Intestinal Microbiome and Antimicrobial Resistivity: A Study in Recent Times

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Abstract

The world has recently witnessed a pandemic and is now challenged by continuous environmental changes. Human health is in constant jeopardy with the rise in bacterial, fungal, and viral infections. Antibiotics are the most widely used medication for the treatment of any infection. The urban population does not always maintain a healthy lifestyle due to the fast-paced nature of life. West Bengal the eastern state of India is no exception to this directive. Rampant use of antibiotics and their frequent consumption has widely increased over the years. This is posing a serious threat to the healthy microbiome of the human intestine. It is resulting in a decline of the healthy microbiota and the development of antibiotic resistance. The study aims to understand the effect of antibiotic consumption in the post-COVID scenario on the gut microbiome of the West Bengal population. The population includes both rural and urban as it takes into account the different lifestyles.

Keywords: Antibiotics, Antimicrobial Resistance, Antibiotic Use in India, Gut Microbiome.

Introduction

The COVID-19 pandemic struck the world and caused great havoc. Many people died; a trail of recurrent infections was left behind in the survivors. Climate change is also posing a serious threat to human health. There is always a fluctuation of temperatures and seasonal changes are ideal causes of viral, and bacterial infections. People also suffer from various kinds of fungal infections. Human health is always at stake. Antibiotics are mostly used to treat any kind of infection [1, 2]. Generally, the most prescribed antibiotics fall under the range of broad spectrum as these work on a wide range of disease-causing bacteria (gram-positive and gram-negative) [3].

We also see that there is a difference in lifestyle between healthy and urban populations and this also plays a crucial role. Life moves at a fast pace in urban areas as compared to rural areas. The urban population does not always have the chance to follow a healthy diet. However, they have easy access to a good healthcare system. On the other hand, the rural population follows a healthy diet, their life is slow-paced but they do not have easy access to a good healthcare system.

Gut microbiota plays a fundamental role in the development of both local and systemic immunity [4]. The human gut is full of diverse bacteria, and many harbor resistance against a broad range of antibiotics [1, 6]. This includes

pathogenic species featured in the CDC's Antibiotic Resistance Threats Report [1, 2], such as vancomycin-resistant *Enterococci* and carbapenem-resistant Enterobacteriaceae [1]. The different phyla comprising the gut microbiota are depicted in Figure 1 [20]. The gut microbiome is under constant threat from antibiotic use and unhealthy lifestyles. Over-the-counter buying of antibiotics without proper prescription at pharmacy shops is very common in India. This is easily accessible to the urban population. This results in unregulated sales of antibiotics. It is also observed that people generally do not always complete the entire course of antibiotics. They stop the medication in between as soon as there are visible signs of recovery. These two factors are leading to antibiotic abuse [5].

Antibiotic medicines are now impacting the gastrointestinal system and disrupting the gut microbiome [3, 5]. Generally, the early symptoms of an unhealthy gut during antibiotic consumption are irritable bowel syndrome and diarrhea [3, 4]. Antibiotics can result in several negative consequences on the gut microbiota, from reduced diversity of species, alteration in metabolic activity, and the selection of antibiotic-resistant organisms, resulting in downstream effects such as antibiotic-associated diarrhea and recurring C difficile infections [9]. There is also evidence that early exposure to antibiotics can impact gastrointestinal, immunological, and neurocognitive systems. This is problematic due to the increased use of antibiotics, which suggests a future increase in the prevalence of acute conditions. To address this challenge, continuing research on the composition and function of the gut microbiota is necessary [9].

With due course of time, this leads to the development of multidrug-resistant organisms in the gut microbiome and thus begins the antimicrobial resistance [3, 4].

The antimicrobial resistance makes the disease-causing parasites flourish even in the presence of the medication which at one point had impacted their growth [8]. This leads to more complications in recovery and in some extreme cases the disease-causing pathogen can be resistant to the medications that are presently available [8].
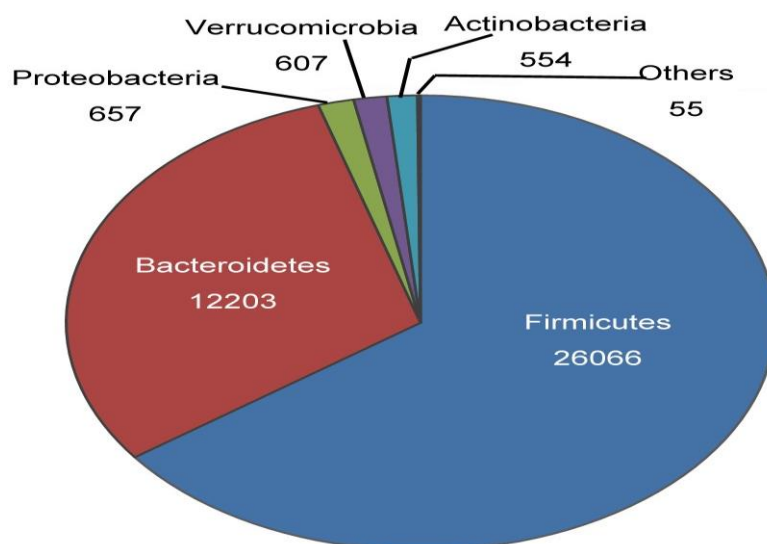

Figure 1. Gut Microbial Composition. The pie chart shows the distribution of gut bacteria obtained by searching RDP browser. Others are: Spirochaetes, Fusobacteria, Deferribacteres, Cyanobacteria, Planctomycetes, Lentisphaerae, TM7 and Tenericutes. Of the thirteen phyla, the Firmicutes and Bacteroidetes occupy 65% and 30% of the pie, respectively, while the rest eleven phyla take up 5%.

Factors Affecting Gut Health

COVID-19 pandemic: The world was gripped by the COVID-19 pandemic and it caused massive havoc. The not-so-advanced healthcare system of India was exposed to the lack of oxygen and essential drugs required for the treatment of COVID-19 [12]. Additionally, during the pandemic period, there was a drastic decline in seeking non-COVID-19 disease-related healthcare services [12]. There were different analyses conducted and all of them revealed a strong relationship between the increase in antibiotic consumption and COVID-19 cases. The utilization of hospital antibiotics, measured in terms of DDD, exhibited a 26% increase in 2021 when compared with 2019 [13]. Despite the ineffectiveness of antibiotics in treating COVID-19, they were prescribed to individuals with suspected or confirmed cases of COVID-19 for several reasons. These reasons include the challenges in excluding bacterial coinfection during initial presentation and the potential occurrence of secondary bacterial infections throughout the disease [14,15]. The empirical use of antibiotics for patients with COVID-19 raises concerns about their overuse and the subsequent harm associated with AMR [16]. Azithromycin has been frequently prescribed in the treatment of COVID-19 globally [17]. The COVID-19 pandemic renewed attention to the need to tackle antibiotic misuse and AMR. Although less than 10% of hospitalized and community-based patients with COVID-19 worldwide are diagnosed with a secondary bacterial infection requiring antibiotics, an estimated 75% of patients receive antibiotic prescriptions [18].

Climate change: Climate change is affecting the health directly causing more sickness and death. It is directly contributing to humanitarian emergencies from heatwaves, wildfires, floods, tropical storms, and hurricanes and they are increasing in scale, frequency, and intensity. Temperature and precipitation changes enhance the spread of vector-borne diseases [19]. India's inadequate health systems make our population particularly vulnerable to the impact of climate risks on health. Although we commonly say that climate change affects human health, it remains challenging to accurately estimate the scale and impact of many climate-sensitive health risks. However, scientific advances progressively allow us to attribute an increase in morbidity and mortality to global warming, and more accurately determine the risks and scale of these health threats [19]. In more indirect ways, it affects nutrition, reduces working hours, and increases climate-induced stress [19].

Lifestyle: As stated earlier, the lifestyle difference between healthy and urban populations also plays a crucial role. The fast-paced urban lifestyle becomes limiting in following a healthy diet. However, the urban population has easy access to a good healthcare system. On the contrary, the rural population follows a healthy diet, their life is slow-paced but they do not have easy access to a good healthcare system. Lifestyle and food habits are also contributing factors to the health of the gut microbiome [1, 4, 10]. The use of probiotics instead of antibiotic therapy to address certain health conditions in humans may alleviate these antibiotic-mediated selective pressures [10].

Diet: It is now widely recognized that diet and other environmental factors play a role in impacting the composition and metabolic activity of the human gut microbiota, which in turn impacts health. Molecular technologies have greatly advanced our understanding of the complexity and diversity of the gut microbial communities within and between individuals. Diet, particularly macronutrients, has a major role in shaping the composition and activity of these complex populations [21].

The maintenance of a diverse and thriving population of beneficial gut bacteria helps to keep harmful bacteria at bay by competing for nutrients and sites of colonization. The physical and mental well-being of any individual is dependent on the food we eat, the environment we live in, and other socio-economic factors [28]. Dietary means, particularly the use of a range of fibers, maybe the best way of maintaining a healthy gut microbiota population [21]. The importance of proper nutrition has already been highlighted during COVID-19 [28]. The general principle is to eat a balanced diet containing seasonal fruits and green vegetables as well as take nutritional supplements as advised by a nutritionist. Proper nutrition includes protein supplements especially plant and seafood proteins, macro and microelements-rich diet, and regular intake of leafy vegetables as a source of vitamins and mineral supplements. Vitamins show immunomodulatory and antioxidative responses, they modulate the expression of genes in immune cells and also help in the differentiation and maturity of immune cells [29]. Good nutritive food is always vital and helps in building immunity [30]. A good immune system easily can fight against infection and decline stressful conditions in human beings [3].

Microbes colonize the human gut during or shortly after birth. The complexities and variability of adult gut microbial populations have become increasingly evident in recent years [21]. The variability may relate to the influence of numerous factors, including diet and host genetics [21]. The composition and activity of gut bacteria can vary according to (and possibly a result of) life events, including puberty, ovarian cycle, pregnancy, and menopause [22]. The impact of non-dietary lifestyle factors on the gut microbiota is also being recognized in present times. The most impactful factors are smoking, lack of exercise, stress, and obesity. Smoking can significantly impact the large bowel (and potentially the microbiota) as they are risk factors for Colorectal Cancer [24].

Stress: Another lifestyle factor, stress, has an impact on colonic motor activity via the gut-brain axis which can alter gut microbiota profiles, including lower numbers of potentially beneficial Lactobacillus [23]. The COVID-19 pandemic has caused anxiety and stress to all beings and this results in turn into sleep disturbances, so it's a vicious cycle as stress and sleep disturbances are complementary to each other [30]. To get good sleep it has been advised that people should consume food containing or promoting the synthesis of serotonin and melatonin at dinner [30]. The diet should be inclusive of varieties of plant species along with roots, leaves, fruits, and seeds like almonds, bananas, cherries, and oats which contain melatonin and/or serotonin or tryptophan. Milk and milk products are the main sources of tryptophan, which is the sleep-inducing amino acid [30]. The sedentary lifestyle of the urban population has increased the incidence of Obesity which is associated with excess energy intake. Exercise plays an important influence on any shifts in microbial populations that are associated with obesity. Geographical location and traveling to different places also influence the gut microbiome. Antibiotics are the most commonly used method of treatment for any bacterial, viral, and fungal infection. The use of antibiotics has increased significantly over some time. They play a crucial role in tackling infections however, their inappropriate use led to the development of multi-drug resistant organisms resulting in antimicrobial resistance or AMR. As a consequence, the most commonly used antibiotics now lose their effectiveness in treating the infection resulting in prolonged hospitalization, a rise in healthcare expenses, and loss of life (in severe cases).

Antibiotic consumption and antibiotic resistance: In India, it is very common to buy antibiotics from pharmacy shops without a

proper prescription. This over-the-counter buy results in unregulated sales of antibiotics. The urban population has easy access to this as compared to the rural population. It is also quite common for patients to not complete the entire course of antibiotics. They tend to stop intake of medicine as soon as recovery signs are visible. These are all various forms of antibiotic abuse. Antimicrobial resistance is posing a serious threat in India and across the world [3, 4. 8, 10]. Globally, India tops the list of countries with the highest antibiotic consumption, and highest AMR. Inappropriate use of antibiotics is one of the central drivers of AMR, and this misuse or overuse of drugs remains a significant problem in India. Lack of effective regulations, and/or failure to implement the regulations is one of the main reasons behind the inappropriate use of antibiotics. The results conducted from past research across countries revealed that very often, clinicians prescribe antibiotics when they are not required, or they prescribe the wrong antibiotics to patients. Often there are circumstances where pharmacy staff are not fully qualified to sell these medicines, or they sell them without prescriptions. All these cumulative factors lead to AMR if patients consume the wrong drug or dosage and for the wrong duration [25].

India being a densely populated country has a high prevalence of communicable diseases [7, 8]. Along with this, a majority of the population has restrictive access to basic healthcare and it is also very challenging to spread awareness about prevention techniques [7]. These are also some of the factors that are accelerating antibiotic resistance.

The spread of antibiotic resistance needs to be stopped. It is the cumulative responsibility of healthcare professionals and patients to be aware of antimicrobial resistance, reduce the overuse of antibiotics, follow a healthy lifestyle and proper diet, and complete the full course of antibiotics [7].

Importance of Stool: A stool sample is most widely used for understanding the gut microbiota; it is not just a waste material. The organs responsible for stool formation and the process of stool formation are depicted in Figure 2 [27]. The stool test can help understand any underlying gastrointestinal infection. Few stool tests are easily used in the primary diagnosis of disorders such as gastrointestinal infections, malabsorption syndromes, and inflammatory bowel diseases. Routine stool tests can prevent unnecessary laboratory investigations. There are various investigations performed in stool analysis and they are microscopic examination, chemical, immunologic, and microbiologic tests. Stool samples can be examined for leukocytes, occult blood, fat, sugars (reducing substances), pH, pancreatic enzymes, alpha-1 antitrypsin, calprotectin, and infectious causes (bacteria, viruses, and parasites). Stool samples are also macroscopically checked in terms of color, consistency, quantity, shape, odor, and mucus [26]. There are numerous associations between gut microbiota and human health, it is particularly important to analyze the relationship between changes in gut microbiota and disease occurrence, progression, and prognosis [11]. A stool test can detect parasitic infections, bacterial overgrowth, signs of cancer, or pathogenic bacteria like Clostridium difficile, and E. coli. The samples that are immediately frozen after collection have been widely regarded as the gold standard for gut microbiota profiling [11].
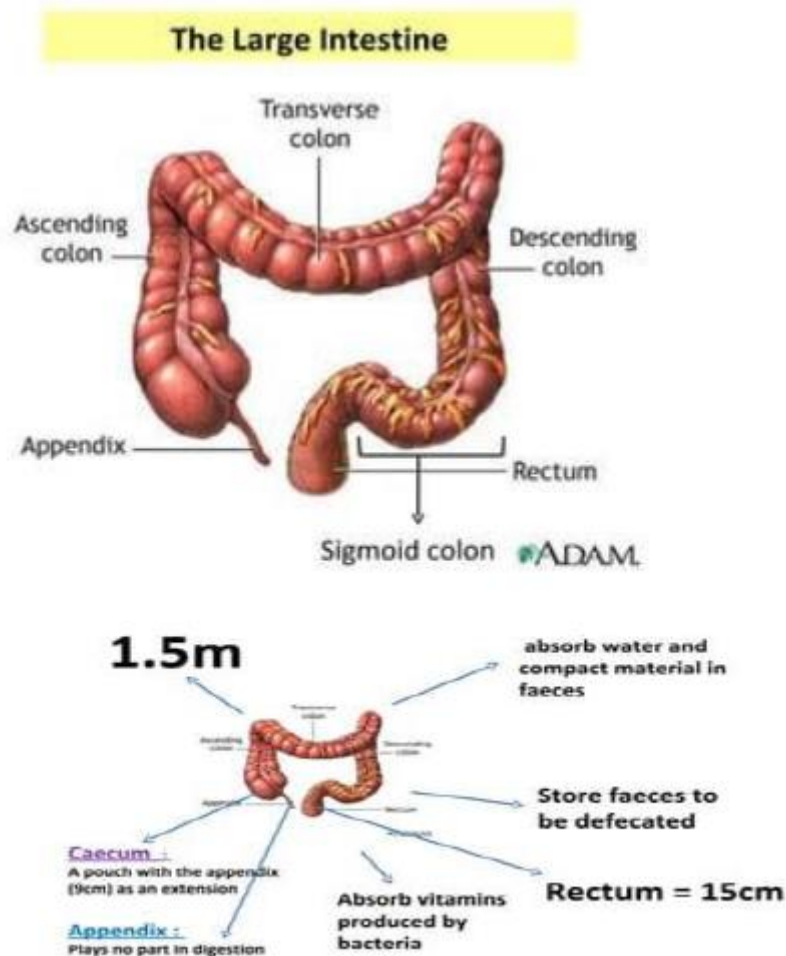
The Large Intestine

1.5m

- absorb water and compact material in faeces
- Store faeces to be defecated
- Rectum = 15cm

Caecum :
A pouch with the appendix (9cm) as an extension

Appendix :
Plays no part in digestion

Absorb vitamins produced by bacteria

Figure 2: Stool Formation in Human Body

Discussion

Climate change has an impact on overall human health quality. Gut microbiota is a mirror of how the health of humans is. It plays a fundamental role in the development of both local and systemic immunity. The gut microbiome is home to different species of bacteria, some of which are naturally resistant to a broad range of antibiotics. The diet and lifestyle have an intense influence on the gut health. Food items like probiotics help in the growth of good bacteria which in turn increases the immune system. Antibiotics are the most widely used mode of treatment for any kind of bacterial, viral, and fungal infections. Broad-spectrum antibiotics are mostly used as it encompasses a lot of infections. Over-the-counter buying of antibiotics without a medical prescription is very common in India. The urban population has easy access to good healthcare, whereas, the rural population has limited access to good healthcare. It is often observed that people do not complete the entire course of antibiotics; it is stopped midway as soon as there are signs of recovery. Diarrhoea and Irritable Bowel Syndrome are some of the common symptoms related to frequent antibiotic consumption. Unregulated sales of antibiotics, frequent consumption, and incomplete dosage are different forms of antibiotic abuse which is leading to antibiotic resistivity. India is grappling with the threat of antimicrobial resistivity and it is spreading very rapidly. Antimicrobial resistivity leads to prolongation of illness and hospitalization. Healthcare professionals and patients are equally

responsible for spreading awareness about antimicrobial resistance and healthier ways of consuming antibiotics.

Conclusion

The world is being continuously challenged with climate changes and health problems. The lifestyle is also changing in the fast-paced life. Antibiotic consumption has significantly increased; antibiotic abuse is on the rise. All these point towards antimicrobial resistance. Understanding more about antibiotic resistance and its effects is the need of the hour. This will pave the path to understanding how effective the presently available antibiotics in the market remain to the disease-causing microbes and whether there is a requirement for new antimicrobial drugs.

Conflict of Interest

I hereby declare that there is no conflict of interest.

Acknowledgements

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