

# Strong evidence demonstrates the relationship between autism spectrum disorder and loss of strains of Escherichia coli bacteria

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**Abstract:** Despite the great interest that autism receives in various specialties, there is still a need for further investigation and understanding of its pathophysiological mechanisms. In this article, we will highlight the potential role of Escherichia coli bacteria in the occurrence of autism spectrum disorder.

Recent studies have explored the possible relationship between Escherichia coli (E. coli) and autism. Escherichia coli is a common bacterium in the environment, including the human intestine.

Urinary tract infections caused by Escherichia coli (E. coli) are among the most common bacterial infections affecting pregnant women, and antibiotics directed at killing strains of E. coli once they have exited the colon and caused inflammatory diseases are becoming increasingly popular.

In this article, we will study the possible relationship of these bacteria, if eliminated, to the occurrence of neurological disorders in the child before birth and during the breastfeeding period. We will also provide a range of evidence. Related to biomarkers that demonstrate the strength of the relationship between the missing activity of Escherichia coli strains and the biological disorders observed in people with autism spectrum disorder.

In addition, we will present and discuss therapeutic interventions and strategies for infection prevention and control, especially alternative treatments to avoid causing harm to the fetus or infant.

**Keywords:** autism spectrum disorder, Escherichia coli, Antibiotics, Genetic activity.

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## **1-Background:**

Autism spectrum disorder (ASD) is a prevalent neurological condition that affects communication, social interaction, and behavior, typically appearing in early childhood and lasting throughout a person's life (Mukherjee & Mukherjee, 2018).

The Algerian Ministry of Health indicates, through the website “Autism in Algeria”, which it launched to support and keep pace with researchers, educators and parents to better understand and receive support and specialized knowledge, that there are approximately 5,000 children with autism in the country.

And in the United States of America the Centers for Disease Control and Prevention (CDC) reports that One in every 39 children suffer from autism, making it one of the most common developmental disorders after intellectual disability.

Recent studies have highlighted a potential relationship between E. coli bacteria and autism, emphasizing the need for further investigation (Horváth & Perman, 2002). The Centers for Disease Control and Prevention (CDC) reports that nearly a 24 million children over the world suffer from autism, making it one of the most common developmental disorders after intellectual disability (Mukherjee & Mukherjee, 2018). Individuals with ASD may experience difficulty with verbal and non-verbal communication, social interactions, repetitive behaviors, and specific interests, with varying severity and extent of symptoms (Chakraborty et al., 2020). Moreover, there is a strong link between gastrointestinal symptoms and the severity of autism, with lower levels of certain gut bacteria observed in individuals with ASD, partly due to probiotic usage (Deng et al., 2022).

E. coli bacteria are commonly found in the intestines of humans and animals, with some strains causing severe illness, especially in cases of food- or water-borne infections, leading to symptoms such as diarrhea, vomiting, fever, and abdominal pain (Horváth & Perman, 2002). The CDC estimates approximately 265,000 cases of E. coli infections in the United States annually, prompting preventive campaigns to mitigate the impact of these infections (Horváth & Perman, 2002). It also took preventive measures that would reduce the number of people infected, as the guardian authorities adopted a set of measures, the most important of which is giving antibiotics to animals intended for consumption in order to kill Escherichia coli bacteria for fear of transmitting them to citizens when they consume meat and causing epidemic waves. This measure has serious consequences because a pregnant woman's consumption of meat treated with antibiotics is similar to her consumption of antibiotics, and studies have confirmed that there is a relationship between the consumption of antibiotics by pregnant and breastfeeding women and an increased risk of the child developing autism. (Lau et al., 2013)

In conjunction with the increase in the number of people with autism in USA, as the records the largest percentage of people with autism, far from global rates that do not exceed one autism case for every 160 births on average.

Additionally, urinary tract infections, often affecting pregnant women due to the pressure of pregnancy on the colon and hormonal disorders, are closely linked to E. coli. (Wuwuti et al., 2022).

In this article, we will try to answer the following question: What are the arguments that strengthen the possible relationship between autism and the bacteria Escherichia coli?

## **2-Urinary tract infections and their relationship to autism:**

Urinary tract infections (UTIs) are a common type of bacterial infection that can occur in any part of the urinary system, including the kidneys and bladder. While anyone can get a UTI, they are more prevalent in women than men, Especially pregnant and breastfeeding women due to hormonal disorders, pregnancy stress, and the risk of infection due to weak immunity.

Research has indicated a possible link between urinary tract infections, especially those caused by Escherichia coli bacteria, and autism. (Billips et al., 2007; Fatimah et al., 2021) One study found that pregnant women who had a UTI during pregnancy were more likely to

have a child with autism than those who did not have a UTI. While the precise mechanisms underlying this relationship are still not well understood.

(Zerbo, 2015)

The inflammatory response triggered by urinary infections during pregnancy may play a role in affecting brain development and increasing the risk of autism (Agace et al., 1993). Furthermore, the impact of *E. coli* may be amplified by other factors, such as changes in the gut microbiome or immune system dysfunction, Hormonal disorders ultimately affecting brain development and increasing the risk of autism (Selim et al., 2018). However, research findings on the potential link between *E. coli* bacteria and autism disorder have yielded mixed results, with some studies reporting an association (Wang et al, 2017), while others found no such association (Hasanzadeh et al, 2020).

It is worth mentioning that treatment of urinary tract infections during pregnancy can reduce the risk of harmful outcomes for the fetus and the development of neurodevelopmental disorders such as autism, especially the necessity of avoiding antibiotics because they are a source of danger to the integrity of the microorganisms in the intestine and colon, which means that the fetus is exposed to the loss of its genetic activity. He is in his mother's womb because antibiotics reach him through the placenta.

### **3- Autism and antibiotics directed to kill pathogenic *Escherichia coli* bacteria**

It should be noted that there are many studies that have linked taking antibiotics during pregnancy and breastfeeding and the child developing autism spectrum disorder. (Atladóttir et al, 2012)

The study examined antibiotic use in Swedish pregnancies and early childhood (2006–2016) and its association with autism and ADHD in children. Findings revealed 25.9% maternal antibiotic use and 41.6% early-life exposure, notably penicillin. Both maternal and early-life antibiotic exposure showed increased risks for autism (OR = 1.16–1.46) and ADHD (OR = 1.29–1.90), suggesting a potential dose-response relationship. This highlights a possible link between antibiotic use and neurodevelopmental disorders, emphasizing the need for further investigation into their causal relationship and mechanisms involved. (Njotto et al, 2023)

Many recent studies suggest that prenatal exposure to antibiotics may increase the risk of developing ADHD and ASD later in life. (Li et al, 2023)

It should be noted that Epidemiological and twin studies suggest that ADHD frequently co-occurs with and shares genetic susceptibility with autism spectrum disorder (ASD) and ASD-related traits. (Lin et al, 2023)

### **4-Glutathione metabolism problems in people with autism and its relationship to *Escherichia coli* bacteria**

The GSH(Glutathione) plays a key role in the detoxification of xenobiotics and maintenance of balance in intracellular redox pathways. Recent data showed that imbalances in the GSH redox system are an important factor in the pathophysiology of ASD. (Bjørklund et al, 2021) GSH is abundant in all mammalian cells, where it represents the only thiol-endowed peptide with a significant role in the cellular redox balance.

The role of an impaired GSH signaling pathway in ASD is yet poorly understood. To date, very few clinical trials suggesting the role of GSH/GSSG in ASD. These limited studies addressing the role of an unbalanced reduced/oxidized glutathione ratio (GSH/GSSG) as a possible causal factor in ASD

Several studies have indicated that children with autism spectrum disorders have altered glutathione metabolism which could play a key role in the condition. (Main et al, 2012)

If we searched for the relationship of *Escherichia coli* bacteria to glutathione metabolism, we would find that they have a direct and strong relationship with it, which was confirmed through laboratory studies, which reached that the  $\gamma$ -glutamyl transpeptidase from *Escherichia coli*, is a key enzyme in glutathione metabolism, and its reaction intermediate, Researchers have determined the crystal structure of GGT from *Escherichia coli* K-12, which is one of the strains of *Escherichia coli* bacteria with beneficial genetic and biological activity in IBS, and

which may be one of the strains that eliminated, whether by antibiotics or for any other reason. It puts the child at risk of developing autism. (Okada et al, 2006)

### **5- Autism spectrum disorder and abnormal sulfur metabolism**

Sulfur is a ubiquitous element of the Earth crust, is an essential component of life.

There are multiple lines of evidence for an impaired sulfur amino acid (SAA) metabolism in autism spectrum disorder (ASD) (Indika et al, 2021).

On the other hand, many studies confirm the relationship between Escherichia bacteria and sulfur metabolism, (Sekowska et al, 2000) (Gyaneshwar et al, 2005).

The study by Sekowska et al. (2000) demonstrates the close relationship between Escherichia coli bacteria and sulfur metabolism. The researchers' analysis of the mechanisms involved in acetyl nicotinamide adenine dinucleotide (NAD) compensation in E. coli revealed that the availability of sulfur plays a crucial role in regulating this process. The study also uncovered multiple chemical reactions that control sulfur metabolism and its impact on bacterial strains.

On the other hand, Gyaneshwar et al. (2005) showed that E. coli bacteria have the ability to convert organic sulfur compounds into gaseous hydrogen. They discovered a correlation between the conversion of sulfur compounds and the development of E. coli's capability to utilize gaseous hydrogen as an energy source, highlighting the role of sulfur in E. coli metabolism and its adaptation to the environment.

In summary, both studies provide strong evidence for the relationship between E. coli bacteria and sulfur metabolism, shedding light on the importance of chemical reactions occurring within bacteria to adapt to their surrounding environment.

### **6- Epidemic waves of Escherichia coli bacteria and autism:**

Epidemic waves of Escherichia coli bacteria and autism:

Epidemiological studies conducted by the World Health Organization reported a significant increase in the prevalence of autism spectrum disorder (ASD) in the United States of America, and when observing the health situation in the United States of America, we find that Escherichia coli is an endemic disease and leads to epidemic waves every year, One of the proposed hypotheses to explain this disorder is the excessive use of antibiotics directed to kill Escherichia coli bacteria when they cause disease, in pregnant and breastfeeding women. This exposes fetuses and infants to the risk of losing beneficial strains in the colon while they are in a state of extreme weakness, leading to the loss of their genetic activity. And thus, the occurrence of autism spectrum disorder.

These findings highlight the need for continued and rigorous investigation into the underlying mechanisms of autism and potential risk factors.

One theory is that E. coli infections during pregnancy may lead to the production of inflammatory molecules that can cross the placenta and affect fetal brain development.

Another possibility is that toxins produced by E. coli bacteria could directly damage the developing brain, leading to neurodevelopmental disorders such as autism. Additionally, some researchers suggest that the gut-brain axis may play a role in the observed link, with E. coli infections disrupting the microbiome and affecting brain function. As with any emerging area of research, it is important to consider multiple hypotheses and approaches in understanding the potential mechanisms underlying the link between E. coli bacteria and autism disorder. Additionally, further studies are needed to confirm and refine these theories, and to explore other potential mechanisms that may contribute to this complex relationship. (Urakubo et al,2001)

### **7- public awareness about the potential link between Escherichia coli bacteria and autism**

Efforts to increase public awareness and support for individuals with autism should include community-based programs, public education campaigns, and early intervention services. These programs can provide families with the tools and resources necessary to support their ones with autism, while also promoting inclusion and acceptance of individuals with the

disorder in society. Moreover, research and advocacy organizations must continue to push for further research into the link between *Escherichia coli* bacteria and autism disorder. This research is necessary to develop effective preventive strategies and treatments for individuals with the disorder. To ensure the success of these efforts, it is essential to engage with a range of stakeholders, including policymakers, healthcare providers, community leaders, and individuals with autism and their families. With increased public awareness and support, we can work towards a future where individuals with autism can achieve their full potential and lead fulfilling lives.

### **8- Ethical Considerations and Controversies**

As with any scientific study, the relationship between *Escherichia coli* bacteria and autism disorder has been subject to ethical considerations and controversies. Research involving human subjects must adhere to strict ethical guidelines to ensure the safety and well-being of participants. Furthermore, the potential implications of the findings must also be carefully evaluated. Some critics have raised concerns about the possible stigmatization of individuals with autism or those who carry *Escherichia coli* bacteria. Others have questioned the validity of the research and the extent to which it can be generalized to the wider population. Some have even suggested that the focus on a bacterial cause of autism may detract from other important research areas. Despite these controversies, responsible and transparent research practices can help mitigate potential risks and maximize the benefits of scientific inquiry. Collaboration between researchers and community stakeholders can help ensure that studies are conducted with due regard for ethical considerations and that findings are appropriately communicated to the public.

### **9- Conclusion**

The potential link between *E. coli* bacteria and autism disorder is an area of increasing interest and concern. Available evidence indicates that the biological indicators that confirm this relationship are many and complex, especially in the field of molecular biology, microbiology, and in the field of biochemistry.

Urinary tract infections caused by *Escherichia coli* during pregnancy may contribute primarily to the development of autism in some individuals.

However, the danger does not lie in the infections themselves, but rather in how they are treated, which uses antibiotics directed to kill *Escherichia coli* bacteria specifically, and sometimes broad-spectrum antibiotics are used to treat them during the mother's pregnancy or breastfeeding period, and this is what constitutes a real danger. It affects the bacterial balance in the colon of the fetus or infant, exposing him to the loss of genetic activity of strains of *Escherichia coli* bacteria and entering into a spiral of neurological, behavioral and psychological disorders.

Preventive measures, such as improving hygiene practices and treating infections in a timely and natural way, may help autism prevention efforts succeed. However, more research is needed to better understand the mechanisms behind this association and to develop more effective prevention strategies. Furthermore, public awareness and support for affected individuals and their families is crucial,

We must also unite efforts to enhance our understanding of the relationship between *Escherichia coli* bacteria and autism, which will enable us to take important steps towards improving public health through prevention, and then move to support efforts to find a final treatment for this complex disorder.

### **10- Recommendations**

By identifying of the potential link between *Escherichia coli* bacteria and autism disorder, preventive measures are of utmost importance.

Among the preventive measures we mention:

- 1 - It is necessary to monitor the child's temperature continuously in the event of his illness, because high temperatures lead to the killing of beneficial intestinal bacteria that are sensitive to heat, and thus the loss of their broad genetic activity, most notably *Escherichia coli*.
- 2- Avoid taking antibiotics by pregnant or breastfeeding women

3- Do not take excessive amounts of antacids during pregnancy, because they cause a change in the environment suitable for the life of microorganisms in the fetus' intestines, which are in a state of weakness and small numbers, which exposes the child to their loss.

4- The pregnant woman's commitment to eating healthy and avoiding excessive use of hydrogenated oils and unhealthy foods

5- Pregnant women should take extra care to avoid urinary tract infections, such as by drinking plenty of water. Seeking prompt treatment for any symptoms of urinary infections is essential to prevent their spread.

6- dietary modulation followed by administration of microbiota modulators is a promising option for treating ASD-related behavioral and gastrointestinal symptoms

These strategies should be thoroughly evaluated for safety and efficacy before widespread implementation. The study of *Escherichia coli* bacteria and their relationship to autism disorder remains an active area of research. By taking preventive measures and conducting further research, we can potentially reduce the risk of autism in vulnerable populations and improve public health outcomes.

7- It is a start to reconsider the established idea of the brain's control over mental processes, which blatantly contradicts what the Holy Qur'an stated that the mind exists in the human heart, as the Qur'an emphasizes that sensory input reaches the heart, who processes it and decides how to interact with it mentally and emotionally. Then, it is sent to the brain as it is the executive system for the heart's commands.

We firmly believe that working to confirm this Qur'anic truth is essential to understanding the causal mechanism for the occurrence of neurological diseases and functional sensory disabilities, such as autism, functional mental disability, functional blindness, functional hearing loss, and all diseases whose cause remains unknown to this day.

There is confusion among researchers about the mechanism of operation of the internal cardiac nervous system, as well as the work of the brain and its relationship to the heart.

It should be noted that cases of functional hearing loss have been confirmed to occur due to some types of antibiotics, such as the drug ciprofloxacin, which causes hearing loss as a serious side effect

. This confirms that the strong relationship between bacteria and human mental activity is a very strong relationship, but it is between bacteria. And the heart, specifically the immune macrophage cells residing in the heart and not between the bacteria and the brain, and this is what removes the blood-brain barrier that baffled scientists when they tried how bacteria affect the mind in the presence of this barrier.

8- We propose to investigate the possibility that the transfer of sensory input from the senses to the internal cardiac nervous system occurs through signaling proteins, and that the transfer from the heart to the macrophage cells residing in the heart and then to the brain is via the beta-amyloid protein produced by cardiac macrophage cells.

9- The presence or absence of beta-amyloid protein in the cerebrospinal fluid of people with autism spectrum disorder should be examined.

10- Given the huge amount of laboratory studies trying to understand the cause of autism spectrum disorder, to no avail, the matter has become a vicious circle.

We must Encouraging researchers interested in understanding the causal mechanism of autism spectrum disorder to conduct interdisciplinary studies aimed at providing transformative knowledge that moves us from a misunderstanding Given the huge amount of laboratory studies trying to understand the cause of autism spectrum disorder, to no avail, the matter has become a vicious circle. to a new beginning from creative perspectives.

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