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Original Research Article

Investigating risk factors for developing autism, cerebral palsy and down syndrome in a Trinidadian population

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ABSTRACT

Background: Autism, Cerebral Palsy and Down Syndrome are three lifelong, non-curable common developmental disorders that affect approximately 1 in 59, 1 in 323, and 1 in 700 children respectively. This research is to study the effects of prenatal, perinatal, and postnatal factors on the development of Autism, Cerebral Palsy (CP) and Down Syndrome (DS) in a Trinidadian population.
Methods: This was a descriptive case-control study comprised 75 subjects, with 25 cases from each of the three disorders investigated, i.e. autism, CP and DS.
Results: The highest risk of autism was associated with mothers having high stress levels (p=0.002), high blood pressure (0.042), and low iron levels (p=0.012) during the pregnancy, as well as having a family history of autism (p=0.002) and residing in an air polluted area (p=0.034). The highest risk of cerebral palsy was associated with a child being born preterm (case 24%, control 0; p=0.009), experiencing postnatal complications (case 80%, control 4%, p=0.000), having a birth weight less than 2500 g (p=0.002), having an abnormal appearance at birth (p=0.045), specifically the prevalence of blue baby (case 20%, control 0) and abnormal appearance (case 12%, control 4%), a case father having a low educational level (p=0.002), a case of mother having gestational diabetes during the pregnancy (p=0.037) and having older mothers (p=0.033) and fathers (p=0.033) than the controls. The highest risk of down syndrome was associated with mothers having high stress (p=0.017) and blood pressure (p=0.021) during pregnancy.
Conclusions: The findings of our research confirm that autism, CP and DS are multi-factorial developmental disorders. A combination of environmental conditions, genetics, prenatal and postnatal factors are associated with an increased risk of developing autism, cerebral and down syndrome.

Keywords: Autism, Cerebral palsy, Down syndrome, Perinatal, Postnatal, Prenatal

INTRODUCTION

Autism, Cerebral Palsy and Down Syndrome are three lifelong, non-curable common developmental disorders that affect approximately 1 in 59, 1 in 323, and 1 in 700 children respectively as stated by CDC. As the underlying cause of these three is unknown, the etiology of the development of these disorders is multi-factorial. Prenatal, perinatal, or postnatal factors have been proposed by different researchers to have significant impact on their development. This study seeks to establish associations between various factors and an increased risk of developing these three disorders in a Trinidadian population.

Autism or Autism Spectrum Disorders (ASD), is a non-progressive neuro-developmental disorder typically appearing before the age of three. Classically, it involves a triad of impairments in communication skills, social interaction, and repetitive behavior and restrictive interests.

Two major factors of Autism are birth weight (<2500g) and gestational age (<33 wks. to <37 wks.), but different articles found conflicting evidence. A 2008 Atlanta study focused on birth weight and gestational age in their study, finding a somewhat increased risk to birth weight <2500g for Autism (12%) and for preterm birth <37wks (14%).[1] For low birth weight (<2500g), which is an indicator of reduced growth, strong associations were evident, yet no association was found in another study with a significantly smaller sample size than the others - this may account for the lack of correlation.[2] Gestational ages of <33 wks and <35 wks., are an indicator of preterm birth, which is also a risk factor for Autism.[1,2]

Parental age indicated a strong association between advanced maternal age (>/= 35 yrs), others found no statistically significant correlation.[2-5]A similar correlation was found with paternal age.[2,3,6] Socioeconomic status also proved to be a risk factor as children with Autism tended to have more highly educated parents.[2,6]

Prenatal risk factors found were the parental psychiatric history, use of prenatal and intrapartum pharmaceutical agents.[2,7] e.g., Thalidomide (small risk), and maternal infection during the pregnancy.[7] Perinatal complications that had evidenced as risk factors included labour induction, use of maternal epidural caudal anesthesia, foetal distress; delivery by emergency or elective Caesarean section, uterine bleeding, and breech presentation.[2,3,5,8] Postnatal or neonatal factors associated with Autism were infants with low Apgar score (<6 at 1 minute) and those who require neonatal care & assisted ventilation.[3]

From the research reviewed, results are mostly inconsistent. This may be due to study design differences, no adjustments in the study for confounding factors and in a few cases due to small sample sizes, which would have had insufficient cases to effectively detect the effect of individual factors.[9]

Cerebral Palsy is a neuromuscular disorder causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behavior and/or a seizure disorder. Cerebral palsy is the leading cause of childhood disability affecting function and development. The brain lesions that cause cerebral palsy occur from the fetal or neonatal period to up to age 3 years. The sub-classifications of the disorder are spastic, dyskinetic, ataxic, hypotonic and mixed, which for the purpose of this study, will all be referred to under their umbrella term, Cerebral Palsy.

The main risk factors uncovered were birth weight and gestational age. Decreased gestational age (preterm <37wks) were noted as a strong risk factor.[9,10] Increased risk of CP was also common with early (37 wks) as well as late delivery (42 wks) in one study. Low birth weight (<2500g) was also a significant factor with most studies citing this as greatly increasing the risk for CP.[9-12] From reviewing the research, several other factors (demographic, socioeconomic, prenatal, perinatal and postnatal) increasing the risk of CP were discovered. Prenatal factors include maternal alcohol use, maternal smoking, maternal antibiotic use and intrapartum hypoxia.[9,12,13] Socioeconomic factors such as less educated parents were associated with increased risk of developing CP.[9] Maternal age was found as a risk factor for CP. One study cited mothers >/= 35 years as being at increased risk, whereas two articles cited younger mothers (<18 yrs) as being at increased risk.[9]

Perinatal/delivery complications with increased CP risk are breech presentation, forceps delivery, vacuum delivery, labour induction, C-section, abruption placentae, prolonged labour, PROM (premature rupture of membranes) asphyxia and maternal infections which carry significant risk.[9-13] Maternal infection and other inflammatory processes such as neonatal sepsis and pre-eclampsia have strong associations with the risk of CP, and thus may have a pathological role in CP aetiology.[4,10,13] Infections were found as the major cause of acquired CP (42.9%), leading to circulatory collapses that accounts for CP.[11] A 2005 Washington population-based study found that prematurity and maternal infection both significantly increase the risk of CP by 20 times.[14]

The main neonatal complications/ birth characteristics found to be of significant risk/association factor are a low Apgar score (<4 at 5minutes) and the need for the infant to be admitted into neonatal special care unit and require mechanical ventilation.[6,10,12]

Down Syndrome or Trisomy 21 is most common genetic birth defect caused by presence of an extra copy of genetic material on chromosome 21. It is characterized by intellectual disability, dysmorphic facial features and other distinctive phenotypic traits. Down Syndrome (DS) is different from the other two disorders in that, one factor, advanced maternal age (>/=35 yrs.), has been cited by countless researchers as the main maternal factor that increases risk for developing DS. So much so that it is considered an established risk factor, forming the basis for prenatal genetic screening offered to pregnant women of a certain age. Increasing maternal age (>/= 35 yrs.) was found to increase the risk of developing DS in several DS-related studies that were reviewed.[14,15] Other research has investigated other factors but to a lesser extent as the focus has been on advancing maternal age, and the reasons behind that causative factor.

Table 1: List of factors investigated.

Prenatal factors	Perinatal factors	Postnatal factors	Other factors
Maternal prenatal lifestyle Smoking Illegal drug use High stress levels Prescription drug use Supplement use Alcohol use Other	Birth characteristics Birth weight Birth order (parity) Gestational age at birth	Postnatal complications Birth injury Baby put under oxygen Baby placed under UV light	Demographic factors Maternal age of delivery Paternal age of delivery
Complications during pregnancy High blood pressure Low iron levels Gestational diabetes Asthmatic attacks	Type of delivery Traditional vaginal delivery Emergency caesarean section Elective caesarean section Forceps delivery Under anaesthesia Other	Problems as an infant Proper appetite Normal bowel movements Incessant crying Seizures Jaundice Colic High fever Frequent infections Skin rashes Allergies Vomiting Diarrhoea Constipation Feeding Problems Other problems	Socioeconomic factors Highest educational level of mother Highest educational level of father
Exposure to second-hand smoke as a fetus	Complications during delivery	Appearance of child at birth	Environmental factors Air pollution in/around area
Maternal reproductive health Abortion/Miscarriages Fertility problems Attendance at antenatal clinic (duration and irregularity) Number of ultrasounds taken		Exposure to second-hand smoke as a baby/infant	Genetic factors: Family history of disorder, and their familial relationship Complications during the birth of other children (if applicable)

The main limitation here was small sample sizes in some cases. This can lead to inaccurate results as in one study of only 35 cases, resulted in no significant antenatal and intrapartal associations being found.[16] There were also differences in study design and in the selection of participants and control groups, which could account for any discrepancies seen in the research literature. Underlying causes remained unknown but what is known is that some studies have identified them as parameters that increase in the chances of a child developing Autism, Cerebral Palsy or Down syndrome. These three disorders are thus complex in its causation thus a study of several risk factors is necessary in order to have a holistic approach to what exactly puts a child at risk of developing Autism, Cerebral Palsy, or Down's Syndrome. A summary of the risk factors investigated can be seen in Table 1.

METHODS

Data were obtained using a questionnaire which investigated general demographic characteristics, as well as various prenatal, perinatal, and postnatal factors. The main variables investigated are listed in Table 1. Data was collected via direct completion of questionnaires, parental interviews and an online version of the questionnaire. The target population of cases was Trinidadians within the ages of 0-25 years diagnosed with Autism, Cerebral Palsy or Down syndrome, and their parents/guardians. The different subgroups of these disorders were not differentiated in this study. The study was conducted over a period of 9 months. The inclusion criteria are all subjects between the ages of 0-18 seen at the clinic and contacted within the three societies, between our data collection period of 5 months. The exclusion criteria will be participants not contacted within that period, who falls out of age range, and whose parents/guardians cannot be contacted, or decline to participate.

Data collection

The questionnaires were either directly filled out by parents/guardians, via interviews, or via an online survey format of the questionnaire. Several organizations and national societies were targeted and involved in this

study, namely, the Special Needs Dental Clinic at Eric Williams Medical Sciences Complex, Memisa Centre, Lady Hochoy Home, Immortelle Centre, the Down Syndrome Family Network, Autistic Society of Trinidad and Tobago and the Cerebral Palsy Society of Trinidad and Tobago. The sample size was 25 cases per disorder.

In total, 88 case questionnaires were completed, and 13 of those were excluded: 6 questionnaires due to the participants not having Autism, Cerebral Palsy nor Down Syndrome but rather another disorder that was not relevant to this study, or a combination of disorders, which was not the focus of this study, and 7 questionnaires due to missing information in 5 or more factors investigated within the questionnaire. This left 25 cases per disorder progressing to analysis.

Twenty-eight control questionnaires were collected, and three were excluded due to missing information, leaving 25 control cases to be subsequently analyzed.

Statistical analysis

The responses for each factor were recorded and tabulated, then analyzed using the SPSS version 16-Statistical Package for the Social Sciences. A χ^2-test was used for analysis of categorical variables (Table 4) and t-test was used for continuous variables (Table 3), with $p < 0.05$ being considered significant (95% critical value).

RESULTS

After the exclusion of cases that did not meet the criteria for the study, a total of 75 cases were identified (25 Autism cases, 25 Cerebral Palsy cases, 25 Down Syndrome cases), and 25 control subjects as well. Given that this study is in effect a three-part study, the results will be separated by disorder.

Autism

Demographics (Table 2) of the 25 cases of autism, 64% were male while 36% were autistic females. The ethnicity with the male greatest occurrence of autism was found to be African (44%), with the parents reflecting the same ethnicities and percentages as the children.

No autistic children were diagnosed at birth or within the first year as having the disease. 24-35 months old children having the highest rate of diagnosis (36%) among all the cases. The greatest occurrence of children being born with autism also presented for the first-born child (44%), the second greatest occurrence being the third born child (24%), and successive children having a decreased rate (Table 3).

Prenatal Complications - the prenatal factors investigated being listed in Table 1. Of all the factors investigated high stress levels (p value 0.002), high blood pressure (p value 0.042) and low iron levels (p value 0.012) were most likely to be associated with developing the disease. These three factors were also statistically higher than the control group (Table 4).

Perinatal complications

The perinatal factors investigated being listed in Table 1. No particular factor was unusual, with the majority of both the case and control group having full term and traditional/vaginal deliveries.

Postnatal complications

The postnatal factors investigated being listed in Table 1. High fever (p=0.037) and constipation (p=0.042) of the babies were more common in the case group when compared to the control group.

Other Factors - the other factors investigated being listed in Table 1. 32% of the case group was found to have air pollution in/around the area where they live (p=0.034), while none from the control group had this problem. Also, 32 % of the case group had a family history of autism (p=0.002).

These two factors having a high probability of association with developing the disease. Another notable factor is that both the mother and father of children born with autism were generally older than those of the control group.

Cerebral palsy

Demographics of the 25 cases of cerebral palsy, 60% were male while, 40% were females. The ethnicity with the greatest occurrence of autism was found to be Indian (48%). The most common paternal ethnicity also being Indian (56%) and maternal being Indian (48%). The most diagnosis of cerebral palsy in children occurred between birth and 11 months and 12 to 23 months (32% and 28% respectively). The greatest occurrence of children being born with cerebral palsy also presented for the first-born child (52%), the second greatest occurrence being the second born child (36%), and successive children having a decreased rate.

Prenatal complications

The prenatal factors investigated being listed in table 1. gestational diabetes (p value 0.037) was the only factor of possible association discovered, while it can be noted mothers of children born with cerebral palsy generally had higher stress levels.

Perinatal complications

The perinatal factors investigated being listed in Table 1. On comparison of the case group to the control group, almost a quarter of the case group was born preterm (24%), a possible connection.

Table 2: Demographic characteristics of the sample investigated.

		Child's disorder			Total
		Autism (n=25)	Cerebral palsy (n=25)	Down syndrome (n=25)	
Age of child	0-5 years	7 (28%)	6	6	19
	6-10 years	8 (32%)	9	4	21
	11-15 years	4 (16%)	4	12	20
	16 - 20 years	3 (12%)	4	0	7
	21 -25 years	3 (12%)	2	3	8
Gender of child	Female	9 (36%)	10	10	29
	Male	16 (64%)	15	15	46
Ethnicity of child	African	11 (44%)	4	4	19
	Asian	1 (4%)	0	0	1
	Indian	3 (12%)	12	6	21
	Mixed	9 (36%)	9	15	33
	Spanish	1 (4%)	0	0	1
Ethnicity of mother	African	13	6	6	25
	Asian	1	0	1	2
	Indian	14	14	7	25
	Mixed	6	5	11	22
	Spanish	1	0	0	1
Ethnicity of father	African	12	5	6	23
	Asian	1	0	0	1
	Indian	5	12	6	23
	Mixed	6	8	13	27
	Spanish	1	0	0	1

Table 3: Compared with controls for continuous prenatal, antenatal, postnatal and other* variables investigated.

Autism	Controls			Cerebral palsy	Controls			Down syndrome	Controls		
		t-test	p+ value			t- test	p+ value			t- test	p+ value
No. cases (%) 2 (10.5%) 0 12(63.2%) 5 (26.3%) Mean (SD) 2948.11 (897.748)	No. cases (%) 0 3 (12%) 13 (52%) 9 (36%) Mean (SD) 3288.84 (582.434)	1.525	0.135	No. cases (%) 2 (8.7%) 7 (30.4%) 12(52.2%) 2 (8.7%) Mean (SD) 2679.87 (722.327)	No. cases (%) 0 3 (12%) 13 (52%) 9 (36%) Mean(SD) 3288.84 (582.434)	3.227	0.002	No. cases (%) 1 (4.2%) 7 (29.2%) 12 (50%) 4 (16.7%) Mean (SD) 2797.46 (617.285)	No. cases (%) 0 3 (12%) 13 (52%) 9 (36%) Mean (SD) 3288.84 (582.434)	2.867	0.006
Mean (SD) 27.40 (7.522)	Mean (SD) 24.76 (4.400)	1.515	0.136	Mean (SD) 28.40 (7.000)	Mean (SD) 24.76 (4.400)	2.201	0.033	Mean (SD) 33.24 (7.043)	Mean (SD) 24.76 (4.400)	5.106	0.000
Mean (SD) 30.83 (6.384)	Mean (SD) 28.00 (5.323)	1.690	0.098	Mean (SD) 32.46 (8.043)	Mean (SD) 28.00 (5.323)	2.297	0.026	Mean (SD) 37.76 (10.138)	Mean (SD) 28.00 (5.323)	4.262	0.000
Mean (SD) 2.24 (1.422)	Mean (SD) 1.60 (0.866)	1.922	0.061	Mean (SD) 1.64 (0.810)	Mean (SD) 1.60 (0.866)	0.169	0.867	Mean (SD) 2.55 (1.535)	Mean (SD) 1.60 (0.866)	2.642	0.011
Mean (SD) 1.28 (1.458)	Mean (SD) 1.60 (1.041)	0.893	0.376	Mean (SD) 1.48 (1.262)	Mean(SD) 1.60 (1.041)	0.367	0.715	Mean (SD) 1.84 (1.463)	Mean (SD) 1.60 (1.041)	0.642	0.525
MEAN (SD) 0.72 (0.980)	MEAN (SD) 0.60 (1.155)	0.396	0.694	MEAN (SD) 0.52 (0.823)	MEAN(SD) 0.60 (1.155)	0.282	0.779	MEAN (SD) 0.72 (1.242)	MEAN(SD) 0.60 (1.155)	0.354	0.725

┼ p <0.05 Indicates a statistically significant association
* Refer to Table 1 for a list of the Other factors

Table 4: Compared with controls for categorical prenatal, antenatal, postnatal and other* variables investigated.

Risk factor	Autism (n=25)	Controls (n=25)			Cerebral palsy (n = 25)	Controls (n = 25)			Down syndrome (n = 25)	Controls (n= 25)		
	No. cases (%)		X^2 test	P ┼ value	No. cases (%)		X^2 test	P ┼ value	No. cases (%)		X^2 test	p ┼ value
Prenatal factors												
Maternal prenatal lifestyle												
Smoking	4(16)	1(4)	2.000	0.157	2(8)	1(4)	0.355	0.552	3(12)	1(4)	1.087	0.297
Illegal drug use	1(4)	2(8)	0.355	0.552	0(0)	2(8)	2.083	0.149	1(4)	2(8)	0.355	0.552
High stress levels	12 (48)	2(8)	9.921	0.002	7(28)	2(8)	3.388	0.066	9(36)	2(8)	5.711	0.017
Prescription drug use	1(4)	1(4)	0.000	1.000	0(0)	1(4)	1.020	0.312	3(12)	1(4)	1.087	0.297
Special diet No salt Vegetarian Low carb and low fat	 0 0 0	 0 2(8) 0	2.083	0.149	 0 0 0	 0 2(8) 0	2.083	0.149	 1(4) 1(4) 1(4)	 0 2(8) 0	2.356	0.502
Supplement use	13 (52)	10 (40)	0.725	0.395	12(48)	10(40)	0.325	0.569	13(52)	10 (40)	0.725	0.395
Alcohol use 1-3 times/week 1-3 times per fortnight 1-3 times/month A few times	 1(4) 1(4) 2(8) 0	 0 0 0 0	4.348	0.226	 2(8) 0 3(12) 0	 0 0 0 0	5.556	0.062	 1(4) 2(8) 0 2(8)	 0 0 0 0	0.556	0.135
Complications during pregnancy												
High blood pressure	6(24)	1(4)	4.153	0.042	4(16)	1(4)	2.000	0.157	7(28)	1(4)	5.357	0.021
Low iron levels	11 (44)	3(12)	6.349	0.012	4(16)	3(12)	0.166	0.684	3(12)	3(12)	0.000	1.000
Gestational diabetes	0	0	-	-	4(16)	0	4.348	0.037	3(12)	0	3.191	0.074
Other Asthmatic attacks Low blood pressure Hemorrhaging due to car accident	 0 0 0	 0 0 0	2.381	0.123	 1(4) 1(4) 1(4)	 0 0 0	3.191	0.363	 0 1(4) 1(4)	 0 0 0	2.083	0.353
Exposure to second hand smoke as a foetus	10 (40)	4(16)	3.579	0.059	3(12)	4(16)	1.143	0.565	5 (20)	4(16)	0.136	0.713
Maternal reproductive health												
Fertility problems	1(4)	2(8)	0.355	0.552	1(4)	2(8)	0.355	0.552	6(24)	2(8)	2.381	0.123
Regular antenatal clinic attendance	23 (92)	23 (92)	0.000	1.000	24(96)	23(92)	0.355	0.552	22(88)	23 (92)	0.222	0.637
Starting month of antenatal care First trimester Second trimester Third trimester	 18(72) 6(24) 1(4)	 20(80) 5(20) 0	1.196	0.550	 18(75) 5(20.8) 1(4.2)	 20(80) 5(20) 0	1.085	0.581	 16(72.7) 6(27.3) 0	 20(80) 5(20) 0	0.345	0.557
Perinatal factors												

Birth characteristics												
Gestational age at birth Full term Preterm Overdue	3(92) 1(4) 1(4)	25(100) 0 0	2.083	0.353	19(76) 6(24) 0	25(100) 0 0	6.818	0.009	21(84) 4(16) 0	25(100) 0 0	4.348	0.037
Type of delivery			1.526	0.676			3.526	0.474			3.443	0.487
Traditional vaginal delivery Emergency caesarean section Elective caesarean section Forceps delivery Under anaesthesia	19 (76) 5(20) 0 0 1(4)	20 (80) 3(12) 1(4) 0 1(4)			19(76) 5(20) 0 1(4) 0	20(80) 3(12) 1(4) 0 1(4)			17(68) 2(8) 3(12) 2(8) 1(4)	20 (80) 3(12) 1(4) 0 1(4)		
Complications during delivery	2(8)	3(12)	0.222	0.637	9(36)	3(12)	5.324	0.070	6(24)	3(12)	1.220	0.269
Postnatal factors												
Postnatal complications	5(20)	1(4)	3.030	0.082	20(80)	1(4)	29.639	0.000	8(32)	1(4)	6.640	0.010
Appearance of child at birth			2.000	0.572			8.025	0.045			2.021	0.364
Normal Pale and delicate Blue baby (cyanotic) Abnormal	21(84) 3(12) 1(4) 0	21(84) 3(12) 0 1(4)			13(52) 4(16) 5(20) 3(12)	21(84) 3(12) 0 1(4)			17(68) 7(28) 0 1 (4)	21(84) 3(12) 0 1(4)		
Problems as an infant/baby												
Proper appetite Normal bowel movements Incessant crying Seizures Jaundice Colic High fever Frequent infections Skin rashes Allergies Vomiting Diarrhoea Constipation Feeding problems Other problems Congenital heart defect Viral encephalitis Meningitis	2(8) 19(76) 12(48) 1(4) 1(4) 1(4) 4(16) 0 2(8) 1(4) 4(16) 0 6(24) 3(12) 0	6(24) 18(72) 6(24) 0 1(4) 2(8) 0 0 2(8) 2(8) 1(4) 1(4) 1(4) 2(8) 0	2.381 0.104 3.125 1.020 0.000 0.355 4.348 - 0.000 0.355 2.000 1.020 4.153 0.222 -	0.123 0.747 0.077 0.312 1.000 0.552 0.037 - 1.000 0.552 0.157 0.312 0.042 0.637 -	6(24) 9(36) 9(36) 13(52) 7(28) 1(4) 6(24) 7(28) 4(16) 1(4) 9(36) 3(12) 9(36) 13(52) 1(4)	19(76) 18(72) 6(24) 0 1(4) 2(8) 0 0 2(8) 2(8) 1(4) 1(4) 1(4) 2(8) 0	13.520 6.522 0.857 17.568 5.357 0.355 6.818 8.140 0.758 0.355 8.000 1.087 8.000 11.524 3.191	0.000 0.011 0.355 0.000 0.021 0.355 0.009 0.004 0.384 0.355 0.005 0.297 0.005 0.001 0.363	21(84) 14(56) 4(16) 0 6(24) 1(4) 4(16) 4(16) 4(16) 3(12) 5(20) 2(8) 3(12) 6(24) 6(24)	19(76) 18(72) 6(24) 0 1(4) 2(8) 0 0 2(8) 2(8) 1(4) 1(4) 1(4) 2(8) 0	0.500 1.389 0.500 - 4.153 0.355 4.348 4.348 0.758 0.222 3.030 0.355 1.087 2.381 6.818	0.480 0.239 0.480 - 0.042 0.552 0.037 0.037 0.384 0.637 0.082 0.552 0.297 0.123 0.009
Exposure to second hand smoke as a baby/infant	6(24)	5(20)	0.117	0.733	4(16)	5(20)	0.136	0.713	8(32)	5(20)	0.936	0.333

Other factors											
Socioeconomic factors											
Highest education level of mother			7.571	0.056			3.301	0.192			3.193	0.363
None	1(4)	0							1(4)	0		
Primary	6(24)	1(4)			5(20)	1(4)			4(16)	1(4)		
Secondary	15(60)	15(60)			14(56)	15(60)			13(52)	15(60)		
Tertiary	3(12)	9(36)			6(24)	9(36)			7(28)	9(36)		
Highest education level of father			4.725	0.094			12.424	0.002			7.692	0.021
None	0	0			0	0			0	0		
Primary	4(16.7)	0			9(36)	0			5(20)	0		
Secondary	17(70.8)	20(80)			10(40)	20(80)			12(48)	20(80)		
Tertiary	3(12.5)	5(20)			6(24)	5(20)			8(32)	5(20)		
Environmental factors												
Air pollution in/around living area	8(32)	2(8)	4.500	0.034	5(40)	2(8)	1.495	0.221	6(24)	2(8)	2.381	0.123
Genetic factors												
Family history of disorder	8(32)	0	9.524	0.002	3(12)	0	3.191	0.074	10 (40)	0	12.500	0.000
Complications during the birth of other children	1(4)	4(16)	2.000	0.157	1(4)	0	2.891	0.236	3 (12)	4 (16)	1.690	0.430

* Refer to table 1 for a list of the other factors

┼ p <0.05 indicates a statistically significant association

Postnatal complications

The postnatal factors investigated being listed in Table 1. On comparison of the case group to the control group (and even the other two case groups), cerebral palsy children suffered from the most post-natal complications. A staggering 80% of the 25 cases (p value 0.000) suffered from postnatal complications, whereas only 4% of the control group had complications. Only 20% of the cases had babies that appeared blue/ cyanotic and 12% had an abnormal appearance (p =0.045). Other notable factors included a minority of the cases having proper appetite (p value 0.000) or normal bowel movements (p=0.011), and a large amount having suffered from seizures (p value 0.000), jaundice (p=0.021), high fever (p=0.009), frequent infections (p value 0.004), vomiting (p value 0.005), constipation (p value 0.005) and feeding problems (p=0.001).

These factors are highly unlikely to not have been associated with the development of cerebral palsy in these cases. The other factors investigated being listed in Table 1. The ages of both parents were found to be older in children born with cerebral palsy when compared to the control group. The mean age of the mother was 28.40 (p=0.033) and the mean age of the father being 32.46 (p =0.026). Having children later in life may therefore increase the likelihood of children born with CP. the final factor of possible relation is the highest level of education attained by the parents with all parents of the control group attaining at least a secondary level whereas only 40% of the case group attained this same level and 36 % only reaching the primary level (p=0.002).

Down syndrome

Demographics of the 25 cases of down syndrome, 60% were male while 40% were down syndrome females. The ethnicity with the greatest occurrence of autism was found to be mixed (60%). Most down syndrome children born to mixed fathers (52%) and mixed mothers (44%). The majority of cases being diagnosed at birth as having down syndrome (76%) and none diagnosed later than 59 months. The greatest occurrence of children being born with down syndrome also presented for the first-born child (60%), the second greatest occurrence being the second born child (24%), and successive children having a decreased rate.

Prenatal complications

The prenatal factors investigated being listed in Table 1. like all the prior diseases, ds are also associated with high stress levels, 36% of the cases (p=0.017), and high blood pressure, with 28% of the mothers suffering from this (p=0.021).

Perinatal complications

The perinatal factors investigated being listed in Table 1. compared to the control group, 16% of the case group

was born preterm whereas 100% of the control group was born full term, possibly indicating this as another factor.

Postnatal complications

The postnatal factors investigated being listed in table 1. a large number of the case group suffered from postnatal complications, 32% (p value 0.010) as compared to 4% from the control group. The main complications being the occurrence of jaundice in 24% (p=0.042), high fever in 16% (p=0.037), frequent infections in 16 % also (p=0.037) and other problems particularly congenital heart defects in 24% (p=0.009).

Other factors

The other factors investigated being listed in Table 1. on comparison of both groups the mean ages of both parents at birth was considerably older in the case group than the control. The mean age of the mother being 33.24 (p=0.000) and the mean age of the father being 37.76 (p=0.000). The age of the parents undoubtedly affecting the probability of being born with down syndrome. like the previous disease, the highest level of education of the case group was generally lower than the control group (p=0.021), with 20% of the case group obtaining a primary level education.

DISCUSSION

This report studies the relationship between various risk factors, and the development of Autism, Cerebral Palsy and Down syndrome, and also offers explanations for the associations found in the study.

Autism

Although some research has cited parental age ≥35yrs carries an increased risk of developing Autism, this study found no such correlation. Additionally, gestational age and birth weight were cited as major factors in other research but was not found to be so in this study. Prenatal risk factors such as maternal infection during Pregnancy, use of prenatal and intra-partum pharmaceutical agents were seen in other research but this study found new prenatal maternal factors. This suggests that there may be some factors affecting the development of the baby in the womb that may predispose a child to having Autism. In the case of our study, these factors were found to be high stress levels, high blood pressure and low iron levels.[3,4,7,8] Postnatal factors those showed associations with Autism were infants with a low Apgar score (<6 at 1 minute) and those requiring neonatal care and assisted ventilation.[3]

The postnatal factors found in this study are high fever and constipation as a baby, indicating that subnormal health as a baby, whether requiring neonatal care or having a high fever, has some association to developing Autism.

Additionally, this study found an association with air pollution, and a strong association with the presence of a family history of Autism, and the development of Autism, something that had not been found in other research. This suggests that there may be a genetic and environmental influence on Autism.

Cerebral palsy

Decreased gestational age (preterm birth) was found to be a strong risk factor and can be explained with the theory that fetuses that eventually develops CP will generally have an abnormal time of delivery, whether preterm or post-term. The underlying mechanisms for this association remain unclear. CP could be disrupting the time of delivery or delivery time causing them to be born at different times. Low birth weight was also found to be a strong factor, and its mechanism can be described in the same way as preterm birth. These two factors can be confounding though as babies born prematurely are more likely to have a low birth weight.

As postnatal and perinatal complications are common in CP individuals, it can be said that CP is caused due to prenatal complications as well as damage to the infant in the course of delivery and right after birth to warrant them to need postnatal interventions such as ventilation and UV lighting, affecting the appearance of the baby and leading to postnatal problems such as poor appetite, seizures and frequent infections.[1,6,10]

Less educated parents were found to be at an increased risk of developing CP in the literature and this was also found in our study, particularly with fathers that had attained up to Primary level of education.[17] Prenatally, there was also an association between gestational diabetes and the child getting CP, again pointing to the health of the fetus having some kind of effect on whether the child develops CP.

The risk of a child being born with genetic abnormalities increases as both parents age and this was reflected in our results where both maternal and paternal age were found to be associated with an increased risk of developing CP with the average maternal age as 28.40 and paternal as 32.46. Studies did not universally find a certain ‘age-group’ thereafter the risk increases significantly, but it agreed that advancing age is a factor.

Down syndrome

First, both maternal and paternal age were confirmed as risk factors, as several studies have found links between advanced maternal age to increase the risk of developing DS.[6,14] Although some theories have been put forward for the etiology of DS w.r.t. maternal age, its correlation is still largely unresolved. As with CP, a possible logical explanation is that as parental age increases, the risk of the child developing genetic abnormalities likewise increases.

The 1999 California study investigated other risk factors such as parity, educational and socioeconomic status, but no significant links were found. Our study contradicts this as increased parity and low level of paternal education were both found to be statistically significant as a risk factor for DS. Also, as a genetic disorder, of course, a family history of the disorder was expected to yield some correlation, and it was found to be a significant factor in DS development. Prematurity and low birth weight were found also to be associated with DS as well as postnatal complications, experiencing problems as a baby (jaundice, high fever, frequent infections), and prenatal factors such as high stress levels and high blood pressure. This combination of factors suggests that there is various triggers for DS, including the health of the baby while in the womb, and subsequently the health of the baby right after birth. The strength of this study lies in the fact that it is unique, and the new associations found in it undoubtedly shows a need for more research to be dedicated to these disorders, especially in light of their increasing prevalence both internationally and unassumingly locally as well.

The main limitation of this study is the small sample size obtained. The original target was 150 case participants, with 50 cases from each disorder, but the target was revised when several limitations were encountered. This was due to several reasons including poor response rates in institutions contacted, the unwillingness of home coordinators to assist us in our research, and the absence of a parent/guardian to complete the questionnaire on behalf of the affected children, whether due to them being deceased, or being mentally incapable. These were especially true for some of the homes that we contacted. The 75 cases that data was collected for does represent a good geographic range as the data were received from several parts of the country.

CONCLUSION

In the final analysis, the main risk factors for Autism, Cerebral Palsy, and Down Syndrome identified within the research are high-stress levels, prenatally low iron levels of the mother, a hereditary or genetic link; advancing age of the parents, decreased gestational age (preterm), low birth weight, postnatal complications; advanced maternal and paternal age, hereditary or genetic linkage, preterm births, and low birth weight. Moreover, it can be concluded that the underlying causes for the diseases are multi factorial.

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