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Effect of antibiotics on physical and physiological development of children under 5—A scoping review

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Abstract:

The scoping review aimed to investigate and compile the effects of antibiotics on children under the age of five's physiological development. A PubMed, CINAHL, and Medline online database search was conducted, and related studies were included in the databases to carry out a more detailed search of the available literature utilizing keywords like "Antibiotics in children's"; "Children under 5"; and "Physiological Development, Physical Development," as well as Boolean operators to generate papers pertinent which were correlating with the objective of the study. It is imperative to demonstrate that a comprehensive, wide-ranging, and exhaustive search was carried out. MeSH words used for the search. MeSH is an is an effective tool for indexing and classifying literature on biology and health. MeSH terms are affixed to articles to enable precise and effective literature searches, guaranteeing that scholars, medical professionals, and other users can locate pertinent data within the extensive PubMed database. MeSH provides researchers with a standardized and structured method of indexing topics in the field of medicine and related disciplines, which aids in the identification and organization of pertinent articles during scoping reviews. PRISMA checklist was followed while doing the data collection and data extraction. The findings revealed that antibiotics hurt the physical and physiological development of children under 5. The study findings show that after exposure to antibiotics children get obese, it also affects the gut microbiota. Antibiotics also have an impact on the language and behaviors of children under 5. It also shows that children are more prone to get different medical disorders. These results highlight how crucial it is to make well-informed decisions about the use of antibiotics in pediatric care. To sum up, giving antibiotics to kids younger than five can have a big impact on how their bodies develop. This study also provides and implements guidelines that consider the possible long-term effects on the development of children under the age of five when prescribing antibiotics. Encourage healthcare professionals, parents, and other caregivers to learn about the proper use of antibiotics for young children as well as the possible risks of overusing or not using antibiotics at all. Promote funding and research for alternative approaches, such as targeted vaccines or probiotics, to treat and prevent infections in young children.

Keywords:

Antibiotics in children, drug effects on physiology, physical development, physiological development

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Introduction

Cognitive development and the establishment of a trajectory for continuous acquisition of typical cognitive skills are supported by the amazing development of the central nervous system, which starts in the prenatal period and continues throughout infancy. The establishment of a stable gut microbial colony in the gastrointestinal tract takes place concurrently with the growth and specialization of the brain. The gut-brain axis, a complex network of systems that connects the gut and the brain and controls physiological function, develops to set the physiological stage for future health. The gut microbiota's composition is altered by

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external stimuli that strongly influence the development of these organs and regulatory systems throughout critical periods.[1] Antibiotics have saved millions of lives and alleviated the suffering caused by infections, making them a blessing to human civilization.[2] Of all the drugs provided to children, antibiotics are the most frequently prescribed therapy and can be a lifesaver for children with bacterial illnesses.[3] Children frequently contract viral diseases, many of which affect preschoolers and lead to a high prescription antibiotic medicine use rate.[4] Antibiotics change the taxonomic makeup of the microbiome and decrease the diversity of the gut microbiota; this decrease in microbial richness is regarded as harmful to health.[5] Concern over the effects of early antibiotic use on children's long-term health and physiological development has grown over time.[6] Intervention studies carried out in low-income countries have shown a growth-promoting impact associated with the use of antibiotics in newborns and children. The formation of gut microbiota has been discovered to be significantly impacted by antibiotic exposure.[7] Early-life antibiotic usage has been shown to induce dysbiosis, which modifies the makeup of the intestinal microbiota and reduces microbial diversity. An increase in antibiotic-resistant bacteria and a decrease in helpful bacteria can arise from this dysbiosis brought on by early drug exposure. Research on animals has verified that modifying the gut microbiota during infancy with antibiotics can result in long-lasting physiological impacts, even after the microbiota has been restored.[8] Antibiotics are widely used to stimulate livestock's growth; however, it's still unclear exactly how this affects childhood obesity.[9] The formation of gut microbiota has been discovered to be significantly impacted by antibiotic exposure. Early-life antibiotic usage has been shown to induce dysbiosis, which modifies the makeup of the intestinal microbiota and reduces microbial diversity. I've tagged this as incomplete and am unable to come up with a reply. An increase in antibiotic-resistant bacteria and a decrease in helpful bacteria can arise from this dysbiosis brought on by early drug exposure. Research on animals has verified that modifying the gut microbiota during infancy with antibiotics can result in long-lasting physiological impacts, even after the microbiota has been restored.[10] According to a number of studies, children who were exposed to antibiotics during their early years of life are more likely to experience hay fever and food allergies. Moreover, an increased risk of inflammatory bowel disease has also been linked to early-life antibiotic use. Because antibiotics have been shown to decrease microbial diversity and change the balance of gut bacteria, it is thought that a disturbed gut microbiota contributes to the etiology of many illnesses.[11] Antibiotics are frequently used in the treatment of pediatric infections, and this is due to a number of contributing factors. These include the high rate of illnesses in this age group, the belief that antibiotics are an effective form of treatment, and the impact of societal structures on the decisions that parents and healthcare professionals make regarding the use of antibiotics. Mothers who are concerned about serious illnesses and feel antibiotics can reduce complications may be persuaded to seek antibiotic treatment for their children due to the societal association and representation of antibiotics as symbols of safe and effective treatment.[12] Numerous studies have emphasized the patterns and trends of pediatric antibiotic use in both hospital and outpatient settings. A brief course of antibiotics can alter a child's microbiota for up to six months, which may contribute to the development of chronic illnesses such as malnourishment, metabolic disorders, and autoimmune diseases. Additionally, children who are exposed to antibiotics run the danger of getting resistant bacteria, which could have a negative impact on their health in the long run. Understanding the trends and risk factors related to antibiotic prescriptions in this demographic is crucial to developing strategies and interventions to optimize antibiotic usage in children.[13] Antibiotic misuse, which includes giving prescriptions for viral respiratory illnesses when there is no benefit, is a recognized problem in the pediatric population and has caused great societal concern.[14] Antibiotic use, however, is not without its drawbacks. It has been demonstrated that the use of antibiotics alters the microbiome in both adults and newborns, causing an imbalance that may have detrimental long-term implications on health.[15] Serious infectious infections are prevented or treated using antibiotics, which also mitigate their effects. Due to their apparent safety and exceptional performance, they are frequently used without a demonstrable need.[16] Due to their impact on the microbiome, antibiotic exposure during critical developmental periods has raised concerns about the rising prevalence of childhood-onset health issues such as obesity, food allergies, ADHD, and asthma.[17] The microbial communities that inhabit the human body are crucial for the growth of the host's immunity, metabolism, and behavior.[18] Their establishment reflects selection over an evolutionary timescale, coinciding with host growth.[19] The transmission and development of the microbiome are adversely affected by cesarean delivery, formula feeding, and pre- and postnatal antibiotic exposure.[20] As a result, these practices may jeopardize the health of children. An increasing body of epidemiological research links the emergence of numerous illnesses to perturbations in the early-life microbiome[21] While the human microbiome's causative function remains unresolved, research on mice supports the idea that disruptions to the microbiome during critical developmental stages have long-term health effects.[22,23]

The threat posed by antibiotic resistance to public health is critical, particularly with regard to children. Data from the World Health Organization indicates that infections with bacteria resistant to multiple drugs result in 700,000 deaths annually, of which 200,000 or so are infant deaths. Approximately 70% of youngsters in a cohort of New Zealanders born in the middle of the 1990s had taken antibiotics within the first year of their lives.[24]

Almost all children have been treated with antibiotics for these common infections by the time they are five years old, with amoxicillin being the most commonly administered antibiotic.[25]

Early-life antibiotic exposure may have an impact on developmental outcomes through the formation of bidirectional linkages between the gut microbiota and the central nervous system during infancy and childhood. Since prescribing antibiotics for pediatric illnesses would be unethical, observational studies are the primary means of investigating this link in human populations. It is possible to investigate relationships between antibiotic exposure and neurodevelopment through longitudinal cohort studies that include data on both antibiotic use and developmental stages from infancy through childhood. In contrast to children who were exposed to antibiotics for the first time after the age of 12 months, our initial study on this subject indicated a negative correlation between exposure to antibiotics during the first year of life with negative behavioral, emotional, and cognitive results.[24]

This result was further supported by a different cohort study that found children who were given antibiotics during the first six months of life had increased issues with executive function, including impulsivity, attention, anxiety, and metacognitive skills, and significantly lower verbal and overall cognitive ability scores at age 11 on psychologist-administered intelligence tests.[26]

Research suggests that gene interactions with chronic antibiotic exposure throughout child raise the risk of mood disorders later in life. Long-term antibiotic use during childhood is linked to an elevated risk of anxiety and depression.[27]

The importance of doing this review is that it talks about how antibiotics might affect a child's growth, immune system, and gut microbiota, among other aspects of development. Nursing practice may be significantly impacted by this knowledge in a number of ways. First of all, it emphasizes how important it is for nurses to keep a close eye on young children's use of antibiotics. They need to be informed about the possible negative effects and issues that can arise from using antibiotics, like antibiotic resistance and disruption of the child's gut flora. To ensure that decisions about the appropriate use of antibiotics are made with knowledge, nursing practice should include comprehensive evaluations of a child's health history, including prior antibiotic use. Second, the paper highlights how crucial antibiotic stewardship is to nursing practice. It is the duty of nurses to promote the use of vaccinations and other alternatives, such as prudent antibiotic prescribing practices, when necessary. The article also recommends that nurses inform parents and other caregivers about the possible advantages and disadvantages of antibiotics. This entails teaching them on the appropriate use and dosage of antibiotics in addition to the significance of finishing the entire course of treatment. In addition, encouraging open communication, addressing any concerns, and educating parents about the possible long-term effects of antibiotics on their child's development are all important aspects of nursing practice

Materials and Methods

This review is for scoping. A range of online search engines were also used to locate databases that might include references. The specific criteria for selecting the studies were directly inspired by the review questions. There were written explanations provided for both inclusion and exclusion. Included were studies that emphasized children under five or defined their target demographic as infants or toddlers under five. Antibiotics of any kind are taken into consideration while treating youngsters. Children's physiological development, including height, weight, obesity, heart rate, respiration, cognitive function, and gastrointestinal function, has been evaluated in connection to antibiotic use. Every single result obtained satisfied the inclusion criterion. Reviews, abstract ideas, conference proceedings, letters, commentary, remarks, opinions, and book chapters were disregarded in favor of studies—with or without a comparison group—that were relevant to our research questions and addressed our research issues. Studies written in languages other than English were excluded. Using extensive critical evaluation principles, a more comprehensive quality assessment of the chosen studies was conducted. PEO criteria were considered, PEO criteria in a scoping review identify the target population, the exposure or intervention of interest, and the anticipated outcomes, aid researchers in methodically locating and mapping pertinent literature. Scoping reviews contribute to a thorough understanding of the available evidence in a particular research area by improving the precision and transparency of the review process by establishing clear PEO criteria. with a focus on the population of children under five who were exposed to antibiotics during their illness. Studies released between 2010 and 2023 will be included in the search. Information

on the use of antibiotics in children, study results, the effect of antibiotics, difficulties encountered, and suggestions will all be taken from publications that meet the eligibility requirements. A narrative summary will be included with the tabular and/or diagrammatic reporting of the results.

Strategies of Data Collection

Several data collection techniques can be used to carry out an extensive scoping assessment on the effects of antibiotics on children's physiological and physical health Search the literature: Use pertinent keywords associated with antibiotics, children's health, and physiological results to conduct a thorough search of databases like PubMed, Scopus, and Google Scholar. The databases that were chosen for this study were used throughout the whole data collection process. We looked through Medline, PubMed, and CINAHL. To lessen data saturation, logical operators and keywords were used in the search. It is imperative to demonstrate that a comprehensive, wide-ranging, and exhaustive search was carried out. MeSH words used for the search. Search strategy involved ((“Antibiotics in children”[MeSH Terms] OR (“Antibiotics”[MeSH Terms] AND “children under 5”[MeSH Terms])) OR ((((((“children *”[Title/Abstract] OR OR “pre-schooler”[Title/Abstract]) OR ““toddler*”[Title/Abstract]) OR “infant*”[Title/Abstract]) OR “child*”[Title/Abstract]) AND (((“Health*”[Title/Abstract] OR “physical *”[Title/Abstract]) OR “physiological”[Title/Abstract]) OR “development”[Title/Abstract]))) AND (“Growth”[MeSH Terms] OR ((((((((((((“G and D”[Title/Abstract] Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) criteria were followed. To guarantee research-endorsed updated methods for providing for expectant mothers, we only included publications from the previous 12 years.

Study selection

After conducting independent reviews of all the publications that were discovered using MESH terms in database searches, two writers collaborated with a third author to resolve any discrepancies. The full texts of the selected studies from level one were acquired, and each was subjected to an independent evaluation by the same two writers to ascertain eligibility. The reasons for exclusion were carefully categorized and documented. Data extraction. Each report's data was gathered independently by two reviewers. Using a typical proforma, information about the study's design, duration, participant characteristics, intervention description, impact of antibiotics, outcomes for children under five, findings, and limitations were all collected. Separately, two reviewers gathered information.

Quality and bias assessment

The following criteria can be used to assess the scoping review's quality and bias assessment:

Using a randomized controlled trial bias risk assessment tool, as advised by the international Cochrane manual 5, is mentioned in the first source.[28] This source suggests that the risk of bias in the randomized controlled trials that were included was evaluated using a trustworthy and well-known instrument. The source also states that the quality of the chosen research was evaluated by two reviewers separately, indicating a rigorous and exhaustive evaluation process.[29]

The second source also suggests evaluating bias risk using the Cochrane collaboration tool. In the research community, this instrument is well-known for assessing trial bias in randomized controlled trials. Additionally, the source claims that two researchers assessed the bias risk independently and cross-checked the findings, demonstrating a thorough and exacting evaluation procedure.[30]

The Cochrane Risk of Bias tool, a highly recognized instrument for assessing bias in randomized control trials, is also mentioned in the third source.[31] The source also states that the tool's primary objective is to evaluate the trial's internal validity and bias risk at various stages.[32]

Ethics and dissemination

This study will not involve any human subjects, nor will any data be directly gathered from them. Since the scoping review will solely rely on data that has been published, ethical approval is not necessary. The results of this investigation will be shared by means of talks at conferences, articles published in peer-reviewed journals, and conversations within professional networks.

Search results

After conducting a Boolean search for pertinent terms, 200 entries were found. As a result, only 78 records could be found in CINAHL, 38 in Medline, and 84 in PubMed. PRISMA flow diagrams were created and are shown in Figure 1. A few items were removed since they had no bearing on the study's topic. The abstracts of every article were looked at after the duplicates were eliminated. After 58 duplicates were eliminated, 142 records were deemed appropriate and qualified for the following screening. After 127 records were rejected for various reasons (antibiotics had no effect on physical or physiological development in 47 cases, and the age group of more than five years in 80 cases), two independent authors conducted the screening. Seven articles were eliminated from the remaining fifteen because there

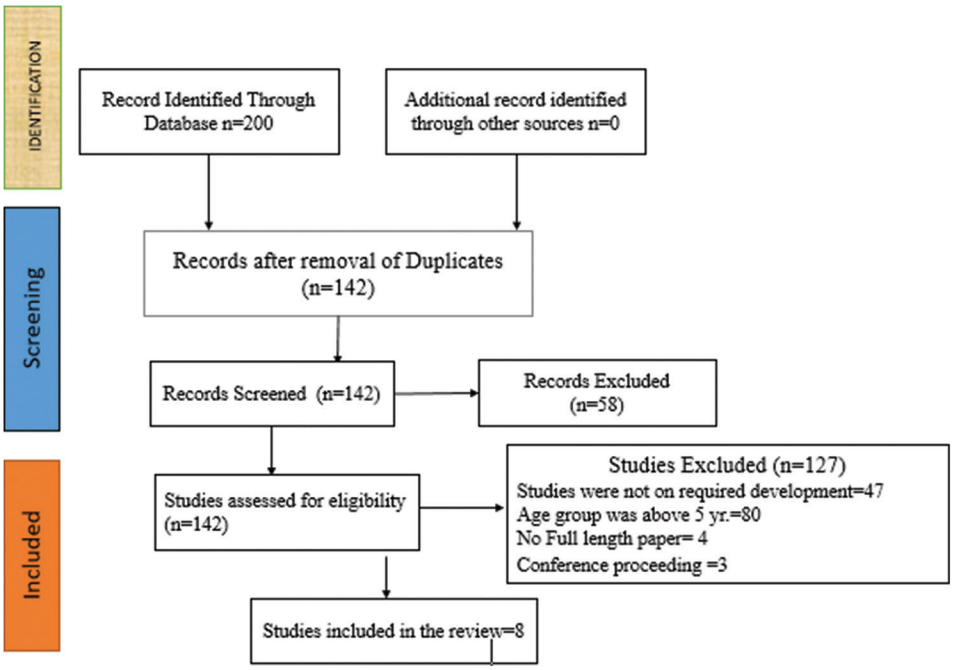

Figure 1: PRISMA diagram describing the study selection process

were no full-length papers (n = 4) or conference proceedings (n = 3).

Synthesis of results

The studies are summarized in Table 1. Studies on children under five indicate that obesity is observed following antibiotic exposure. Of these studies, one demonstrates alterations in language and behavior, while the other demonstrates the influence of antibiotics on gut microbiota. One study examines the effects of antibiotics on a number of different medical disorders. Convergent synthesis was used to synthesize the results, and a variety of pre- and post-intervention outcomes were collected and evaluated using self-reports, post-intervention questionnaires, and results that specifically addressed the three sections of the research study—the use of antibiotics, physical development, and physiological development.

Results

Antibiotics and physiological development

Youngsters under the age of five have special physiological traits that put them at risk for antibiotic use.[41]

Antibiotic misuse, including non-prescription use, is a major problem in this population. Many urban Chinese caregivers have reportedly self-medicated their kids with antibiotics, which highlights the need for improved guidelines and instruction regarding antibiotic use in this age group. Furthermore, research has revealed that even though they are useless in treating viral respiratory infections in children, antibiotics are frequently prescribed in these situations. In addition to adding to the issue of antibiotic resistance, this improper use of antibiotics raises the possibility of harmful gastrointestinal effects in young patients.[14] In addition, it is critical to include parents and medical professionals in initiatives aimed at reducing pediatric antibiotic overuse.[42] In conclusion, because of their physiological development and clinical traits, children under the age of five are especially susceptible to the improper use of antibiotics.

Therefore, it is critical to give top priority to initiatives that lessen the overuse and abuse of antibiotics in this population, with an emphasis on teaching caregivers and medical professionals about the proper use of antibiotics and the dangers of misuse. Youngsters younger than five are particularly susceptible to the negative effects of antibiotic use. They are particularly vulnerable to the harmful consequences of overusing antibiotics because of their developing bodies, as well as their heightened responsiveness and sensitivity to medications. Furthermore, giving too many antibiotics to kids younger than five can lead to the development of antibiotic resistance, which will make treating infections later on even harder. It's critical to evaluate parents' awareness of and comprehension of respiratory conditions and their management in order to address this issue. This can assist in creating focused educational initiatives and communication plans to encourage children under five to use antibiotics responsibly. Due

Table 1: Summary of articles reviewed for this scoping review

Author reference	Aim	Design	Sample Size	Impact	Key Findings
Bailey *et al*.[33]	to evaluate the influence of early childhood (ages 24–59 months) antibiotic prescriptions on childhood obesity.	Cohort Study	65 480 children	Anthropometric measurements were used to directly determine the outcomes of obesity.	Early childhood obesity has been linked to repeated exposure to broad-spectrum antibiotics between the ages of 0 and 23 months.
Gerber *et al*.[34]	to evaluate the relationship between childhood weight gain and early antibiotic exposure.	Retrospective longitudinal	38614 38522 92 twins	Weight was measured between the ages of six months and seven years during preventive health visits.	Antibiotic exposure during the first six months of life did not differ statistically significantly from no exposure in terms of weight gain until age seven.
Ventin-Holmberg *et al*.[35]	The purpose was to look into how antibiotics affect a baby's gut microbiota.	Cohort	37 21 in Exp gr 16 in Control group	antibiotic use affected the gut mycobiota,	Antibiotic use altered the gut microbiota, as evidenced by a greater relative abundance of Candida and greater diversity and richness in infants receiving antibiotic treatment.
Scott *et al*.[36]	to evaluate the relationship between obesity at age 4 and antibiotic exposure prior to age 2.	Cohort Study	21,714	Increased risk of child obesity	Early childhood obesity is linked to the administration of three or more antibiotic courses before a child turns two years old.
Kelly *et al*.[37]	Analyze the relationship between early childhood use of general practice (GP) healthcare, body mass index (BMI), and health.	prospective cohort study.	13,858	Increased childhood obesity	Obesity in children has been linked to a number of worse health outcomes, including more frequent use of primary healthcare.
Uzan-Yulzari *et al*.[38]	the relationship between a child's growth until the age of six years old and antibiotic exposure during and after the neonatal period	Cohort study	1,151	Increased BMI	neonatal boys who were exposed to antibiotics gained less weight and gained more height, but boys who used antibiotics later in infancy and childhood gained more weight and both boys' and girls' BMIs increased.
Slykerman *et al*.[39]	to examine, after adjusting for a number of variables, such as otitis media, the association between the age at which a child is exposed to antibiotics for the first time and their cognitive and behavioral development at 4.5 years of age.	Cohort Study	5589	Lower executive function scores, receptive language ability, and behavioral issues were linked to infants exposed to antibiotics during their first year of life.	antibiotic exposure during potentially delicate developmental windows is linked to later-life receptive language and behavior.
Zaira Avearsa[40]	To determine the degree to which exposure to antibiotics during the first two years of life is linked to the risk of immunological, metabolic, and neurobehavioral disorders that manifest in childhood.	Cohort Study	14572	An increased risk of childhood-onset asthma, allergic rhinitis, atopic dermatitis, celiac disease, overweight, obesity, and attention deficit hyperactivity disorder was linked to early antibiotic exposure.	The current study discovers strong correlations between early exposure to antibiotics and a number of different childhood-onset health conditions.

to their physiological development and clinical traits, children under the age of five are especially susceptible to the improper use of antibiotics. As a result, initiatives to strengthen legislation and education regarding the use of antibiotics in this age group should be undertaken.[43]

Discussion

Although it is well known that antibiotic exposure can have unintended side effects, little previous research has examined how antibiotic use affects children's physical and physiological development. Due to their frequent exposure to antibiotics and the sensitive period of microbiome development that is childhood, to improve antibiotic stewardship practices, researchers must examine how exposure to antibiotics affects children's physical and physiological development. This scoping review set out to identify existing gaps in the field, highlight the known effects of antibiotics on the development of the body and mind, and highlight potential bias across studies. Because antibiotics are widely available, the study's findings draw attention to the current risk that using them poses to children under the age of five as well as the effects that it has on those children's physical and physiological health. These findings have global implications. Children's physiological development may be negatively impacted by antibiotic misuse and abuse.

In the present study, findings show that after antibiotic exposure children are more prone to get obesity as five studies have shown the correlation of antibiotics exposure and obesity. One study also shows that antibiotic Exposure has an effect on during receptive language and behavior. Another study shown that antibiotic use altered the gut microbiota, and it affected the children's immunity. One study shows that exposure children to antibiotics makes them prone to different health diseases like asthma, allergic rhinitis, etc., The synthesis of this scoping review shows that antibiotics have detrimental effects on the physical and physiological development of the children under 5.

The study findings are supported by the studies that previously showed the impact of antibiotics.

The maturation of the gut microbiota community is necessary for a child's healthy development, but antibiotic exposure can impede this process. Antibiotic abuse and overuse in children can have a negative impact on their physiological development. Antibiotic exposure can interfere with the gut microbiota community's maturation, which is essential for a child's healthy development.[42,44] This interference can affect bone, adipose, and muscle tissue growth in addition to immune system development. Concern over the overuse of antibiotics and its effect on bacterial resistance is also growing.[45] These results highlight the critical need to lessen children's overuse and abuse of antibiotics.[42] The improper use of antibiotics in children, such as when they are prescribed for viral respiratory infections for which there is no benefit, is a well-known issue that has raised significant social concern.[14] In addition to antibiotic resistance, improper antibiotic use in children can have adverse gastrointestinal effects. Strategies that evaluate parents' knowledge and comprehension of respiratory illnesses and their treatment must be developed in order to address the problem of antibiotic overuse in children.[14] In the West, the most common kind of medication prescribed to kids, even newborns, is an antibiotic. Antibiotic treatments can have unfavorable effects in addition to changing once-fatal infections into relatively mild illnesses. It has been demonstrated that antibiotics significantly change the composition of gut microbiota in humans, animals, and child models. Antibiotic effects on the gut microbiota may result in additional health issues because the microbiota is essential for immunity, metabolism, and endocrinology. In this review, we provide an overview of how antibiotics affect children's microbiomes and discuss how these effects are related to long-term issues with behavior, obesity, allergies, autoimmunity, and other conditions.[46]

Conclusion

The scoping review aimed to explore and summarize the impact of antibiotics on the physical and physiological development of children under 5. The purpose of the scoping review was to investigate and compile the effects of antibiotics on children under the age of five's physiological development. It is clear from the reviewed sources that the management of children's illnesses is significantly influenced by the practices, knowledge, and attitudes of parents regarding the use of antibiotics.[47] These results highlight how crucial it is to make well-informed decisions about the use of antibiotics in pediatric care. To sum up, giving antibiotics to kids younger than five can have a big impact on how their bodies develop. Healthcare professionals must inform parents about the proper use of antibiotics and the possible risks that come with misusing them. This will lessen the possibility of harm to children's physical and physiological development and encourage the responsible use of antibiotics. It also draws attention to the necessity of more studies and initiatives to deal with the abuse and overuse of antibiotics in this susceptible group. Additionally, given the specific dosage, medication formulations, and monitoring requirements for children, governments and health systems must prioritize providing access to antibiotics for the treatment of neonatal infections in developing nations. The results highlight the significance of using antibiotics responsibly and the necessity for lawmakers and healthcare professionals to give education, interventions, and access to the right medications top priority when treating neonatal infections in developing nations.[48] The scoping review concludes by highlighting the possible effects of antibiotics on children under the

age of five's physical and physiological development. By doing this, we can safeguard kids from the possible harm that comes with overusing antibiotics and support their normal physiological growth.

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Ethical Approval considerations

Ethical approval was taken for this study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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