Journal of Pharmaceutical Research International

Volume 36, Issue 4, Page 33-45, 2024; Article no.JPRI.115437
ISSN: 2456-9119, NLM ID: 101716968
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Influence of Gut Resistome on Humans with Autism Spectrum Disorder

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2024/v36i47510

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/115437

Review Article

Received: 28/01/2024
Accepted: 02/04/2024
Published: 08/04/2024

ABSTRACT

Recent studies have shed light on the connection between the gut resistome and individuals with autism spectrum disorder (ASD). Environmental factors such as premature birth and exposure to drugs in utero can have a significant impact on children with ASD. Microorganisms present in wastewater, hospitals, and animal production wastewaters have been found to contain various antibiotic-resistant genes (ARGs) that encode resistance to a broad spectrum of antibiotics. Environmental variables are currently considered potential etiological agents of this condition, as genetics alone cannot explain its primary origin. Numerous bacteria found in the gut microbiota (GM) have an impact on human health. Furthermore, a microbe impacted by birth mode, lifestyle, and genetics is present in the intestine. To produce different compounds that affect the host, train the host's immunity, modify drug action and metabolism, regulate gut endocrine function, and eliminate toxins, for example, GM is essential to achieving the intended target for treatment application.

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Keywords: Gut endocrine function; autism spectrum disorder; environmental stresses; Microorganisms.

1. INTRODUCTION

Autism spectrum disorder (ASD) is a major neurodevelopmental issue that affects roughly 1% of the general population. ASD symptoms include repetitive behaviours and trouble with social communication [1]. Epidemiological studies indicate that children with ASD often experience emotional and behavioural difficulties, such as anxiety, sadness, hyperactivity, inattention, and aggressive behaviours, in addition to the innate signs of the disorder [1]. Environmental stresses such as early birth and drug exposure in utero can have an impact on kids with ASD [2,3]. Furthermore, the pathophysiology of ASD is associated with maternal infection during pregnancy, which raises the likelihood that the child would experience ASD [4]. According to the Centers for Disease Control (CDC), one in 54 children in the US has ASD, indicating that the prevalence of ASD is rising globally [5]. In certain situations, the diagnosis of ASD can be made as early as 18 months of age. However, a definitive diagnosis might take longer, or in certain situations, it might not be discovered until the patient is a teenager or an adult [6]. The aetiology of ASD remains uncertain despite numerous explanations being postulated by environmental and genetic variables [6]. According to a wealth of research, alterations in the makeup and function of the gut microbiota (GM) are considered crucial components of ASD [7,8]. According to Kovtun et al. (2020), GM plays a part in communication between the brain and the gut. Additionally, through its interactions with the immune system, the gut microbiome may impact brain function [9]. Furthermore, long-term disruption of GM, which is linked to the emergence of gastrointestinal (GI) symptoms, may result from early-life antibiotic exposure [10-12]. Nonetheless, according to Schulfer et al. (2018), antibiotics are necessary for the treatment of several illnesses, including TB and gonorrhoea, and alterations in the GM composition may be linked to ASD [13].

Thousands of bacterial species comprise the gut microbiome, home to a reservoir of antibiotic resistance genes (ARGs) known as the resistome [14]. In various settings, including the gut, soils, human, animal, and ocean, resistome—a collection of antibiotic resistance genes (ARGs) in a microbial community or on a single microorganism—has been studied [15]. According to Martinez (2014) and Munita and Arias (2016), susceptible bacteria can develop antibiotic resistance by accumulating mutations or acquiring resistance genes through transformation, transduction, and conjugation [16,17]. These genes provide the cell with resistance to antibiotics. A mutation can be acquired or innate. Furthermore, using antibiotics and bacteria that pose a risk to humans and animals can accelerate the development of antibiotic-resistant genes (ARG). Microorganisms found in wastewaters, hospitals, and animal production wastewaters have been found to harbour hundreds of distinct ARGs that encode resistance to a broad spectrum of antibiotics [18]. To make it easier to characterise and identify ARGs, the Antibiotic Resistance Genes Database (ARDB) is a database that contains the majority of the publicly available data on antibiotic resistance. An extensive amount of information is annotated for each type of resistance and gene, including sequencing, resistance profile, protein databases, ontology, mechanism of action, COG (Clusters of Orthologous Genes), and CDD (Conserved Domain Database) annotations [19]. Examples of ARGs that have been found in the environment include those that are resistant to vancomycin, sulfamethoxazole, trimethoprim, ciprofloxacin, quinolone, or tetracycline (e.g., *sul I*, *sul IItet(A)*, *tet(B)*, *tet(C)*, *tet(G)*, *tet(M)*, *tet(W)*, and *tet(O)*). According to studies, ear infections may raise the chance of ASD, and postnatal antibiotic exposure—particularly the usage of paracetamol and antibiotics—has been linked to ASD [20]. Compared to their contemporaries, children with autism are known to receive an excessive amount of antibiotic treatment [14]. Furthermore, Sharma and colleagues (2016) provided evidence of a connection between ASD and resistome [21].

2. AUTISM SPECTRUM DISORDER (ASD)

According to Pulikkan, Mazumder, and Grace (2019), autism spectrum disorder (ASD) is regarded as a severe neuropsychiatric and neurodevelopmental illness with an unclear aetiology and pathogenesis [22]. Individual differences may exist in the restrictive, repetitive, communicative, and social issues associated with ASD [23]. ASD is associated with a wide range of comorbidities, such as abnormalities in

sensory processing, impaired neural processing, altered brain development, motor deficits, gastrointestinal (GI) disturbances, deficits in verbal and language communication skills, and impairments in intellect and abstract reasoning [24]. Up to 90% of children with ASD have aberrant sensory perception, which is a characteristic of the illness [25]. Furthermore, there is a higher prevalence of GI symptoms in people with ASD, including food intolerance, inflammatory diseases, constipation, flatulence, reflux, gastrointestinal problems, and indicators of irritable bowel syndrome (IBS) [26]. The Centres for Disease Control and Prevention (CDC) stated that roughly one in 44 American children had ASD in 2021, indicating an increase in the frequency of ASD cases. 2.81 incidences of ASD were reported per 1,000 children in Saudi Arabia, with Makkah and Jeddah having the highest prevalence [27]. Furthermore, compared to other wealthy nations, the prevalence of ASD is said to be slightly greater [28]. Moreover, Hayat et al. (2019) estimate that the prevalence of ASD in the Arab Gulf countries ranges from 1.4 to 29/10,000. [29]. Globally, males are more prone to having Autism Spectrum Disorder (ASD) than females. Boys have a 4.5 times greater infection rate than girls [30]. ASD manifests in the first three years of life [26]. Autism can be diagnosed as early as 18 to 24 months of age; at this time, distinguishable symptoms from other developmental delays can be made. As early as 18 to 24 months of age, autism can be diagnosed, and it is possible to differentiate between the disorder's distinctive symptoms and other developmental abnormalities [31]. The diagnosis of ASD can be challenging because its symptoms are similar to those of different psychiatric conditions. Moreover, ASD has a neurodevelopmental basis, and social and non-social symptoms, such as unusually narrow interests, communication and relationship difficulties, and highly repetitive and restrictive behavioural patterns, are used to diagnose the disorder. There is strong evidence that the genetic component of heritability for ASD ranges from 60% to 83%, even when the exact cause of the disorder is unknown [32,33]. Furthermore, a growing body of research indicates that ASD may be brought on by several diseases [34]. Environmental variables are currently considered potential etiological agents of this condition, as genetics alone cannot explain its primary origin [35]. A growing number of studies employ indirect methods to deduce the aetiology of ASD from epidemiological data [36]. Genetics, epigenetics, and environmental variables are only a few of the numerous risk factors for ASD. Though their exact role in ASD is unknown, the microbiota is the most crucial component. It may be able to comprehend the aetiology of ASD through the relationship between ASD and gut resistome [1]. All of the genes that confer antibiotic resistance in both pathogenic and non-pathogenic bacteria populations are known as the resistome. Several investigations have elucidated the connection between gut microbiota and ASD. Constipation is a gastrointestinal syndrome that affects 20% of children with ASD, making up a more significant percentage of affected persons than healthy children. By contrast, the ASD person's diarrhoea rate was 19% greater than that of the healthy person. Substantial evidence links GM to ASD through effects on the immune system and metabolism [1,37].

3. MICROBIOME

The human gastrointestinal tract (GI) harbours around a thousand distinct microbiome species. The term "human gut microbiome" (GM) refers to the genes and microorganisms found in environmental settings [38]. Numerous bacteria found in GM have an impact on human health. Furthermore, a microbe impacted by birth mode, lifestyle, and genetics is present in the intestine. In order to produce different compounds that affect the host, train the host's immunity, modify drug action and metabolism, regulate gut endocrine function, and eliminate toxins, for example, GM is essential to achieving the intended target for treatment application [39]. According to Sarkar et al. (2010), microbiome alteration results in a critical therapeutic target for sustaining the course of treatment and overall disease wellness. Several investigations have indicated that gut microbiota impacts the immune system, mucosal tissues, and various organs [40]. Variations in the makeup and function of an individual's gut microbiome have been related to inflammatory, metabolic, neurological, cardiovascular, and respiratory disorders [41]. Infection and smoking are the two most significant environmental factors that affect oral/intestinal dysbiosis, arthritic result, and onset [42]. Since germ-free mice do not develop experimental arthritis, the microbiome may be involved in the disease's aetiology One of the hallmarks of chronic autoimmune inflammatory disease Rheumatoid arthritis (RA) is joint degeneration. Without treatment, RA patients' gut microbiota differed significantly from healthy controls[43]. According to Wells et al. (2020),

there appears to be a reduction in the genetic diversity of rheumatoid arthritis patients compared to healthy controls. Furthermore, *Prevotella* species, including *Prevotella copri*, were more prevalent in the compositional level of bacteria in RA patients[44]. Additionally, *Prevotella copri* was shown to be more abundant in the colon in recent preclinical phase research on RA patients in European nations, suggesting that dysbiosis occurs before arthritis develops [45]. The aetiology of irritable bowel syndrome (IBS) is linked to dysbiosis in the gut, and there is a decrease in *facalibacterium* and an increase in *collinsella* in RA [46,47]. Numerous researchers have demonstrated that gut microbiota dysbiosis may be crucial in neurological and psychiatric illnesses [48].

The gut microbiota of individuals with ASD is different; research found that the number of Prevotellaceae and Porphyromonadaceae was higher in healthy mice compared to autistic mice, as well as an increased number of Erysipelotrichaceae, Alcaligenaceae, and Ruminococcaceae [49]. According to research on animals, the gut microbiota can influence social behaviour, communication, stress, and depression [50]. Furthermore, faecal microbiota transplantation can transfer behavioural features between mice strains [15]. Furthermore, new research indicates that behavioural characteristic alterations may be influenced by microbiota [51]. In addition, GM has been linked in numerous studies to the advancement of pancreatic cancer [22,52,53]. The study conducted by Ren (2017) revealed that the stool microbiome of patients with pancreatic cancer was more diverse and composed of known lipopolysaccharide (LPS)-producing taxa and pathogens, such as *Enterobacter*, *Veillonella*, *Hallella*, *Selenomonas*, *Prevotella*, and *Klebsiella* species, than the microbiome of healthy controls [53].

4. RESISTOME

A collection of environmental antibiotic resistance genes, or ARGs, is an antibiotic resistome [54]. According to Moore et al. (2013), the resistome is formed after birth or the first few months of life [55]. According to Yi et al. (2022), the microbiota serves as a reservoir for resistomes or ARGs [56]. According to Stecher and Hardt (2011), colonisation resistance is a method the gut microbiota uses to resist different infections [57]. . Numerous factors can impact ARGs, such as the use of live microbial therapies, antibiotics, the severity of the illness, the hospital setting, nursing, agriculture, location, and nutrition (Fig. 1) [58]. In addition, metagenomics based on next-generation sequencing technologies, the human microbiomes, and their resistome found in the skin, respiratory tract, and gut have been evaluated. Understanding the dynamics of the human resistome and how it relates to the health sectors is crucial for controlling ARG that flows from the other sectors to the human sector, especially ARG transfer to bacteria that cause disease [59]. The human microbiome's commensal bacteria serve as clinical ARGs' primary reservoir and transmission route [60]. Several research studies have uncovered its function by interpreting the gut resistome and contrasting its similarities with pathogens [61-63]. A suggested indirect effect has drawn more attention to resistome: commensal species may share their resistome with pathobionts or pathogens, potentially passing it on to clinically and virulently relevant strains [64]. Commensal bacteria may be the source of the resistome that supported the discovery of the *vanB* genes in the vancomycin-resistant gut that was separated from *Eggerthella* lenta and *Clostridium innocuum* [65].

5. ANTIBIOTIC RESISTANCE GENES (ARGS)

A collection of antibiotic resistance genes (ARGs) in a microbial community or on a single bacterium is referred to as a resistome. Resistome has been studied in a variety of settings, including the human gut, soils, animals, and oceans (Fig. 2) [66]. Furthermore, metagenomic whole-genome shotgun sequencing (mWGS) will make additional ARGs available as newly sequenced bacterial genomes become available [67]. ARGs are categorised as intrinsic (originating from the producers) or acquired (from other bacteria) resistant (Fig. 3) [68].

ARGs, which shield the cell from antibiotics, can develop from susceptible bacteria by accumulating mutations or obtaining resistance genes through transformation, transduction, and conjugation [16]. Moreover, global cell adaptations, ribosomal protection protein, antibiotic target replacement, inactivation, and antibiotic modifications (Fig. 4) are the primary mechanisms of antibiotic resistance. These mechanisms include changing the antibiotic target by lowering the affinity of the binding site for the antibiotic. Drug efflux, drug target

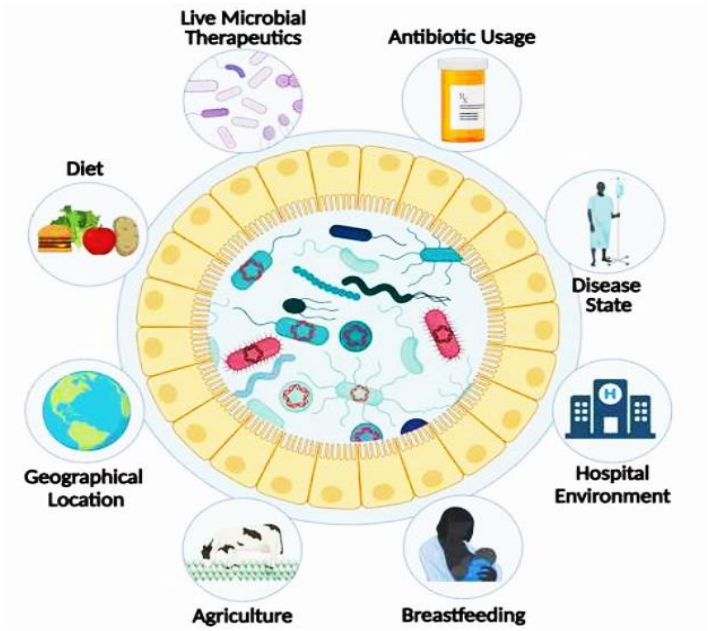

Fig. 1. Collection of environmental antibiotic resistance genes

modification, and drug inactivation were the methods of acquired resistance; drug efflux, limiting uptake, and drug inactivation might be intrinsic resistance mechanisms [69]. As previously indicated, these mechanisms may be innate to the microorganisms or acquired from other microbes [69].

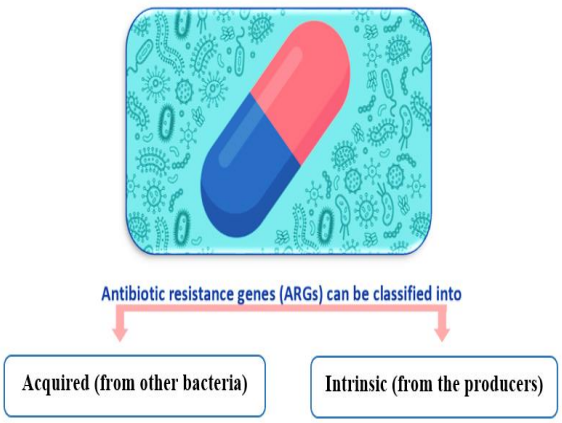

Fig. 2. Description of the reservoir of ARGs. Taken after Cuadrat et al. (2020) [66]

The five primary categories of antimicrobial processes are depolarising the cell membrane, blocking bacterial pathways, blocking the creation of proteins and nucleic acids, and inhibiting cell walls. Table 1 displays examples of how antimicrobial group-based mechanisms work. Moreover, resistance levels within the bacterial groupings may vary dramatically. Minimum inhibitory concentration (MIC) is used to quantify susceptibility and resistance. The range of MICs for any antibiotic among different. bacterial species is known as drug susceptibility. The species is thought to have intrinsic resistance to the medication even if it is in the resistant portion of the MIC range. The genes that bacteria acquire and the species they belong to determine their resistance levels [69].

Natural resistance can be produced by intrinsic genes always expressed in the species or by naturally occurring genes in bacteria that are expressed only to the resistant levels following antibiotic exposure. The feature that all bacteria have in common is intrinsic resistance, which has nothing to do with horizontal gene transfer or prior exposure to antibiotics (Table 2). For instance, the structure and function of the lipopolysaccharide (LPS) layer in gram-negative bacteria acts as a barrier to a wide range of molecules, giving the bacteria an inherent resistance to various antimicrobial drugs. For example, because *Mycobacteria* has a lipid outer membrane, hydrophobic drugs—like rifampicin and fluoroquinolones—have easy access to the cell, while hydrophilic drugs are more restricted in their absorption [70-72]. Moreover, Mycoplasma is inherently resistant to antibiotics that attack the cell wall, such as β-lactams and glycopeptides [73]. Gram-positive bacteria have an outer barrier that keeps drugs from entering the cell. For instance, enterococci's cell wall

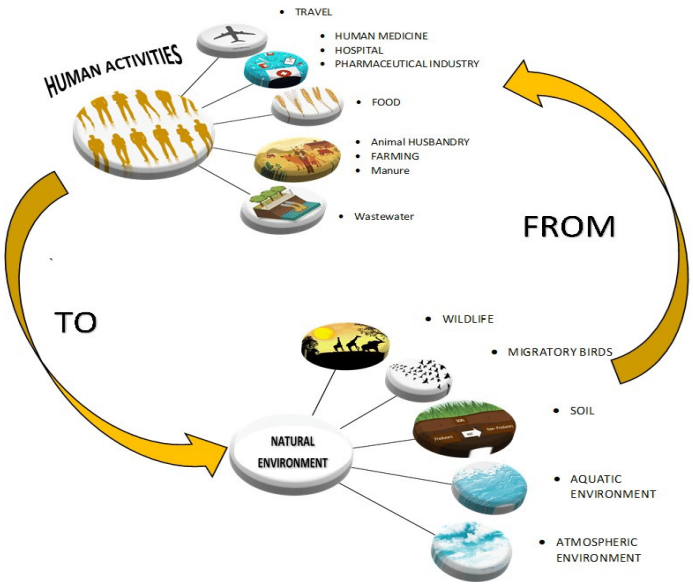

Fig. 3. The classification of ARGs. Taken after Hu et al. (2017) [68]

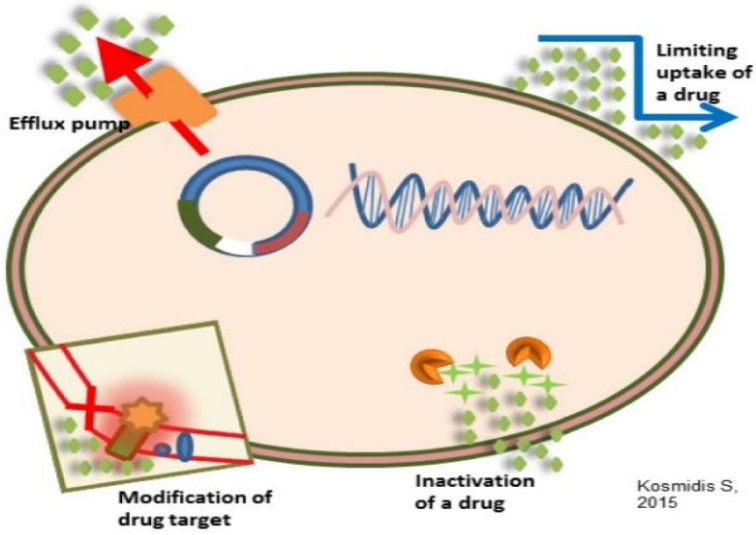

Fig. 4. Types of antimicrobial resistance mechanisms in bacteria. Taken after Munita and Arias (2016) [17]

contains polar compounds that hinder cell wall penetration and confer an inherent resistance to aminoglycosides [70]. Gram-positive *Staphylococcus aureus* bacteria are resistant to vancomycin. Vancomycin-resistant *S. aureus* (VISA) strains have produced a thickened cell wall, which hinders the drug's ability to enter the cell and confers resistance [70,74].

The acquisition of ARGs can be made temporarily or permanently. Plasmid-mediated transmission of resistance genes is the most frequent method of acquiring foreign genetic material; however, bacteriophage transfer is uncommon. However, some bacterial species—like *Acinetobacter* spp.—can obtain genetic material directly from the environment [72]. Additionally, specific genes, such as those that encode antibiotic-modifying enzymes, drug targets, regulators that regulate drug transporters, and drug transporters, may experience mutations that result in antimicrobial resistance [16]. Moreover, the organism determines a great deal of the mutations that contribute to antibiotic resistance. For example, when *S. aureus* develops a methicillin resistance,

Table 1. The actions of ARGs are based on the antimicrobial groups. Taken after [69]

Action of ARGs	Antimicrobial drug groups
Inhibit cell wall synthesis.	B-Lactmas, Cephalosporins, Penicillins
Inhibit protein synthesis.	Aminoglycosides, Tetracyclines, Macrolides
Inhibit nucleic acid synthesis.	Fluoroquinolones

Table 2. Some bacterial species have intrinsic resistance to antimicrobial drugs. Taken after several reports [70-72]

Organism	Intrinsic resistance
Bacteroides (anaerobes)	Aminoglycosides, many β-lactams, quinolones
Enterococci	Aminoglycosides, cephalosporins, lincosamides
Escherichia coli	Macrolides
Klebsiella spp.	Ampicillin
Acinetobacter spp.	Ampicillin, glycopeptides

the bacterial growth rate is dramatically reduced [16]. High resistance levels in subsequent bacterial generations may be selected using very low or low doses of antibacterial drugs (sub-inhibitory) [75].

6. PENICILLIN-BINDING PROTEINS (PBPS)

The bacterial cells alter the structure and/or quantity of Penicillin-binding proteins (PBPs), which allows the agents to withstand the effects of numerous antimicrobial drugs. Gram-positive bacteria have this process as one of their resistance mechanisms to β-lactam antibiotics. PBPs are transpeptidases that are involved in the cell wall's peptidoglycan production. Therefore, altering the PBP value, either up or down, has an impact on the drug's capacity to bind. PBPs alter the amount of antimicrobial that binds to that target, resulting in structural changes. For instance, PBP2a in *S. aureus* causes resistance by acquiring the *mecA* gene, which can either reduce or prevent the capacity of a medication to bind [16,69]. Furthermore, by depolarising a cell membrane, the glycopeptide vancomycin prevents the formation of cell walls and lipopeptides. Because of the thick LPS coating, gram-negative bacteria are intrinsically resistant to these medications [76,77]. Vancomycin-resistant Enterococci (VRE) and methicillin-resistant *S aureus* (MRSA) are two types of enterococci where resistance to the antibiotic is a significant problem. On the other hand, resistance is caused by the acquisition of *van* genes, which alters the structure of peptidoglycan precursors and lowers vancomycin's binding capacity [70,74]. Furthermore, a mutation in *mprF* is an important mechanism that inhibits calcium binding by changing the cell membrane's charge to a positive state. As a result, daptomycin cannot bind because of the inhibition of calcium [6,78]. The targeting of ribosomal subunits' antimicrobial resistance can arise through ribosomal methylation or ribosomal mutation (aminoglycosides, oxazolidinones) [78]. Additionally, in bacterial and some eucaryotic organisms, such as *Pneumocystis carinii* [79]. *Toxoplasma gondii*), and *Plasmodium falciparum* [79], the enzyme dihydropteroate synthase (DHPS; EC 2.5.1.15) catalyses the biosynthesis of dihydropteroic acid. Synthetic antibacterial agents include sulfonamides (SULs) and trimethoprim (TMP). While TMP treats acute urinary tract infections, the early SUL chemicals were long used to prevent urinary tract infections. Human cells do not possess this enzyme activity. SUL medications function as DHPS competitive inhibitors, preventing the bacterial cell from producing folate, which results in [80]. Over the past few years, TMP resistance and significant SUL resistance have seen a noticeable increase. Pathogenic bacteria have exhibited remarkable evolutionary adaptability to the presence of TMP and SUL, as evidenced by their methods of resistance and spread. Despite this, Huovinen et al. (1995) reported alterations in the chromosomal architecture and regulatory processes of the *dhps* and *dhfr* genes, which code for the target enzymes DHPS and DHFR, respectively [81].

7. β-LACTAMASES

A four-sided β-lactam ring makes up the unique core structure shared by all β-lactam medications. Three main mechanisms were identified for resistance to β-lactam medications: the drug being hydrolysed by β-lactamase

enzymes, the drug altering its ability to bind to PBP to prevent interaction, and the existence of efflux pumps that can extrude β-lactam medications [82]. Different types of efflux pumps, known as multi-drug (MDR), can transport more significant quantities of chemicals. Their purpose is to remove harmful molecules from the bacterial cell. Furthermore, many of these pumps' resistance level is affected by the accessible carbon source [83]. Cephalosporinases and penicillinases are two types of β-lactamases that block β-lactam medications by hydrolysing a specific location within the β-lactam ring, causing the ring to open. Furthermore, according to Bush and Jacoby (2010), open-ring medications are unable to attach to their intended PBP [84]. β-lactamase enzymes are categorised based on features related to their structure and/or molecular functions. They fall under four major structural types. Gram-positive bacteria primarily contain β-lactamases from group A [84,85].

These enzymes can be inherited from the bacterial chromosome or acquired through a plasmid. Gram-negative bacteria belonging to the Enterobacteriaceae family possess β-lactamase genes on their chromosomes. This enzyme is also present in other Gram-negative bacteria, such as *Acinetobacter* spp., *Pseudomonas* spp., and *Aeromonas* spp. Enterobacteriaceae is a common family that contains β-lactamase genes transmitted by plasmids [86]. The ampicillin resistance gene, *ampC*, chromosomally encodes the first β-lactamase described, derived from *E. coli*. The majority of the time, this gene is expressed at a low level; nevertheless, mutations lead to an overexpression of the gene. Penicillins and the first generation of some cephalosporins are affected by β-lactamases encoded by the *AmpC* gene [85,87-89].

Table 3 displays a summary of the elements of antimicrobial resistance.

The human microbiome's commensal bacteria serve as clinical ARGs' primary reservoir and transmission route [60]. Several researchers [61,62] have unravelled the role of gut resistome and compared its similarity with those of pathogens. Rarely does commensal bacteria transfer ARG to pathogens. Pathogenic

Table 3. Examples of antimicrobial resistance elements. Taken after a few reports [85,87-89]

Drug	Drug uptake limitation	Drug target modification	Drug inactivation	Efflux Pumps
β-Lactams	Decreased numbers of porins, no outer cell wall	Gram-positive alterations in PBPs	Gram-positive, gram-negative β-lactamases	Resistance-nodulation-division (RND)
Cephalosporins	Changed selectivity of porin			
Penicillins Glycopeptides	Thickened cell wall, no outer cell wall	Modified peptidoglycan		
Lipopeptides		Modified net cell surface charge		
Aminoglycosides	Cell wall polarity	Ribosomal mutation, methylation	Aminoglycoside modifying enzymes, acetylation, phosphorylation, adenylation	RND
Tetracyclines	Decreased numbers of porins	Ribosomal protection	Antibiotic modification, oxidation	Major facilitator superfamily (MFS), RND
Macrolides		Ribosomal mutation methylation		ATP-binding cassette (ABC) MFS

bacteria and the human gut have nearly comparable ARGs and genetic settings, indicating GM's significance in forming clinical ARGs [63]. Geographical location, chemotherapeutics (such as antibiotics), and dietary modifications have all been linked to associations between the animal gut and environmental and human gut resistomes [90-92].

8. ASD AND MICROBIOME

Early-life antibiotic exposure can alter the microbiota composition, which may be a factor in ASD [93]. GI problems in ASD are explained by the fact that children with ASD are treated with a greater quantity of antibiotics than healthy children [14]. Moreover, oral antibiotics promote the growth of anaerobic bacteria in the gut, including *Desulfovibrio*, *Clostridium*, and phylum Bacteroidetes, which may exacerbate GI symptoms and autistic behaviours in people with ASD [94]. Compared to broad-spectrum and moderate-spectrum antibiotics, which increased the effect of ASD, the impact of using narrow-spectrum antibiotics was limited concerning autism [95]. It has been demonstrated that using several antibiotic classes while pregnant may marginally raise the incidence of ASD [20]. In the second and third trimesters of pregnancy, penicillin use was documented in 50% of instances of ASD. It has been demonstrated that taking sulfonamides when pregnant increases the likelihood that the child will become infantile [64]. Antibiotic use and ASD have not yet been proven to be related [14].

9. CONCLUSION

The connection between the gut microbiome, antibiotic resistance genes (ARGs), and autism spectrum disorder (ASD) is complex. Environmental factors like early birth, maternal infection during pregnancy, and antibiotic exposure are implicated in the onset and severity of ASD symptoms. The gut microbiome, which comprises diverse bacterial species and genetic reservoirs, is crucial for modulating immune responses influencing brain function and overall health.

Studies have shown that individuals with ASD have changes in their gut microbiota composition and an increased prevalence of antibiotic-resistant genes (ARGs). This finding suggests a potential link between gut dysbiosis, antibiotic exposure, and the manifestation of ASD symptoms. Furthermore, commensal bacteria in the gut can acquire and transmit ARGs, indicating the interconnection between environmental factors and human health. Therefore, Understanding the mechanisms underlying antibiotic resistance and its impact on the gut microbiome is crucial to developing targeted interventions and therapeutic strategies for individuals with ASD. Future research should focus on understanding the complex interplay between environmental exposures, microbial dynamics, and neurodevelopmental outcomes in ASD. By untangling these intricate relationships, we can develop personalised approaches to ASD management, improving the quality of life for affected individuals.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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