International Journal of Psychology and Counselling Vol. 3(8), pp. 130-136, November 2011
Available online at http://www.academicjournals.org/IJPC
ISSN 2141-2499 ©2011 Academic Journals

Full Length Research Paper

Study of Some Environmental and genetic determinants of autism in Egyptian children

El Sawy MA[1], Awadalla HI[2]*, Mohamed RR[3], Zaki OK[4] and Mohamed OA[5]

[1]Genetics Unit and Pediatric Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt.
[2]Medical Science Department, Institute of Environmental Studies and Research, Ain Shams University, Cairo, Egypt.
[3]New Renewable Institute of Energy and Electricity, Medical Department, Ain Shams University, Cairo, Egypt.
[4]Genetic Unit, Ain Shams University Hospital, Cairo, Egypt.
[5]Department of Medical Studies, Institute of Post Graduate Childhood Studies, Ain Shams University, Cairo, Egypt.

Accepted 21 July, 2011

Autism is a neuro-developmental disorder of unknown cause. Both genetic and environmental influences are claimed to contribute to the etiology of autism. Several studies were done to determine the factors that contribute to the expression of the symptoms. We studied genetic, epigenetic and environmental factors that may influence the neurodevelopmental alteration that can cause vulnerability to autism. We did a controlled study on 44 patients who volunteered to participate at two Egyptian health clinics over 10 months duration. Full clinical evaluation, Cytogenetic analysis, biocard celiac test were done to detect anti-t TG Ig A antibodies for gluten sensitivity test; and quantase neonatal phenylalanine screening was done to detect the phenylalanine level in blood using ELISA. A part of significant positive family history, and no significant association were found between autism and the studied parameters. This study points to the important role of genetic susceptibility compared to the environmental factors and the role of family studies for determining the susceptible individuals to autism.

Key words: Autism, genetics and environmental interaction.

INTRODUCTION

Communication problems form one of the key diagnostic criteria for autism, but there is a wide variety of manifestations. Autism provides a model for studying the important distinction between language and communication, and demonstrates the vital part which mind-reading plays in normal human verbal and non-verbal interaction (Frith and Happe, 1994). Autism is a neurodevelopmental behavioral disorder usually presented before 36 months characterized by impairment of social contact and communication, restricted and repetitive interest and behaviors (Newschaffer et al., 2007).

Other characteristics include sensory dysfunction, inappropriate laughing and giggling, little of no eye contact, apparent insensitivity to pain and preference to be alone.

In the last 20 years, there had been an increase in the incidence of autism, unexplained by genetics alone, nor can this increase be secondary to only increased awareness (Chakrabarti and Fombonne, 2001).

The causative factors of autism are biological in nature and involve the brain. It is believed that a combination of genetic factors, viral factors, prenatal complication and post natal defects contribute to the development of autism (Caronna et al., 2008). Environmental influences in autism can be infections, general pre and perinatal factors, family history and drug and chemical exposures. A good example of this is provided by a genetic condition called phenylketonuria (Baieli et al., 2003).

Over the past two decades, systematic family and twin studies have shown that genetic factors play a crucially important role in causing apparently idiopathic form of the

*Corresponding author. E-mail: hala_awadalla@yahoo.com.

condition (Szpir, 2006).

This conclusion is supported by the fact that about 3% of siblings of a child with autism also develop autism (Folestein and Rosen, 2001). It is thought that this 3% rate is higher in reality. This is because the prevalence catenation simply counts the number of siblings with autism, and does not take into account the stoppage phenomenon, where by parents with a child with severe leaning disabilities choose not to have further children (Williams et al., 2006).

Till date, research in autism has failed to identify any major environmental factor that contributes to its causation. Recent research has cast doubt on significance of pregnancy and birth complication in development of autism (May - Benson et al., 2009).

The most obvious interpretation of the association of autism with some prenatal viral infections is that brain damaging medical condition may add to increasing the risk for autism. These specific prenatal pathogens include herpes simplex, rubella and syphilis. Rubella has been most commonly reported to be associated with autism (Kolevzon et al., 2007).

Also, drug intake is considered a very important factor. Suggestion of early prenatal xenobiotics could play a role in autism etiology, also valporic acid and other anticonvulsants drugs (Amdt et al., 2005). Hypothyroidism might influence the initiation or expression of autism (Rodier and Hyman, 1998). Induction of labour is increasingly used. This might be considered as a risk factor for autism (Hultman et al., 2002).

Some researchers discussed Post Natal Factors in the etiology of autism. Neonatal jaundice is a very common condition. If serum bilirubin reaches high levels, it can be toxic to the brain and can cause direct insults on it (Bilder et al., 2009).

Another factor could be vaccination, MMR vaccine and any mercury and thimerosal (preservative containing ethyl mercury) - containing vaccines. Ethyl mercury is a known fetal neurotoxin that causes severe neurologic injury at high doses and developmental delays and neurologic dysfunction at lower doses (Pichichero et al., 2008). A 1998 study in Lancet (Wakefield et al., 1998) proposed the initial MMR-autism link. His report has led intentionally or otherwise to the erroneous assumption by the media and parents of a cause and effect relation between MMR immunisation, inflammatory bowel disease, and developmental disorder, resulting in parental confusion about the safety of immunization (Wakefield et al., 1998). Gluten sensitivity is considered a dietary defect that is also accused of having a role in the etiology of autism (Potts and Bellows, 2006).

Despite all studies mentioned above, there is no general acceptance of the main causes leading to autism. Since autism is one of the disorders that cause impairment in children and its etiology is still not clear, the aim of the study is to establish the possibility of some genetic, pre, post natal factors role in the etiology of autism.

METHODS

Subjects

This study is a case – control study. A total of consecutive 44 patients (38 males and 6 females) attending Ain- Shams University, Genetic Department Clinic, from September 2008 to June 2009, with age range of 3 to 12 years old, were used for this study . The control group (38 males and 6 females) was from a matching age and sex group consecutively selected from the National Institute of Research Clinic.

Diagnosis was done by a qualified psychologist, psychiatrist or neurologist according to DSM-IV criteria. DSM-IV is the diagnostic criterion for the five Pervasive Developmental Disorders (PDDs), also known as Autism Spectrum Disorders (ASDs), as defined by the Diagnostic and Statistical Manual of Mental Disorders (Diagnostic and Statistical Manual of Mental Disorders, 1994). Autism is defined as exhibiting at least symptoms of qualitative impairment in social interaction, communication, restricted and repetitive behavior. The assessment of severity of symptoms was done by using Childhood Autism Rating Scale (CARS); its 15 items include 14 specific domains plus one category of impression of autism. It is based in a rating scale from 1 to 4 that is scored with information from parents' report, observation of the child's available records (Schopler et al., 1986).

Then, the parents were asked to complete a questionnaire regarding the perinatal history, family history, child's medical and behavioral history. Family tree construction was also done.

Three milliliters venous blood was collected using sterile syringes previously flushed with preservative free heparin 5000 IU/ml.

Samples were used immediately or within few hours from collection provided they are kept at room temperature or refrigerated above 4°C.

One milliliter was put in culture for cytogenetic analysis; the analysis involved the examination of phytohaemagglutinin stimulated T cell population by blocking cell division at metaphase stage with an inhibitor of spindle formation (Colecemid). This is followed by hypotonic treatment of cultured cells. Slide making, fixing, and staining with G-banding technique were done. Analysis of available metaphases was done using light microscope and image system (cystoscane applied imaging) (Rooney and Czepulkowski, 1992; Mitelman, 1995).

Two milliliters of the venous blood were collected on EDTA (1.5 mg/ml) for gluten sensitivity test. We used Biocard Celiac test to detect the anti-t TG IgA antibodies. It is a rapid immuno chromato graphic test. If the sample contains anti t TG Ig A antibodies, these will bind with the gold labeled antibodies with t TG derived from red blood cells and with the stationary reagents in the test membrane forming a visible, red test line. The test also contains total Ig A measuring system. Red line in the control window shows that there are Ig A antibodies in the sample. This will make it impossible to get false negative results in the case of Ig A deficiency (Korponay - syzabo et al., 2005;Nemec et al., 2006; Raivio et al., 2006).

Three drops of fresh blood were collected on Whatman 903 specimen collection paper to test for phenylketonuria by the Quantase Neonatal Pheylalanine Screening Assay using ELISA. It makes use of the enzyme phenylalanine dehydrgenase which catalyses the NAD-dependent oxidative deamination of phenylalanine to L-phenylpyruvate and ammonia. The NADH produced is measured colorimetically using a tetrazolium/ intermediate electron acceptor detection system (Slazyk and Hannon, 1993).

Table 1. Comparison of socio demographic factors among studied groups.

Socio demographic factors		Studied groups				χ^2	p
		Cases (44)	100%	Control (44)	100%		
Gender	Male	38	86.4	38	86.4	0.00	1.00
	Female	6	13.6	6	13.6		
Maternal age (year)	20-30	36	81.8	26	59.1	5.7	0.05
	30-40	7	15.9	17	30.6		
	≥40	1	2.3	1	2.3		
Paternal age (year)	20-30	14	31.9	12	27.3	0.86	0.65
	30-40	24	54.5	28	63.6		
	≥40	6	13.6	4	9.1		
Maternal education	Primary	2	4.5	1	2.3	1.06	0.5
	Secondary	12	27.3	16	36.3		
	University	30	68.2	27	61.4		
Paternal education	Primary	1	2.3	3	6.8	2.79	0.2
	Secondary	11	25.0	16	36.4		
	University	32	72.7	25	56.8		
Maternal occupation	House Wife	25	56.8	22	50.0	1.22	0.5
	Employee	18	40.9	19	43.2		
	Professional	1	2.3	3	6.8		
Paternal occupation	Worker	3	6.8	4	9.1	0.2	0.9
	Employee	31	70.5	31	70.5		
	Professional	10	22.7	9	20.4		
Residence	Rural	3	6.8	2	4.5	0.00	1.00
	Urban	41	93.2	42	95.5		

Results were analyzed using SPSS for windows. Statistical analysis for differences between the groups was assessed by χ^2 tests and analysis of variance of P values of < 0.05 was considered significant.

RESULTS

Table 1 summarizes socio-demographic characteristics of the studied subjects. Most of the samples (86.4%) were males, and 81.8% of mothers in the cases were between age group 20 to 30 while 59.1% of the controls were in the same age group. More than half (54.5%) of the case fathers were in the 30 to 40 age group while 63.6% of the control fathers were in the same age group. For education, the highest percentage for parents in both groups was the university education.

The maternal occupation that was highly demonstrated in the sample was the house wives and for the paternal side they worked as employee. More than 90% of the studied groups were urbans. So, it appears that there were no significant differences between the case and control groups as regards socio-demographic factors.

Table 2 shows the familial factors that were suspected to have a role in the etiology of autism. Consanguinity and the order of child birth in the family seemed to be insignificantly different between both groups. On the other hand positive family history was significant between the two groups.

Two of the cases were brothers and both suffered from autism. Another case had a first degree cousin (on the mother's side) who also had autism. Another two cases had relatives with learning disabilities and only one mother suffered depression and was on treatment.

Table 3 presents some of the medical factors that are accused of having a role in autism. Considering the antenatal, natal and postnatal factors (maternal infections and drug intake,) there were no significant differences in the case group in comparison to the control group.

Table 2. Comparison of familial factors among studied groups.

Familial factors		Studied groups				χ^2	*p*
		Cases (44)	100%	Control (44)	100%		
Consanguinity	Positive	8	18.2	4	9.1	1.45	0.2
	Negative	36	81.8	40	90.9		
Positive family history	Positive	6	13.6	0	0.0	4.4	0.03
	Negative	38	86.4	44	100		
Order of child	1st	28	63.7	26	59.1	1.3	0.5
	2nd	10	22.7	8	18.2		
	≥3rd	6	13.6	10	22.7		

Table 3. Comparison of Medical factors among studied groups.

Medical factors		Studied groups				χ^2	p
		Cases (44)	100%	Control (44)	100%		
TORCH	Positive	1	2.3	2	4.5	0.00	1.00
	Negative	43	97.7	42	95.5		
Drug intake	Positive	11	25.0	7	15.9	1.1	0.29
	Negative	33	75.0	37	84.1		
Method of delivery	Spontaneous vaginal	15	34.1	24	54.5	5.7	0.12
	Caesarean section	26	59.1	19	43.2		
	Instrumental	3	6.8	1	2.3		
Neonatal jaundice	Positive	11	25.0	9	20.5	3.12	0.07
	Negative	33	75.0	35	79.5		
Phenylketonuria	Normal< 2	40	90.9	44	100	2.36	0.14
	Border line (2-2.5)	4	9.1	0.0	0.0		

Regarding the method of delivery, more than half (59.1%) of the cases mothers were delivered by caesarean section while equal percent (43.2%) of mothers in the case group was delivered by normal delivery or Caesarean section, yet it seemed to be insignificant.

Post natal factors as neonatal jaundice was also found insignificant. Only 4 autistic children were found to have border line results when tested for phenylketonuria which is not considered as a risk factor for autism.

Only one mother in the case group suffered from toxoplasmosis while two mothers did in the control group. One quarter of the cases mothers took drugs while 15.9% received it in the control group.

For hypothyroidism, one mother suffered from it in the case group. As regard the MMR vaccine, both groups were 100% vaccinated. Gluten sensitivity test detected only one positive case while it came negative for the rest cases as well as the control group. Cytogenetic analysis was negative for both case and control group (data not presented in tables).

DISCUSSION

Results from our study demonstrated no significant differences in the incidence of the various tested factors among autistic children compared with the control group, except for the positive family history factor.

There was no evidence of any association between socio-demographic factors and the development of autism in current study. Early studies suggested that a high socioeconomic status was common in families with autistic children (Gardener et al., 2009). Over the past 25 years an increasing proportion of cases had been found in the low socioeconomic group (Reichen berg et al., 2006).

That finding may well be supported by the increased awareness of the disorder and the increased availability of child health services (Grether et al., 2009).

An example of a potential confounder that is possibly more important in Middle Eastern Population is cons had no role in autism. These findings confirmed the results of Saleh et al. (2009), where theydid not provide any evidence of a direct link between consanguinity and autism in Saudi Arabia. Sasanfar et al. (2010) found that consanguinity had no role in a study done on the Iranian population. On the contrary, other investigators found that possible parenteral consanguinity increases the likelihood of autosomal recessive diseases, autism, learning disorders and behavionral disturbances (Dotta et al., 2009).

This study did not show a higher incidence of first or fourth born individuals in the autistic group compared to the general population, as many other studies failed to do so (Fombonne, 2002). However, this result is in disagreement with Bolten et al. (1997) that autistic children tend to be first or fourth born more commonly than that of control. An explanation for such a phenomenon was most widely believed to be due to the reproductive stoppage rules (Grether et al., 2009).

The current study demonstrated significant differences in the incidence of positive family history among autistic children compared with control group. Klauch (2006) declared that in some cases, parents and other relatives of autistic children show mild impairments in social and communicative skills. Consistent with our results, Delong and Nohna (2008) found that affective or emotional disorders occur more frequently than average within families of people with autism.

The results of this study revealed that there was a consistent association of unfavorable events in pregnancy, delivery and neonatal phase and autism. Bolten et al. (1994) suggested additional differentiation between complications based on the severity as determined by the selection of obstetric complication know to be associated with a high risk of developmental disorder.

This study found no association between autism and maternal infection. Consistent with the findings of the present study, results of exposure to cytomegalo virus from case reports were very difficult to interpret because the virus was so common (Gillberg and Coleman, 1992). Also, data on the coincidence of autism with exposure to more common conditions such as influenza had been negative (Rodier and Hyman, 1998). Stubbs et al. (1984) reported no significant correlation between toxoplasmosis and autistic disorders.

One quarter (25%) of the cases and 15.9% of control mothers received drugs which were safe antibiotics and tocolytic drugs. Consistent with the results of the present study, Lidsky and Schneider (2005) reported no drug intake correlation to the autistic disorder as well.

In the current study, only one mother of a case suffered from hypothyroidism and received treatment. Although hypothyroidism seems to be an eligible factor in autistic disorder, still little proof was recorded to support this hypothesis (Román, 2007).

More than half (59.1%) of cases and 43.2% of control group delivered by caesarean section, yet it seemed to have no impact on the etiology of autism. Other studies contradicted this and thought caesarean section is a risk factor for autism (Lauritsen et al., 2005). Kolevzon et al. (2007) disapproved that Caesarean section to be accused as a risk factor for autism, despite the obvious increase in its incidence nowadays.

Post natal factors for example hyperbilirubinemia is also alarming and suspected in the etiology of autism. In the current study there was no statistically significant relationship between neonatal jaundice and autism, supporting the belief of many researchers (Gauderner et al., 2009). On the other hand, a few suggested that hyperbilirubinemia occurred more frequently than expected among children later diagnosed with autism (Maimburg et al., 2008).

All cases and controls were vaccinated with MMR. Thus, no difference between MMR vaccination could be shown. Other studies failed to show an association between MMR vaccination and autism (Hornig et al., 2008).

In the present study, only one case showed sensitivity to gluten and this was insignificant. This result was in accordance with those of Smith et al. (2009) that there was no sufficient evidence to support the beneficial effect of casein and gluten free diet in autistic children. On the contrary, Morric and Aegin (2009) claimed that gluten sensitivity could play an important role in the pathophysiology of autism. So, gluten sensitivity and its relationship to autistic disorder still is a controversial issue.

Results from our study revealed no significant difference between both groups when tested for phenylketonuria (autosomal recessive genetic disorder). This was in agreement with Fombonne (2003), even researchers that confirm pheuylketonuria as one of the cause of autism found its prevalence to be very low (Steiner et al., 2007).

This study revealed no significant contribution of genetic factor to the etiology of autism. So, it appears that to date, only a small percentage of autistic disorders have been associated with specific genetic or chromosomal abnormalities. Even then, we would speculate that within this group, more than one genetic locus will be found (Rapoport, 2009).

As a result, there is no conclusive factor that can be elicited as being a risk for autistic disorder affection, except may be for positive family history within the families of autistic children. The main limitation of the study is the small sample size, and further work on large scale is recommended. Another limitation is the fact that this study failed to explore correlations between drug intake and severity of the cases of autism.

Conclusion

In this study, we have tried to stress the interrelationships that are likely to exist between genetic and environmental causes of autism. Few environmental factors identified are still involved in a tiny fraction of cases. The vast majority of individuals with autism do not have any one of these infrequent non-genetic or rare genetic cases.

But, however no matter how rare the cause is or whether genetic or environmental, these factors have the potential to provide clues to the etiology and neurobiology of autism. What is known about environmental agents does not account for many cases, but it is a source of information on the nature of autism. It is critical that we use all the data at our disposal to unravel the causes of the disorder.

RECOMMENDATIONS

1. Multiple parallel scientific, epidemiologic and clinical approaches are needed to rapidly improve our understanding of ASD, its origin and its prevalence;
2. Future studies using larger case group from the same population. In such a replicated sample it would be ideal to have information on autism as well as environmental risk exposures for both parents and children. Stress on the role of genetic susceptibility compared to environmental factors and the role of family studies to determine the susceptible genes. This can help to find susceptible individuals to autism;
3. Clinical standardization of autistic disorders phenotyping and so identify meaningful patterns in the date;
4. Developmental surveillance should be carried out, screening tools should be administrated regularly at the 9, 18, 24, 30 month visits for early developmental intervention;
5. Siblings of children with autism should be monitored carefully. Screening should be performed not only for autism, but also, language delays, learning difficulties, social problems and anxiety or depressive symptoms.

ACKNOWLEDGMENTS

The authors are grateful to the Genetic unit, Ain Shams University and National Center for Research for their great help. We thank all individuals who participated in the study by willingly giving samples.

REFERENCES

Amdt TL, Stodgell CJ, Rodier PM (2005). The teratology of autism. Int. J. Dev. Neurosci., 23 (2-3): 189-99.
Association Psychiatric Association: Diagnostic and statistical manual of mental Disorders. Washington DC 4th edition (1994).
Baieli S, Pavone L, Meli C, Fiumara A, Coleman M (2003). Autism and phenylketonurea. J. Autism Dev. Disord., 33(2):201-4.
Bolten P, Macdonald H, Pickles A, Rios P, Goode S, Crowson M, Bailey A, Rutter M (1994). "A case – control family history of autism. J child Psychol. Psychiatry, 35 (5): 877-900.
Bolten PF, Murphy M, MacDonald H (1997). Obestetric complication in autism: con sequences or causes of the condition? J. Am. Acad. Child. Adolesc. Psycliatry, 36: 272-281.
Caronna EB, Milumsky JM, Tager- Flusberg H (2008). Autism spectrum disorders: clinical and research Frontiers. Arch. Dis. Child, 93(6): 518-523.
Chakrabarti S, Fombome E (2001). Pervasive developmental disorders in preschool children. JAMA, 285(24): 3093-9.
Datta AK, Mandol S, Chaya SB (2009). Autism and Mental retardation with convulsions in tuberous sclerosis: a case report. Cases J., 2: 7061.
Bilder D, Pinborough-Zimmerman J, Miller J, McMahon W (2009). Prenatal, Perinatal, Neonatal factors associated with autism spectrum disorder. Pediatrics, 123(5): 1293-1300.
Delong R, Nohna C (2008). Psychiatric family history and Neurological disease in autistic spectrum disorders. Dev. Med. Child Neurol., 36(15): 441- 448.
Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition (DSM-IV) (1994). Published by the American Psychiatric Association, Washington D.C.
Folstein SE, Rosen-Sheidley B (2001). Genetics of autism: complex etiology for a heterogeneous disorder. Nat. Rev. Genet., 2(12): 943-955.
Fombonne E (2002). Epidemiological trends in rates of autism. Mol. Physiol., 7(suppl 2): 54-56.
Fombonne E (2003). Epidemiological surveys of Autism and other pervasive Developmental Disorders: an update. J. Autism Dev. Disord., 3(4): 365-383.
Fridman R (2008). Autism Gene Discoveries may Support Behaviour Therapy. J. Neurol., 8(16): 1-16.
Frith U, Happe´ F (1994). Language and communication in autistic disorders. Phil Trans R Soc Lond B, 346: 97-104.
Gardener H, Spiegelman D, Buka SL (2009). Prenatal risk factors for autism comprehensive meta-analysis. Br. J. Psychiatry, 195(1): 7-14.
Gauderner H, Spiegelman D, Stephen L (2009). Prenatal risk factors for autism comprebensive meta analysis. Br. J. Psychiatry, 195: 7-14.
Gillberg C, Coleman M (1992). The Biology of the Autistic Syndromes. 2nd ed. London, Mackeith Press, p. 90.
Grether JK, Anderson MC, Croen LA, Smith D, Windham GC (2009). Risk of autism and Increasing Maternal and Paternal age in a large North American Population, Am. J. Epidemiol., 170(9): 1118-1126.
Grether JK, Rosen NJ, Smith KS (2009). Investigation of shifts in autism reporting in the California Department of Develop mental services. J. Autism Dev. Disord., 39(10): 1412-1419.
Hultman CM, Sparén P, Cnattingius S (2002). Perinatal risk Factors for infantile autism. Epidemiology 13: 417-423.
Klauck SM (2006). Genetics of Autism Spectrum disorder Europeon J. Human Genetics 14, 714-720.
Kolevzon A, Gross R, Reichenberg A (2007). Prenatal and Perinatal risk factors for Autism. Arch. pediatrics Adole. Sci. Med., 161(4): 326-333.
Kolevzon RG, Reichenberg A (2007). Prenatal and Perinatal risk factors for Autism: A Review and Integration of Findings. Arch Pediatr. Adolesc. Med. April; 161 (4): 326-333.
Korponay-Syzabo IR, Laurila RK, Opre J, Király R, Kovács JB, Kaukinen K, Fésüs L, Mäki M (2005). Coeliac disease case finding and diet monitoring by point of care testing. Aliment. Pharmacot. Ther., 22: 729-737.
Lauritsen MB, Pedersen CB, Mortensen PB (2005). Effects of familial risk factors and place of birth on the risk of autism a nationwide register- based study. J. Child Psychol. Psychiatry, 46: 963-971.
Lidisky TI, Schneider JS (2003). Lead neurotoxicity in children: basic mechanisms and clinical correlates. Brain, 126(1): 5-19
Hornig M, Briese T, Buie T, Bauman ML, Lauwers G, Siemetzki U, Hummel K, Rota PA, Bellini WJ, O'Leary JJ, Sheils O, Alden E, Pickering L, Lipkin WI (2008). Lack of association between Measles Virus vaccine and Autism with enteropathy. A case control study. PLOS ONE, 3(9): e 3140.
Maimburg RD, Vaeth M, Schendel DE, Bech BH, Olsen J, Thorsen P (2008). Neonatal Jaundice: a risk factor for infantile autism? Pediatr.

Perinat. Epidemiol., 22 (6): 562-568
May-Benson TA, Kooman JA, Teasdale A (2009). Incidence of pre, perinatal, Post nhatal birth and developmental Promblems of children with sensory processing disorder and children with autism spectrum disorder. Front Integr. Neurosci., 3(31): 18-21.
Mitelman F (1995). ISCN, an international System For Human cytogenetics nomenclature. Basel: Krager.
Morric R, Aegin MC (2009). Syndrome of allergy, apraxia and malabsorption: characterization of a neuro developmental phenotype that responds to omega 3 and Vit E Supplementation Alter. There. Health Med., 15(4) 34-43.
Nemec G, Ventura A, Stegano M, Di Leo G, Baldas V, Tommasini A, Ferrara F, Taddio A, Città A, Sblattero D, Marzari R, Not T (2006). Not Looking for celiac disease. Diagnostic accuracy of two rapid comenrcial assays Am. J. Gaastroenterol., 101: 1-4.
Newschaffer CJ, Croen LA, Daniels J Giarelli E, Grether JK, Levy SE, Mandell DS, Miller LA, Pinto-Martin J, Reaven J, Reynolds AM, Rice CE, Schendel D, Windham GC (2007). The epidemiology of autism spectrum disorders. Annual Rev. Public Health, 28: 235-58.
Pichichero ME, Gentle A, Giglio N, Umido V, Clarkson T, Cernichiari E, Zareba G, Gotelli C, Gotelli M, Yan L, Treanor J (2008). Mercury levels in newborns and infants after Receipt of thimerasal contaning vaccines. Pediatrics, 121(2): e. 208-214.
Potts M, Bellows B (2006). Autism and diet. J. Epidemiol. Community Health, 60(5): 375-375.
Raivio T, kaukinen K, Nemes E, Laurila K, Collin P, Kovács JB, Mäki M, Korponay-Szabó IR (2006). Self Transglutaminase – based rapid celica antibody disease antibody detection by lateral flow method. Aliment Pharmacol. Ther., 24: 147-154.
Rapoport JL (2009). Autism spectrum Disorders and child hood onset schizophrenia. J. Am. academy Child Adolescent Psychiatry, 48(1): 10-18.
Reichenberg A, Gross R, Weiser M, Bresnahan M, Silverman J, Harlap S, Rabinowitz J, Shulman C, Malaspina D, Lubin G, Knobler HY, Davidson, M. & Susser, E (2006). Advancing Paternal age and autism. Arch. Gen. Psychiatry, 63 (9): 1026-1032.
Rodier PM, Hyman SL (1998). Early environmental factors in autism. Mental Retardation and Developmental Disabilities. Res. Rev., 4(2): 121-128.
Rogers SJ (2009). What are infant siblings teaching us about autism in infancy. Autism Res. Jun; 2 (3): 125-37.
Román GG (2009). Autism: transient in utero hypothyroxinemia related to maternal flavonoid ingestion during pregnancy and to other environmental antithuroid agents. J. Neurol. Sci., 276(I 1): 15-26.
Rooney DE, Czepulkowzki PH (1992). A practical approach constitutional analysis: Human cytogenetics, (eps). Rooney DE, Czepulkowzki PH Second edition, New York, Oxford University Press.
Saleh M, Elham H, Ehaziuddin M (2009). Autism in Saudi Arabio, Presentation, Clinical correlates and comorbidity. Transcult. Psychiatry, 46(2): 340-347.
Sasanfar R, Haddad SA, Tolouei A, Ghadami M, Yu D, Santangelo SL (2010). Parental age increases the risk for autism in an Iranian population sample. Mol. Autism, 1: 2, doi:10.1186/2040-2392-1-2.
Schopler E, Reichler R, Renner B (1986). The childhood autism rating scale (CARS) for diagnostic screening and classification of autism, New York: Irvington.
Slazyk WE, Hannon WH (1993). In Laboratory methods for Neonatal screening (Therrell BL. ed) American Public Health Association, Washington DC., p. 23.
Smith RA, Farnworth H, Weight B, Allgar V (2009). Are there more bowel Symptoms in children with autism compared to normal. Autism, 13(4): 343-355.
Steiner CE, Acosta AX, Guerreiro MM, Marques-de-Faria AP (2007). Genotype and natural history in unrelated individuals with phenlketonuria and autistic behaviours. Arq. Neurosci., 65(2A): 202-5.
Stubbs EG, Elizabeth Ash E and Williams PS (1984). Autism and cytomegalovirus. J. Autism Dev. Disord. 14 (2): 183-189.
Szpir M (2006). Tracing the origins of autism: a spectrum of new studies. Environ. Health Prespect., 114(7): A 412-8.
Wakefield AJ, Murch SH, Anthony A, Linnell J,Casson D M, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Harvey P, Valentine A, Davies SE, Walker-Smith JA (1998). Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. Lancet. 351(9103): 637-641.
Williams JG, Higgins JPT, Brayne CEG (2006). Systematic review of prevalence studies of Autism spectrum disorders. Arch Dis. Child 91 (1): 8-15.