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Journal of Neuroscience and Neurological Surgery
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Review Article

The Prevention of the Birth of an Autistic Child is Simpler than its Cure

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Received date: January 30, 2023; Accepted date: February 17, 2023; Published date: February 27, 2023

Citation: Ayushi Goyal and Milind Parle (2023), The Prevention of the Birth of an Autistic Child is Simpler than its Cure, *J Neuroscience and Neurological Surgery.* 13(2); DOI:**10.31579/2578-8868/262**

Abstract

Impressive intellect and extrovert nature exhibited by the child spring from both, the supremacy of protective factors during nine months of the gestation period and the favorable genes of the parents. There is no approved allopathic, homeopathic, or ayurvedic medicine for the treatment of autism spectrum disorder or any neurodevelopmental childhood disease for that matter. The challenges faced by the lady during pregnancy and the delivery of the child, therefore need to be delicately addressed so that the birth of an abnormal child does not occur in the first place. The intellectual and physical personality of the unborn child is dependent on the sound health of the pregnant lady during gestation, proper nutrition, and a loving home environment. Thus, the prevention of the birth of an autistic child is the only reasonable option available at present and appears to be simpler than its cure. We believe that the society at large in India and around the world would greatly benefit from this review article.

Key words: autism; protective; risk; pregnant lady; transition

Introduction

Preamble: Autism Spectrum Disorder (ASD) is an irreversible, lifelong disability adversely affecting the victim as well as the family of the victim, for the whole of their lives since there is no appropriate medicine available today for treating this childhood disorder. ASD is a chronic, multi-factorial, neurodevelopmental childhood disorder in which toddlers grow in an unorthodox fashion. It is characterized by poor communication, deficiencies in cognition, abnormal behavior, and defective reciprocal social interaction. [1]. The exact cause of ASD is yet not identified, therefore it's a tough task to treat this complex, heterogeneous disorder with allopathic medicines [2]. Furthermore, no biomarker has been attributed to be responsible for the pathogenesis of ASD. In this scenario, a comprehensive strategy involving alternative systems of medicines needs to be adopted to boost the life quality of the family having an autistic child. Several nutritional strategies have been proven in recent research to lessen the severity of the basic symptoms of ASD like repetitive behavior, social and communication issues, self-harm, tantrums, and violence [3]. Developmental abnormalities in the unborn child seem to be associated with the quality of the pregnant mother's diet, fitness, and lifestyle [4]. The mother's daily diet and caring family ambiance influence the growth and robustness of the child [5]. Thus, appropriate and timely measures, when adopted during the sensitive phases of the pregnancy would help in preventing the birth of an abnormal child. The authors have identified both, the protective factors and risk factors precisely operating during pregnancy and made a modest attempt to give concrete recommendations to prevent the birth of a retarded child in the first place, thereby warding off the consequent embarrassment. We believe that the society at large in India and around the world would greatly benefit from this review article.

Prevalence: Autism Spectrum Disorder (ASD) is currently regarded as a toddler disorder with the highest prevalence of 1.00% worldwide because it's a lifelong burden and has no known cure. ASD has generated a significant deal of attention among researchers. Lately, a dramatic increase has been reported in ASD cases globally [6, 7]. The rise in the frequency of autistic cases may be due to better autism diagnosis and increased public knowledge [8]. The frequency of Autism has been tracked globally over the past three decades by ongoing epidemiological surveys. Autism cases have been steadily increasing, according to regular surveillance in many countries. There were 62 million ASD patients reported worldwide in 2016. ASD was diagnosed in one out of every 59 (1.7%) eight-year-olds, as per the "Autism and Developmental Disabilities Monitoring (ADDM) Network" estimates [9]. ASD affects 1 out of every 89 children in European nations, which is approximately the same in the United States [10]. The incidence of ASD is substantially higher in boys than in girls, according to several publications

in the literature. [11,12]. Autism may go unnoticed, be misdiagnosed, or be detected at an advanced age in girls since there is not much information available about female instances of autism [13,14]. Recent research suggests that the higher frequency of Autism in boys than in girls may be due to a "female protective effect". All racial and ethnic groups, whether in wealthy or underdeveloped nations, have been reported to exhibit autism instances. According to the "Centers for Disease Control," autism affects about 185 out of every 10,000 children in the United States, 152 out of every 10,000 in Canada, 161 out of every 10,000 in Japan, and 100 out of every 10,000 children in France. Italy, Holland, and Germany have the lowest prevalence rates [15]. India is a very populous country with almost 1300 million inhabitants, of whom 430 million are children between the ages of 0 and 15. ASD is estimated to affect more than 2 million children in India [16]. In India, the prevalence of autism in children under the age of 10 was found to be 15 instances per 1000, with the majority of these cases coming from villages [17]. This complex illness afflicting babies probably goes underdiagnosed in India and continues to remain undocumented. [16, 18, 19].

Historical Background: Although autistic behavior has persisted for thousands of years, it has just been precisely identified, coined the nomenclature as Autism Spectrum Disorder (ASD), and has its unique traits and clinical symptoms recognized in the last eight years only. The creation of the conceptual framework for ASD has been appropriately credited to Swiss physician Paul Eugen Bleuler, Austrian child specialist Hans Asperger, and Austrian-American psychiatrist and social activist Leo Kanner [19]. However, the role of Russian lady psychiatrist GrunyaEfmovnaSukhareva, who first labeled the illness as schizoid psychopathy in 1925 and changed its term to autistic psychopathy in 1959, was left unacknowledged [19]. The phrase "autistic children" was first used to describe people with developmental disabilities in 1944 by a Viennese child specialist named A. Ronald, who was working in Darjeeling, West Bengal (India). The techniques utilized by Tito's mother and detailed in Tito Mukhopadhyay's book [written by an eleven-year-old, Bangalore kid suffering from autism] "Beyond the Silence: My Life, the World, and Autism" have generated a lot of interest worldwide [19]. In recent years, there has been a tremendous increase in autism awareness in India.

Types of Developmental Disorders: Attention Deficit Hyperactivity Disorder (ADHD), autism, learning problems, intellectual disability, motor disorders, cerebral palsy, Asperger's disorder, down's syndrome, vision & hearing impairments, and Rett syndrome are only a few examples of developmental disorders.

Comorbidities: Autism is frequently associated with co-morbid conditions such as depression, schizophrenia, schizoaffective disorder, anxiety disorder, bipolar affective disorder, epilepsy, Down syndrome, Tourette syndrome, hypothyroidism, intellectual disorder, metabolic disorders, hypertension, etc. [19, 20].

Symptoms and Diagnosis: The clinical signs and symptoms of autism spectrum disorder (ASD) appear in the early developing years of the child and persist throughout the child's life. Together with persistent difficulties with social interaction and reciprocal communication, ASD is characterized by abnormal behavior, and constrained activities. These clinical symptoms are present from early childhood through adulthood to old age and cause substantial deficiencies in social, occupational, or fundamental functioning domains [2]. ASD may consist of a mix of primary symptoms that are universal and secondary symptoms that vary significantly and are suggestive of other co-morbidities [21]. Despite the extensive investigation into developmental abnormalities for more than a century, no trustworthy biomarker is identified to help in the precise detection of ASD. As a result, ASD is still diagnosed precisely based on symptoms classified in the domains of social skills and behavioral patterns, with the help of the caregiver's experience.

Causes /Risk factors of ASD: The risk factors acknowledged widely by scientists, which contribute to the birth of an abnormal child include defective genes of the parents, toxic environment, compromised immune system of the expectant mother, prenatal, and perinatal factors, gynecological interventions, and postnatal factors, which work independently or in combination to alter the functional capacity of the brain of the abnormal child. **Genetic make-up:** Genetic make-up appears to play an integral role in causing autism. Several reports suggest that autismcould be an inherited disorder. No particular gene mutation has been recognized with ASD. However, an individual gene appears to play a very trivial role in ASD, even though more than 400 genes are found to be strongly associated and 200 genes weakly associated. More recent research points to the possibility that ASD is a multi-factorial, multi-path-way genetic disorder that doesn't obey classical Mendelian inheritance [2]. Advances in computational technologies and datamining are expected to disentangle the genetic aspects of ASD. The genetic architecture of ASD is extremely diverse. Mutated genes interfere with normal physiological functions including appropriate brain development, synapses, and bones and muscle formation, thereby producing autistic symptoms. **Adverse environment:** The adverse environment [2] is emerging as a powerful determinant for the development of ASD, although this may be a precipitating factor in individuals having susceptible genes but not a primary causative factor alone **(Fig. 1)**. Cumulative neurotoxicant exposure during the sensitive phase of pregnancy periods affects the normal development of the neonate, resulting in mental retardation by interfering with neuronal circuit formation causing disorganization of various parts of the fetal brain. A toxic environment could be an absolute cause of fetal brain damage and may stimulate gene mutation in susceptible individuals. Toxicants suspected to be involved in ASD include insecticides, polychlorinated biphenyls (PCBs), harmful wastes,air/ water pollutants, mercury, radiation, diesel exhaust, volatile organic compounds, nitrogen dioxide, and heavy metals [2].Investigations have been carried out to study the influence of adverse environments at various stages of pregnancy. Interestingly, a link was observed between polluted air and ASD. Therewas a positive correlation between the cumulative presence of particulate matter in the vicinity of expecting mothers during the third trimester of pregnancy and autism. In another investigation, an interconnection between post-partum nitrogen dioxide (a vehicular pollutant) and autism was observed [2]. Studiesindicate that the pathogenesis of ASD involves a complicated interplay between genetic factors and adverse environment which act synergistically or laterally during vulnerable times of embryonic development, imparting increased sensitivity to thetoxic effects of the environment thereby enhancing the probability of developing a child with autism. **Prenatal, Perinatal, and Postnatal Factors:** ASD might be considered, at least in some cases, a disorder of fetal programming. Consumptionof medicines (such as thalidomide, valproic acid, misoprostol, and acetaminophen) having teratogenic effects, and use of alcohol, or tobacco during pregnancy constitute important prenatal factors causing ASD [2, 27]. It is a well-established fact that exposureto certain substances like mercury, lead, polychlorinated biphenyls, phthalates, pesticides, insecticides, and radiation during the prenatal period produces autism in children **(Fig. 1)**. Maternal infection during pregnancy can result in behavioral abnormalities and neuropathologies in the neonate. The uterine ambiance has a profound impact on the development of the fetus. The compromised mother's health can deeply affect the long-term mental and physical health of the developing embryo. Other prenatal factors, like short inter-pregnancy spacing, abnormal gestational age, multiple pregnancies, gestational hemorrhage, gestational diabetes, and advanced parental age might be linked to an increased incidence of ASD [2]. **Gynecological Interventions:** Gynecological interventions that are used in Assisted Reproductive Technologies (ART) such as hormonal stimulation, egg retrieval, in vitro fertilization, intra-cytoplasmic sperm injection, micromanipulation of gametes, and exposure to the culture medium, could subject the gametes and early embryos to uterine stress and may be associated with an increased risk of developmental disorders [2]. Children conceived using ART are at a higher risk for birthdefects. In reality, artificial

insemination, hormonal imbalance, advanced parental age, pre-term deliveries, and lowbirth weight constitute major risk factors for developing autism. Current research seems to suggest that obstetric interventions, Cesarean Sections (CS), and/or oxytocin-induced labor are all likely to cause ASD in children [2]. **Heavy Metal Toxicity:** Recent ecological studies suggest a critical contribution of metal toxins in autism. Both Aluminum and Mercury appear to be the main culprits, which can penetrate the blood-brain barrier and exhibit severe adverse effectson the brain as well as the immune system. Intake of these toxicmetals by ladies of child-bearing age enhances the susceptibility of a child to ASD [20, 21]. The continuous presence of mercury as a contaminant in the surrounding environment (air, soil, and water), packed eatables, and seafood increases the likelihoodof developing autism symptoms. Elevated heavy metal concentrations (arsenic and mercury) have been detected in the blood and urine of children suffering from autism. Lead, cadmium, aluminum, and arsenic toxicity have also been associated with the development of ASD-likesymptoms [2]. **Dysfunctional Immune System:** Maternal immune system activation and the production of pro-inflammatory cytokines are risk factors for autism. Pregnancy-induced immune suppression makes a woman more vulnerable to infections. Besides, obese and underweight motherscarry an enhanced risk of ASD in newborns. Maternal obesity results in an activated immune system and inflamed uterine ambiance consequently leading to neurodevelopmental impairments in the offspring. On the other hand, malnutrition of the mother evokes a physiological stress response producing neuronal damage mediated via excessive secretion of pro-inflammatory factors [2]. Of late enhanced concentrations of maternal cytokines and chemokine during pregnancy have been linked to the development of ASD with intellectual disability in the child [2]. **Age of Parents:** The effects of aging on human genetic traitsare well documented, particularly in early embryonic development. Several investigators showed the age of parents' ≥35 years imparted a higher risk of bearing a child with autism [2]. Furthermore, parents with advanced age had a greater risk of a first-born child being abnormal as compared tothe later-born children. The most likely underlying mechanism for older fathers to have an abnormal child can be attributed tolower sperm count due to de novo mutations, precipitated by continuous toxic environmental exposure **(Fig. 1)**. Whereas, the multiple reasons for older women to bear abnormal children appearto be hormonal imbalance, incompatible uterus, use of contraceptives, and adverse environment [2]. The intensity of interplay between the risk factors and the protective factors affecting the growing embryo, while in the womb of the mother ultimately determines the extent of the abnormality in the newborn. This degree of abnormality decides whether the infant would suffer from Asperger's syndrome, Pervasive Developmental Disorder, classical autism, or any other childhood disorder.

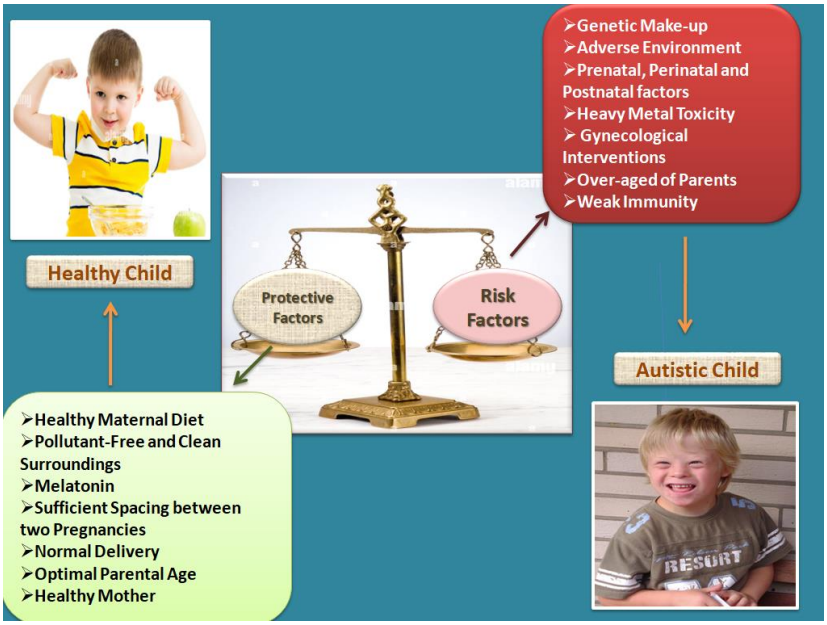

Figure 1: Supremacy of Protective Factors over Risk Factors Yield a Healthy-Baby

Pathogenesis of Autism Spectrum Disorder: The term "autism spectrum disorder" refers to a variety of disorders including "Classic Autistic disorder, Asperger's disorder, Childhood disintegrative disorder, and Pervasive developmental disorder not otherwise defined (PDDNOS)". Due to the considerable clinical and genetic heterogeneity, the pathogenesis of ASD is still up for debate. However, no single gene has a clear-cut impact on the occurrence of this disorder. More than 400 genes are closely linked with ASD and 200 genes are marginally connected [20]. The pathogenesis of ASD appears to be a complex interplay of susceptible genes, adverse surroundings, conceiving circumstances, prenatal factors, perinatal factors, and gynecological interventions **(Figure. 1)**. The adverse environment (2) comprising of exposure to heavy metals, pesticides, smoke, and toxic chemicals at vulnerable times of gestation, is arising as a key predictor for the development of autism. No single biomarker can be attributed to being involved intimately in the pathogenesis. This increases sensitivity to environmental toxins and thus raises the likelihood that a child will become autistic. The composite interaction between susceptible genes and an adverse environment results in the formation of abnormal synapses and unstable neuronal networks in the fetal brain. **(Figure. 1)** The intensity of interplay between the risk factors and the protective factors while the growing embryo is in the womb of the mother ultimately determines the extent of abnormality in the newborn, whether the infant is suffering from Asperger's syndrome, Pervasive Developmental Disorder, classical autism or any other childhood disorder. There exists a delicate physiological equilibrium between the risk and protective factors within the transforming physique of an expectant mother. Autism results when the risk factors dominate over the protective factors.

Challenges Faced by the Lady during Pregnancy: A happy, successful, and nurturing home environment has a positive and calming effect on the temperament of the unborn kid. Every lady has to undergo pregnancy sometime in her life, and the first pregnancy poses several challenges. These challenges become unbearable when the lady is illiterate, married in a non-cooperative family, and faces poor financial support **(Figure. 2)**. The actual

cause of autism has not yet been discovered. Risk factors such as compromised immune system, mitochondrial dysfunction, mating circumstances, prenatal, perinatal, and postnatal factors, unfavorable environment, gynecological manipulations, and susceptible genes are among the conventionally recognized pathological and non-pathological conditions causing ASD [22]. These conditions can act alone or in combination to impair the brain function of the unborn child. Researchers working on ASD have a focus on adverse environmental exposure at susceptible times as a culprit. Consecutive exposure to neurotoxicants during vulnerable pregnancies disrupts the development of neural circuits and disorganizes many areas of the fetal brain, which results in mental retardation and aberrant behavior in the offspring. Although the unfavorable environment may not be the sole underlying cause of ASD but a potent precipitating factor in individuals. A hazardous environment, however, may be a crucial factor in prenatal brain injury and may encourage gene changes in susceptible ladies. Pollutants present in the atmosphere around expectant mothers during the last phase of pregnancy appear to be positively correlated with the future birth of an autistic child. Moreover, there is a link between autism and the post-partum presence of nitrogen dioxide, a carcinogen, in the vicinity of the newborn [2, 13, and 23]. At least in certain instances, ASD could be regarded as a fetal programming disorder. The use of teratogenic medications (such as thalidomide, valproic acid, misoprostol, and acetaminophen) and alcohol or tobacco usage **(Figure. 1)** during pregnancy are significant prenatal risk factors for ASD [24, 25]. Neonatal neuropathologies and aberrant behavior can arise from maternal infection during pregnancy [26]. The fetus's development is significantly influenced by the environment inside the uterus. Epigenetic and imprinting diseases are more likely to occur in children conceived with ART [26]. ASD and other developmental illnesses may be directly related to obstetric interventions, artificial insemination, older parental age, cesarean sections (CS), and/or oxytocin-induced labor, according to recent studies. Toxic exposure of pregnant ladies to lead, cadmium, mercury **(Figure. 1),** aluminum, and/or arsenic has been linked to the birth of an abnormal child. Elevated maternal cytokine and chemokine concentrations during pregnancy are found to be related to the birth of an autistic child with a low IQ [27]. Autism incidence is also increased by the physical immaturity of younger parents, the embryo's deficient intrauterine development, and poor maternal care **(Figure. 2)**. Furthermore, parents in their late thirties show a higher risk of delivering an abnormal child. Usually, ladies of poor families are heavily burdened with household chores, especially because modern gadgets like washing machines, refrigerators, microwaves, etc. are unaffordable **(Figure. 2)**. Such a lady is left alone and faces the tension herself since she has no other world than the four walls of the house. The physical and intellectual personality of her unborn child is dependent on her sound health during gestation, proper nutrition, stress-free, and a loving home environment.

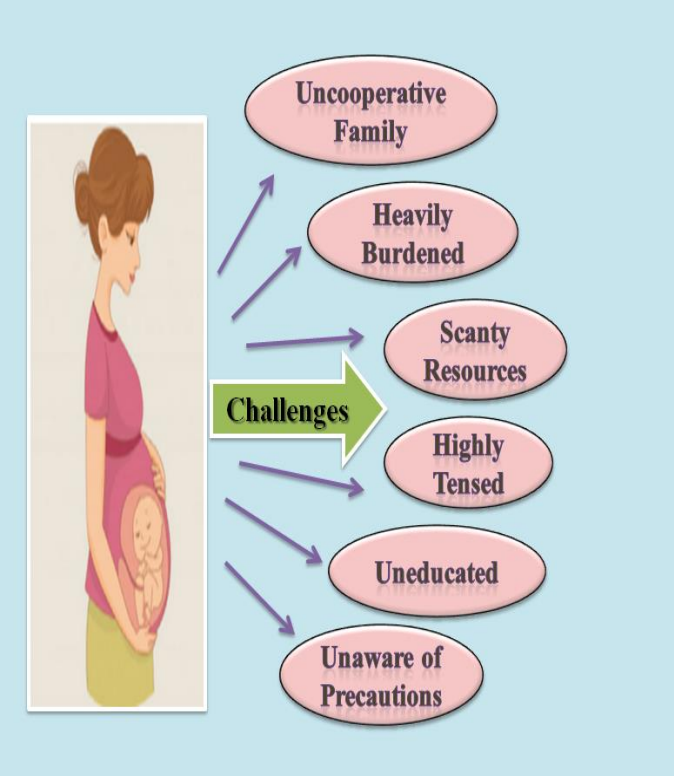

Figure 2: Challenges Faced by the Pregnant Lady

Protective Factors: Protective factors, when identified precisely would play a crucial role in preventing the occurrence of ASD in the first place. The protective factors which help in diminishing the frequency of the birth of an abnormal child include a favorable family atmosphere coupled with proper maternal care, proper maternal diet, a pollutant-free green environment around the premises, optimal parental age, sufficient gap between two children, **(Figure. 1)** absence of gynecological interventions, facilitation of normal delivery, good maternal health. **Healthy Maternal Diet**: Pregnant ladies with fatty acid deficiency showed a decrease in ASD risk when their meandaily fatty acid intake was maintained at ≥600 µg in the peri-conception period and/or during the first month of pregnancy.The increase in Polyunsaturated Fatty Acids (PUFA), especially omega-3 fatty acids, during prenatal maternal diet was associated with a decreased ASD risk. Prenatal vitamin D supplementation decreased the likelihood that the unborn child will acquire ASD. [20]. Higher iron and calcium intake during the last phase of pregnancy and particularly during breastfeeding was associatedwith reduced ASD risk [2, 28]. **Melatonin:** There is no concrete evidence indicating the beneficial effect of melatonin supplements during pregnancy. Melatonin is a natural hormone secreted by the placenta even during pregnancy. However recent research findings suggest that melatonin supplementation during pregnancy could potentially decrease the risk of pre-term birth, preeclampsia, and intra-uterine growth restrictions. Furthermore, melatonin has been shown to impart

neuroprotection to the growing neonate when administered during pregnancy **(Figure. 1)**. Melatonin synthesis is frequently impaired in children with ASD and their mothers. Therefore, consumption of this hormone during pregnancy could act as a neuroprotective factor, decreasing the risk of neurodevelopmental disorders, including ASD [29]. Additionally, melatonin has been proven to streamline the sleep-wake cycle as a unique advantage during pregnancy. However, further clinical investigations need to be carried out to confirm the beneficial role of melatonin supplements during pregnancy. **Family Ambiance:** The entire family present in the vicinity of the expecting mother has a big role to play in creating positive vibrations, and a cooperative ambiance thereby supporting the pregnant lady in creating constructive thoughts **(Figure. 2)** and an optimistic attitude. It must be remembered that pregnancy is not a disease but a physiological phenomenon happening in healthy women's life as a temporary phase. The expecting mother should not feel isolated or overstressed **(Figure. 2)** in carrying out household chores thereby overburdening the physical body carrying the fetus. **Pollutant-free, Green, and Clean Surroundings around the Premises:** Pollutant-free and clean surroundings around the Premises create a positive impact on the mind and body of the expecting mother. This conducive environment rules out the toxic effects of heavy metals (Lead, Aluminum, Arsenic, and Mercury) likely to be present as contaminants in the surrounding air, soil, and water. **Optimal Parental Age:** There is sufficient evidence in the literature suggesting that the optimal age of parents should be in the range of 20 to 35 years **(Fig. 1)**. When the age of the Parents is less than 20 years there is a danger of inadequate intrauterine development of the fetus due to an immature uterus which could lead to preterm delivery, miscarriage, or the birth of an abnormal child. On another hand parents, aged above 35 years may prove to be incompatible and over-mature for smooth conception thereby interfering with the proper formation of the embryo. The culprits are the hormonal imbalance present in the older woman and/or the low sperm count of the father. **Sufficient Spacing between Two Pregnancies:** helps the mother's body to recover fully from the previous delivery episode and facilitates the right growth of the embryo within the uterus during subsequent gestation. **Healthy Mother**: Obese and underweight mothers carry a higher risk of delivering an abnormal child as compared to healthy mothers. There is a low risk of bacterial and viral infections when the immune system of the expecting mother is strong (30) which promotes a smooth and natural delivery of a healthy baby. **Limited Gynecological Intervention:** normal delivery as opposed to cesarean section goes a long way in providing a protective shield against the development of an autistic child. The complexity of ASD can be disentangled by studying the inter-relationship of multiple risks and protective factors associated with ASD. The diversity of these factors makes it difficult to determine which factor represents the primary cause and which other factors interact with this primary cause and their possible mechanism of influence. No single therapy/ approach fits exactly all kinds of patients. The authors recommend that focusing on the protective factors antepartum and post-partum might prove to be an effective method for the prevention of ASD. The intellectual and physical personality of the unborn child is dependent on the sound health of the pregnant lady during gestation, proper nutrition, and a stress-free and loving home environment. Thus, appropriate and timely measures, when adopted during the sensitive phases of the pregnancy would help in preventing the birth of an abnormal child. The authors have documented both, the protective factors and the risk factors precisely **(Figure. 1)** operating during pregnancy. Focusing on and consolidating the protective factors would go a long way in preventing the birth of an abnormal child in the first place, thereby warding off the consequent embarrassment. Thus, the prevention of the birth of an autistic child is the only workable option available at present and appears to be simpler than its cure.

Consequences of the Lifelong Illness: One of the main consequences of autism spectrum disease is the progression of ASD into schizophrenia, which makes the youngster uncooperative and extremely aggressive, necessitating hospitalization. Epileptic seizures can develop in ASD sufferers, which is another dangerous complication. If the epileptic episodes are not swiftly treated with anti-convulsants, instant death may occur. **Economic Impact:** Any type of chronic mental illness places a significant financial burden on the caretakers. ASD can also contribute to low educational grades and employment difficulties, for the sufferer. Many patients with ASD struggle to maintain healthy communication and social interactions, thereby making it hard to live independently. Nonetheless, even today, in industrialized nations, a sizable portion of patients with autism are unable to work full-time to support themselves. The expenditure towards the treatment of the ASD patient comprises the ongoing need for medical attention, expensive medications, the charges of specialists, and trainer fees. The majority of supportive resources for ASD are still concentrated in the biggest cities in developing nations like India. ASD has a significant economic impact that includes direct medical and non-medical bills, for the patient as well as the indirect productivity loss by the caretaker. Yet, the general public, especially in low-income areas and developing countries, is still uninformed of the services given by governmental and voluntary organizations, which causes the affected people and their families to suffer continuously. To encompass all areas of the spectrum and make autism more empathetic to the general population, the media must represent autism more comprehensively. **Transition into Adulthood and Old Age:** Marriage and lifelong friendships are beyond consideration for such sufferers. As a permanent neurological disorder, ASD displays an unusual pattern of development that has an unsettling effect on how adults and elderly people behave [31]. The necessity to have a structured transition from a child with an autism spectrum disorder to an adult is becoming widely acknowledged in recent times. However, there is relatively not much research in this area. In particular, it is not clear how to best meet the requirements of developing a toddler with ASD into an adult, their transition into a senior citizen, unemployment aspects, and treatment options over the lifespan [27, 31]. Consideration must be given to developmental changes related to the child's growth, maturity, middle age, and old age while establishing a treatment program. Regardless of the beneficial role played by the groups supporting ASD patients and the awareness attempts of the media, there is improper coordination between healthcare systems, service providers, accessible support measures, and ASD patients [32].

Allopathic Remedies: There is no treatment available to physicians for the therapeutic management of the patient suffering from autism spectrum disorder, due to the intricacy of ASD's appearance, co-morbid disorders, and age-related response variability. Drug therapy for core ASD symptoms is typically complex. There are no US-FDA-approved medications that alleviate the primary symptoms of ASD, particularly the deficiencies in reciprocal social interaction and abnormal behavior. Therefore, the only option available to pediatricians is to target co-morbid conditions and various ASD-associated symptoms like self-injury, aggression, and sleeplessness. Thus, it's an ardent task to treat this incurable childhood disorder. The quality of life of both, the autistic child and his family are severely affected in addition to the pathetic and helpless condition of the sufferer. The authors have identified supportive protective factors inclusive of nutrients, which would help the expectant lady to maintain a fit and healthy body during pregnancy and labor, which would effectively prevent the birth of an abnormal child suffering from autism or any other neonatal abnormality in the first place.

Healthy Eating during Pregnancy: The most significant physical change in a lady occurs during pregnancy. During pregnancy practically every aspect of her body goes through some sort of alteration. An expecting mother during pregnancy usually hates several foods that she formerly loved. There may also be foods, which the pregnant lady never liked before but now develops a craving for these food items. The nutrients beneficial during pregnancy are illustrated in **Figure. 3.** Since breastfeeding and pregnancy both require more calories, mothers who breastfeed may also develop cravings of their own and undoubtedly continue to have greater appetites. The best defense against all kinds of infections in an infant is provided by breast milk**.**

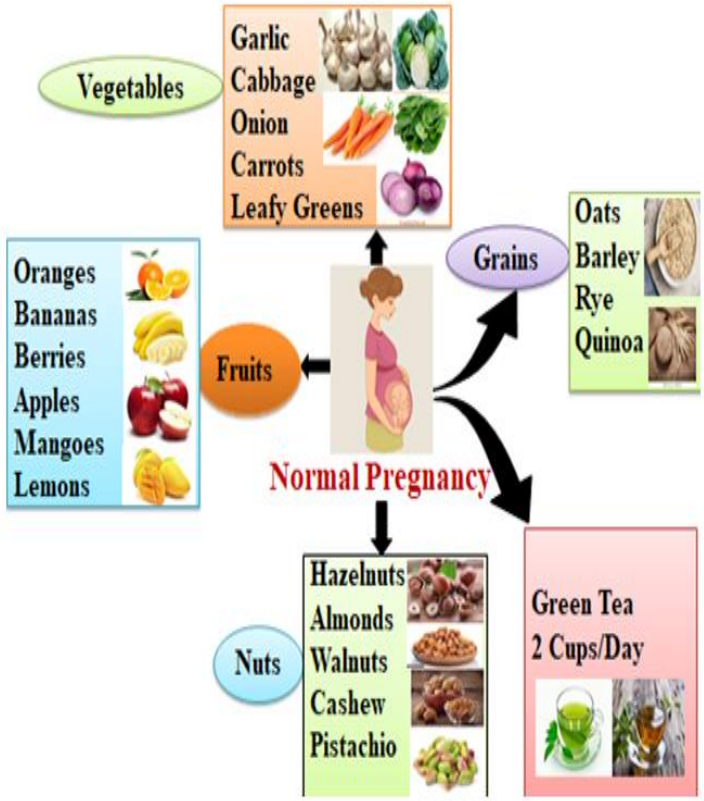

Figure 3: Beneficial Nutrients during Pregnancy

Why Does Pregnancy Cause Food Cravings?

Significant hormonal changes occur during pregnancy, especially in the first trimester. The hormones of pregnancy may alter the types of desires of the lady. The sensory perception of food, the sense of smell, and the mood can all be impacted by hormones, which will change the kinds of meals the pregnant lady craves. Several ladies who are expecting a child claim that they develop bloodhound-like senses during pregnancy and can detect odors from a large distance. Pregnant ladies need more nutrients **(Figure. 3)** like calcium and iron. As a result, there would be a craving for such dishes that contain these ingredients. Some of the urges and dislikes are motivated by a desire to keep the mother and the developing child safe. One of the most intriguing aspects of craving is how individual preferences for certain meals can be influenced by the culture in which we are raised. Women in the United States, for instance, frequently crave chocolates, women in Japan frequently crave rice, and women in India mostly crave citrus fruits like tamarind, and anwala. Dieting during pregnancy is not a good idea. On the other hand, the pregnant lady needs to concentrate on a healthy and balanced diet **(Figure. 3)**, so that she remains fit for bearing labor and the postpartum phase. Averages of 500 extra calories per day in addition to a normal diet are recommended during pregnancy, which is subjective. In addition, a few nutrients like calcium, folic acid, iron, and proteins are essential to facilitate babies' growth and keep the lady healthy and fit **(Figure. 3)**.

Nutrition Needs During Pregnancy: Women have definite dietary needs throughout their lives, notably during pregnancy, the postpartum period, and during nursing, because these are the times when they are most vulnerable to nutritional deficiencies. Women are advised to eat healthy food to safeguard their as well as their offspring's survival and welfare **(Figure. 3)**. Women's diets are influenced by several factors, such as food access, affordability, the know-how of the family, gender inequality, and social and cultural norms that may limit women's ability to make decisions about their nutrition. Additionally, the short interval between two successive pregnancies and the reduced physical activity of the lady contributes to the birth of an autistic child. The lack of essential nutrients during pregnancy, such as iodine, iron, folate, calcium, and zinc, can cause anemia, pre-eclampsia, hemorrhage, and mortality in the mothers. Furthermore, stillbirth, low birth weight, or an autistic child may result from the deficiency of essential nutrients **(Figure. 4)**. Women of childbearing age who used calcium and multivitamin supplements along with their diet had a lower risk of ASD in their unborn children [20]. Nutrients containing Omega-3 fatty acids are necessary for the diet of the lady for the normal brain growth of the neonate and decent social skills. Midwives can also play the role of a counselor for expectant mothers or women who are planning pregnancies so that there are no negative effects on the nutritional status of the expectant mothers.

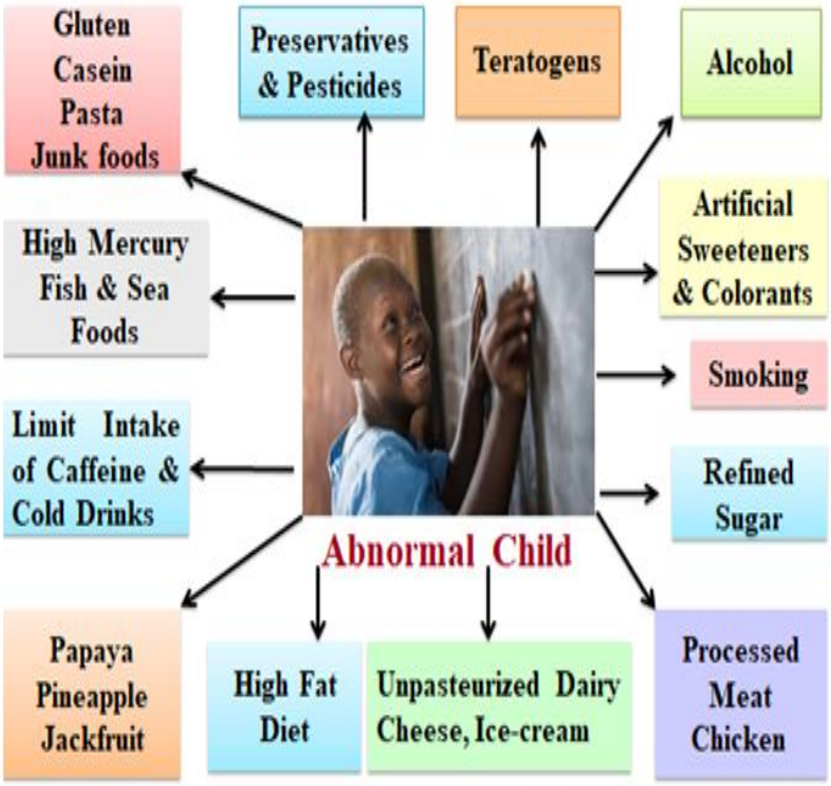

Figure 4: Harmful Food Items

Prevention is better than Cure: The most well-known and frequently discussed childhood disease with high worldwide prevalence right now without any knowledge of the biomarkers is Autism Spectrum Disorder (ASD). The neurochemistry and causes of classical autism are still unknown, even though research in this area has steadily progressed. Furthermore, the lack of a reliable animal model to study the pathophysiology of ASD has made matters even more difficult. The authors recommend that concentrating on the protective factors which become functional during the antepartum and postpartum phases may work out to be a successful strategy for the prevention of ASD. A smart diet choice during the prenatal and postnatal periods can lessen the difficulties of neuro-cognitive impairments linked to ASD. The harmful food items interfering with the normal growth of a neonate have been depicted in **Figure. 4**. Upcoming challenges include a greater understanding of the interplay between the risk factors and the compensatory physiological mechanisms operating naturally within the body of a pregnant lady. The knowledge we have about the protective factors that positively influence the lives and health of expectant mothers along with their unborn neonates in various nations, cultures, and communities needs to be carefully applied. Wisdom derived from the "Autistic voices" and practical implementation of the lessons learned from the feedback obtained from the teenagers with autism and their families would undoubtedly boost the quality of life of all the stakeholders [27]. There is no approved allopathic, homeopathic, or ayurvedic medicine available today for the treatment of autism spectrum disorder or any neurodevelopmental childhood disease for that matter. The challenges faced by the lady during pregnancy and the delivery of the child, therefore need to be delicately addressed so that the birth of an abnormal child does not occur in the first place. The intellectual and physical personality of the unborn child is dependent on the sound health of the pregnant lady during gestation, proper nutrition, and a loving home environment. Thus, the prevention of the birth of an autistic child is a workable option under the present circumstances and appears to be simpler than its cure. Overall, we have already overcome a few roadblocks and are in a lot better position today than we were yesterday, but we still have a long journey ahead and plenty of challenges to face.

Conclusion

Every lady has to undergo pregnancy sometime in her life, and the first pregnancy poses several challenges. These challenges become unbearable when the lady is illiterate, married in a non-cooperative family, and faces poor financial support**.** Extensive investigations are underway all over the globe to identify the specific biomarkers involved in autism and target sites in the brain and periphery for discovering useful allopathic medicines to manage children suffering from developmental childhood abnormalities in general and autism spectrum disorder in particular. At present, there is neither any drug approved by the US FDA for the treatment of autism nor complementary therapies of any use. Therefore, it becomes compelling to prevent this lifelong irreversible developmental disorder in the first place, by focusing on environmental factors, mating factors, prenatal factors, perinatal factors, and the challenges faced by the lady during pregnancy and delivery of the child. There is strong evidence in favor of a close connection between childhood developmental disorders, particularly autism, and the diet of the lady during pregnancy. Developmental abnormalities in the unborn child seem to be associated with the quality of the pregnant mother's diet, fitness, and lifestyle. The mental, emotional, and physical personality of the unborn child is dependent on the sound health of the pregnant lady during gestation and a stress-free loving home environment. Thus, appropriate and timely measures, when adopted during the sensitive phases of the pregnancy would help in preventing the birth of an abnormal child. The authors have identified precisely both, the protective factors and risk factors operating during pregnancy and made a modest attempt to give concrete recommendations to prevent the birth of an abnormal child in the first place, thereby warding off the consequent embarrassment. We believe that the society at large in India and around the world would greatly benefit from this review article. Thus, the

prevention of the birth of an autistic child is the only practical option available today and appears to be simpler than its cure.

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DOI:10.31579/2578-8868/262