secondary factors.^{2,3}

Classification of chronic constipation

According to the Rome IV criteria, chronic constipation disorders can be classified into four subtypes in the absence of any organic gastrointestinal pathology¹:

- Functional constipation
- Irritable bowel syndrome (IBS) with constipation
- Opioid-induced constipation, and
- Functional defecation disorders, which encompass inadequate defecatory propulsion and dyssynergic defecation.

Criteria for functional constipation

The Rome IV criteria for diagnosing functional constipation require the presence of two or more of the following symptoms within the last 6 months:^{1,4}

- Fewer than 3 spontaneous bowel movements per week
- Straining for more than 25% of defecation attempts
- Experiencing lumpy or hard stools for at least 25% of defecation attempts

- Sensation of anorectal obstruction or blockage during at least 25% of defecation attempts
- Sensation of incomplete defecation for at least 25% of defecation attempts
- Manual maneuvering is needed to facilitate defecation during at least 25% of defecation attempts.

Functional constipation is also diagnosed when two specific conditions are satisfied: Loose stools rarely present without the use of laxatives and the failure to meet the Rome IV criteria for irritable bowel syndrome (IBS) as abdominal pain is either absent, not predominant, or occurs less than 1 day per week.⁴

Opiate users should be excluded from a functional constipation diagnosis, as they likely have opioid-induced constipation.¹

Burden of constipation

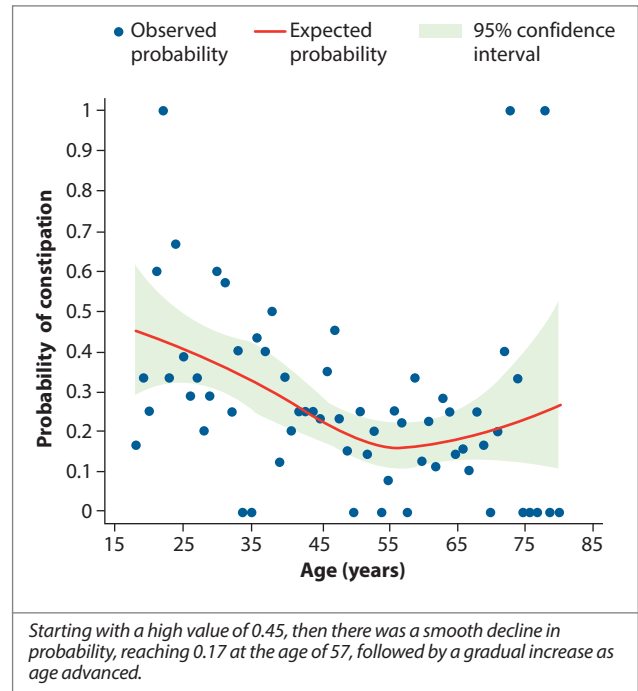
Based on meta-analysis, global prevalence of chronic constipation is estimated at around 14%. It is more prevalent in women, older individuals, and those with

lower socioeconomic status. This condition significantly affects work performance and daily activities thus diminishes quality of life. Also, it imposes a considerable burden on healthcare resources.^{1,2}

Constipation across different phases of women's life

- The elevated occurrence of constipation in women can be linked to biological issues related to estrogen and progesterone. These issues activate the autonomic nervous system, potentially leading to the development of constipation and affecting gastrointestinal motility.^{2,3}
- Women of reproductive age, particularly during menstrual cycles, may face a notable prevalence of constipation. Moreover, the involvement of the female pelvic floor in the biomechanics of gastrointestinal emptying contributes to constipation.²
- Several evidence emphasizes the need for comprehensive understanding and management of constipation, recognizing its substantial prevalence and the susceptibility of females to this condition.³
- Verkuijl *et al.* in their study found that probability of functional constipation varies at different phases of ages in men as well as women with lowest probability at around 55 years of age (Figure 1.1).⁵

Figure 1.1: The trend in the probability of constipation in females at various ages⁵



The prevalence of constipation at different stages of women's lives has been thoroughly examined through numerous studies across diverse populations. A comprehensive overview of these findings is presented in Table 1.1.^{3,6-12}

Table 1.1: Prevalence and factors associated with constipation in different phases of women's life^{3,6-12}

Life phases	Constipation prevalence	Reasons associated with constipation
Childhood ⁶	Constipation was more prevalent among girls (9–10 years old) compared to boys, with ranges of 5.1% for girls and 2.8% for boys	Watching TV for long periods, food consumption frequency, being overweight, frequent irritability, and rare interaction with parents
Reproductive age group women ³	<ul style="list-style-type: none"> • Young adult (19–24 years old): 21.7% • Adult (25–39 years old): 47.8% • Middle-aged (40–49 years old): 30.5% 	Clinical factors such as hemorrhoids, pain and a burning sensation, and sexual dysfunction
Pregnancy ⁷	<ul style="list-style-type: none"> • Prevalence of constipation is 2–3 fold more as compared to nonpregnant women • Prevalence of constipation was 40% during pregnancy vs. 21% in control group; 44% of women had constipation during 2nd trimester while 36% of women had constipation during 3rd trimester 	The impact of placental sex hormones on gastrointestinal transit time and motility, alterations in mechanical processes as pregnancy progresses, changes in water absorption, dietary influences, decreased physical activity during gestation and also history of constipation is a risk factor
Postpartum ⁷	<ul style="list-style-type: none"> • 52% of postpartum women had constipation • In early postpartum period, 47% of women with vaginal delivery and 57% of women with caesarean delivery had constipation • 1 month after postpartum, 9% of women with vaginal delivery and 15% of women with caesarean delivery had constipation 	Anal sphincter injury induced by childbirth, pelvic floor muscle injuries and pudendal nerve tears as well as reduced exercise, and dehydration.

Continued on next page...

...continued from previous page

Life phases	Constipation prevalence	Reasons associated with constipation
Menopausal/ postmenopausal ^{8,9}	18.43% of postmenopausal women show functional constipation vs. 14.60% of pre-menopause women	Stress perception, tension, anxiety, and cortisol hormone
Elderly ¹⁰⁻¹²	<ul style="list-style-type: none"> Constipation becomes more common with age In population studies of individuals >65 years old, 26% of women are constipated compared to 16% of men In a subgroup of patients aged 84 years, the prevalence of constipation increased to 34% in women vs. 26% in men Elderly women are 2–3 times more likely to report constipation than elderly men 	Risk factors include – Immobility, weakness of the abdominal and pelvic floor muscles, malnutrition, rectal hyposensitivity, ignoring a “defecation call,” chronic medical conditions (metabolic, neurologic, cardiovascular), chronic medication use (analgesics, calcium channel blockers, antihypertensive drugs, and antipsychotics), and aging effects on colonic motility; psychological, social, and behavioral factors

Common causes of constipation in Indian women

According to the Indian consensus on chronic constipation in adults, constipation is a common

health concern in India wherein female population is expected to suffer more than males.¹³

The National Health Portal of India reported that 22% of Indian adults experience chronic constipation.¹⁴

Unhealthy lifestyle and dietary habits	<ul style="list-style-type: none"> Epidemiological surveys reported sedentary lifestyle, irregular and inadequate toilet time, insufficient dietary fiber, and fluid intake as some of the factors contributing to chronic constipation in Indian people.¹³ Increased attraction of children towards unhealthy fast food/junk food/empty calorie food (e.g. wafers, pizza, chips, colas, burgers, etc.) which lacks in micronutrients such as vitamins, minerals or amino acids and fiber but has high energy contribute to diseases like constipation.¹⁵ In a study by Kaur <i>et al.</i> it was found that among a group of 30 children aged 6–12 years (including 13 girls), the second most prevalent health issue was constipation (86.66%), with obesity being the most common (93.33%).¹⁵
Inadequate sanitation	<ul style="list-style-type: none"> Women in India, particularly in rural regions, encounter sanitation challenges stemming from the absence of toilets, poor toilet conditions, or reluctance to use them despite access availability.¹⁶ In rural areas, open defecation is prevalent, often rooted in patriarchal family structures resistant to toilet installation due to traditional sanitary customs influenced by societal norms. Women feel ashamed and embarrassed to be seen defecating during the day, leading them to suppress their urge until nighttime to use open spaces for sanitation. This often result in reduced food and water intake, leading to chronic constipation and urinary incontinence. The sense of shame is not confined to open defecation but also extends to using private toilets in the presence of family elders.¹⁶ Similarly, for women in cities, mainly low-income residents/slum residents, bathroom use is restricted due to inadequate toilet infrastructure. Urban public toilets are overcrowded and are often inadequately maintained, sewage overflows, poorly lit, and face water scarcity. This deficiency in sanitation infrastructure makes some residents, particularly women, to adopt unhealthy practices such as withholding urine and limiting liquid intake to minimize visits to these facilities.¹⁷ Consequently, these habits contribute to health issues such as stomach aches and constipation.¹⁷

This emphasizes the importance of raising awareness about constipation and its adverse effects on health, particularly among women in India.

Key highlights

- Constipation is a common health concern in Indian women.¹³
- The prevalence and influencing factors of constipation change at different stages in a woman's life.^{3,5-12}
- Eating junk food, less fluid consumption, holding urge due to sanitation challenges are the key contributing factors for health issues like constipation among Indian women.^{13,15-17}

References

1. Aziz I, Whitehead WE, Palsson OS, et al. An approach to the diagnosis and management of Rome IV functional disorders of chronic constipation. *Expert Rev Gastroenterol Hepatol.* 2020;14(1):39-46.
2. Dantas AAG, Pereira ARR, de Castro SS, et al. Is constipation associated with worse functioning in adult women? A cross-sectional study. *J Multidiscip Healthc.* 2020;13:883-89.
3. Dantas AAG, Barbosa IR, Castro SS, et al. Prevalence and factors associated with constipation in premenopausal women: A community-based study. *Arq Gastroenterol.* 2020;57(2):188-92.
4. Yamamoto S, Ohashi W, Yamaguchi Y, et al. Background factors involved in the epidemiology of functional constipation in the Japanese population: A cross-sectional study. *Biopsychosoc Med.* 2022;16(1):8. Doi.org/10.1186/s13030-022-00237-2
5. Verkuijl SJ, Meinds RJ, Trzpis M, et al. The influence of demographic characteristics on constipation symptoms: A detailed overview. *BMC Gastroenterol.* 2020;20(1):168. Doi.org/10.1186/s12876-020-01306-y
6. Yamada M, Sekine M, Tatsuse T. Psychological stress, family environment, and constipation in Japanese children: The Toyama Birth Cohort Study. *J Epidemiol.* 2019;29(6):220-26.
7. Kuronen M, Hantunen S, Alanne L, et al. Pregnancy, puerperium and perinatal constipation - An observational hybrid survey on pregnant and postpartum women and their age-matched non-pregnant controls. *BJOG.* 2021;128(6):1057-64.
8. Brigstocke S, Nee J, Ballou S, et al. Women's health factors and altered bowel habits: Results of a National Health and Nutrition Examination Survey. *GastroHep [Internet].* 2021;3(3):141-50.
9. Kirka AS, Oksuz SK, Gul DK. Constipation and its effects on quality of life in menopausal women. *Int. J. Caring Sci.* 2021;14(1):269-75.
10. De Giorgio R, Ruggeri E, Stanghellini V, et al. Chronic constipation in the elderly: A primer for the gastroenterologist. *BMC Gastroenterol.* 2015;15:130. Doi. 10.1186/s12876-015-0366-3
11. Shamloufard P, Kern M, Hooshmand S. Bowel function of postmenopausal women: Effects of daily consumption of dried plum. *Int J Food Prop.* 2017;20(12):3006-13.
12. Mari A, Mahamid M, Amara H, et al. Chronic constipation in the elderly patient: Updates in evaluation and management. *Korean J Fam Med.* 2020;41(3):139-45.
13. Ghoshal UC, Sachdeva S, Pratap N, et al. Indian consensus on chronic constipation in adults: A joint position statement of the Indian Motility and Functional Diseases Association and the Indian Society of Gastroenterology. *Indian J Gastroenterol.* 2018;37(6):526-44.
14. Kumar R, Ramakrishnan SR, Kulkarni A. Chronic constipation with associated comorbid conditions: A physician survey on clinical perspectives on its diagnosis and management. *Int J Adv Med.* 2023;10(10):695-704.
15. Kaur N, Qumar N, Agarwal S. Relationship between fast food and consumption and health of late childhood. *Int J Res – Granthaalayah.* 2016;4(6):72-81.
16. Chaudhari O. Impact of sanitation insecurity on women: A case from rural Odisha in India. *Sanitation.* 2023;7(2):43-58.
17. Kumar R. For many Indian women, lack of toilet access poses health risks. [Internet] 2022. [Cited 2024 Feb 23]. Available from: <https://undark.org/2022/07/20/for-many-indian-women-lack-of-toilet-access-poses-health-risks/>



Dr. Chandrakant Sankalecha

MD, FICOG

Consultant, Sankalecha Hospital,
Nashik.

Member Executive committee, Gestosis India Association

PATHOPHYSIOLOGY OF CONSTIPATION

Functional constipation can be classified as slow transit constipation and outlet dysfunction constipation. Slow transit constipation refers to the delayed passage of fecal contents via colon and is more prevalent in women. Outlet dysfunction manifests as compromised rectal evacuation.¹

Pathophysiology of constipation

Constipation can result from various pathophysiological factors affecting the following:²

- Colonic absorption
- Colonic motility
- Behavioral/psychological aspects

Slow transit constipation

- The exact pathophysiology of slow transit constipation is incompletely understood.¹
- Adequate water and solute secretion into the intestinal lumen are crucial for lubrication influencing the stool consistency.²
- Stool consistency is linked to water content, which in turn correlates with colonic transit time. "Prolonged transit time leads to increased water absorption, resulting in firmer stool consistency. This process may contribute to difficulties in evacuating small hard stools (Bristol Stool Form Scale [BSFS] type 1) or large hard stools (BSFS type 2).²
- Various factors contribute to slow transit constipation. They include alterations in colonic muscle or nerve activity, disruptions in enteric neurotransmitters, and the loss of interstitial cells of Cajal. These electrically active cells are believed to serve as the pacemakers for the intestines.¹
- Additionally, studies suggest that an excess production of methane by colonic bacteria may contribute to slow transit in certain patients. Opioid-induced constipation is frequently associated with slow transit and is believed to stem from heightened non-propulsive segmental motility

and reduced propulsive peristalsis, triggered by the activation of μ -opioid receptors.¹

- A reduction in the frequency of larger peristaltic contractions, also known as high-amplitude propagated contractions (HAPCs), can be one of the pathophysiological mechanism contributing to constipation by hindering the effective propulsion of stools along the colonic lumen.²

Outlet dysfunction constipation

- Functional and physiological abnormalities in the anorectum can contribute to constipation.²
- Outer dysfunction can occur due to insufficient rectal propulsive forces, heightened resistance to evacuation, or a combination of both.¹
- Dyssynergic defecation, a subtype of outlet dysfunction, is characterized by inadequate relaxation or paradoxical contraction of the anorectal muscles during attempts to pass stools.¹
- While the exact pathophysiology of dyssynergic defecation remains incompletely understood, factors such as anxiety, psychological stress, and the chronicity of constipation are believed to contribute to its development.¹
- Dyssynergia may manifest with pathologic behaviors like avoidance of defecation, mostly linked to conditions like painful anal fissures, and may be associated with comorbidities such as back injury, brain-gut dysfunction, eating disorders, and a history of sexual or physical abuse.²
- The least common cause of dyssynergic defecation include mechanical factors such as rectal intussusception, prolapse, rectocele, and abnormal perineal descent.²

Factors influencing constipation in women

Various theories have been proposed for higher prevalence of constipation in women than men.³ Overall, the factors influencing constipation in women can be classified as:

- **Anatomical factors:** Normal defecation requires coordinated action of various anatomical factors like anal sphincters, puborectalis muscles (pelvic floor), and rectal curvatures.⁴ Factors influencing constipation involve complex interactions within the gastrointestinal (GI) tract, nervous system, and pelvic muscles. Key contributors for constipation include reduced colonic motility, delayed transit of stool, impaired rectal sensation, and ineffective coordination of pelvic floor muscles during defecation.⁵ Pelvic floor dysfunction, characterized by paradoxical contraction or insufficient relaxation of pelvic floor muscles when attempting to defecate, is associated with conditions like dyssynergic defecation.⁶
- **Hormonal factors:** In the premenstrual phase, ovaries secrete estrogen and progesterone. These hormones decelerate gut motility, frequently leading to constipation. With menstruation, there is a sudden drop in these hormones and an increase in prostaglandins, which lead to diarrhea during the first few days. The proximity of the uterus to the intestine is believed to be a factor in these digestive changes.⁷ During menopause, stress hormones like cortisol is one of the major players in constipation.⁸
- **Neurological factors:** The intestinal function is governed and controlled by the intricate neural networks of the enteric nervous system (ENS). Dysfunction of ENS is at times a major underlying factor in the pathogenesis of chronic constipation.⁹
- **Lifestyle factors:** The secretory and sensory mechanisms of gut functions are affected by lifestyle factors like diet i.e. intake of fluid and fiber.² Chronic constipation is often attributed to insufficient fiber intake, characterized by lack of fruits, vegetables, and other fiber-rich foods, as well as inadequate consumption of drinking water or liquids. Additionally, consumption of iron and calcium supplements contribute to developing constipation.¹⁰

Factors variably responsible for constipation across different life phases of women are discussed below:

Childhood period

- Childhood constipation is often idiopathic. Children usually withhold stools after difficult bowel movements. This leads to water absorption, sometimes leading to rectal distension and loss of sensation.²
- Around one-fourth of childhood constipation cases persist into adulthood.² Additionally, lifestyle factors such as physical inactivity, inadequate intake of fruits and vegetables, watching TV for longer time, eating high calorie and fiber-less fast food like pizza, burger, chips, etc. can lead to constipation in children, specially in girls.^{11,12}
- Psychological factors like stress, less interaction with parents and anxiety may contribute to increased muscle tone, leading to dyssynergic defecation.^{2,11}

Women of reproductive age

- Women of reproductive age show higher prevalence of constipation.^{13,14}
- Estrogen and progesterone affect gut motility through autonomic nervous system.^{13,14}
- Other factors can be altered biomechanical aspects involved in bowel movement due to impaired pelvic floor muscle.^{13,14}
- Furthermore, hemorrhoids, pain and a burning sensation, and sexual dysfunction can cause constipation.¹⁴

Pregnancy

- During antenatal and postnatal period, constipation ranks as the second most prevalent GI symptom after nausea.¹⁵
- The history of constipation in previous pregnancy increases the risk of constipation during the next pregnancy.¹⁶
- In early pregnancy, progesterone plays a major role in causing constipation by inducing relaxation of smooth muscle, leading to hypomotility of the small and large bowels. Also, there is an increased absorption of water during pregnancy due to higher levels of aldosterone induced by estrogen and progesterone.¹⁶
- Iron supplement during pregnancy can exacerbate constipation.¹⁶

- During late pregnancy, mechanical factors add to constipation. The movement of solid feces is hampered by overdistended uterus which may obstruct defecation.¹⁶
- Vaginal delivery and with high parity raises the risk of defecation problems linked to pelvic floor dysfunction.¹⁷
- Dietary factors and reduced mobility are additional contributing factors to constipation during pregnancy.¹⁵

Postpartum

- Discomfort at the episiotomy site, the influence of hormones, the consumption of iron supplements during pregnancy, and hemorrhoids may elevate the likelihood of postpartum constipation.¹⁸
- Anal sphincter injury during childbirth, pelvic floor muscle injuries, or pudendal nerve tears as well as reduced water intake and exercise can contribute to the postpartum constipation.¹⁵

Postmenopausal

- In postmenopausal women, factors like reproductive hormones, have not been reported to influence the risk of constipation.^{8,19}
- In contrast, stress perception, tension, anxiety, and cortisol play a significant role in constipation.⁸

Elderly

- Factors contributing to constipation in aging include structural and functional changes in the GI tract, particularly in the colon and anorectal region. These

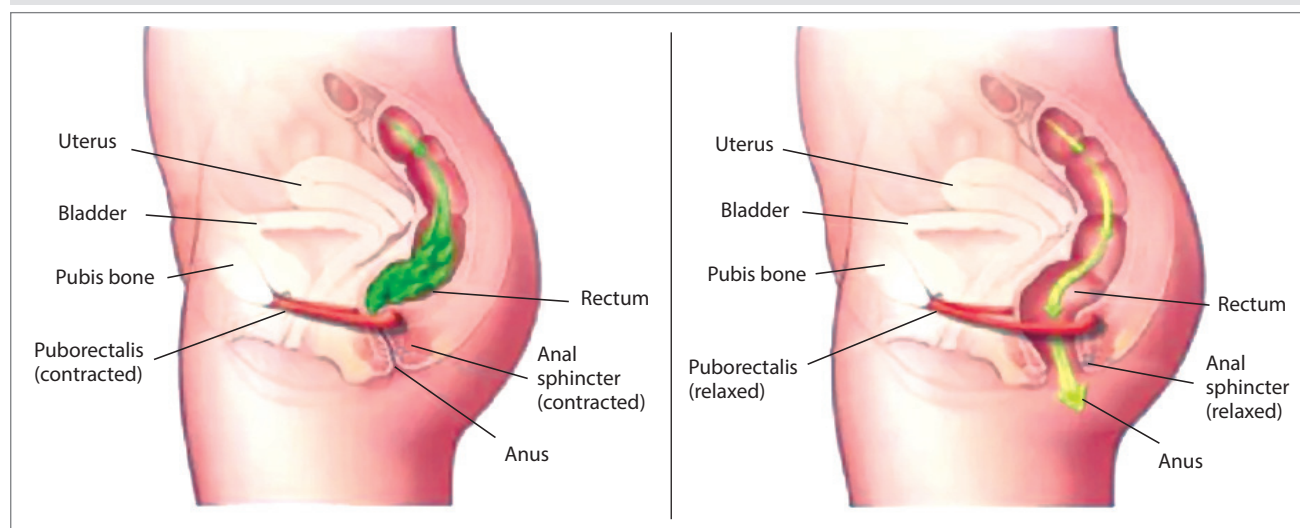
alterations can disrupt bowel habits and evacuation mechanisms.²⁰

- In elderly individuals, complete disruption of the pelvic floor or restricted to bowel (e.g., rectocele, intussusception, internal, or external rectal prolapse), along with decreased rectal sensation, are causes of chronic constipation. These conditions also encompass the result or potential complications of pelvic and perineum surgical procedures.²⁰
- Tissue atrophy leading to reduced distensibility contributes to alteration in the pelvic floor. Pudendal nerve injury, particularly in women, can play a role in constipation. It may cause abnormal perineal descent, resulting in prolapse of the anal canal or anterior rectal mucosa, thereby affecting rectal emptying.²⁰
- It has been reported that women who have had vaginal or laparoscopic hysterectomies are twice as likely to experience obstructive defecation.¹⁷

Constipation and pelvic floor dysfunction: A vicious cycle

To facilitate excretion, it is necessary to maintain relaxation in the external sphincter and puborectalis muscles. When the puborectalis muscle relaxes, it allows the anorectal angle to open, facilitating the passage of feces. The expulsion of feces is aided by intra-abdominal pressure and the execution of the Valsalva maneuver, as depicted in Figure 2.1. Failure or lack of coordination in these actions may lead to constipation.²¹

Figure 2.1: Role of pelvic floor muscles in defecation²¹



Constipation experienced during pregnancy and after childbirth has the potential to induce pelvic floor dysfunction, leading to fecal incontinence or pelvic organ prolapse. The excessive straining associated with constipation may inflict damage on the pudendal nerve, impairing the function of the pelvic floor musculature. Additionally, severe constipation can contribute to the development of hemorrhoids or rectal prolapse, further exacerbating pelvic organ prolapse. Conversely, injuries to the pelvic floor muscles and anal sphincters during labor may result in postpartum constipation.¹⁵

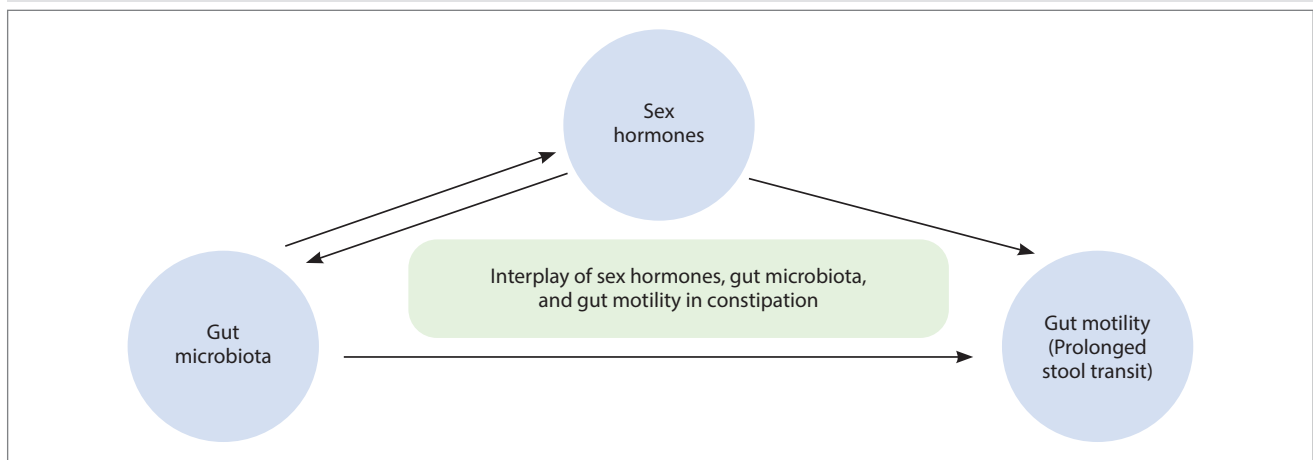
Gut health in women and its association with constipation

- The gut microbiome, a collection of around 40 trillion microbes in the GI tract, plays a vital role in humans' well-being.²²
- This microbial community interacts with metabolism, nervous system, immune system, and endocrine system, influencing psychological functions.²²
- The disruption of gut microbial communities (dysbiosis) can lead to functional GI disorders like constipation.²²
- The gut microbiota significantly influences intestinal motility.²³
- Studies have found a connection between chronic constipation and dysbiosis, with an increase in methanogenic bacteria, especially *Methanobrevibacter smithii*, slowing down small intestine movement by enhancing non-propagating contractions.^{23,24}

- Gut microbiota differs across genders, with women generally having lower Bacteroides but higher alpha (α) diversity than men.²⁵
- Li *et al.* found that in women with chronic constipation, there is a decrease in Proteobacteria and butyrate-producing bacteria, along with an increase in Bacteroides.²³
- Estrogen and progesterone play a crucial role in prolonging stool transit.²²
- There are bidirectional interactions between gut microbiota and sex hormones.²²
- During pregnancy, the body undergoes changes in the immune system, hormones, and metabolism. These results in increased pro-inflammatory cytokines leading to low-grade inflammation affecting the composition of maternal gut microbiota, including changes in diversity and abundance of specific bacterias. These alterations continue into the postpartum period.²⁶
- Hormones, including steroids, influence gut movement through various mechanisms. Overexpression of progesterone receptors, especially P4R, might be a factor in pregnancy-related constipation.²²

This intricate interplay of hormones, microbiota, and gut motility provides insights into sex-specific differences in constipation (Figure 2.2). Ongoing research on the crosstalk between host hormones, microbiota, and constipation during pregnancy holds promise for understanding this complex physiological mechanism.²²

Figure 2.2: Complex link between sex hormones, gut microbiota, and gut motility in constipation²²



Key highlights

- Constipation results from various pathophysiological factors affecting colonic absorption, motility, and behavioral and psychological aspects.²
- Various factors contribute to the higher prevalence of constipation in women, including anatomical, hormonal, neurological, and lifestyle considerations.⁴⁻¹⁰
- Dysbiosis in the gut microbiome can lead to functional GI disorders like constipation.²²
- Gender differences in the gut microbiome, hormonal influences, and the complex interplay between hormones, microbiota, and gut motility contribute to constipation in women.^{22,26}

References

1. Jani B, Marsicano E. Constipation: Evaluation and management. *Mo Med*. 2018;115(3):236-40.
2. Heidelbaugh J, Martinez de Andino N, Pineles D, et al. Diagnosing constipation spectrum disorders in a primary care setting. *J Clin Med*. 2021;10(5):1092. Doi.org/10.3390/jcm10051092
3. Verkuijl SJ, Meinds RJ, Trzpis M, et al. The influence of demographic characteristics on constipation symptoms: A detailed overview. *BMC Gastroenterol*. 2020;20(1):168. Doi.org/10.1186/s12876-020-01306-y
4. Andrews CN, Storr M. The pathophysiology of chronic constipation. *Can J Gastroenterol*. 2011;25(Suppl B):16B-21B.
5. Diaz S, Bittar K, Hashmi MF, et al. Constipation. [Updated 2023 Nov 12]. In: StatPearls. Treasure Island (FL): StatPearls Publishing. [Internet]. 2024. [Cited 2024 Feb. 27]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK513291>
6. Grimes WR, Stratton M. Pelvic floor dysfunction. [Updated 2023 Jun 26]. In: StatPearls. Treasure Island (FL): StatPearls Publishing. [Internet]. 2024. [Cited 2024 Feb. 27]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK559246/>
7. Judkins TC, Dennis-Wall JC, Sims SM, et al. Stool frequency and form and gastrointestinal symptoms differ by day of the menstrual cycle in healthy adult women taking oral contraceptives: A prospective observational study. *BMC Womens Health*. 2020;20(1):136. Doi.org/10.1186/s12905-020-01000-x
8. Callan NGL, Mitchell ES, Heitkemper MM, et al. Constipation and diarrhea during the menopause transition and early postmenopause: Observations from the Seattle Midlife Women's Health Study. *Menopause*. 2018;25(6):615-24.
9. Wang L, Lv WQ, Yang JT, et al. Enteric nervous system damage caused by abnormal intestinal butyrate metabolism may lead to functional constipation. *Front Microbiol*. 2023;14:1117905. Doi: 10.3389/fmicb.2023.1117905
10. Forootan M, Bagheri N, Darvishi M. Chronic constipation: A review of literature. *Medicine (Baltimore)*. 2018;97(20):e10631. Doi: 10.1097/MD.0000000000010631.
11. Yamada M, Sekine M, Tatsuse T. Psychological stress, family environment, and constipation in Japanese children: The Toyama Birth Cohort Study. *J Epidemiol*. 2019;29(6):220-26.
12. Kaur N, Kumar S, Agarwal S. Relationship between fast food consumption and health of late childhood. *Int J Res. – Granthaalayah*. 2016;4(6):72-81.
13. Dantas AAG, Pereira ARR, de Castro SS, et al. Is constipation associated with worse functioning in adult women? A cross-sectional study. *J Multidiscip Healthc*. 2020;13:883-89.
14. Dantas AAG, Barbosa IR, Castro SS, et al. Prevalence and factors associated with constipation in premenopausal women: A community-based study. *Arq Gastroenterol*. 2020;57(2):188-92.
15. Kuronen M, Hantunen S, Alanne L, et al. Pregnancy, puerperium and perinatal constipation - An observational hybrid survey on pregnant and postpartum women and their age-matched non-pregnant controls. *BJOG*. 2021;128(6):1057-64.
16. Gomes CF, Sousa M, Lourenço I, et al. Gastrointestinal diseases during pregnancy: What does the gastroenterologist need to know? *Ann Gastroenterol*. 2018;31(4):385-94.
17. Black CJ, Ford AC. Chronic idiopathic constipation in adults: Epidemiology, pathophysiology, diagnosis and clinical management. *Med J Aust*. 2018;209(2):86-91.
18. Turawa EB, Musekiwa A, Rohwer AC. Interventions for preventing postpartum constipation. *Cochrane Database Syst Rev*. 2015(9):CD011625. Doi: 10.1002/14651858.CD011625.pub2
19. Brigstocke S, Nee J, Ballou S, et al. Women's health factors and altered bowel habits: Results of a National Health And Nutrition Examination Survey. *Gastro Hep*. 2021;3(3):141-50.
20. Mannella P, Palla G, Bellini M, et al. The female pelvic floor through midlife and aging. *Maturitas*. 2013;76(3):230-4.
21. Bahmani A, Arab AM, Khorasany B, et al. Systematic review: The role of pelvic floor muscles dysfunction in constipation. *Physical Treatments*. 2015;4(4):177-82.
22. Pan R, Wang L, Xu X, et al. Crosstalk between the gut microbiome and colonic motility in chronic constipation: Potential mechanisms and microbiota modulation. *Nutrients*. 2022;14(18):3704. Doi.org/10.3390/nu14183704
23. Iancu MA, Profir M, Roşu OA, et al. Revisiting the intestinal microbiome and its role in diarrhea and constipation. *Microorganisms*. 2023;11(9):2177. Doi: 10.3390/microorganisms11092177.
24. Ohkusa T, Koido S, Nishikawa Y, et al. Gut microbiota and chronic constipation: A review and update. *Front Med (Lausanne)*. 2019;6:19. Doi: 10.3389/fmed.2019.00019
25. Siddiqui R, Makhlof Z, Alharbi AM, et al. The gut microbiome and female health. *Biology (Basel)*. 2022;11(11):1683. Doi.org/10.3390/biology11111683
26. Weerasuriya W, Saunders JE, Markel L, et al. Maternal gut microbiota in the postpartum period: A systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2023;285:130-47.

CLINICAL PRESENTATION, CAUSES, AND RISK FACTORS OF CONSTIPATION



Dr. Gorakh G Mandrupkar

MBBS, DGO, FICOG
Consultant, Reproductive Medicine
Angel IVF, Pune.
Vice President, Gestosis India Association

The clinical presentation of constipation is influenced by patient factors such as gender, age, race, and socioeconomic status.¹

Women experience constipation 2.2 times more than men, and prevalence increases with age, especially in those over 65 years. Hence, recognizing the clinical presentation and identifying alarm signs and symptoms is essential for prompt diagnosis and successful management.¹

Clinical presentation

The term constipation is used to describe the symptoms caused by difficulties in defecation. It is often characterized by the following:^{1,2}

- Infrequent bowel movements
- Hard or lumpy stools
- Excessive straining
- Feeling of incomplete evacuation or blockage
- Sometime use of manual maneuvers for defecation

- Abdominal cramping
- Bloating

The Rome IV criteria helps in diagnosis of constipation with the key tool of Bristol Stool Form Scale (BSFS). BSFS categorizes stool form on a graded 7-point scale, ranging from separate hard lumps that are challenging to evacuate (BSFS type 1) to mushy, watery stools (BSFS type 7) as shown in Figure 3.1.¹

Table 3.1 shows Rome IV diagnostic criteria of chronic idiopathic constipation and irritable bowel syndrome with constipation (IBS-C).¹

Figure: 3.1: Bristol Stool Form Scale¹








Type 1		Separate hard lumps like nuts (hard to pass)
Type 2		Sausage-shaped, but lumpy
Type 3		Like a sausage, but with cracks on its surface
Type 4		Like a sausage or snake; smooth and soft
Type 5		Soft blobs with clear-cut edges (passes easily)
Type 6		Fluffy pieces with ragged edges; a mushy stool
Type 7		Watery, no solid pieces; entirely liquid

Table 3.1: Rome IV diagnostic criteria of chronic idiopathic constipation and irritable bowel syndrome with constipation¹

	Rome IV criteria	Other considerations
Chronic idiopathic constipation (CIC)	<p>Patients must exhibit at least two of the following criteria within the past 3 months:</p> <ul style="list-style-type: none"> • Less than 3 bowel movements per week • Straining over 25% of bowel movements • Experiencing lumpy or hard stools (Bristol Stool Form Scale [BSFS] type 1 or 2) in more than 25% of bowel movements • Sensation of incomplete defecation in over 25% of bowel movements • Sensation of anorectal obstruction/blockage in over 25% of bowel movements • Using manual maneuvers to facilitate over 25% of bowel movements • Patients who do not meet the Rome IV criteria for IBS-C. 	<ul style="list-style-type: none"> • Patients who exhibit some similar symptoms to IBS-C but who do not meet IBS-C criteria are diagnosed with CIC • Frequency of bowel movements is primary consideration for the diagnosis of CIC • Patients with CIC may encounter bloating, abdominal pain, or discomfort, but the symptoms are not regarded as primary indicators of CIC
Irritable bowel syndrome with constipation (IBS-C)	<ul style="list-style-type: none"> • Recurrent abdominal pain occurring at least once a week • Alterations in stool frequency • Alterations in stool consistency • Bowel movements BSFS type 1 or 2 ($\geq 25\%$) • Bowel movements BSFS type 6 or 7 ($< 25\%$) 	<ul style="list-style-type: none"> • For diagnosis of IBS, patients should exhibit abdominal pain • Presence of abdominal bloating is common but not obligatory • Relief from abdominal pain or discomfort upon defecation may be experienced

Causes of constipation

- Constipation arises from a multifaceted pathogenesis, encompassing factors such as dietary choices, genetic predisposition, colonic motility, absorption, as well as behavioral, biological, and pharmaceutical elements.³
- The causes of constipation can be classified as primary or secondary.^{3,4}

Primary causes: Include slow transit or outlet obstruction.

Secondary causes include the following:

- Simple dehydration or less liquid intake
- Endocrine and metabolic disturbances due to diabetes, hypothyroidism, hyperthyroidism, hypercalcemia, pregnancy, porphyria, panhypopituitarism, and pheochromocytoma
- Neurological disorders like Parkinsonism, dementia, multiple sclerosis, spinal cord lesions, autonomic neuropathy, etc.
- Myopathic disorders like scleroderma, myotonic dystrophy, and amyloidosis
- Structural disorders like colon cancer, strictures, a large rectocele, abnormal narrowing of the intestine, or rectum
- Psychological conditions like eating disorder, depression, and anxiety

- Pregnancy
- Connective tissue disorders like lupus
- Anorectal conditions such as anal strictures, anal fissures, and hemorrhoids can impede the timely evacuation of stool and worsen chronic constipation by causing discomfort during the passage of feces.

While evaluating patients for constipation, secondary causes are ruled out first, then evaluation for primary constipation is carried out.⁴

Risk factors for constipation

Factors that increase the risk of constipation comprise the following:^{3,4}

- Advanced age
 - Common factors of constipation in elderly include lack of normal bowel movements, aging, lack of proper diet, lack of adequate fluid intake, lack of adequate physical activity, illness or the use of drugs.
 - The occurrence of anatomical abnormalities like rectocele, pelvic floor dyssynergia, and prolapse tends to be greater among the elderly, as reported.
 - Severe constipation is notably more prevalent among elderly women compared to elderly men.
- Diet low in fiber
- Low socioeconomic status

- Immobility
- Previous abdominal or pelvic surgery
- Use of multiple medications

Overall, constipation is influenced by various factors such as socioeconomic status, parental education, physical activity, medications, depression, abuse, and

daily life events. The extensive and diverse range of these factors suggests that many pathophysiological elements can lead to similar symptoms, often remaining undetectable in early stages. Due to the intricate interplay among these factors, caution is necessary when implementing therapeutic approaches based solely on one aspect of the condition.³

Key highlights

- Recognizing the clinical presentation of constipation, including the frequency of bowel movements, straining, incomplete evacuation, stool consistency, and associated symptoms, is essential for healthcare providers.^{1,2}
- While evaluating patient with constipation, ruling out secondary causes of constipation is necessary to establish the diagnosis of primary constipation.⁴
- Severe constipation is notably more prevalent among elderly women compared to elderly men.³
- In the later stages of pregnancy, constipation risk elevates due to heightened levels of sex hormones, decreased intestinal movement, and delayed intestinal emptying caused by mechanical pressure.³

References

1. Heidelbaugh J, Martinez de Andino N, Pineles D, et al. Diagnosing constipation spectrum disorders in a primary care setting. *J Clin Med.* 2021;10(5):1092. Doi.org/10.3390/jcm10051092
2. Aziz I, Whitehead WE, Palsson OS, et al. An approach to the diagnosis and management of Rome IV functional disorders of chronic constipation. *Expert Rev Gastroenterol Hepatol.* 2020;14(1):39-46.
3. Forootan M, Bagheri N, Darvishi M. Chronic constipation: A review of literature. *Medicine (Baltimore).* 2018;97(20):e10631. Doi: 10.1097/MD.00000000000010631.
4. Jani B, Marsicano E. Constipation: Evaluation and management. *Mo Med.* 2018;115(3):236-40.



Dr. Charmila Ayyavoo

MD, DGO, DFP, FICOG, PGDCR

Director, Aditi Hospital & Parvathy Ayyavoo Fertility Center, Trichy
Associate Professor, Dhanalakshmi Srinivasan Medical College &
Hospital, Perambalur.
Vice President, FOGSI (2024–25)

CLINICAL EVALUATION OF CONSTIPATION

Clinical evaluation of constipation involves a detailed clinical history, clinical examination, and basic laboratory tests. Additional investigations for organic pathology are determined by the presence of alarm features.¹

Clinical history

- Constipation assessment commences with a comprehensive patient history, encompassing bowel habits (Table 4.1), dietary details, and family history.²
- The initial evaluation helps identify primary and secondary causes, along with potential alarm symptoms (Table 4.2).²
- Key historical clues, such as prolonged sitting and excessive straining, can indicate pelvic floor dysfunction.²

Table 4.1: Checklist for detailed bowel habit history²

- Frequency of natural bowel movements per week
- Assessment of stool consistency by using the Bristol Stool Form Scale
- Determination of prolonged straining during evacuation
- Identification of bloating or abdominal pain
- Evaluation of support on digitization, perineal, or vaginal pressure for stool passage
- Counting the occurrences of the urge to defecate
- The impact of ignoring the urge to defecate due to work or functional constraint
- Comprehensive review of all medications, medical history, and previous surgeries.

Table 4.2: Alarm signs and symptoms to be assessed while evaluating constipation²

- Unintentional weight loss
- Hematochezia
- Family history of colon cancer or inflammatory bowel disease
- Detectable blood in stool through occult blood testing
- Iron deficiency anemia
- Sudden onset of constipation
- Significant alteration in recent bowel habits

- Pain relief upon bowel movements suggests a functional cause. Duration, nature, and stool consistency, assessed by the Bristol Stool Form Scale (BSFS), aid in diagnosing transit disorders.^{1,2}
- Additionally, the medical history inquiry explores gastrointestinal symptoms (abdominal pain, bloating, vomiting) and potential neurological causes (Parkinson's disease and multiple sclerosis), endocrine disorders, such as hypothyroidism and hypercalcemia or medication-induced constipation.^{1,3}
- Obstetric and gynecological history is crucial for women, considering the impact of surgeries and childbirth on defecatory symptoms.³

A thorough clinical history, including medication and surgical procedures, is essential for accurate diagnosis and tailored treatment.⁴

- Vigilance for red flag symptoms, like weight loss or rectal bleeding, prompts urgent investigations.³
- A systematic approach involves assessing risk factors like medical conditions, medications, toileting facilities, mobility, and nutritional and fluid intake. Questionnaires, such as the Patient Assessment of Constipation Quality of Life (PAC-QoL), assist in understanding the impact on QoL. Structured questioning covers current bowel problems, precipitating factors, bowel movement frequency, stool consistency, straining, laxative use, diet, and overall impact on life.⁴

Physical examination

- During a thorough physical examination, abdominal and digital rectal examinations should be conducted to help identify the underlying cause of chronic constipation.⁵
- Clinicians should check for abdominal masses and lymphadenopathy.¹
- They should inspect the anal orifice for fissures or mass lesions. Then, they should perform a digital rectal examination to feel anorectal strictures.¹

A complete digital rectal exam

The digital rectal examination goes beyond visual inspection, revealing unseen anatomic abnormalities.² It is crucial in chronic constipation to assess rectal tone, puborectalis muscle function, anal contraction during defecation, and perineal descent.⁵ Evaluation of resting tone, sphincter squeeze, and Valsalva maneuvers during the digital examination allows the clinician to assess sphincter functionality. Sharp, knife-like pain during the exam may indicate active mucosal injury, such as acute or chronic fissure, ulcer, or inflammation. Additionally, fecal impaction can be identified through digital rectal examination.² Collaboration with specialists such as gastroenterologists, colorectal surgeons, and pelvic floor-trained physical therapists may be necessary to investigate causes of constipation.⁵ Paradoxical anal contraction may suggest dyssynergic defecation, a condition where coordination issues among abdominal, rectoanal, and pelvic floor muscles occur during attempts for defecation. Digital rectal examination has a sensitivity of 75% and specificity of 87% for detecting dyssynergic defecation.¹ Palpable abnormalities may necessitate further testing, including imaging or manometric studies.⁵

Laboratory investigations

- A series of tests should be done for evaluation of constipation, aiding in the identification of potential underlying causes that may range from treatable conditions (such as hypothyroidism) to those requiring early detection (such as colon cancer).^{6,7}
- As per guidelines, a complete blood cell count is the initial step, with further testing guided by the patient's medical history and physical examination

findings. While metabolic assessments, including thyroid-stimulating hormone, serum glucose, creatinine, and calcium tests, are commonly conducted during the evaluation of patients experiencing constipation, there is a lack of evidence regarding their diagnostic effectiveness and cost efficiency.⁶

Structural examination of colon in case of alarm symptoms

A colonoscopy or imaging should be carried out in cases of constipation with alarm features such as weight loss, abdominal pain, and hematochezia. No significant diagnostic benefit exists in performing these procedures without alarm symptoms, and there is no proven link between chronic constipation and colorectal cancer. Structural evaluation is recommended in patients with alarm symptoms, abrupt onset of constipation, or those older than the screening age for colonoscopy. Identifying a secondary cause through evaluation allows for appropriate treatment.^{1,6}

In postmenopausal women presenting with recent onset constipation, localized lower abdominal pain, bloating, or distension, a transabdominal/vaginal ultrasound scan is advised to rule out underlying causes such as ovarian cancer.¹

Anorectal manometry

Anorectal manometry offers crucial insights into anorectal sensory and motor functions, anal sphincter pressures, and anorectal reflexes.⁸ This evaluation is recommended in patients suspected of having a functional defecation disorder, characterized by inadequate defecatory propulsion and/or dyssynergic defecation. It should occur either after the initial digital rectal examination or if standard medical therapy has proven ineffective.¹

Balloon expulsion test (BET)

- BET is employed for detecting pelvic floor dyssynergia. During this test, a rectal balloon filled with 25 mL or 50 mL of water, or air, and/or a silicone-filled stool-like device is used. This can be conducted concurrently with anorectal manometry or as an independent examination.⁷

- Individuals who experience regular bowel movements can successfully release the balloon within a minute. If a patient encounter challenges in expelling the balloon within this timeframe, it may indicate the possibility of dyssynergic defecation.⁶

Other studies

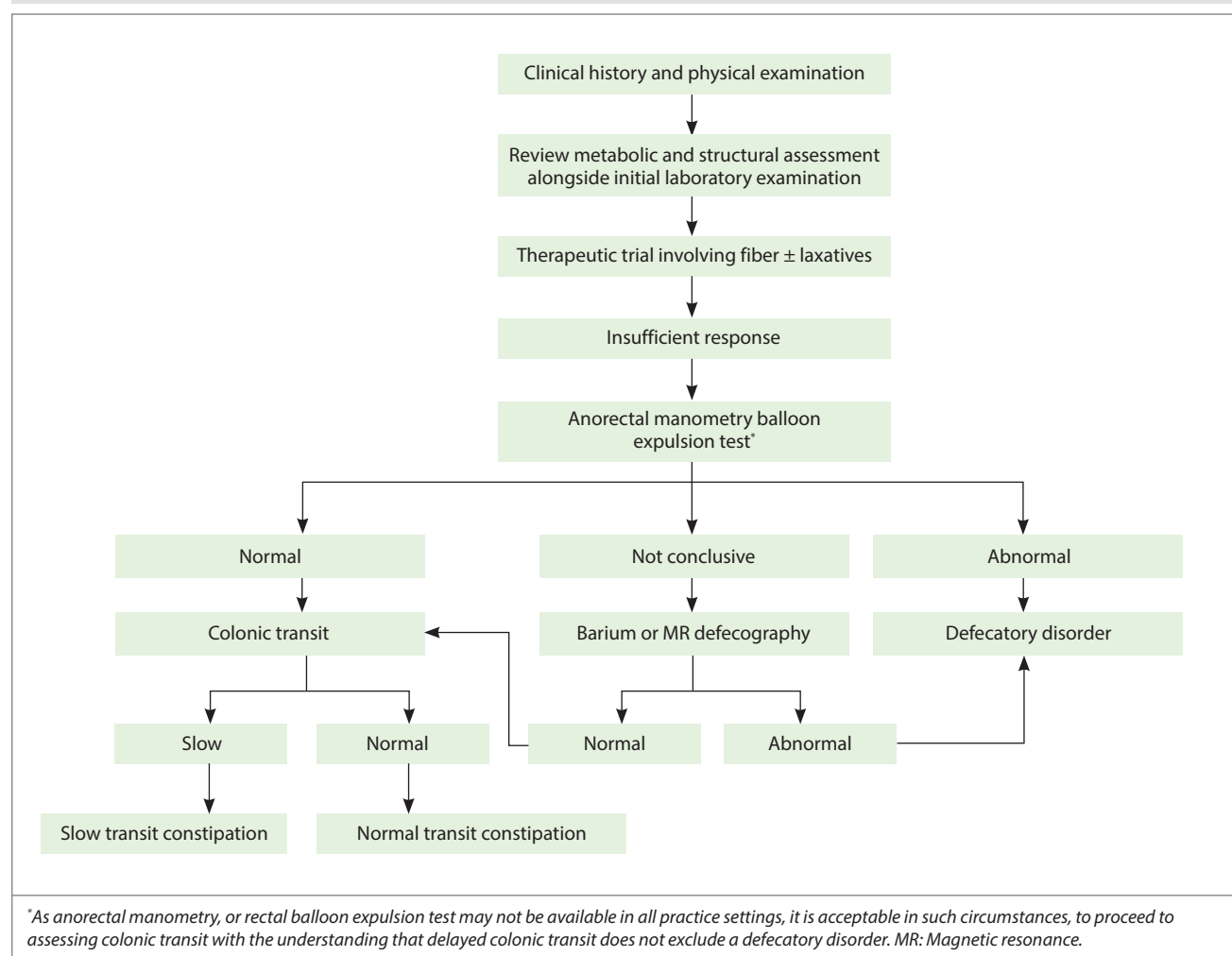
- Once outlet dysfunction has been ruled out through anorectal manometry and balloon expulsion tests, the assessment should proceed to evaluate colonic transit.⁶ This can be accomplished using radiopaque markers (sitzmark study), a wireless motility capsule, or radionuclide scintigraphy.^{6,7}
- Defecography and magnetic resonance defecography (MRD) are additional tests for

evaluating pelvic anatomy during attempted defecation.⁶

Diagnostic algorithm for diagnosis of constipation

- Managing primary constipation can present difficulties for primary care physicians, as well as specialists, due to its multifaceted nature. When constipation and its related symptoms appears severe, and fail to respond to initial conservative and first-line treatments, or their root cause remains unclear, it is advisable to consider referring the patient to a specialist for further evaluation and management. Figure 4.1 shows the algorithmic approach for the diagnosis of constipation.⁵

Figure 4.1: Diagnostic algorithm for the evaluation of constipation⁵



Key highlights

- The assessment of chronic constipation involves a systematic approach, incorporating a detailed clinical history, clinical examination, and basic laboratory tests, guided by alarm features to investigate potential organic pathology.¹
- A comprehensive patient history, covering bowel habits, diet, and family medical history, along with tools like the Bristol Stool Form Scale, aids in identifying primary and secondary causes, including transit disorders.²
- Understanding a woman's obstetric and gynecological history is vital, as surgeries and childbirth can significantly affect defecatory symptoms.³
- Physical examination, including abdominal and digital rectal exams, is crucial for uncovering underlying causes, with the digital rectal examination assessing anorectal function and identifying issues like dyssynergic defecation.⁵
- For postmenopausal women experiencing new-onset constipation, along with localized lower abdominal pain, bloating, or distension, it is recommended to undergo a transabdominal/vaginal ultrasound scan to exclude potential underlying causes like ovarian cancer.¹

References

1. Aziz I, Whitehead WE, Palsson OS, et al. An approach to the diagnosis and management of Rome IV functional disorders of chronic constipation. *Expert Rev Gastroenterol Hepatol.* 2020;14(1):39-46.
2. Costilla VC, Foxx-Orenstein AE. Constipation in adults: Diagnosis and management. *Curr Treat Options Gastroenterol.* 2014;12(3):310-21.
3. Black CJ, Ford AC. Chronic idiopathic constipation in adults: Epidemiology, pathophysiology, diagnosis and clinical management. *Med J Aust.* 2018;209(2):86-91.
4. Collins BR, O'Brien L. Prevention and management of constipation in adults. *Nurs Stand.* 2015;29(32):49-58.
5. Heidelbaugh J, Martinez de Andino N, Pineles D, et al. Diagnosing constipation spectrum disorders in a primary care setting. *J Clin Med.* 2021;10(5):1092. Doi.org/10.3390/jcm10051092
6. Jani B, Marsicano E. Constipation: Evaluation and management. *Mo Med.* 2018;115(3):236-40.
7. Forootan M, Bagheri N, Darvishi M. Chronic constipation: A review of literature. *Medicine (Baltimore).* 2018;97(20):e10631. Doi.org/10.1097/MD.00000000000010631
8. Mari A, Mahamid M, Amara H, et al. Chronic constipation in the elderly patient: Updates in evaluation and management. *Korean J Fam Med.* 2020;41(3):139-45.



Dr. Basab Mukherjee

MBBS (Vellore), MD (Vellore),

FRCOG (London), FICOG

Director, Ankuran Fertility & Fetal Medicine Centre,
Kolkata.

President elect, Bengal Society of Obstetrics and Gynecology

ALARM SIGNS AND SYMPTOMS IN CONSTIPATION

Primary care physicians should meticulously gather a comprehensive clinical history to rule out alarm symptoms, indicative of potentially severe health issues, and assess for prevalent comorbidities that could be underlying secondary causes of constipation.¹ Only patients with alarm symptoms or those meeting colorectal cancer screening criteria should undergo diagnostic colonoscopy.²

Alarming symptoms associated with constipation

Unintentional weight loss: Unexplained weight loss may indicate the severity of a disease or a consequence of an undiagnosed condition. In the gastrointestinal system, weight loss can be associated with benign conditions such as Crohn's disease, celiac disease, and irritable bowel syndrome, or it may indicate a malignancy.³

Iron deficiency anemia: It is often the first indication of an underlying gastrointestinal malignancy, celiac disease, or gastritis.⁴

Hematochezia (rectal bleeding/bloody bowel movements): Hematochezia is the passage of visible blood from the rectum, usually signifying lower gastrointestinal bleeding. The most frequent causes in adults are diverticulosis and hemorrhoids, both generally benign, although such bleeding can be a warning sign for colorectal cancer.⁵

Severe, persistent, and treatment-refractory constipation: The majority of individuals with chronic constipation can be treated using conventional methods. However, a subset of patients remains unresponsive to standard medical approaches even after thorough clinical evaluation. These individuals require more comprehensive diagnostic assessments to understand the underlying causes and may benefit from tailored therapeutic interventions.⁶

Alterations in bowel habits occurring after the age of 50: With increasing age, a rise in the likelihood of colorectal cancer among individuals experiencing changes in bowel habits as the solitary symptom has been reported.⁷

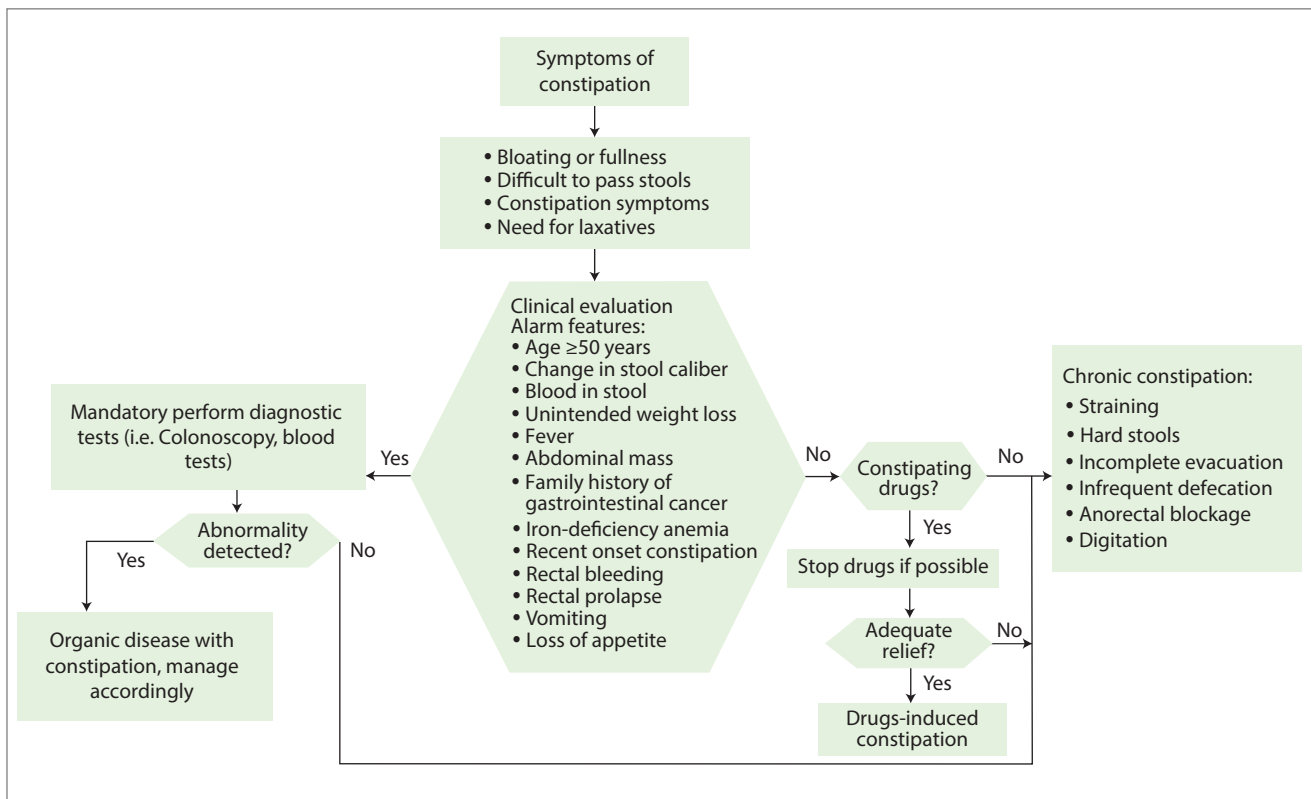
Sudden onset of constipation in elderly individuals: Constipation is a commonly experienced issue among older adults, often perceived as a minor concern. Clinicians should remain vigilant for signs of malignancy, such as unintended weight loss, anemia, rectal bleeding, or sudden changes in bowel habits.⁸

Signs of inflammatory bowel disease: Ulcerative colitis typically manifests as bloody diarrhea, with or without mucus. Tenesmus, coupled with abdominal pain, is frequently described. The combination of right lower quadrant pain, weight loss, and non-bloody diarrhea indicates a potential flare-up of Crohn's disease.⁹

Symptoms indicating organic disorder: Secondary causes of constipation are associated with organic disease, systemic conditions, or medication use. Secondary causes are usually initially investigated through patient history, physical examination, and diagnostic tests.¹⁰

A strong family history of colorectal cancer: A family history of colorectal cancer is a recognized risk factor for colorectal cancer, encompassing both genetic and shared environmental risks.¹¹

Algorithmic assessment of constipation based on alarm features¹²



Key highlights

- Primary care physicians should possess knowledge of alarm signs and symptoms that warrant referral, or expedited referral, to a gastroenterologist or another suitable specialist when necessary.¹
- In patients presenting with constipation, it is crucial to conduct a comprehensive medical history to identify and exclude any alarm features.¹
- Alarm symptoms include alterations in bowel habits occurring after the age of 50, sudden onset of constipation in older adults, presence of blood in stools, unexplained weight loss, anemia, signs of inflammatory bowel disease, symptoms indicative of organic disorder, and a significant family history of colorectal cancer.²
- If no alarm symptoms are present, primary care physicians can often manage constipation by employing empiric therapy and monitoring outcomes, particularly if there are comorbidities that may be contributing to the condition.¹

References

1. Heidelbaugh J, Martinez de Andino N, Pineles D, et al. Diagnosing constipation spectrum disorders in a primary care setting. *J Clin Med*. 2021;10(5):1092. DOI.org/10.3390/jcm10051092
2. Forootan M, Bagheri N, Darvishi M. Chronic constipation: A review of literature. *Medicine (Baltimore)*. 2018;97(20):e10631. Doi.org/10.1097/MD.00000000000010631
3. Bajwa M, Bank L, Yacoub A, et al. Unexplained weight loss in a gastroenterology clinic: 198. *Am J Gastro*. 2017;112 (Suppl 1):S102-S103.
4. Bayraktar UD, Bayraktar S. Treatment of iron deficiency anemia associated with gastrointestinal tract diseases. *World J Gastroenterol*. 2010;16(22):2720-25.
5. Saljoughian M. Gastrointestinal bleeding: An alarming sign. *US Pharm* 34(12):HS12-HS16.
6. Bassotti G, Blandizzi C. Understanding and treating refractory constipation. *World J Gastrointest Pharmacol Ther*. 2014;5(2):77-85.
7. McCulloch SM, Aziz I, Polster AV, et al. The diagnostic value of a change in bowel habit for colorectal cancer within different age groups. *United European Gastroenterol J*. 2020;8(2):211-19.
8. Chatterjee P. Constipation: More than Just "A Symptom". In: *Health and Wellbeing in Late Life*. Springer, Singapore 2019. https://doi.org/10.1007/978-981-13-8938-2_5
9. McDowell C, Farooq U, Haseeb M. Inflammatory bowel disease. [Updated 2023 Aug 4]. In: *StatPearls. Treasure Island (FL): StatPearls Publishing. [Internet]. 2024. [cited 2024 Jun 11]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470312/>*
10. Andrews CN, Storr M. The pathophysiology of chronic constipation. *Can J Gastroenterol*. 2011;25(Suppl B):16B-21B.
11. Henrikson NB, Webber EM, Goddard KA, et al. Family history and the natural history of colorectal cancer: Systematic review. *Genet Med*. 2015;17(9):702-12
12. Manfredi G, Londoni C, Bellini M, et al. Diagnostic algorithm for constipation and obstructed defecation. In: Ratto C, Parrello A, Dionisi L, et al. (eds). *Coloproctology*. Springer International Publishing; 2016. pages.1-8. DOI: 10.1007/978-3-319-10154-5_29-1

CONSEQUENCES OF CONSTIPATION ON WOMEN'S HEALTH



Dr. Ursula Pandit

MD, ABIM Board certified in Internal Medicine
Consultant, Methodist Mansfield Medical Center Dallas, Texas.



Dr. Suchitra N Pandit

MD, DNB, FRCOG, MRCOG, DFP, FICOG, MNAMS, B. Pharm
Senior Consultant, OBGYN Surya Group of Hospitals, Mumbai. President, FOGSI & ICOG (2014–15)

Constipation has been demonstrated to adversely impact the development of activities pertinent to individuals' health and functioning, such as daily activities, physical, emotional, social, and personal well-being, as well as work/school productivity, lifestyle, and overall quality of life (QoL).¹

Impact of constipation on women's health

In the assessment of an individual's functioning through a biopsychosocial lens, the World Health Organization (WHO) supports the utilization of the World Health Organization Disability Assessment Schedule (WHODAS) 2.0. This tool delineates

an individual's functioning and disability across the following six domains: Cognition, mobility, self-care, interpersonal relationships, life activities, and participation.¹ The WHODAS 2.0 model was employed to examine the association between intestinal constipation and functional impairment in adult females from a clinical perspective.¹

Effects of constipation on women's health

- Women experiencing constipation often encounter challenges in engaging in cognitive and communicative tasks, encompassing difficulties in concentration, memory, problem-solving, learning, and communication.¹
- Women with constipation experience post-mobility issues, including difficulty in standing, moving indoors, going out, and walking long distances. This is linked to abdominal pain and discomfort, impacting their ability to engage in these activities.¹
- The presence of constipation also impairs self-care aspects, affecting self-hygiene, dressing, eating, and the ability to be alone.¹
- Furthermore, research has established an association between constipation and insomnia.¹
- Women with constipation face challenges in community activities, personal dignity, and encounter barriers, potentially linked to associations between constipation and psychological disorders such as anxiety and depression.¹
- Another researcher studying constipation in women reported poor peripheral circulation, abdominal distension, infertility, amenorrhea, diminished female secondary sexual characteristics, and an elevated prevalence of ovarian cysts during clinical investigations.²
- Women with chronic constipation were more likely to experience urogenital symptoms, such as dyspareunia, urinary hesitancy, and a sensation of incomplete bladder emptying.³

Consequences of constipation during pregnancy

- Constipation is the second most prevalent gastrointestinal concern during pregnancy, surpassed only by nausea. Constipation may give rise to significant complications, including the rare occurrence of fecal impaction.⁴
- The association between constipation during pregnancy and hemorrhoids has been conclusively established. Constipation during pregnancy significantly elevates the likelihood of developing perianal diseases both during gestation and up to 6 times more after childbirth.⁵
- Constipation during pregnancy does not pose a significant threat to the well-being of the mother and fetus but it can substantially diminish the quality of life for pregnant women. Symptoms such as rectal fullness, pressure sensations, pain, and straining during defecation, as well as feelings of incomplete excretion, hard and solid stools, abdominal distension, headaches, weakness, cramp-like abdominal pain, loss of appetite, vomiting, abdominal tension, and regional sensitivity in the body can collectively affect the quality of life of pregnant women.⁶
- Genc *et al.* studied the effect of constipation during pregnancy on quality of life using Short Form-36 Health Survey (SF-36) scale. Based on the research findings, pregnant women experiencing constipation exhibited lower mean scores across various quality of life subscales, including physical function, role limitations related to physical problems, pain, vitality, social function, emotional well-being, mental health, and overall perception of health when compared to their counterparts without constipation.⁶

Constipation has a consistently detrimental impact on the quality of life throughout all stages of pregnancy.⁶

- Clinically, constipation may exhibit a correlation with elevated anxiety levels and an overall feeling of discomfort. Prolonged and severe constipation can lead to various complications such as back pain, fecal impaction, and hemorrhoids. Fecal impact might manifest as the involuntary leakage of liquid stool.⁷

Consequences of constipation in postmenopausal women

- In postmenopausal women, occurrence of functional constipation is influenced by hormonal homeostasis, given the intricate changes associated with hormonal alterations during this period. Consequently, postmenopausal women commonly experience a myriad of psychosomatic complaints pertaining to the gastrointestinal tract, including eating disorders, abdominal bloating, and chronic constipation. These issues have a substantial impact on their overall quality of life.⁸
- Blotcher *et al.* conducted a prospective analysis, to study the impact of constipation on cardiovascular health in postmenopausal women. In postmenopausal women, the presence of constipation demonstrated a statistically significant correlation with all major risk factors associated with cardiovascular disease, thereby indicating an elevated likelihood of experiencing cardiovascular events.⁹

A correlation exists between constipation and cardiovascular diseases in postmenopausal women.⁹

- The biological, psychological, and sociological alterations associated with menopause exert substantial influence on a woman's lifestyle and overall well-being. When women experience constipation during this phase, it can adversely impact their physical, mental, and social health, thereby negatively affecting the quality of life.¹⁰

Key highlights

- Pregnant women experiencing constipation showed lower mean scores across various quality of life subscales, including physical function, role limitations due to physical problems, pain, vitality, social function, emotional problems, and mental health.⁶
- Constipation in postmenopausal women is significantly correlated with major cardiovascular disease risk factors, suggesting an increased likelihood of cardiovascular events.⁹

References

1. Dantas AAG, Pereira ARR, de Castro SS, et al. Is constipation associated with worse functioning in adult women? A cross-sectional study. *J Multidiscip Healthc*. 2020;13:883-89.
2. Preston DM, Lennard-Jones JE. Severe chronic constipation of young women: Idiopathic slow transit constipation. *Gut*. 1986;27(1):41-8.
3. Ortega MV, Kim Y, Hung K. et al. Women with chronic constipation have more bothersome urogenital symptoms. *Tech Coloproctol*. 2022;26(1):29-34.
4. Trotter M, Erebara A, Bozzo P. Treating constipation during pregnancy. *Can Fam Physician*. 2012;58(8):836-8.
5. Bužinskienė D, Sabonytė-Balšaitienė Ž, Poškus T. Perianal diseases in pregnancy and after childbirth: Frequency, risk factors, impact on women's quality of life and treatment methods. *Front. Surg*. 9:788823. Doi: 10.3389/fsurg.2022.788823
6. Genc FZ, Hisar F. Quality of life in pregnant women with and without constipation: A comparative study. *Int J Caring Sciences*. 2021;14(3):1697-704.
7. Bonapace Jr ES, Fisher RS. Constipation and diarrhea in pregnancy. *Gastro Clinics of North America*. 1998;27(1):197-211.
8. Blonska A, Chojnacki M, Macieja A, et al. Tryptophan metabolism in postmenopausal women with functional constipation. *Int J Mol Sci*. 2023;25(1):273. Doi: 10.3390/ijms25010273.
9. Salmoirago-Blotcher E, Crawford S, Jackson E, et al. Constipation and risk of cardiovascular disease among postmenopausal women. *Am J Med*. 2011;124(8):714-23.
10. Kirka SA, Oksuz SK, Gul DK et al. Constipation and its effects on quality of life in menopausal women. *Int J Caring Sciences*. 2021;14(1):269-75.



Dr. Girija Wagh

MBBS, MD, FICOG, FICS

Professor & HOD, Dept of OBGYN, Bharathi Vidyapeeth Medical College Hospital, Pune
Senior Consultant, Cloud Nine & Apollo Hospitals, Pune.
Vice President FOGSI (2024–25)

PREVENTION AND MANAGEMENT OF CONSTIPATION

Managing constipation is complex, as it requires addressing diverse factors and underlying causes that vary from person to person.¹ Constipation can be treated using nonpharmacological or pharmacological management approaches.²

Nonpharmacological management of constipation

Given the association between sedentary habits and low-fiber diets with constipation, women should be encouraged to enhance fiber and fluid intake, engage in regular physical activity, and adopt timed toilet training upon exclusion of secondary causes of constipation.^{2,3} These are often effective first-line management strategies.²

Diet and fluid intake

Fiber plays a pivotal role in both adding bulk to and softening stool consistency. Enhancing fiber intake and maintaining adequate hydration stands as the primary therapeutic approach for individuals struggling with chronic constipation. It is imperative to gradually escalate the introduction of fiber to prevent potential abdominal cramping and bloating.^{2,4}

Lifestyle and exercise

A daily routine starting with waking up, doing light exercises like stretching, having a cup of coffee, tea or warm water and eating breakfast within an hour can stimulate the body's natural gastro-colic reflexes to help with regular bowel movements. To optimize outcomes, individuals should be advised to maintain a straight back posture while on the toilet, limit the duration to 5–10 minutes to prevent hemorrhoid congestion, use a footstool to align the anorectal angle, employ deep relaxing breaths, and avoid excessive straining.⁴

Anorectal biofeedback

This therapy involves training patients to employ breathing techniques and relax pelvic floor muscles, enhancing propulsive force for effective evacuation.² It is the preferred choice for dyssynergia-related outlet obstruction. Biofeedback is not effective for functional or delayed transit constipation unless dyssynergia is overlapped. Anorectal biofeedback involves giving patients visual and auditory feedback to enhance intra-abdominal pressure and pelvic floor muscle relaxation, typically offered at tertiary referral centers and through physical therapy.⁴

Pharmacological management of constipation

When nonpharmacological interventions are insufficient for the management of constipation, numerous medications are used to address constipation as discussed below.²

Laxatives in the management of constipation

- Most patients with constipation eventually need to use laxatives during their treatment.³ Laxatives can be categorized into five groups: Bulk-forming, stimulants, stool softeners, osmotic agents, and lubricants.²
- Table 7.1 shows the mechanism of action of each category of laxatives.^{1,2,4}

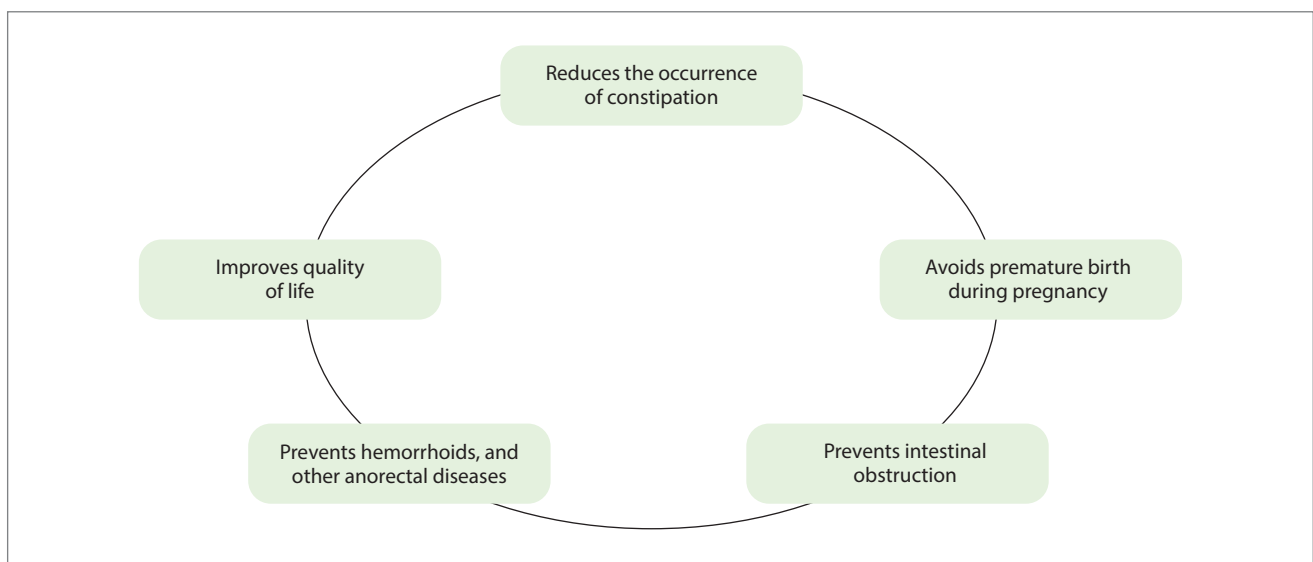
Table 7.1: Categorization and mechanism of laxatives^{1,2,4}

Category	Mechanism	Examples	Possible side-effects or drawbacks
Bulk-forming	Increases the water absorbency properties of stool, stool bulk, consistency, weight, and intraluminal volume	Bran, psyllium, inulin, methylcellulose, calcium polycarbophil	Bloating and flatulence
Osmotic	Generate an osmotic gradient through poorly-absorbed ions and molecules, thereby drawing water into the intestinal lumen. This process leads to the formation of soft stool and enhances intestinal transit	Lactulose, polyethylene glycol, sorbitol, sodium phosphate, magnesium citrate	Abdominal bloating, flatulence, and distention
Stimulants	Directly activate the mucosa or myenteric plexus to trigger vigorous peristaltic contractions; hinder water absorption, thereby enhancing intestinal motility	Senna, bisacodyl, castor oil	Bothersome abdominal cramping and pain, electrolyte imbalance
Stool softeners	Functioning like detergents, they enhance the interaction between stool and water, promoting a softer stool consistency and easing the evacuation of hardened stool	Docusate	Moderate effectiveness
Lubricants	Decrease water absorption and soften stool, allowing easier passage	Mineral oil	Lipoid pneumonia may develop in cases of material aspiration

Laxatives for the management of constipation in women

Criteria for ideal laxative selection ⁵	Factors to consider while prescribing laxatives ⁵
<ul style="list-style-type: none"> • It should exhibit good curative effect and tolerability • It should not be absorbed into the blood • If given in pregnancy, it should not cause developmental defects to the fetus (no teratogenic effect) • If given to lactating women, it should not get transferred into breast milk 	<ul style="list-style-type: none"> • The efficacy, safety, drug dependence, and potency ratio should be considered when prescribing laxatives. • During pregnancy and breastfeeding, laxative choice should be based on ensuring the safety of the mother and the fetus and it must have ideal laxative properties.

Beneficial effects of laxatives⁵



Lactulose: A commonly prescribed osmotic laxative in constipation management

- Lactulose is derived from lactose by the isomerization process.⁶
- Unlike other osmotic laxatives, lactulose exhibits multiple modes of action, leading to numerous pleiotropic benefits.⁶

Lactulose: Detailed mechanism of action

- Figure 7.1 illustrates the various modes of action of oral lactulose; Figure 7.2 depicts the dosage-dependent effects of these same modes of action; the detailed mechanism of action of lactulose is presented in Figure 7.3.⁶
- The amount of lactulose prescribed varies according to the type and severity of the condition being treated.⁶

Figure 7.1: Modes of action of lactulose⁶

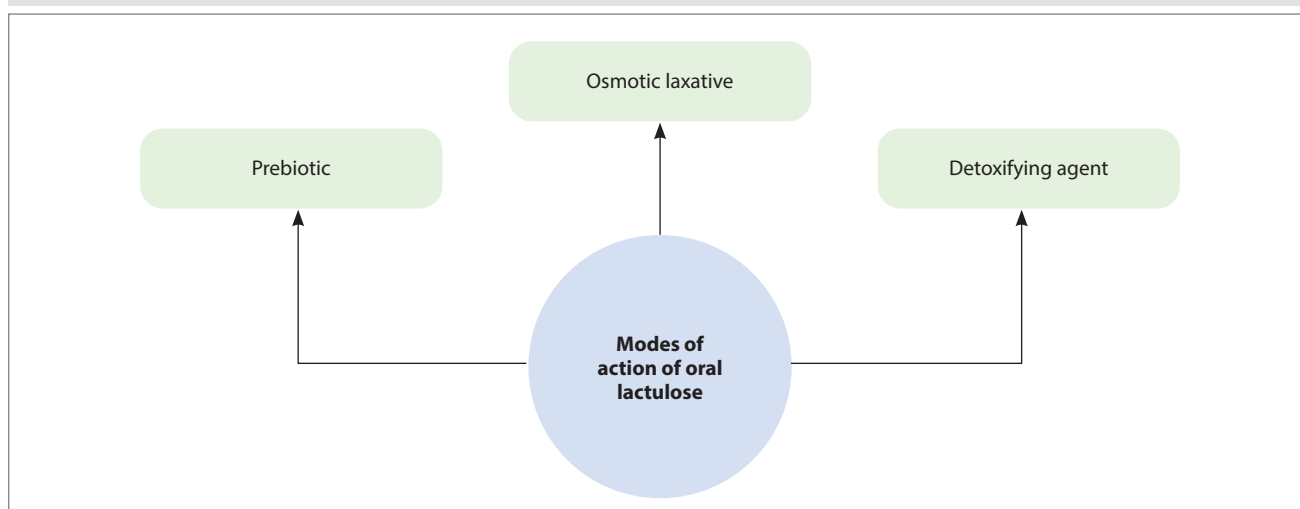
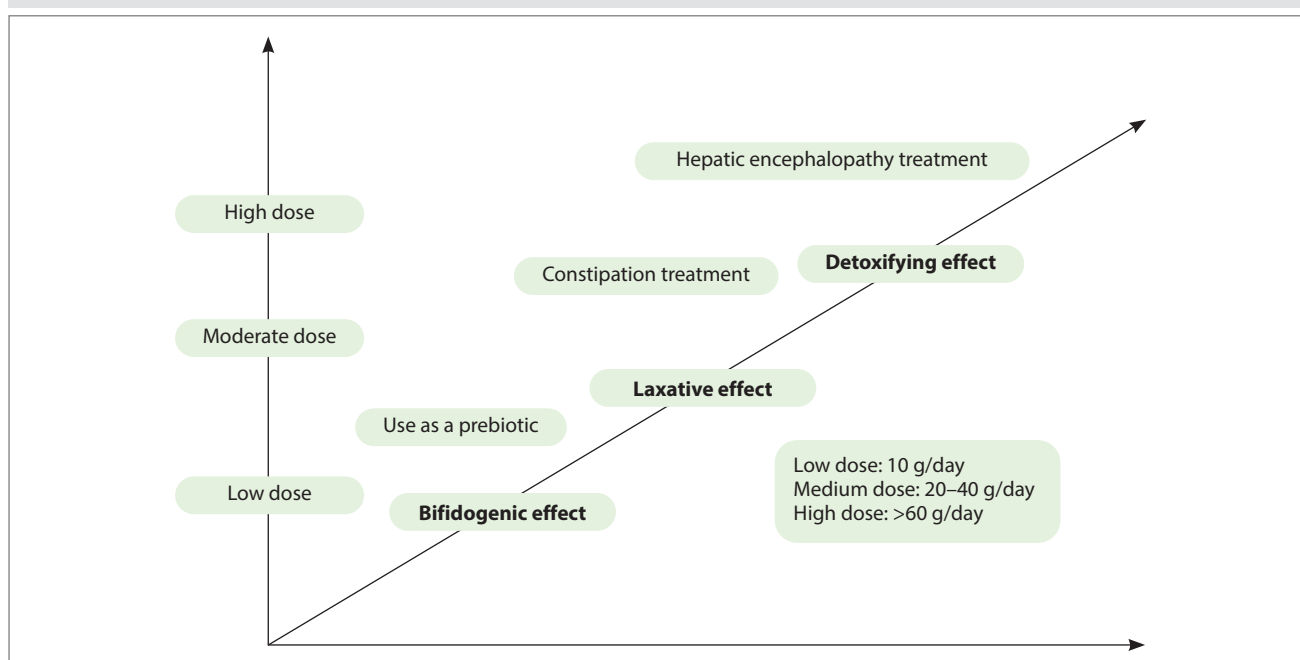


Figure 7.2: Dose-dependent effect of lactulose⁶



Mechanism of action of lactulose

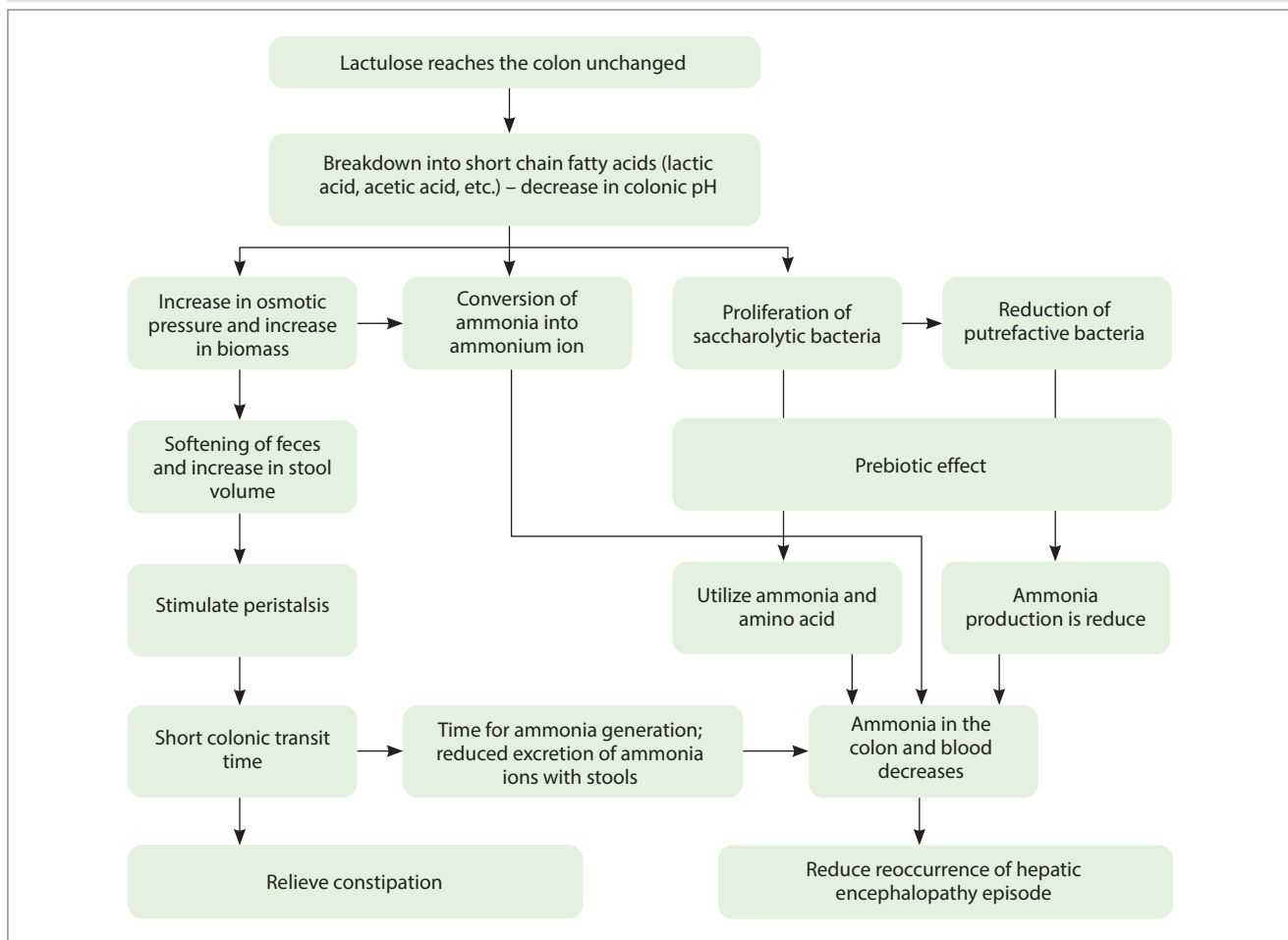
As an osmotic laxative: Lactulose is a nonabsorbable disaccharide of fructose and galactose. Much of the orally ingested lactulose remains unchanged since the human gastrointestinal tract lacks the necessary enzymes for its hydrolysis. Upon reaching the colon, the colonic bacteria transform lactulose into lactic acid, as well as into small amounts of formic and acetic acid. Consequently, the contents of the colon become more acidic, elevating osmotic pressure. This osmotic effect leads to an increase in water content in stools, resulting in softer stools.⁶

As a prebiotic: Prebiotics are compounds that stimulate the proliferation of symbiotic microflora, particularly fecal bifidobacteria and lactobacilli, which contribute to health-promoting effects. The growth of beneficial microorganisms can be boosted through

the prolonged consumption of lactulose, either in low or high doses. Bouhnik *et al.* demonstrated that a daily intake of 10 g of lactulose enhances fecal bifidobacterial counts, meeting the established criteria for lactulose to be classified as a prebiotic.⁶

As a detoxifying agent: Lactulose plays a crucial role in managing hepatic encephalopathy as a detoxifying agent. In the colon, lactulose is broken down by bacteria into short-chain fatty acids, creating an acidic environment. This acidity facilitates the conversion of ammonia (NH_3) to ammonium ions (NH_4^+). Since colonic content is more acidic than blood, ammonia in the blood migrates into the colon and is converted to ammonium ions. Due to the laxative effect of lactulose, the trapped ammonium ions are expelled from the colon and eliminated through feces, aiding in the detoxification process.⁶

Figure 7.3: Mechanism of action of lactulose as osmotic, prebiotic, and detoxifying agent⁶



Efficacy, safety, and tolerability aspects of lactulose

Efficacy ⁵	Safety and tolerability ⁵⁻⁸
<ul style="list-style-type: none"> Significantly improves stool characteristics <hr/> <ul style="list-style-type: none"> In postpartum women, significantly improves bowel motility, characteristics of stool, and reduces hospital stay <hr/> <ul style="list-style-type: none"> In postpartum perineal lacerations, significantly relieves first bowel movement pain and reduces the duration of hospitalization 	<ul style="list-style-type: none"> No serious adverse events following treatment <hr/> <ul style="list-style-type: none"> Not absorbed in the blood hence, no blood sugar fluctuations <hr/> <ul style="list-style-type: none"> Does not affect nutrient absorption <hr/> <ul style="list-style-type: none"> Does not affect fetal development since systemic exposure is negligible <hr/> <ul style="list-style-type: none"> Does not affect breastfeeding since it is not expressed in breast milk <hr/> <ul style="list-style-type: none"> Flatulence may occur after the initial dose of lactulose and are transient in nature <hr/> <ul style="list-style-type: none"> Excessive doses may lead to diarrhea, potentially causing electrolyte imbalance

Lactulose usage for constipation management in women: Evidence analysis

Study	Study design	Study population	Outcomes
During pregnancy			
Muller <i>et al.</i> (1995) ⁹	Multicenter, open, baseline-controlled study	Pregnant women (n = 62) with constipation treated with lactulose for 4 weeks	Defecation frequency was significantly increased after 1 week of treatment (4.0 vs. 2.5 [median per week], p < 0.001), and normalized after 2 weeks, stool consistency was also normalized, lactulose was well or very well tolerated with no report of serious adverse events during the study
Signorelli <i>et al.</i> (1996) ¹⁰	Clinical study	Pregnant women (n = 50) with constipation received glucomannan and lactulose combination treatment for 1–3 months	Treatment normalized weekly defecation frequency and controlled weight gain
Li <i>et al.</i> (2020) ⁵	Randomized controlled clinical study	Pregnant women (n = 113) with constipation received lactulose or polyethylene glycol 4,000 treatment twice daily for 3 weeks	Final effects of both the treatments were comparable, total effective rate was increased, and the quality of life was also improved
During pregnancy and postpartum			
Solovyeva <i>et al.</i> (2013) ¹¹	Prospective interventional study	Pregnant women (n = 63) in the 1 st , 2 nd , and 3 rd trimesters, or postpartum period with constipation occurred during (n = 28) or before pregnancy (n = 35) received 10–40 mL/day lactulose for 15 days	Lactulose restored intestinal transit in all cases, also promoted normal vaginal biotope, with no pyoseptic complications in the postpartum period
Sokur <i>et al.</i> (2013) ¹²	Investigational study	Women (n = 150) with constipation during pregnancy and postpartum received lactulose	Lactulose led to the normalization of stool and a feeling of complete bowel evacuation in 96.7% of pregnant women. It did not trigger intense intestinal motility which eventually could lead to threatened abortion and premature birth
During postpartum			
Huang <i>et al.</i> (2016) ¹³	Randomized clinical trial	Women with postpartum constipation (n = 211); lactulose group received lactulose – 15 mL once daily and 5–15 mL of maintenance dose and control group was blank control	Lactulose group showed significantly better curative effects and symptom improvement, faster relief from constipation, greater number of days without constipation, and shorter defecation time

Study	Study design	Study population	Outcomes
Zhou <i>et al.</i> (2015) ¹⁴	Multicenter clinical survey	Postpartum women with constipation (n = 4,781) received lactulose oral solution – 22 mL/day initial dose and 11–14 mL maintenance dose for 2 weeks and followed up for 4 weeks	Treatment with lactulose for 2 weeks significantly improved stool consistency, daily defecation frequencies, defecating time and dyschezia compared with before lactulose treatment
Eogan <i>et al.</i> (2007) ¹⁵	Randomized clinical trial	Postpartum women (n = 147) who had sustained anal sphincter injury at vaginal birth received lactulose or lactulose + ispaghula husk combination	The study concluded that 10 mL of oral lactulose 3 times a day for the initial 3 postpartum days, followed by an adequate amount of lactulose should be prescribed to ensure a soft stool for the subsequent 10 days after childbirth for women with anal sphincter injury. Lactulose monotherapy showed notable advantage with lower incontinence scores during the immediate postpartum period than the combination treatment
Meng <i>et al.</i> (2015) ¹⁶	Randomized, double-blind, placebo-controlled multi-center clinical study	Women with puerperal constipation (n = 200) therapy group received lactulose (20 mL twice daily) or control group received defecation habits training, diet management and drinking adequate water, etc. for 4 weeks	Lactulose significantly improved defecation frequency per week and stool consistency (efficiency rate 92% vs. 21%; p = 0.000) relative to control group; reoccurrence of constipation was significantly lower in the lactulose group than in the control group (4% vs. 18%, p = 0.001) at 120-days of follow-up.

Recommendations/guidelines for using lactulose in the management of constipation

US Food and Drug Administration (USFDA)⁵	It has approved lactulose for treating constipation in both pregnancy and the postpartum period
World Gastroenterology Organization (WGO)⁵	It has recognized lactulose as a prebiotic for the treatment of constipation
The electronic medicines compendium (emc), UK⁷	<ul style="list-style-type: none"> • Treatment indications for lactulose are constipation, hepatic encephalopathy; hepatic coma • Lactulose can be used during pregnancy. No effects during pregnancy are anticipated, since systemic exposure to lactulose is negligible • Lactulose can be used during breastfeeding. No effects on the breastfed newborn/infant is anticipated since the systemic exposure of the breastfeeding woman to lactulose is negligible.
National Health Service (NHS), UK⁸	<ul style="list-style-type: none"> • Lactulose can be taken during pregnancy. • Lactulose can be taken during breastfeeding, It does not pass into breast milk and hence, it is very unlikely to cause any side effects in the baby
Federation of Obstetrics & Gynecological Societies of India (FOGSI)¹⁷	<ul style="list-style-type: none"> • Lactulose is an effective and safe drug for treating postpartum constipation • Oral lactulose is effective and safe, and it can be considered as the first-line therapy in treating chronic constipation during pregnancy • Lactulose offered good therapeutic benefit and it could be developed as an effective intervention to postpartum women with constipation.
Royal College of Obstetricians and Gynaecologists (RCOG)¹⁸	<ul style="list-style-type: none"> • It advises the use of lactulose for stool softening over a period of approximately 10 days following surgery in women with third or fourth-degree perineal tears (obstetric anal sphincter injury). This is recommended to minimize the risk of wound dehiscence.
German Guideline of the German Society of Gynecology and Obstetrics¹⁹	<ul style="list-style-type: none"> • Administering lactulose prophylactically reduces the discomfort experienced during initial bowel movements following the management of a higher degree perineal tear. • Administration of laxatives for a few days is recommended in order to reduce the mechanical stress on the sutures.

Severe constipation needs specialist referrals, and it is prudent to request for a gastroenterologist or surgical consultation. There may be a need to step-up medications.

Other medications

- Prucalopride is recommended for women with chronic constipation who have not found relief with two laxatives over 6 months. It stimulates colonic motility, with a recommended dosage of 2 mg for adults up to 65 years and 1 mg for those over 65 years. A clinical trial showed its efficacy in improving bowel habits and associated symptoms, patient satisfaction, and quality of life.¹
- Linaclotide, an analog of guanylin, operates by triggering the guanylyl cyclase-C receptor, promoting chloride secretion akin to the enterotoxin found in *Escherichia coli*.³ It is licensed for treating moderate-to-severe irritable bowel syndrome with constipation (IBS-C) since it provides neuromodulatory advantages, offering daily relief with decreased pain, increased fluid secretion, and accelerated intestinal transit.^{1,3}
- Lubiprostone is advised when two categories of laxatives fail with a recommended dose of 24 mg twice daily.¹ It functions as an activator of chloride channels, like the cholera toxin, leading to an augmentation of luminal fluid secretion. It is effective in reducing stool transit time and alleviating symptoms associated with chronic idiopathic constipation.³
- Plecanatide is an additional agent that stimulates the guanylyl cyclase inhibitor, leading to enhanced entry

of chloride and bicarbonate into the lumen through activation of the cystic fibrosis transmembrane conductance regulator (CFTR) ion channel.³

- Tegaserod is a partial agonist for serotonin type 4 (5-HT₄) receptors, believed to initiate a peristaltic reflex through 5-HT₄ activation. This mechanism enhances motor activity and normalizes impaired gastrointestinal motility.³
- Colchicine, a cytotoxin commonly used for gout treatment, is generally not recommended for routine clinical use in managing constipation due to its side effect profile. This caution is especially pertinent when there is impaired renal function. Nonetheless, small-scale studies suggest potential utility in a subset of patients with chronic constipation who do not respond well to standard medical management.³
- Misoprostol, an analogue of prostaglandin E₁, stimulates intraluminal fluid and bicarbonate secretion. In smaller research studies, these effects have been harnessed to alleviate the severity of refractory chronic constipation.³

Surgical management

Surgery might be an last option when individuals experience consistently low quality of life resulting from chronic, resistant delayed colon transit, megacolon, or severe dyssynergia.^{1,4} Surgical interventions may include procedures such as total colectomy with ileorectal anastomosis, sigmoid colectomy, left hemicolectomy, or the creation of an ileostomy.¹ Colostomy is the typical surgical approach for refractory dyssynergia, while for megacolon or significant slow transit, options include colostomy or ileoanal anastomosis.⁴

Key highlights

- There is no universal treatment for constipation due to its multifaceted nature. A tailored approach, considering both nonpharmacological and pharmacological options is crucial for effective management.^{1,2}
- Most patients with constipation eventually need to use laxatives during their treatment.³
- Lactulose, a commonly used laxative in the management of constipation, exhibits osmotic, prebiotic, and detoxifying action.⁶
- Lactulose is safe and effective during pregnancy and postpartum since it improves stool characteristics, bowel movements, does not affect nutrient absorption, has negligible systemic exposure, and does not pass into breast milk.⁵⁻⁸
- Clinical evidence on the lactulose supports its use during pregnancy and postpartum period.^{5,9-16}
- Various guidelines and societies recommend lactulose for the management of constipation during pregnancy and postpartum.^{5,7,8,17,18,19}

References

1. Collins BR, O'Brien L. Prevention, and management of constipation in adults. *Nurs Stand*. 2015;29(32):49-58.
2. Costilla VC, Foxx-Orenstein AE. Constipation: Understanding mechanisms and management. *Clin Geriatr Med*. 2014;30(1):107-15.
3. Jani B, Marsicano E. Constipation: Evaluation and management. *Mo Med*. 2018;115(3):236-240.
4. Costilla VC, Foxx-Orenstein AE. Constipation in adults: Diagnosis and management. *Curr Treat Options Gastroenterol*. 2014;12(3):310-21.
5. Li H, Zhang P, Xue Y. A comparison of the safety and efficacy of polyethylene glycol 4000 and lactulose for the treatment of constipation in pregnant women: A randomized controlled clinical study. *Ann Palliat Med*. 2020;9(6):3785-92.
6. Pranami D, Sharma R, Pathak H. Lactulose: A prebiotic, laxative and detoxifying agent. *Drugs Ther Perspect* 2017;33,:228-33.
7. Electronic medicines compendium (EMC) UK. Duphalac 3.335 g/5 ml oral solution. [Internet]. [cited 2024 Mar 11]. Available from: <https://www.medicines.org.uk/emc/product/5525/smpc>.
8. National Health Service. Pregnancy, breastfeeding and fertility while taking lactulose [Internet]. [cited 2024 Mar 11]. Available from: <https://www.nhs.uk/medicines/lactulose/pregnancy-breastfeeding-and-fertility-while-taking-lactulose/>.
9. Müller M, Jaquenoud E. Behandlung der Obstipation bei Schwangeren. Eine Multizenterstudie in gynäkologischen Praxen [Treatment of constipation in pregnant women. A multicenter study in a gynecological practice]. *Schweiz Med Wochenschr*. 1995;125(36):1689-93.
10. Signorelli P, Croce P, Dedè A. [A clinical study of the use of a combination of glucomannan with lactulose in the constipation of pregnancy]. *Minerva Ginecologica*. 1996;48(12):577-82.
11. Solovyeva AV. Principles of therapy for constipation in pregnant women. *Obstetrics and Gynecology*. 2013;(4):58-60.
12. Sokur TN, Dubrovina NN. Use of lactulose in the treatment of constipation during pregnancy and postpartum. *Journal Obstetrics and Gynecology*. 2013;8:103-107.
13. Huang P, Gou WL, Wang XT, et al. Lactulose oral solution for the treatment of postpartum constipation. *J Biol Regul Homeost Agents*. 2016;30(2):523-8.
14. Zhou Y, Yang X, Fan L, et al. Observations on the curative effect of lactulose for postpartum constipation based on a large sample study. *Int J Clin Exp Med*. 2015;8(10):19167-71.
15. Eogan M, Daly L, Behan M, et al. Randomised clinical trial of a laxative alone versus a laxative and a bulking agent after primary repair of obstetric anal sphincter injury. *BJOG*. 2007;114(6):736-40.
16. Meng S, Pan Y, Deng Q, et al. [Efficacy and safety of lactulose on the treatment of puerperal constipation]. *Zhonghua Yi Xue Za Zhi*. 2015;95(28):2288-90.
17. Patel MC, Biniwali P. Constipation in pregnancy. *Federation of Obstetrics & Gynecological Societies of India (FOGSI). Science integra*. 2018.
18. The management of third- and fourth-degree perineal tears. *Green-top Guideline No. 29*. 2015. Royal College of Obstetricians and Gynaecologists. [Internet]. 2015 [cited 2024 March 11]. Available from: <https://www.rcog.org.uk/media/5jeb5hzu/gtg-29.pdf>
19. Aigmueller T, Bader W, Beilecke K, et al. Management of 3rd and 4th degree perineal tears after vaginal birth. *German guideline of the German Society of Gynecology and Obstetrics (AWMF Registry No. 015/079, October 2014). Geburtshilfe Frauenheilkd*. 2015;75(2):137-44.



Dr. Sanjay Gupte

MD, DGO, FICOG, FRCOG
Director, Gupte Hospital
and Center for Research in
Reproduction
Director, Greenarray Genomic
Research and Solutions, Pune
President, FOGSI (2010–11)



Dr. Arati Shah

MS ObGyn
Director, Pulse hospital,
Consultant, Greenarray Genomics
Research and Solutions,
Ahmedabad

NEW THOUGHTS ON TREATMENT OF GUT DYSBIOSIS LEADING TO CHRONIC CONSTIPATION

Chronic constipation, including functional constipation and constipation-type irritable bowel syndrome, is a prevalent, multifactorial gastrointestinal disorder. Its etiology and pathophysiology remain poorly understood.

Advances in the culture independent technologies have shown the enormous diversity, functional capacity, and age-associated dynamics of the human microbiome. A large number of diverse microbial species reside in the distal gastrointestinal tract, and gut microbiota dysbiosis – imbalances in the composition and function of these intestinal microbes – is associated with diseases ranging from localized gastroenterological disorders including constipation to psychoneurotic, respiratory, metabolic, hepatic, and cardiovascular illnesses.^{1,2} Recently studies using 16S rRNA-based microbiota profiling have demonstrated dysbiosis of gut microbiota in chronic constipation.

Functional constipation (FC: Rome classification II-IV) is typically categorized into:

- Normal transit constipation (NTC)
- Slow transit constipation (STC)
- Defecatory or rectal evacuation disorders, based on specific tests such as colonic transition time, manometry evaluation and defecography.

The defecatory or rectal evacuation disorders is caused by pelvic floor dyssynergia and reduction in intra-abdominal pressure, rectal sensory perception, and rectal contraction, suggests that this type of FC is not related to gut microbiota.

In contrast, NTC and STC are associated with gut microbiota. Most literature from Western countries reports an association between STC and gut

microbiota.³ The compositional difference in gut microbiota has been observed in health and disease conditions.

Eubiosis conditions are effective in controlling various diseases caused by microbes. Several population-based studies have revealed the highly beneficial role of human gut microbiota in healthy people which reside in symbiosis with the host in a healthy state, by controlling nutrient metabolism, defending against pathogens, and delivering signals to immune cells to promote host physiology and immunity.

Phyla Firmicutes, Bacteroides, Actinobacteria, Proteobacteria, and Verrucomicrobia contribute to the significant resident bacterial populations and Verrucomicrobia contribute to the significant resident bacterial populations in the gut microbiome. A normal balance between the host and gut flora is essential for human health, while disruption is linked with various human diseases, like hypertension, obesity, cardiovascular disorders, diabetes, and inflammatory bowel disease.⁴

It was observed that patients with chronic constipation had a relative decrease in obligate bacteria (e.g., *Lactobacillus*, *Bifidobacterium*, and *Bacteroides* spp.) and a parallel increase of potentially pathogenic microorganisms (e.g., *Pseudomonas aeruginosa* and *Campylobacter jejuni*). These alterations may influence intestinal motility and secretory functions by changing the amount

of available physiologically active substances and the metabolic environment of the gut. Another study reported that the levels of Bifidobacteria and Lactobacillus were significantly decreased in adult patients with constipation.⁵

Chronic constipation that is accompanied by abdominal pain is classified as irritable bowel syndrome with constipation (IBS-C: Rome classification II-IV). Gut microbiota have been shown to play a role in IBS-C.

The findings of gut microbiota in functional constipation are inconsistent. Although no clear consensus exists, compared with healthy subjects, IBS-C patients have a lower level of Actinobacteria, including Bifidobacteria, in their fecal samples and a higher level of Bacteroidetes in their mucosa. In most randomized controlled and parallel-group trials, probiotics, prebiotics, synbiotics, antibiotics, and fecal microbiota transplantation (FMT) therapy for chronic constipation were effective with few side effects. There are many studies but with small sample size and the types of probiotics are different, so it is difficult to evaluate the effect.

Microbiome-based medicines can fall into two categories, microbiome-based biomarkers, and therapeutics. Although some dietary interventions, prebiotics, probiotics, antibiotics and FMT are well-established therapeutics, recent work has raised the possibility of live biotherapeutics, and phage therapies for managing and treating a large array of diseases.

Prebiotic supplements

These are used to modulate the composition or activity of the microbiome. Prebiotics aim to increase the levels of beneficial bacteria and may include non-digestible fiber components (for example inulin or oligosaccharides) to stimulate the growth of *Bifidobacterium* and other beneficial microorganisms. Prebiotics are found naturally in human milk, and fructooligosaccharides and galactooligosaccharides are now added to many commercial formulas of infant milk to increase the abundance of bifidobacteria and lactobacilli.

Low-dose lactulose as a prebiotic for improved gut health and enhanced mineral absorption

Lactulose is an artificial disaccharide composed of galactose and fructose, and is produced via isomerization of lactose.⁶ Montgomery and Hudson described it first in 1929,⁷ lactulose gained clinical interest only in 1957, when Petuely found that growth of fecal bacteria from the genus *Bifidobacterium* increased after administration of lactulose to infants. Due to this activity (i.e., enhancement of bifidobacterial growth), Petuely referred to lactulose as the bifidogenic factor, a term still in use today.⁸ Based on the prebiotic and osmotic laxative properties of lactulose, Mayerhofer and Petuely proposed its use to treat constipation in 1959,⁹ and lactulose has been used as a laxative for more than 50 years.¹⁰

In current clinical practice, lactulose is indicated as a laxative for the symptomatic treatment of constipation in children and adults and as a detoxifying agent for the treatment of hepatic encephalopathy (HE) in adults.¹¹ Although chiefly used for medicinal purposes at medium and high doses for the treatment of constipation and HE, respectively, low-dose lactulose can also be used as a prebiotic to stimulate the growth of health-promoting bacteria in the gastrointestinal (GI) tract, or gut.^{6,12}

Prebiotics like lactulose are substrates that are selectively utilized by host microorganisms and confer a health benefit,¹³ multiple preclinical and clinical studies have shown that low doses of lactulose enhance the proliferation of health-promoting gut bacteria (e.g., *Bifidobacterium* and *Lactobacillus* spp.) and increase the production of beneficial metabolites [e.g., short-chain fatty acids (SCFAs)], while inhibiting the growth of potentially pathogenic bacteria (e.g., certain clostridia). SCFAs produced on microbial fermentation of lactulose, acetate which is most abundant, is likely to contribute to immune regulation, which is important within the gut itself, and also systemically for bone health. Low-dose lactulose also enhances the absorption of minerals

like calcium and magnesium from the gut, an effect which may have it stimulate the growth of health-promoting gut bacteria (e.g., *Bifidobacterium* and *Lactobacillus* spp.)

Probiotic supplements

Live or attenuated microorganisms defined as being capable of conferring health benefits on their host when they are given in sufficient quantities and administered continuously.

The probiotics may benefit chronic constipation by: (1) Modifying the altered intestinal microbiota, (2) Probiotic metabolites may alter gut sensation and motility function, and (3) Some probiotics may regulate the intraluminal environment, such as increasing the end products of bacterial fermentation and reducing luminal pH.

Lactobacillus and *Bifidobacterium* species given in sufficient quantities can recolonize the patient's gut with beneficial microbial species. Rationally designed therapeutics can be made containing a personalized consortium of microorganisms dependent on the patient's microbiome.^{6,9}

Synbiotics, a combination of prebiotics and probiotics, are said to have the best efficacy when it comes to treating constipation, with prebiotics increasing the survival of the probiotic supplements.

Subtractive microbiome therapeutics: This involves elimination of deleterious members of the microbiome, for example using chemicals or peptides, bacteriophages or bacteriocins.¹⁰

Fecal microbiota transplants (FMT) to rebalance the gut microbiome, a technique already proven to be extremely successful in tackling *Clostridium difficile* infections and one of the most direct approaches to manipulate the microbiome. There have been some small studies and case reports showing the immediate and effective treatment of chronic constipation using FMT. However, more large scale studies are still needed.⁹

Next generation therapeutics may include recombinant probiotics with engineered characteristics and controllable gene circuits, as this offers an opportunity to improve existing microbial communities.

The major challenge in the field of microbiome therapeutics is the identification of the microbes to address disease complexities. Different microbial strains are suitable for different therapeutic approaches based on their survival within the body. Proper characterization of microbes based on their functional benefits needs to be done before choosing them for treatment.

Conclusion

Constipation is a syndrome indicating various and complex combinations of disorders. Evidence indicates that dysbiosis of gut microbiota may contribute to functional constipation and constipation-type irritable bowel syndrome. Targeting treatments for the dysbiosis of constipation by probiotics, prebiotics, synbiotics, antibiotics, and FMT may be a new option, especially for refractory constipation to conventional therapies.

Key highlights

- Chronic constipation, including functional constipation and constipation-type irritable bowel syndrome, is a prevalent, multifactorial gastrointestinal disorder. Its etiology and pathophysiology remain poorly understood.
- Evidence indicates that dysbiosis of gut microbiota may contribute to functional constipation and constipation-type irritable bowel syndrome
- Targeting treatments for the dysbiosis of constipation by some dietary interventions, prebiotics, probiotics, synbiotics, and fecal microbiota transplant (FMT) are well-established therapeutics.
- Lactulose, a versatile osmotic laxative, demonstrates efficacy in constipation management through its osmotic, prebiotic, and detoxifying actions.
- Synbiotics, a combination of prebiotics and probiotics, are said to have the best efficacy when it comes to treating constipation, with prebiotics increasing the survival of the probiotic supplements.
- Microbiome-based medicines like microbiome-based biomarkers and therapeutics are going to be the modern day approach. Recent work has raised the possibility of live bio therapeutics and phage therapies for managing and treating a large array of diseases.

References

1. Lynch SV, Pedersen O. The human intestinal microbiome in health and disease. *N Engl J Med*. 2016;375(24):2369-2379.
2. Yusuf N, Hamid N, Ma ZF, et al. Exposure to environmental microbiota explains persistent abdominal pain and irritable bowel syndrome after a major flood. *Gut Pathog*. 2017;9:75.
3. Simrén M, Barbara G, Flint HJ, et al. Intestinal microbiota in functional bowel disorders: A Rome foundation report. *Gut*. 2013;62(1):159-76.
4. Afzaal M, Saeed F, Shah YA, et al. Human gut microbiota in health and disease: Unveiling the relationship. *Front Microbiol*. 2022;13:999001.
5. Zhao Y, Yu YB. Intestinal microbiota and chronic constipation. *Springerplus*. 2016;5(1):1130.
6. Pranami D, Sharma R, Pathak H. Lactulose: A prebiotic, laxative and detoxifying agent. *Drugs Ther Perspect* 2017;33:228-233.
7. Karakan T, Tuohy KM, Janssen-van Solingen G. Low-Dose Lactulose as a Prebiotic for Improved Gut Health and Enhanced Mineral Absorption. *Front Nutr*. 2021;8:672925.
8. Petuely F. Der Bifidusfaktor [The Lactobacillus bifidus factor]. *Dtsch Med Wochenschr*. 1957;82(46):1957-60.
9. Mayerhofer F, Petuely F. Untersuchungen zur Regulation der Darmträgheit des Erwachsenen mit Hilfe der Laktulose (Bifidus-Faktor). *Wien Klin Wochenschr*. 1959;71:865-9.
10. Public Assessment Report of the Medicines Evaluation Board in the Netherlands. Lactulose Sandoz 670 mg/ml, syrup. [2012] [Internet]. [Cited 2024 May 27]. Available at: www.geneesmiddeleninformatiebank.nl/Pars/h109595.pdf.
11. Electronic medicines compendium (EMC) UK. Duphalac 3.335 g/5 ml Oral Solution - Summary of Product Characteristics (SmPC) - (emc) [Internet]. Cited 2024 May 27. Available from: <https://www.medicines.org.uk/emc/product/5525/smpc>
12. Olano A, Corzo N. Lactulose as a food ingredient. *J Sci Food Agric [Internet]*. 2009;89(12):1987-90.
13. Gibson GR, Hutkins R, Sanders ME, et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nat Rev Gastroenterol Hepatol*. 2017;14(8):491-502.



Abbott

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

For more information, please contact: Medical Sciences Division, Abbott India Limited,
Floor 16, Godrej BKC, Plot No. C - 68, BKC, Near MCA Club, Bandra (E), Mumbai - 400 051.

