"Correlation of severity of autism with risk factors and EEG abnormalities in children aged 3-12 years attending child guidance clinic at Institute of child health and hospital for children"

Dissertation submitted for

M.D. DEGREE EXAMINATION

BRANCH VII- PAEDIATRIC MEDICINE

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI

INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN

MADRAS MEDICAL COLLEGE

CHENNAI

APRIL 2015

CERTIFICATE

This is to certify that the dissertation titled **" Correlation of severity of autism with risk factors and EEG abnormalities in children aged 3-12 years attending child guidance clinic at Institute of child health and hospital for children "**submitted by **Dr. KAVITHA .H. R ,** to the Faculty of Pediatrics, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the award of M.D., Degree (Pediatrics) during the academic year 2012 – 2015 is a bonafide research work carried out by her under our direct supervision and guidance.

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DECLARATION

I solemnly declare that this dissertation entitled **"Correlation of severity of autism with risk factors and EEG abnormalities in children aged 3-12 years attending child guidance clinic at Institute of child health and hospital for children"** has been prepared by me at Madras Medical College and Institute of child health, during 2012-2015. This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.D. Degree in Pediatrics (Branch-VII).

Signature of Candidate

Place : Chennai

Date :

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INSTITUTIONAL ETHICS COMMITTEE
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EC Reg No.ECR/270/Inst./TN/2013
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CERTIFICATE OF APPROVAL

To

Dr.Kavitha H.R,
Postgraduate in Peadiatrics,
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Dear **Dr. Kavitha H.R,**

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled **"Correlation of severity of autism with risk factors and EEG abnormalities in children aged 3-12 years attending child guidance clinic at Institute of Child Health and Hospital for Children"** No.29042014.

The following members of Ethics Committee were present in the meeting held on 08.04.2014 conducted at Madras Medical College, Chennai-3.

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2.	Prof. Kalaiselvi, M.D, Vice Principal, MMC, Ch-3	-- Member Secretary
3.	Prof. Nandhini, M.D, Inst. of Pharmacology, MMC, Ch-3	-- Member
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6.	Thiru. S. Govindasamy, BA., BL	-- Lawyer
7.	Tmt.Arnold Saulina, MA MSW	-- Social Scientist
8.	Thiru.S.Ramesh Kumar, Administrative Officer, MMC, Ch-3.	-- Lay Person

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
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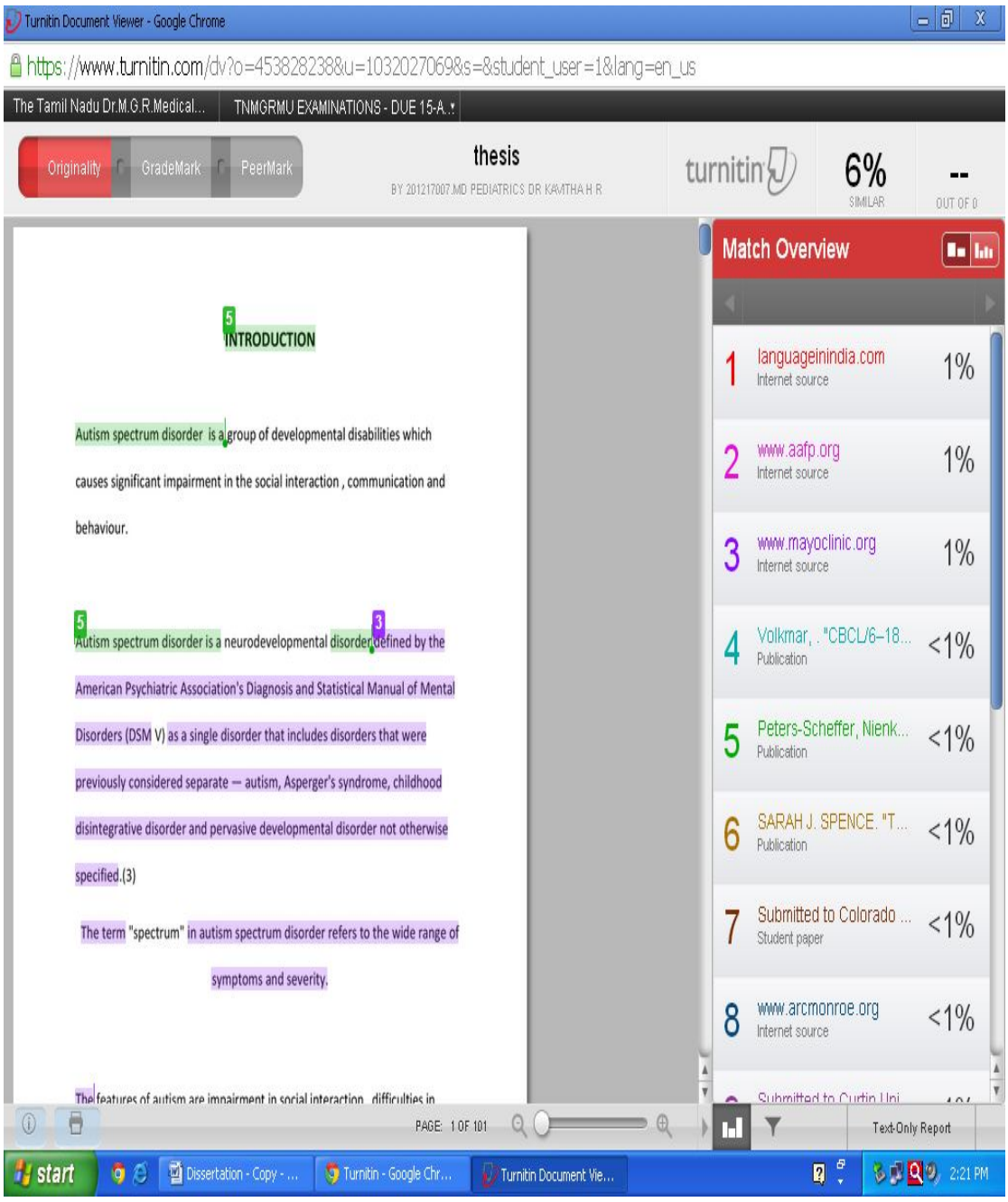
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INTRODUCTION
Autism spectrum disorder is a group of developmental disabilities which causes significant impairment in the social interaction , communication and behaviour.
Autism spectrum disorder is a neurodevelopmental disorder defined by the American Psychiatric Association's Diagnosis and Statistical Manual of Mental Disorders (DSM V) as a single disorder that includes disorders that were previously considered separate — autism, Asperger's syndrome, childhood disintegrative disorder and pervasive developmental disorder not otherwise specified.(3)
The term "spectrum" in autism spectrum disorder refers to the wide range of symptoms and severity.
The features of autism are impairment in social interaction, difficulties in
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INTRODUCTION

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ABSTRACT

"Correlation of severity of autism with risk factors and EEG abnormalities in children aged 3-12 years attending child guidance clinic at Institute of child health and hospital for children"

BACKGROUND

Autism is a neurodevelopmental disorder characterised by significant impairment in the social interaction, communication and behaviour. The exact etiology still remains unknown. Genetic, environmental factors, prenatal, perinatal, postnatal risk factors said to play a role in the pathogenesis of autism. Subclinical epileptiform discharges said to be present in approximately 30% of children with autism which are causally associated with the deficits and severity.

METHODS

Children aged 3 – 12 years diagnosed as autism using DSM – V criteria in child guidance clinic at Institute of child health and hospital for children were enrolled in this study. Prenatal, perinatal and postnatal risk factors of autism data are collected. Severity of autism is assessed by childhood autism rating scale (CARS). Electroencephalogram (EEG) was done to all children in the study.

RESULTS

In the study, out of 72 autistic children 73.6 % (n-53) were in the age group of 3-6 years,19.4% (n-14) were in the age group of 6-9 years and 7 % (n-5)were in 9-12 years. Out of 72 children, 83.3% (n-60) were males and 16.7% (n-12) were females. 41.7% (n-30) had abnormal EEG in the absence of clinical seizures and 58.3% (n-42) children had normal EEG. EEG was correlated with CARS using

spearman’s rho correlation test and found to be significant, P value – 0.005**.** Among the risk factors advanced maternal age at conception, positive family history of psychiatric illness, birth order and multiple birth were significantly correlating to CARS P value- < 0.05**.** Rest of the risk factors were not significantly correlated with CARS.

CONCLUSION

In the study 40.7% children had EEG abnormality, most common pattern of EEG abnormality noted is bilateral epileptiform activity with sharp waves.EEG significantly correlates with CARS , abnormal EEG highly correlates with the severity of autism. Advanced Maternal age at conception ,positive family history of psychiatric illness, birth order and multiple births are the risk factors correlated with the severity of autism. Epileptiform discharges being highly correlated to severity of autism could serve as prognostic tool for these children.

KEY WORDS : Autism , risk factors, severity, CARS, EEG, correlation

INTRODUCTION

Autism spectrum disorder is a group of developmental disabilities which causes significant impairment in the social interaction, communication and behaviour.

Autism spectrum disorder is a neurodevelopmental disorder defined by the American Psychiatric Association's Diagnosis and Statistical Manual of Mental Disorders (DSM V) as a single disorder that includes disorders that were previously considered separate — Autism, Asperger's syndrome, Childhood disintegrative disorder and pervasive developmental disorder not otherwise specified.(1)

The term "spectrum" in autism spectrum disorder refers to the wide range of symptoms and severity.

The features of autism are impairment in social interaction, difficulties in communication, as well as repetitive, restricted, and stereotypical pattern of behaviour. The main feature is impairment in social interaction.(1)

Autism presents before 3 years of age and can be identified at around 18 months. According to DSM 5 the age of manifestation is from the "early developmental period", but the symptoms can present later when the capabilities are inadequate to meet the demands.(1)

Due to increased awareness and simple diagnostic criteria, the prevalence of autism has increased. According to the CDC data, the current prevalence is 1 in 68 children (2). Males are 5 times more commonly affected than females.

The etiology of autism is multifactorial , specific causes aren't yet established , multiple risk factors have been found which can play a role in the etiopathogenesis of autism such as genetics, prenatal and perinatal factors, environmental factors and neurobiological abnormalities.

Neurobiological findings in autism are : (3)

- Increased serotonin levels
- Persistent "primitive" reflexes
- Increased head size(macrocephaly)
- Changes in brain morphology/ cytoarchitecture
- Failure to activate Fusiform face region
- High rates of EEG abnormalities/seizure disorder

These abnormal findings indicates that autism can result because of interruption in the development of brain during fetal growth due to the defects in genes that regulate the growth of brain, environmental factors may have their influence on gene function.

Autistic children do not respond to their names and avoid eye contact, have no bonding with their parents or caregivers. They find it difficult to understand what others think or feel because they have problem in understanding the social cues, like tone of voice or facial expressions, they often have speech delay , cognitive delay and may lack empathy.

Some children development may be normal and then presents with loss of acquired skills in the first 2–3 years. Regression can happen in many areas , such as social, communication, self-help skills and cognition. Language is the most common domain which undergo regression.(4)

Autistic children often involve in stereotypical movements like rocking and twirling, self injurious behavior like biting , head-banging, fail to have interactive play with other children.

Problems with the verbal and non verbal communication is considered as the first warning sign. Some of the warning signs which helps us to suspect autism are :

When a twelve month old child

- Does not babble or coo
- Does not gesture like pointing out or wave bye
- Does not speak single words by 16 months
- Does not speak two-word phrases on his own
- Does not respond or make facial expressions .

Many genetic syndromes and medical conditions are associated with autism. Epilepsy is commonly associated with autism seen in 11-39% of autistic children.(5)

Many checklist screening tools have been developed such as

- Autism Behavior Checklist, a screening instrument can be used by teachers.
- Autism Diagnostic Interview-Revised (ADI-R), a semistructured interview for parents.
- Autism Diagnostic Observation Schedule (ADOS)
- Childhood Autism Rating Scale (CARS), for severity grading

Complete history to determine the risk factors and physical examination to check for the presence any associated medical or genetic conditions and finally DSM V criteria is used for diagnosis of autism.

Management mainly includes educational/behavioral interventions which provides skill-oriented training which improves social and language skills.

Counselling to parents and siblings of autistic child will help them to cope up with the challenges of living with autistic child.

Specific drugs are used to treat associated comorbid symptoms such as antipsychotic medications for severe behavioral problems, anticonvulsant drugs for seizures.

Since the specific reasons for the deficits in autism is not clearly understood and the literature also propose that a significant proportion of autistic children have epileptiform discharges in EEG in the absence of seizures and these EEG abnormalities are causally associated with the deficits (behavioral, communicative and cognitive) in autism.

So we decided to work on the morbidity part and also to find out if there is any significant association between these EEG abnormalities and risk factors with the severity of autism. And also no studies have been conducted in the Indian context which in many ways are quite different from the American or European context when we take in to account the environmental, as well as the genetic makeup of our population.

REVIEW OF LITERATURE

Autism is a neurodevelopmental condition which has strong genetic background (6). The exact etiology of autism is still remains to be established (6) .The first clinical description of autism was given by Leo Kanner, a psychiatrist in 1943 (7). He describes as “the children aloneness from the beginning of life”(7).

Autism is characterized by deficits in social interaction ,social communication and repetitive , restricted or stereotyped behavior, interests or activities and in some cases, cognitive delay . (1)

Age of manifestation is from the "early developmental period", but the symptoms can occur later when the capabilities are inadequate to meet the demands.(1)

Autism is also known as childhood autism, infantile autism and autistic disorder (8).

EPIDEMIOLOGY

The worldwide prevalence is increased 20 to 30 fold . The reasons for recent increase in prevalence is attributed to the increased awareness, changes in diagnostic criteria and availability of services (9,10).

The present prevalence is 14.7 per 1,000 (1 in 68) children (2) . Male : female ratio is 5:1 ,among boys (1 in 42) and girls (1 in 189) (2). The exact reason for male preponderance is not known. But it is suggested that there is a genetic role in inheritance of Autism (11).

ETIOLOGY

The exact etiology of autism still remains unknown. Classified as

1. Idiopathic autism
2. Secondary autism

Idiopathic autism which is a complex heritable disorder which involve multiple genes.

The recurrence risk is 5% - 6% when an older sibling is autistic and still more higher when two autistic children in the family.(6, 12, 13,14)

Inheritance pattern of autistic disorder demonstrate 60% monozygotic concordance and no concordance for dizygotic twins.(15)

Genetic studies have found the defective loci on chromosome 7,15,17,22,2,3,X and 15q –maternally derived duplications which are commonly associated with autism.(6,16,17,18,19)

Environmental factors do play a role in the expression of the already existing genetic factor during early gestation age as a second hit phenomenon.

Some of the risk factors have been implicated in the etiology of autism such as :

- advanced maternal and paternal age (20)
- antenatal infections like rubella (21,22)
- maternal drug intake during pregnancy such as thalidomide, sodium valproate (23)
- Neonatal encephalopathy (24).

Farida El-Baz et al and others have showed that Family h/o psychiatric disease, instrumental delivery, birth asphyxia, neonatal jaundice, increased parental age are significant risk factors. 31% cases showed diffuse epileptiform discharges in EEG (25).

Heidi Jeanet Larsson et al and others study has concluded that the risk factors which are associated with autism are Parental psychiatric history , breech presentation, low apgar score, LBW, GA< 35 weeks, and high parental age (26).

There is no causal association between MMR vaccine and autism which has been proved recently (27).

Secondary autism includes less than 10% of cases which are associated with medical condition or genetic syndromes.

Fragile x syndrome, Tuberous scelorosis, Phenylketonuria, Fetal alcohol syndrome, Angelman’s syndrome, Prader Willi syndrome, Rett’s syndrome, smith-lemli-opitz syndrome, congenital rubella syndrome and epilepsy are some of the disorders associated with autism (11).

PATHOPHYSIOLOGY(28,29)

The commonly identified neuropathologic features are :

1. Subcortical forebrain anomalies of the limbic system
2. Frontal and temporal lobe abnormalities
3. Increased white matter volume
4. Decreased cerebellar Purkinje cells
5. Abnormalities in amygdala and fusiform gyrus (30)
6. Changes in cell number & size in broca's area & inferior olive
7. Brainstem -heterotopias
8. Elevated levels of blood serotonin (31)
9. Mirror neuron system abnormalities (32) - inferior frontal gyrus and the inferior parietal lobule areas associated with empathy processes

The size of the head is normal at birth, thereafter there is rapid increase in head size is noted during 6 -14 months of age. It is followed by decreased or arrested growth of head at a later part of life. 20%-30% of the autistic children have found to have macrocephaly (7).

This abnormal growth results in abnormal neuronal connections in the brain. Even though there are several neuropathological features identified, the routine use of neuroimaging is not useful(11).

CLINICAL PRESENTATION (33)

The clinical diagnosis of autism is most challenging because of the heterogeneity of symptoms. The core features of autism are deficits in social interaction, communication and repetitive, restricted and stereotypical patterns of behavior, interest, and activities.

Significant variation may be seen in the severity of deficits.

Typical presentations are lack of speech, scripted speech, echolalia, and pop-up words, stereotypical behaviours like rocking, finger movements, twirling and hand flapping.

Earlier prespeech deficits, deficits in joint attention is characteristic features of very young children with autism.

Common Prespeech Deficits in Autistic children :

- Reduced or absent use of prespeech gestures (e.g., waving, pointing)

- Delayed onset of babbling past 9 months of age

- Disregard for vocalizations (i.e., lack of response to own name), yet awareness of environmental sounds

- Lack of appropriate gaze

- Lack of expressions such as “oh-oh” or “huh”

- Lack of interest or response to neutral statements

- Lack of recognition of mother's (or father's or consistent caregiver's) voice

- Lack of the alternating pattern of vocalizations between infant and parent that usually occurs at six months of age

- Lack of warm, joyful expressions with gaze

Due to the impairment in the theory of mind skills autistic children have difficulties with empathy, sharing, and comforting know as “mindblindedness”(34).

Co-morbid symptoms are hyperacusis, hyperactivity, Self-injurious behaviours, GDD/MR (intellectual disability) may coexist.

EVALUATION

1. Complete history taking including antenatal, neonatal, peri & post natal events, developmental milestones, behavioral problems and family history regarding similar illness or any psychiatric illness and history regarding co-morbid illness.
2. Clinical examination including general examination, syndromic facies, focal neurological deficits, neurocutaneous markers.
3. Depending on the child’s age developmental assessment and psychometric evaluation to be done.
4. DSM-V criteria for the diagnosis of autism.
5. To identify the etiology and co-morbid condition, laboratory investigation and imaging, karyotyping, DNA testing, EEG, metabolic work up, MECP2 gene, if needed to be done to find out the secondary causes of autism.

Commonly used screening tools include CHAT,M-CHAT, PDD screening test, CARS is used for the grading of severity. Commonly used diagnostic scales include ADOS & ADI-R

Many EEG studies in autism children have been conducted and they have suggested that, significant number of children with autism have epileptiform discharges in EEG in the absence of clinical seizures and these EEG abnormalities are causally correlated with the deficits (behavioral, communicative and cognitive) and also the severity of autism .

Riad M. Elsayed et al have showed that Subclinical EEG abnormalities were noted at higher incidence in autistic children (51.1%), abnormal EEG were highly correlated to autism severity (p value 0.000).Hence concluded that EEG study may serve as a prognostic tool. (35)

Michael G. Chez et al and others have concluded that 60.7% (540) autistic children in their study had abnormal epileptiform discharges in EEG in the absence of seizures . 176 autistic children out of 540 was treated with Sodium valproate, 80 out of 176 patients EEG became

normal and 30 patients showed improvement in the EEG findings compared to first EEG .(36)

Yasuhara et al have showed in their study that Epileptiform activity was noted in (85.8%) 870 out of 1014 autistic children. Epileptic seizure waves noted from frontal lobe (65.6%). The spike discharges in temporal lobe, parietal lobe, occipital lobe and multifocal spike waves were < 10% children.

Finally concluded that treatment of epileptiform activity in EEG may improve the symptoms. (37)

Hideaki Kanemura et al and others have showed that 11 out of 21 (52.4%) children with autism in their study had EEG abnormalities (spike waves) in the absence of epilepsy , 6 out of 11 children (54.5%) had clinical seizures at some point of time in their lives when these children were followed up.

Seizure waves in the frontal region was mainly associated with later development of epilepsy compared to centrotemporal region ($p < 0.003$).

The semiology of seizure commonly identified was partial, partial with secondary generalization in 66.7% (4 out of 6). (38)

Ahmed I. Kotoury et al and others have showed in their study that, EEG abnormalities with macrocephaly when exits together, significantly correlates severity of autism .(39)

DIFFERENTIAL DIAGNOSIS: (11)

- Specific language developmental disorder
- Early onset psychosis
- Stereotypic movement disorder
- Social anxiety
- Childhood onset dementia
- Selective mutism
- Obsessive-compulsive disorder
- Inhibited-type reactive attachment disorder

CO-MORBID MEDICAL DISORDERS (40)

Epilepsy	Rubella embryopathy
Fragile-X syndrome	Tuberous sclerosis
Angelman syndrome	Visual deficits and strabismus
Acoustic hypersensitivity	Moebius sequence
Hypomelanosis of Ito	Phenylketonuria
Hearing deficits	Sex chromosome aneuploidies
CHARGE association	Sotos syndrome
22q11 deletion syndrome	Smith–Magenis syndrome

MANAGEMENT

Autism is a chronic condition which affect almost 1 in 68 children and needs medical and nonmedical care. Primary goal of management includes alleviating core features, treating co-morbid conditions, to maximize the quality of life and functional independence as far as possible.

To attain these primary goals educational and behavioral intervention is the mainstay of management.

The treatment modality includes :

- Applied behavior analysis
- structured teaching
- speech therapy
- occupational therapy

It helps in improving communication and social skills and also decreases maladaptive behavior..

Medical care includes the routine healthcare as of normal children like immunization and nutrition and it also depends on underlying etiology.

Associated problems like epilepsy and other co morbid condition such as sleep disturbances, hyperactivity, aggressive behavior and self-injurious behavior to be addressed accordingly with appropriate drugs.

Family support is the one which decides the prognosis and the outcome. Early stimulation and educating the parents about the need for long term therapy, prognosis and outcome is essential.

PROGNOSIS: (11)

Factors associated with Good Outcome includes,

- Normal intelligence
- Normal adaptive functioning
- Milder autistic symptoms

Factors associated with Poor Outcome includes,

- Lack of joint attention by the age of 4yrs
- Lack of functional speech by the age of 5yrs
- Presence of seizures & intellectual disability
- Comorbid medical &psychiatric illness
- Severe autistic features.

SHORT & LONG TERM OUTCOME (11)

As the age progress many autistic patients stay within the spectrum even as adults and regardless of their cognitive functioning, problems with independent living, social relationships, employment and mental health can persist.

Few patients particularly those with communication abilities may live their independent life in the community with employment. Some may dependent on their families or need placement in facilities outside the home.

As these children grow older, few patients may show change in the symptom profile and risk of self-injurious behaviour, seizures might become more common.

OBJECTIVES

To correlate the severity of autism with prenatal, perinatal and postnatal risk factors and EEG abnormalities.

STUDY JUSTIFICATION

- Prenatal, perinatal and postnatal risk factors are said to play a role in the pathogenesis of autism and Identification of risk factors helps us in early intervention and prevention.
- No studies have been conducted in the Indian context with regard to various risk factors that are associated with severity of autism.
- Though significant proportion of autistic children have epileptiform discharges in EEG in the absence of seizures and these EEG abnormalities are causally associated with the deficits (behavioral, communicative and cognitive), no such studies have been done in the Indian context. And also to find out is there any significant association between these EEG abnormalities with severity of autism.

METHODOLOGY

Study design	:	Descriptive study
Study place	:	Department of Child Psychiatry Child Guidance clinic Institute of child health and hospital for children, Egmore, Chennai
Study period	:	Protocol Preparation-January 2013–March 2013
Sample size	:	72
Data collection	:	April 2013 – June 2014
Data analysis and manuscript preparation	:	July 2014 – August 2014
Submission of report	:	September 2014
Study population	:	Children aged 3 –12 years diagnosed as autism as per DSM 5 criteria

DEFINITIONS

CASE DEFINITION:

Autism is defined as per American Psychiatric association as the onset of symptoms before 3 years of age which reflect delayed or abnormal development in 3 domains : social skills, communication, repetitive and stereotyped pattern of behaviour.

INCLUSION CRITERIA :

- Children aged 3 –12 years diagnosed as autism as per DSM 5 criteria

EXCLUSION CRITERIA :

- Autism with seizure disorder or epilepsy
- Specific genetic syndromes

Children who met the inclusion criteria were recruited for the study. Seventy two children enrolled according to the desired sample size. Written consent was documented from all the parents before enrolling them in to the study.

Ethical committee approval was obtained from the institutional ethics committee.

Conflict of interest : Nil

Financial support : Nil

STUDY MANOEUVRE

- Children aged 3 – 12 years diagnosed as autism using DSM – V criteria in child guidance clinic were enrolled in this study.
- Based on the literature the risk factors of autism are compiled to form a clinical proforma. This proforma questions were asked to all parents of the autistic children.
- Detailed clinical examination was done
- Childhood autism rating scale (CARS) is administered to all the children in the study and severity of autism was assessed.

CARS is fifteen item scale which consists of :

1. Relating to people
2. Imitation
3. Emotional response
4. Body use
5. Object use
6. Adaptation to change
7. Visual response
8. Listening response
9. Taste, smell and touch response and use
10. Fear or nervousness
11. Verbal communication

12. Non verbal communication
13. Activity level
14. Level and consistency of intellectual response
15. General impression

To make a total score, each of the 15 items is given a rating of one to four.

- A rating of 1 suggest that the child behaviour is within normal limit for that age.
- 2 indicates that child behaviour is mildly abnormal compared with the children of same age.
- 3 means child behaviour is moderately abnormal for that age.
- 4 means child behaviour is severly abnormal for a child of that age.

In addition to these 4 ratings, midpoints between them(1.5, 2.5, 3.5) are to be used when the behaviour of the child falls between two values.

Total score :

Non autistic : 15 – 29.5

Mild – moderate autism : 30 – 36.5

Severe autism : 37 - 60

- Electroencephalogram (EEG) was done to all children in the study.

STATISTICAL ANALYSIS

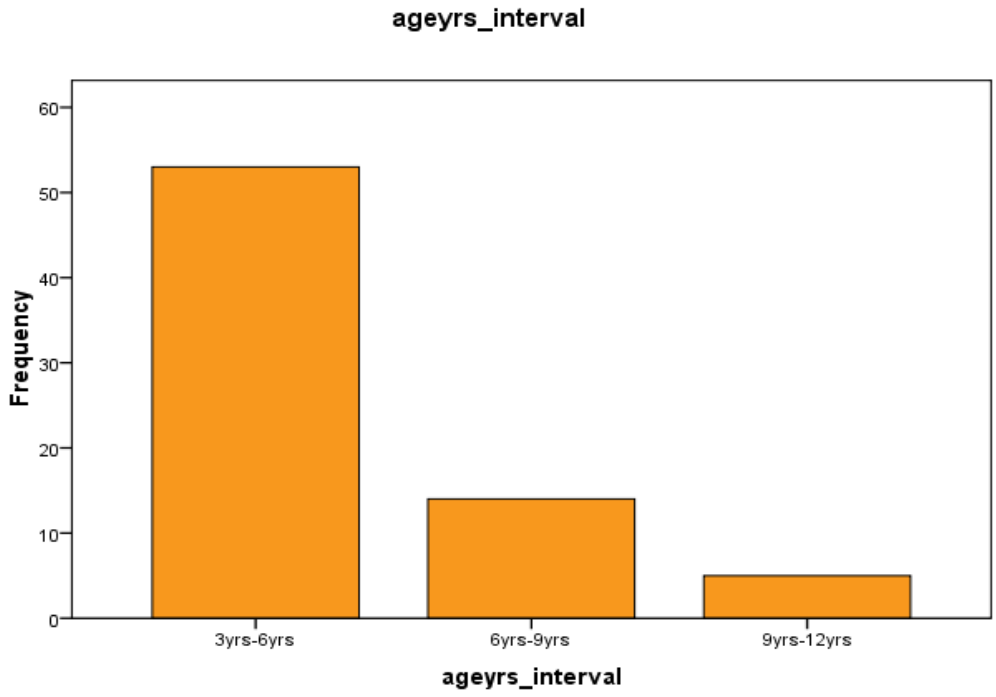
All data entered in data collection form are entered in excel spread sheet and the data was analyzed using the statistical software, SPSS version 17.

- Qualitative data were given using descriptive statistics.
- Quantitative data were given using summary statistics.
- Associated categorical variables were tested using chisquare.
- Relationship between quantitative variables were tested using correlation.

RESULTS

DISTRIBUTION OF PATIENTS BASED ON AGE GROUP

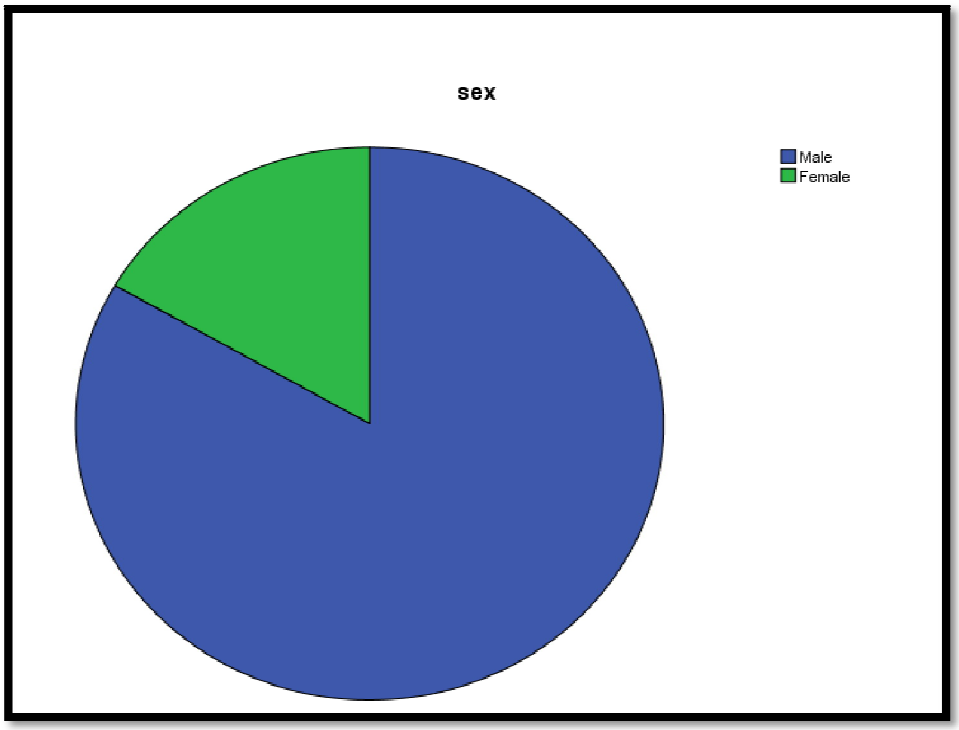
Age group	N	Percent
3yrs-6yrs	53	73.6
6yrs-9yrs	14	19.4
9yrs-12yrs	5	7
Total	**72**	**100.0**



In study population of 72, 73.6 % were seen in the age group of 3-6 years, 19.4% were seen in the age group of 6-9 years and 6.9% were seen in 9-12 years.

DISTRIBUTION OF PATIENTS BASED ON GENDER

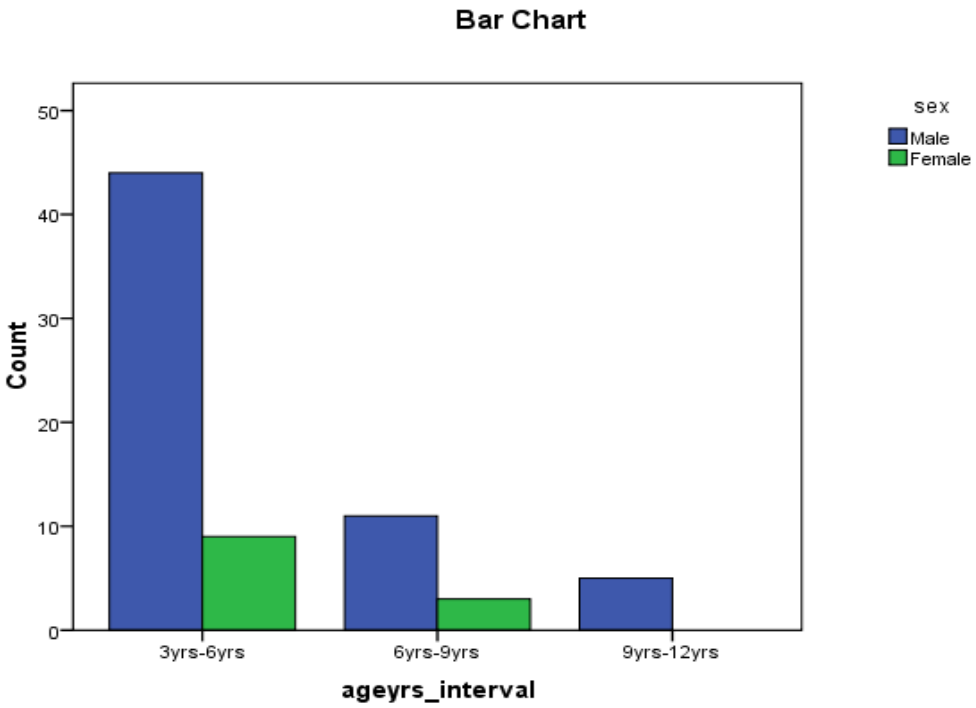
GENDER	N	PERCENT
Male	60	83.3
Female	12	16.7
Total	**72**	**100.0**



In the study population of 72 cases 83.3 % were males and 16.7% were females. Maximum incidence was seen in males

FREQUENCY OF DISTRIBUTION OF PATIENTS BASED ON AGE GROUP & GENDER

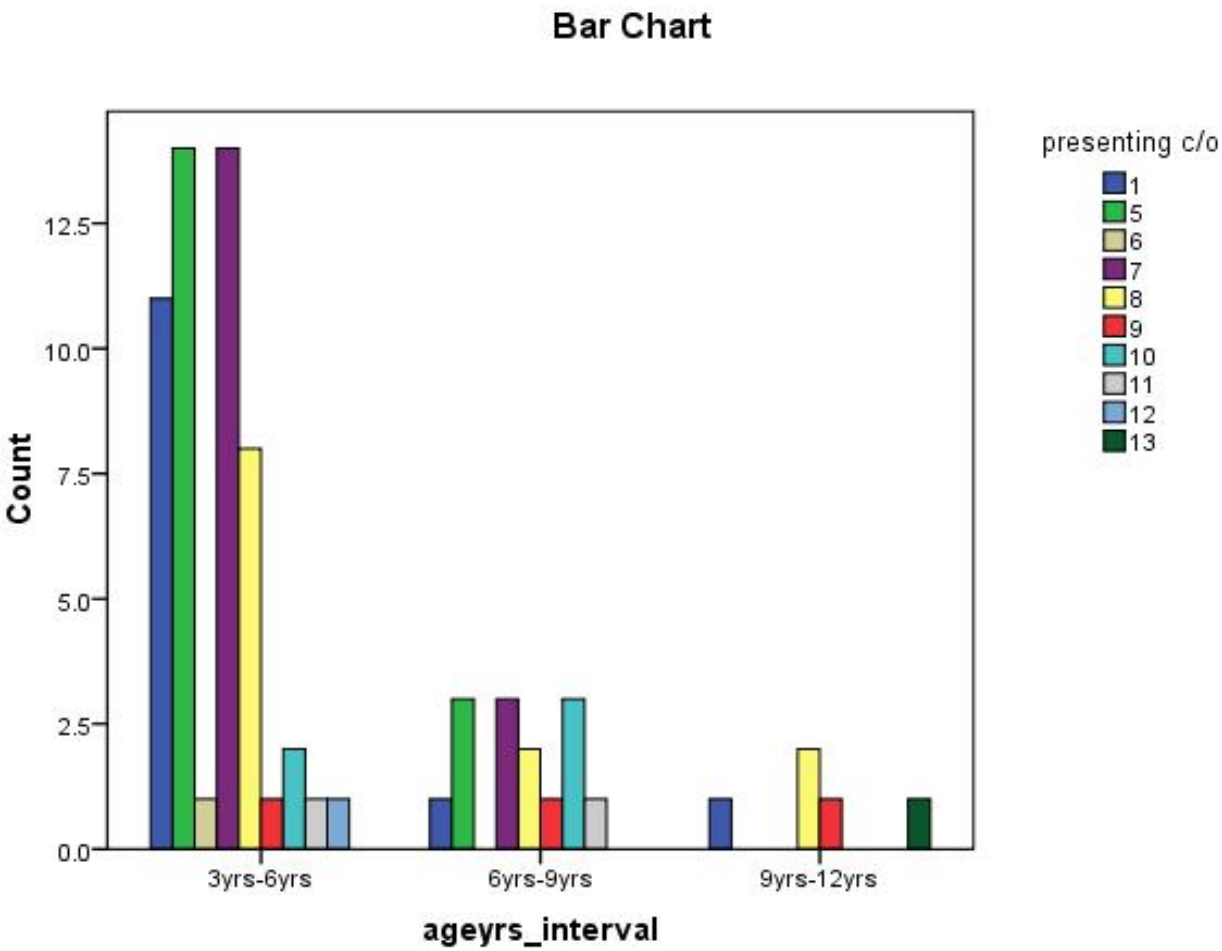
AGE GROUP	GENDER		TOTAL
	MALE	FEMALE	
3yrs-6yrs	44 (83%)	9 (17 %)	53
6yrs-9yrs	11 (78.6%)	3(21.4%)	14
9yrs-12yrs	5 (100%)	0	5
Total	**60(83.3%)**	**12(16.6%)**	**72**



Out of 72 cases there were 83% males and 17% females in the age group 3-6 years, 78.5% male and 21.4% females in 6-9 years group, 100% male in 9-12 years age group**.**

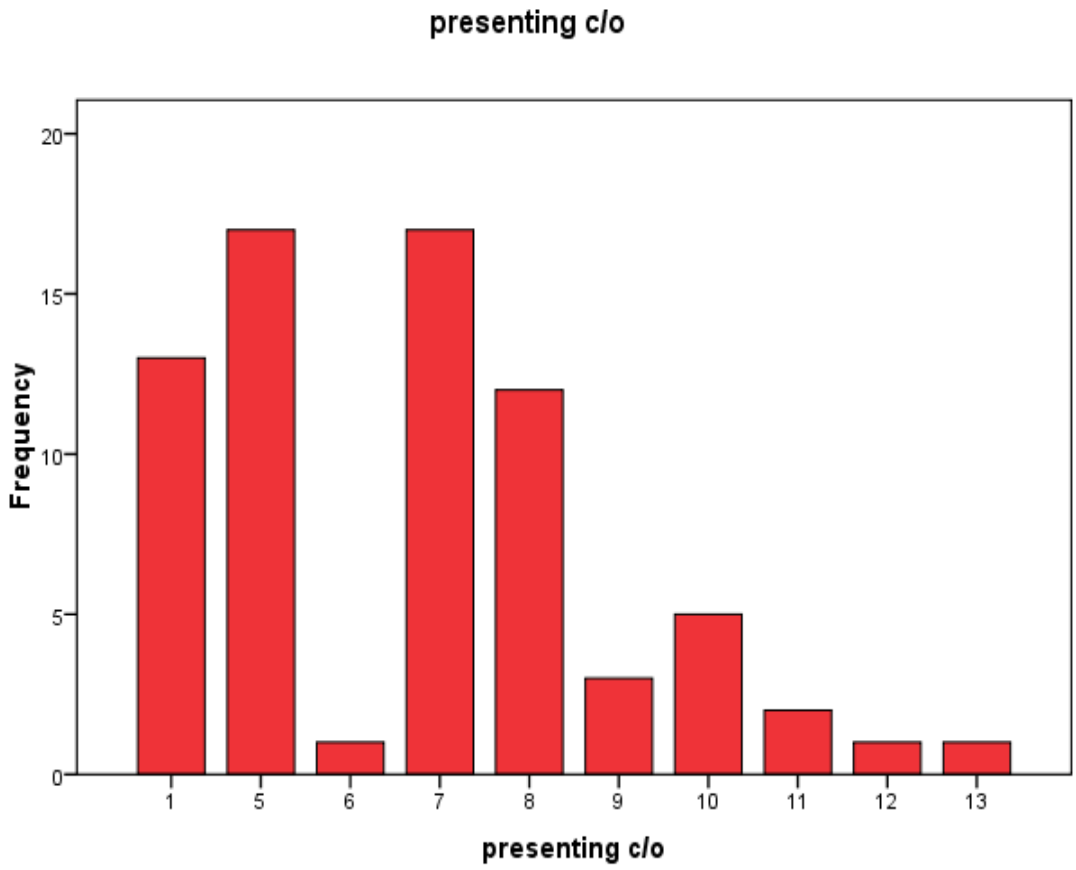
FREQUENCY OF DISTRIBUTIONS OF PATIENTS BASED ON PRESENTING COMPLAINTS

Presenting complaints	Age Intervals				Percent
	3yrs-6yrs	6yrs-9yrs	9yrs-12yrs	Total(N)	
(1)Speech Delay	11	1	1	13	18
(5)Speech delay No eye Contact	14	3	0	17	23.6
(6)Speech delay No eye contact Solitary play	1	0	0	1	1.4
(7)Speech delay No eye contact hyperactivity	14	3	0	17	23.6
(8)Speech delay Hyperactivity	8	2	2	12	16.7
(9) 6 + hyperactivity	1	1	1	3	4.2
(10) 8+ Solitary play	2	3	0	5	6.9
(11)Speech delay Solitary play	1	1	0	2	2.8
(12)8+ Steriotypic movements	1	0	0	1	1.4
(13) Speechdelay Stereotypic movements	0	0	1	1	1.4
Total	**53**	**14**	**5**	**72**	**100.0**



Presenting complaints	1+2-5	1+4+14-12
	1+2+3-6	1+14-13
Speech delay - 1	1+2+4-7	
No eye contact – 2	1+4-8	
Solitary Play – 3	1+2+3+4-9	
Hyper activity – 4	1+3+4-10	
Stereotypies – 14	1+3-11	

Speech delay, absence of eye contact and hyperactivity are the most common presenting complaints in all age group in the study.

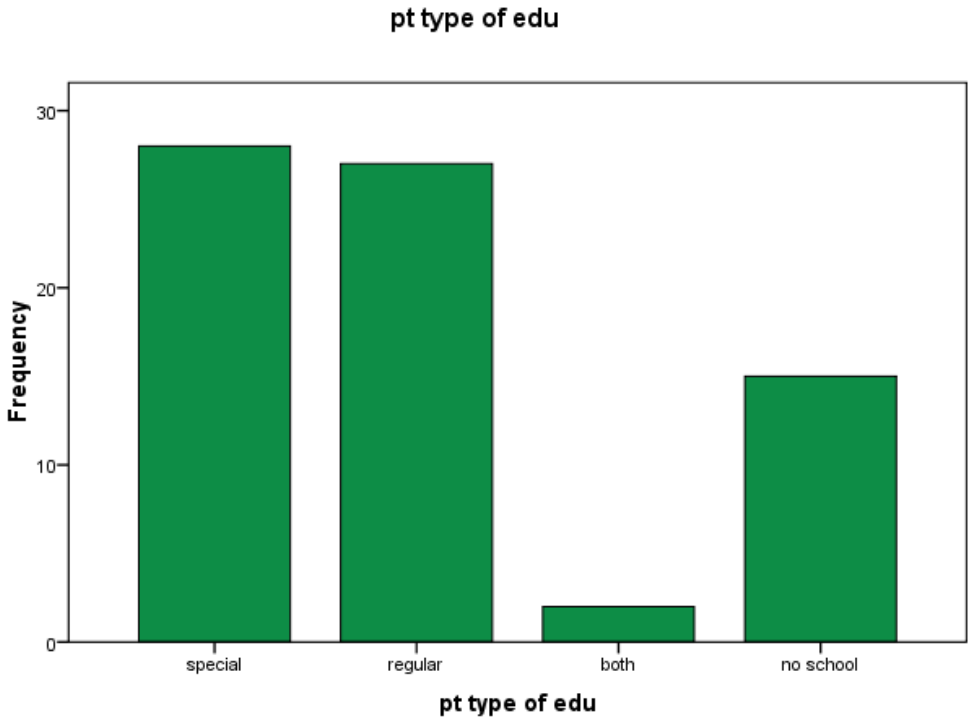


Presenting complaints	1+2-5	1+4+14-12
	1+2+3-6	1+14-13
Speech delay - 1	1+2+4-7	
No eye contact – 2	1+4-8	
Solitary Play – 3	1+2+3+4-9	
Hyper activity – 4	1+3+4-10	
Stereotypies – 14	1+3-11	

Speech delay, absence of eye contact and hyperactivity are the most common presenting complaints in the study.

DISTRIBUTION OF PATIENTS BASED ON TYPE OF EDUCATION

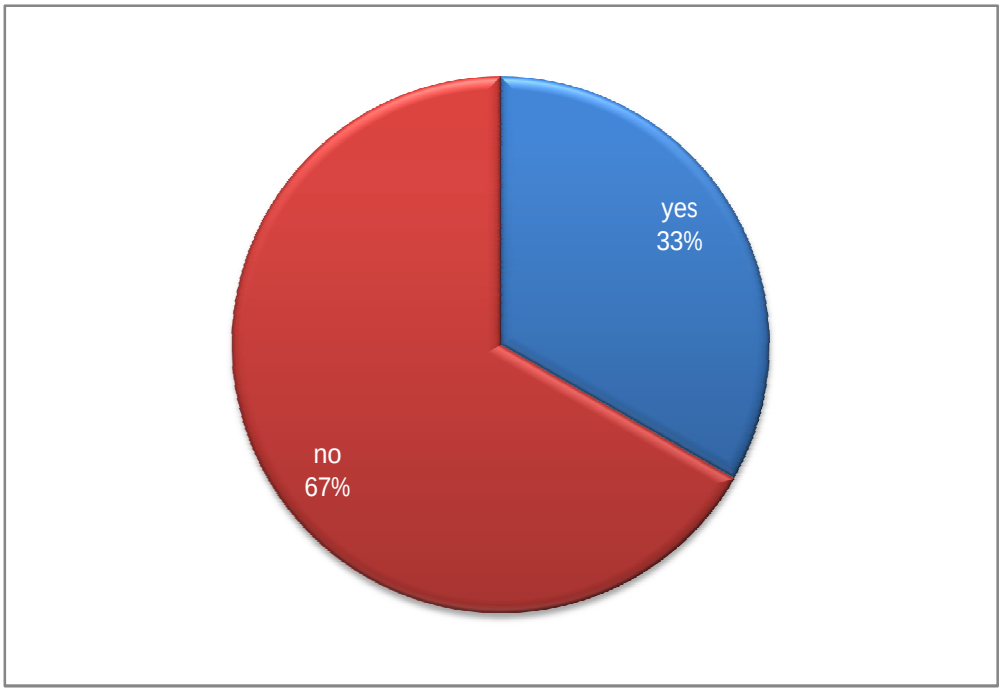
Type of education	N	Percent
Special	28	38.9
Regular	27	37.5
Both	2	2.8
no school	15	20.8
Total	**72**	**100.0**



In the study population of 72 children 38.9 % are attending special school, 37.5 % are attending regular school and 20.8 % are not attending any school.

DISTRIBUTION OF PATIENTS BASED ON DRUG INTAKE

On drugs	N	Percent
Yes	24	33.3
No	48	66.7
Total	**72**	**100.0**



Out of 72 children 32% were on drugs and 68% were not on drugs 75% (18) of children were on T Risperidone and rest on T Trihexyphenidyl.

MEAN CARS AND AGE GROUP

AGE GROUP	CARS	
	MEAN	**STD. DEVIATION**
3yrs-6yrs	33.3	2.2
6yrs-9yrs	33.8	2.8
9yrs-12yrs	36.6	7.7

Mean CARS observed in 3-6 yrs age group is 33.3, 33.8 in 6-9 yrs age group and 36.6 in 9-12 yrs age group.

MEAN CARS AND SEX

SEX	CARS	
	MEAN	**STD. DEVIATION**
Male	33.5	3.0
Female	34.2	3.1

Mean CARS observed in males is 33.5 and 34.2 in females

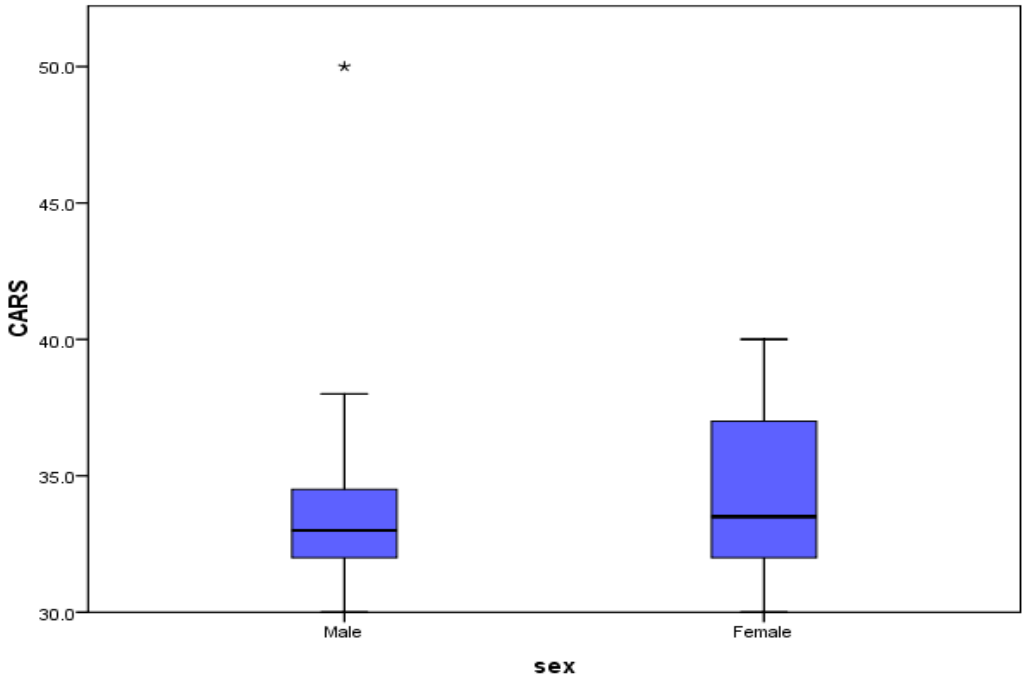
CORRELATION OF CARS WITH AGE

		Age yrs	**CARS**
Age yrs	Pearson correlation	1	.242
	P value		.041*
	N	72	72
CARS	Pearson correlation	.242	1
	P value	.041*	
	N	72	72

- Correlation is significant at the 0.05 level. Age is significantly correlated to CARS, as the age increases severity of autism increases.

CORRELATION OF CARS WITH GENDER

	Spearman's rho	CARS	Gender
CARS	Correlation coefficient	1.000	.082
	P value		.493
	N	72	72
GENDER	Correlation coefficient	.082	1.000
	P value	.493	
	N	72	72



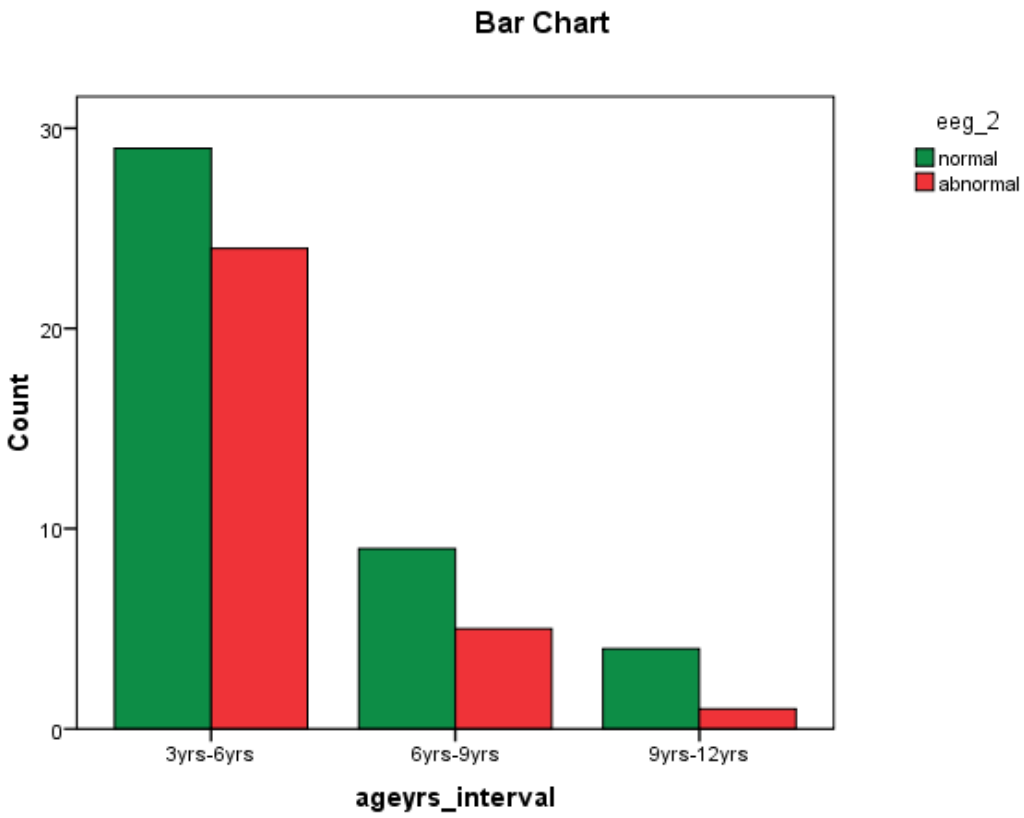
- Correlation of CARS with gender is not significant

FREQUENCY OF DISTRIBUTION BASED ON AGE AND EEG

AGE YRS	EEG		TOTAL
	NORMAL	ABNORMAL	
3yrs-6yrs	29(54.8%)	24(45.2%)	53
6yrs-9yrs	9(64.2%)	5(35.8%)	14
9yrs-12yrs	4(80%)	1(20%)	5
Total	**42**	**30**	**72**

Chi square	Value	Df	P value
	1.455	2	0.483

There is no significant difference between the two EEG groups and age.

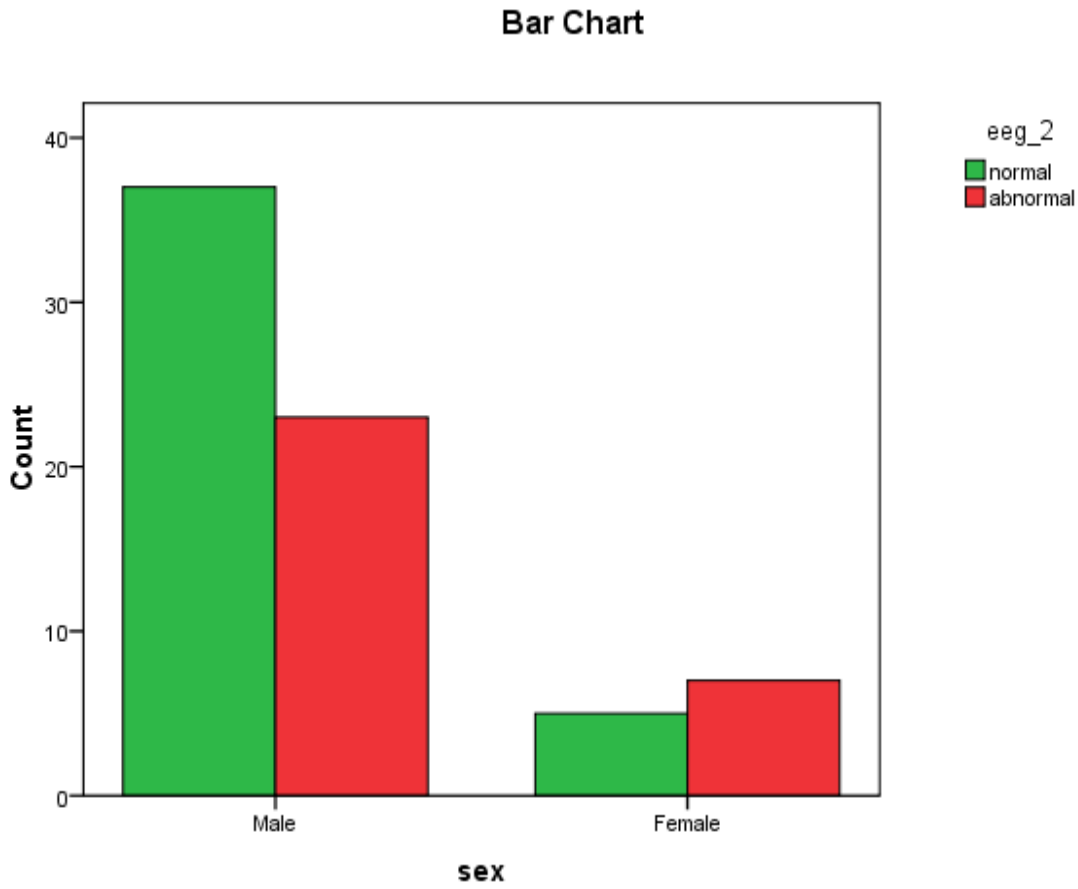


In 3-6 yrs age group 54.8 % children had normal EEG, 45.2 % had abnormal EEG. In 6-9 yrs children 64.2% had normal EEG, 35.8 % had abnormal EEG and in 6-9yrs age group 80% had normal EEG, 20% had abnormal EEG.

DISTRIBUTION OF PATIENTS BASED ON GENDER AND EEG

GENDER	EEG		TOTAL
	NORMAL	ABNORMAL	
Male	37(61.7%)	23(38.3%)	(100%)60
Female	5(41.7%)	7(58.3%)	(100%)12
Total	**42**	**30**	**72**

Chi Square	Value	Df	P Value
	1.646	1	0.200



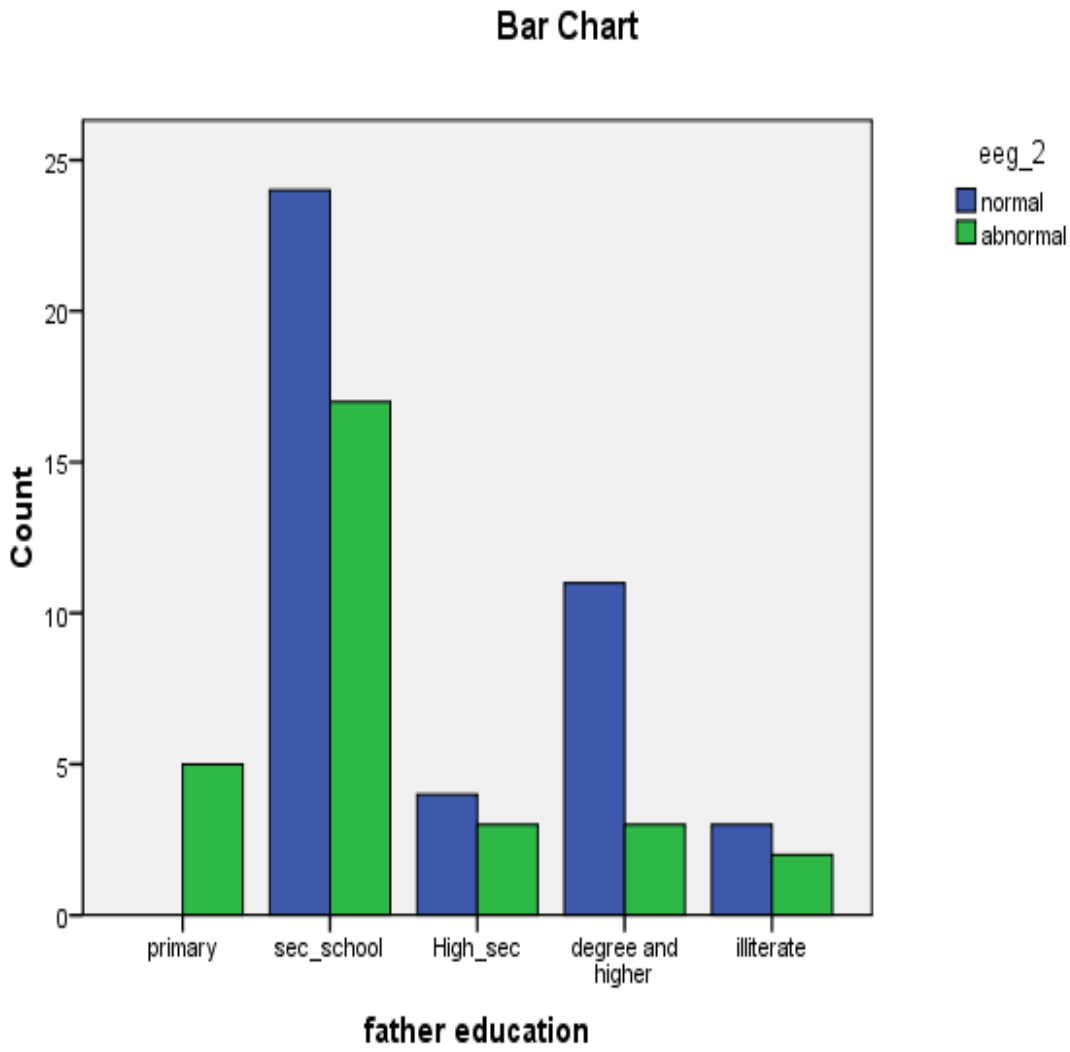
There is no significant difference between the two EEG groups and gender 61.7% (n – 37) males had normal EEG and 38.3% (n- 23) had abnormal EEG. 41.7% (n-5) females had normal EEG and 58.3 %(n-7) had abnormal EEG.

ASSOCIATION BETWEEN EEG AND FATHER'S EDUCATIONAL STATUS

FATHER EDUCATION	EEG		TOTAL	PERCENT
	NORMAL	ABNORMAL		
Primary	0	5	5	7
Sec. School	24	17	41	57
High. Sec	4	3	7	10
Degree and Higher	11	3	14	19
Illiterate	3	2	5	7
Total	**42**	**30**	**72**	**100**

Chi Square	Value	Df	P Value
	9.370	4	0.052

There is no significant difference between the two EEG groups and father's educational status.



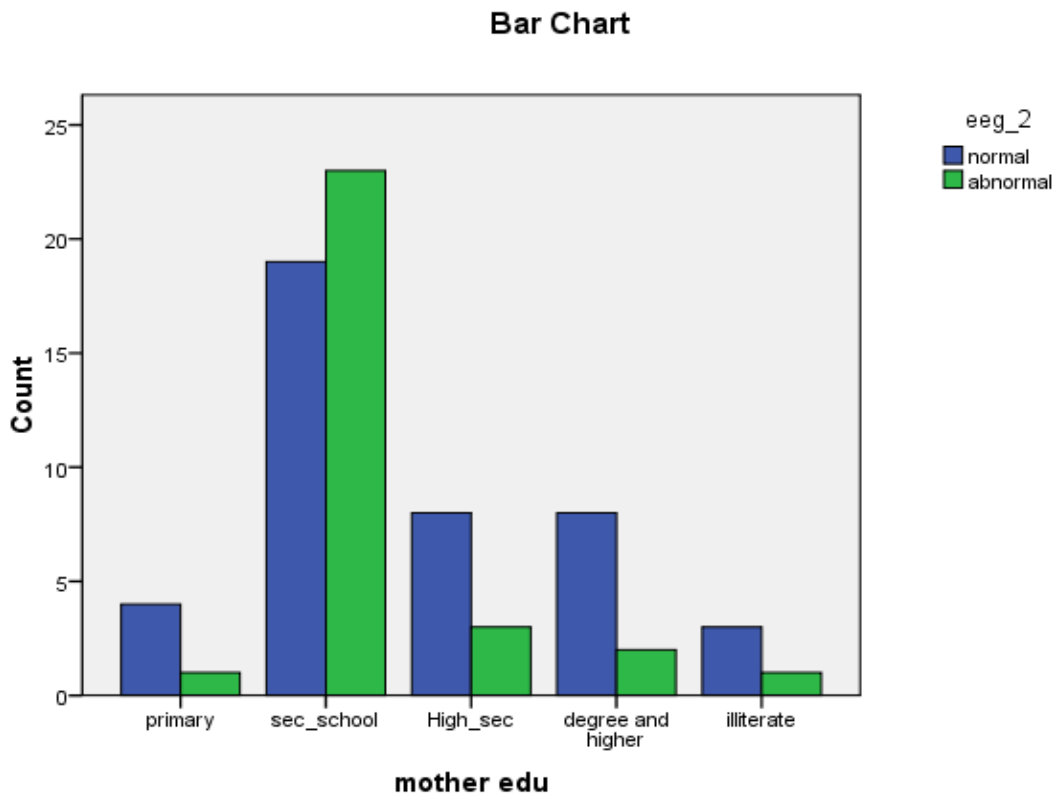
Most of the fathers (50%) had their educational status till secondary school and there is no significant difference between the two EEG groups and father's educational status.

ASSOCIATION BETWEEN EEG AND MOTHER'S EDUCATIONAL STATUS

MOTHER EDUCATION	EEG		TOTAL	PERCENT
	NORMAL	ABNORMAL		
Primary	4	1	5	7
Sec. School	19	23	42	58.3
High. Sec	8	3	11	15.2
Degree and Higher	8	2	10	14
Illiterate	3	1	4	5.5
Total	**42**	**30**	**72**	**100**

Chi Square	Value	Df	P Value
	7.255	4	.123

There is no significant difference between the two EEG groups and mother's educational status.



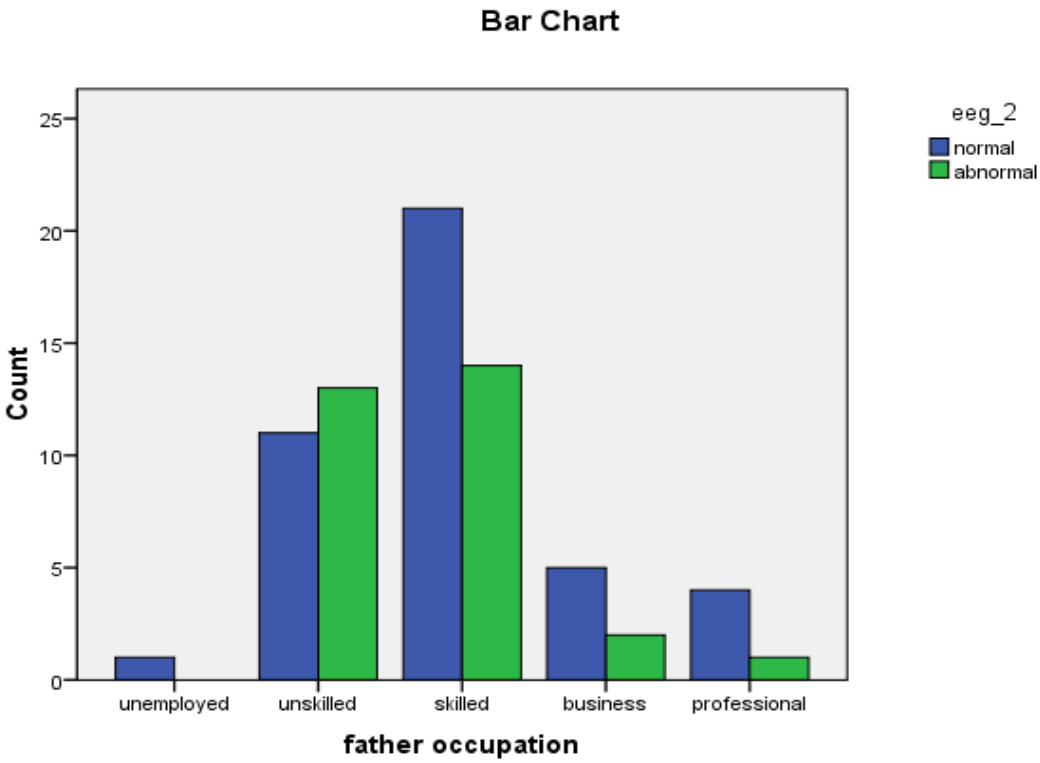
Most of the mothers (58.3%) had their educational status till secondary school and there is no significant difference between the two EEG groups and mother's educational status.

ASSOCIATION BETWEEN EEG AND FATHER'S OCCUPATION

FATHER OCCUPATION	EEG		TOTAL	PERCENT
	NORMAL	ABNORMAL		
Unemployed	1	0	1	1.4
Unskilled	11	13	24	33.3
Skilled	21	14	35	48.6
Business	5	2	7	9.7
Professional	4	1	5	7
Total	**42**	**30**	**72**	**100**

Chi Square	Value	Df	P Value
	3.757	4	0.440

There is no significant difference between the two EEG groups and father's occupation.



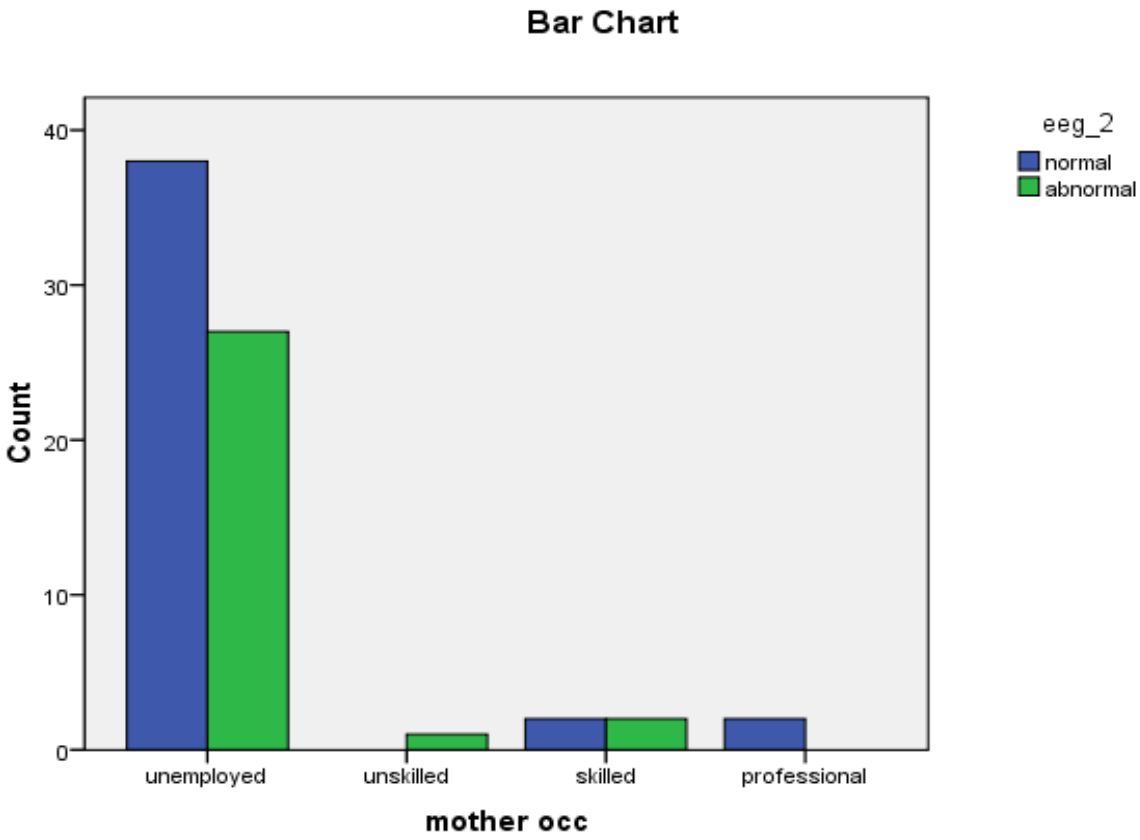
Most of the fathers (48.6%) were skilled workers, 33% unskilled workers, 7% professionals and 9% were business men. There is no significant difference between the two EEG groups and father's occupation status.

ASSOCIATION BETWEEN EEG AND MOTHER'S OCCUPATION

MOTHER OCCUPATION	EEG		TOTAL	PERCENT
	NORMAL	ABNORMAL		
Unemployed	38	27	65	90.3
Unskilled	0	1	1	1.4
Skilled	2	2	4	5.5
Business	0	0	0	0
Professional	2	0	2	2.8
Total	**42**	**30**	**72**	**100**

Chi Square	Value	Df	P Value
	2.943	3	0.400

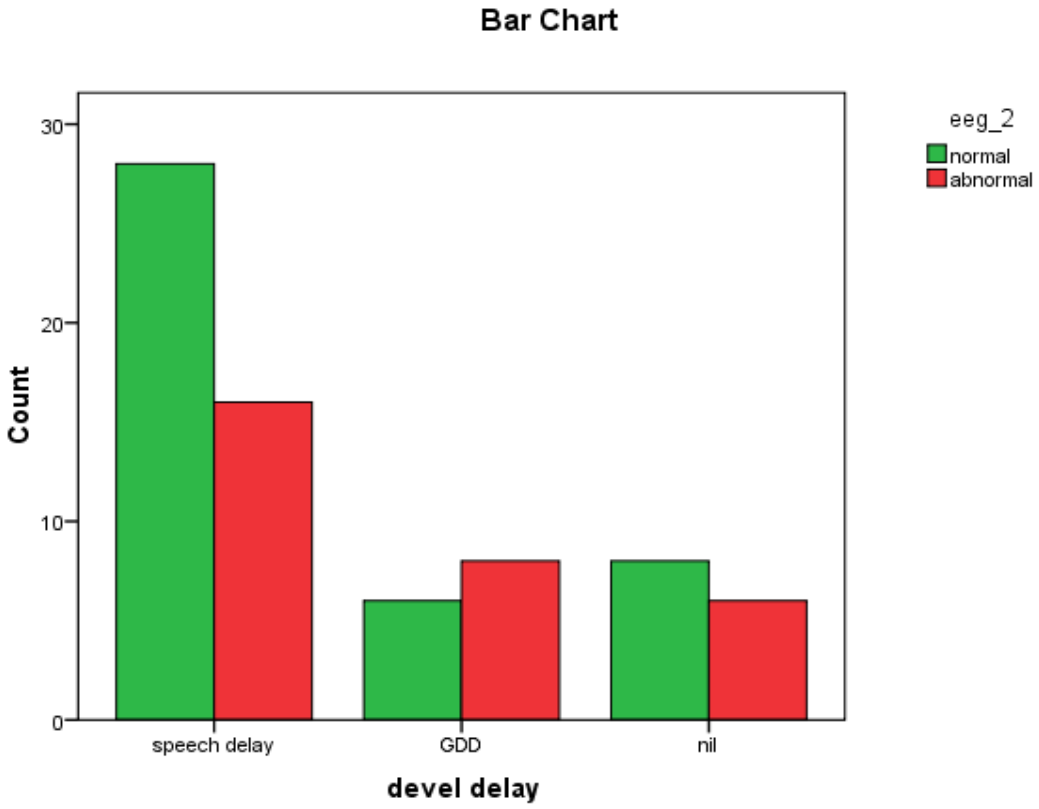
There is no significant difference between the two EEG groups and mother's occupation.



Most of the mothers were (90%) were house wives, 2.8% were professionals. There is no significant difference between the two EEG groups and mother's occupation status.

DISTRIBUTION OF PATIENTS BASED ON PRESENCE OF DEVELOPMENTAL DELAY

TYPE OF DELAY	EEG		TOTAL	PERCENT
	NORMAL	ABNORMAL		
Speech delay	28	16	44	61.2
Global delay	6	8	14	19.4
No delay	8	6	14	19.4
Total	42	30	72	100



61.2% children had speech delay, 19.4% children had global developmental delay and 19.4% children were developmentally normal .

CORRELATION OF CARS WITH DEVELOPMENTAL DELAY

			CARS	Devel. delay
Spearman's rho	CARS	Correlation Coefficient	1.000	.053
		Sig. (2-tailed)	.	.657
		N	72	72
	Devel. delay	Correlation Coefficient	.053	1.000
		Sig. (2-tailed)	.657	.
		N	72	72

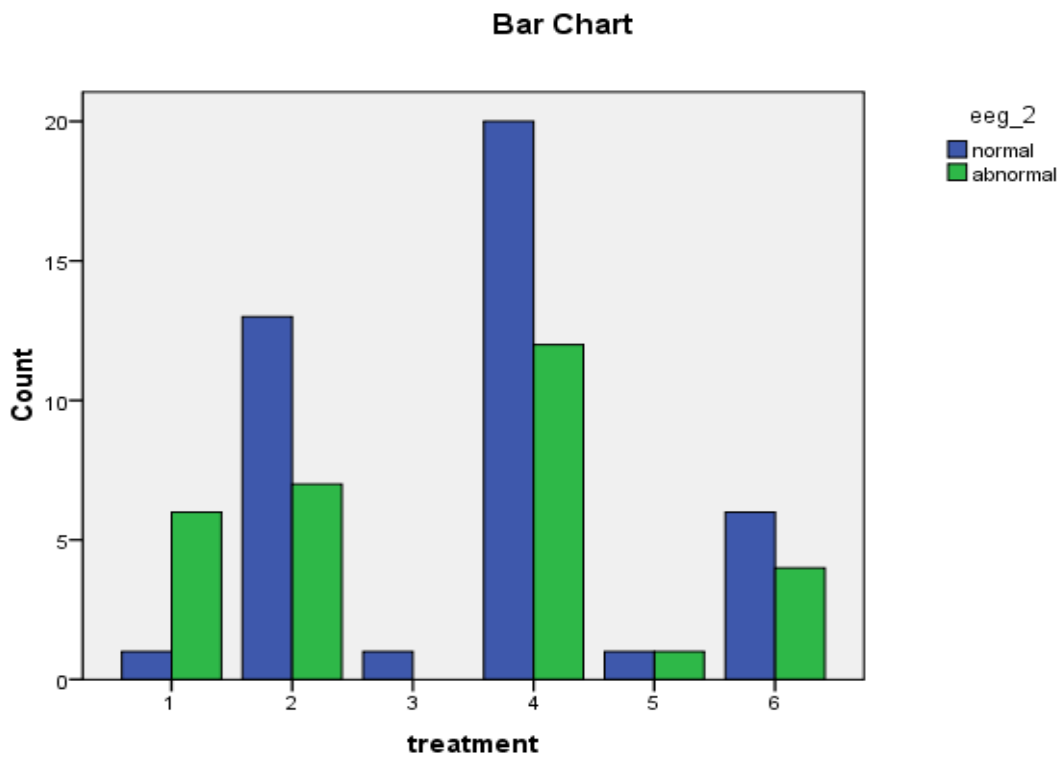
Developmental delay was correlated with severity of autism (CARS) and found to have no statistical significance.

DISTRIBUTION OF PATIENTS BASED ON TREATMENT

Treatment	eeg_2		Total	
	Normal	Abnormal		Percent
1 Speech therapy	1	6	7	9.8
2 Occupational therapy	13	7	20	27.7
3 special educator help	1	0	1	1.3
4 – 1&2	20	12	32	44.4
5- 1,2 &3	1	1	2	2.8
6 nil	6	4	10	14
Total	**42**	**30**	**72**	**100**

Chi Square	Value	Df	P Value
	6.965	5	.223

There is no significant difference between the two EEG groups and treatment modalities.



1. Speech therapy
2. Occupation therapy
3. Special educators help
4. Both 1 and 2
5. 1+2+3
6. nil

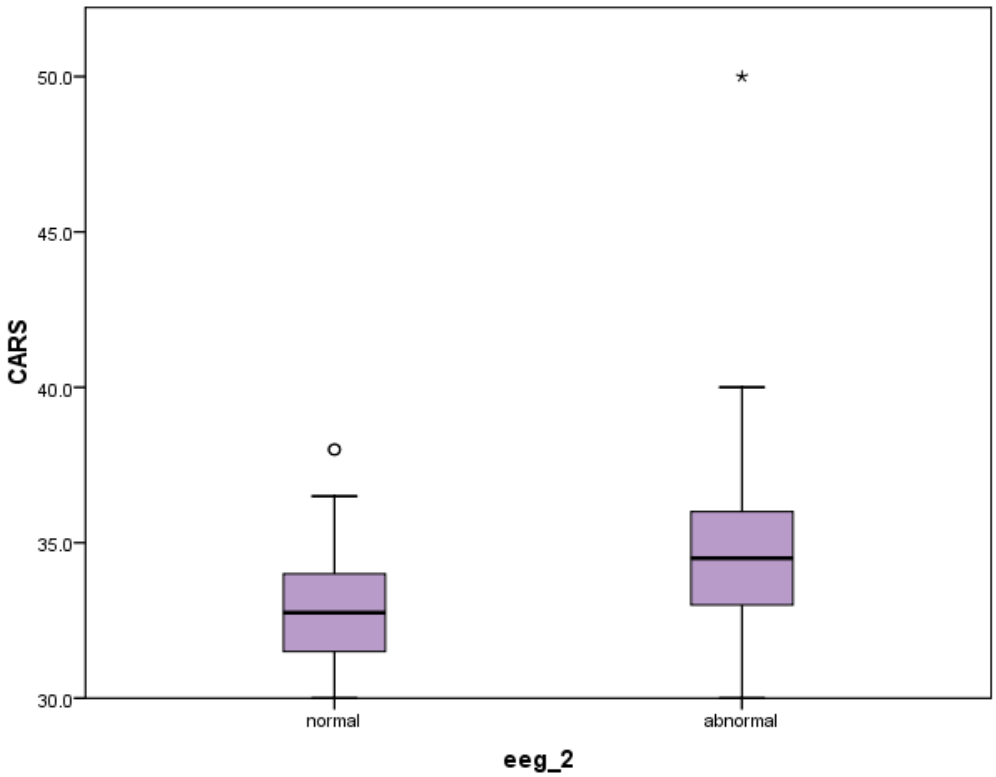
9.8 % children were on speech therapy, 27.7 % were on occupational therapy, 1.3% were on special educator help and rest were receiving combination of therapies. There is no significant difference between the two EEG groups and treatment modalities.

CORRELATION OF EEG AND CARS

Spearman's rho		EEG	CARS
EEG	Correlation Coefficient	1.000	**.326****
	Sig. (2-tailed)	-	**.005**
	N	72	72
CARS	Correlation Coefficient	.326**	1.000
	Sig. (2-tailed)	.005	-
	N	72	72

P value .005

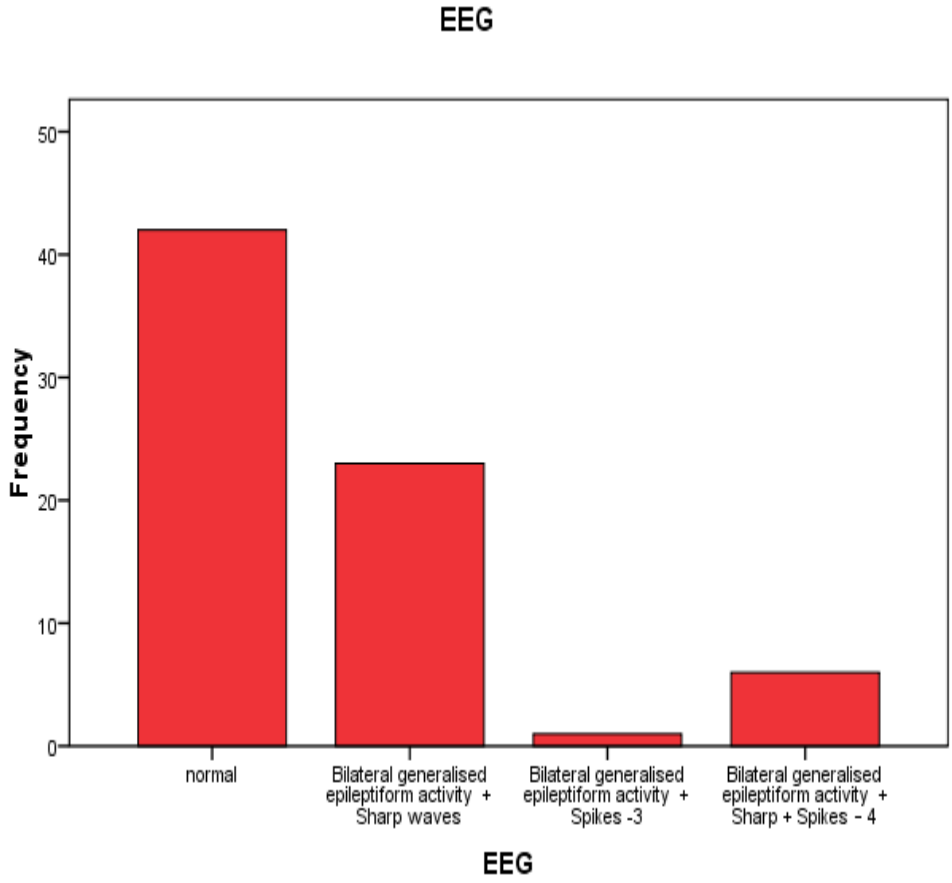
EEG correlates with CARS



EEG is significantly correlated to CARS, P value 0.005, hence abnormal EEG correlates with the severity of autism.

FREQUENCY OF DISTRIBUTION OF PATIENTS BASED ON EEG FINDINGS

EEG	Frequency	Percent
Normal	42	58.3
Bilateral generalised epileptiform activity + Sharp waves	23	31.9
Bilateral generalised epileptiform activity + Spikes	1	1.4
Bilateral generalised epileptiform activity + Sharp + Spikes	6	8.4
Total	**72**	**100.0**

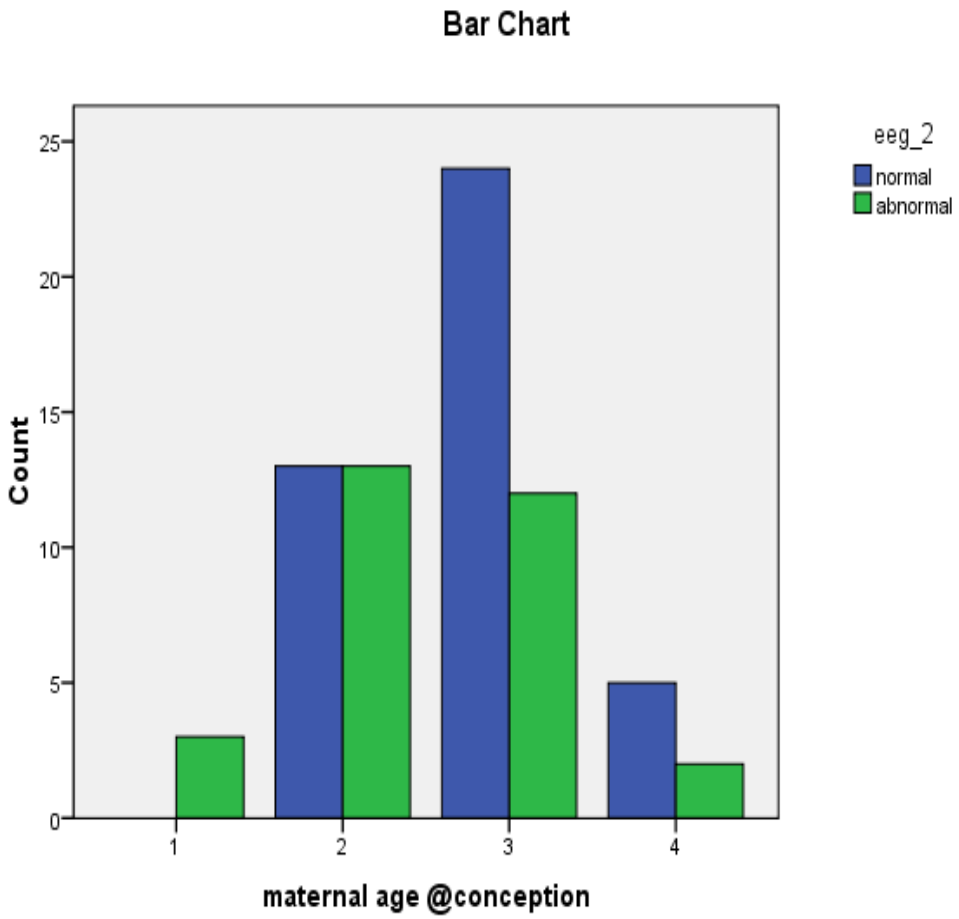


58.3% children had normal EEG, 31.9% had bilateral generalised epileptiform activity with sharp waves, 8.4 % had bilateral generalised epileptiform activity with sharp waves and spike waves, 1.4% had only spike waves.

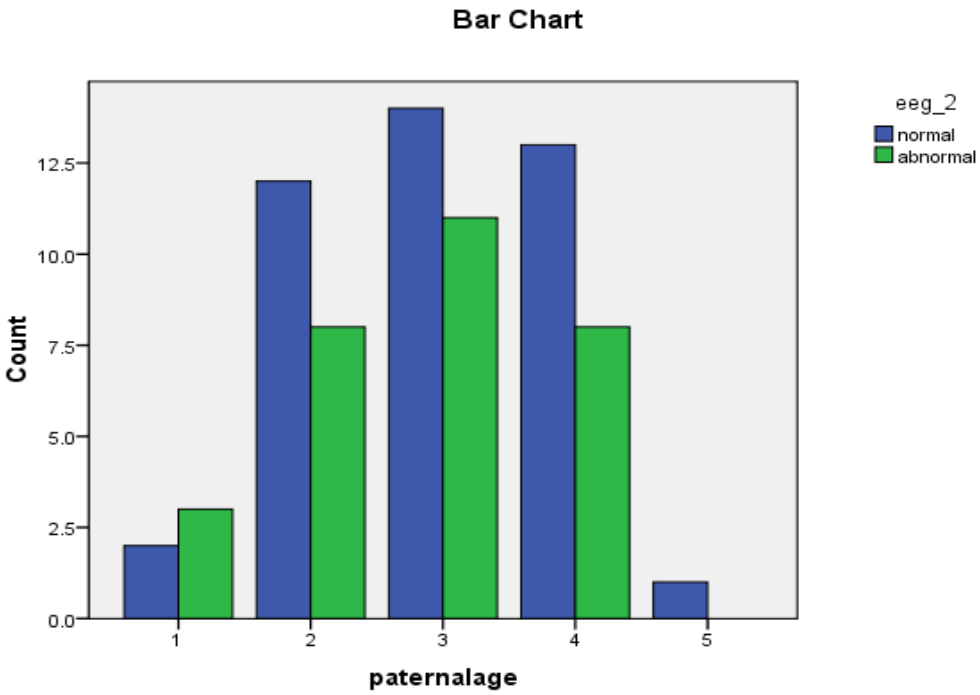
In the study population of 72 patients, 42 patients had normal EEG and 30 patients had abnormal EEG. 17 risk factors of autism were studied, patients were divided into 2 groups, 1st group with normal EEG and 2nd group with abnormal EEG and the association of risk factors were studied between the two groups.

ASSOCIATION OF PRENATAL RISK FACTORS BETWEEN THE TWO GROUPS

Maternal Age at Conception		EEG_2		Total	Percent
		Normal	Abnormal		
	<20 yrs	0	3	3	4.2
	21-25 y	13	13	26	36.1
	26-30y	24	12	36	50
	>30y	5	2	7	9.7
	Total	**42**	**30**	**72**	**100**
Paternal age	<25y	2	3	5	7
	26-30y	13	8	21	29
	31-35y	14	11	25	35
	>35y	13	8	21	29
	Total	**42**	**30**	**72**	**100**
Consanguineous marriage		12	7	19	26.4
Non Consanguineous marriage		30	23	53	73.6
Total		42	30	72	100
psychiatric illness in family	yes	4	6	10	14
	no	38	24	62	86
Total		**42**	**30**	**72**	**100**



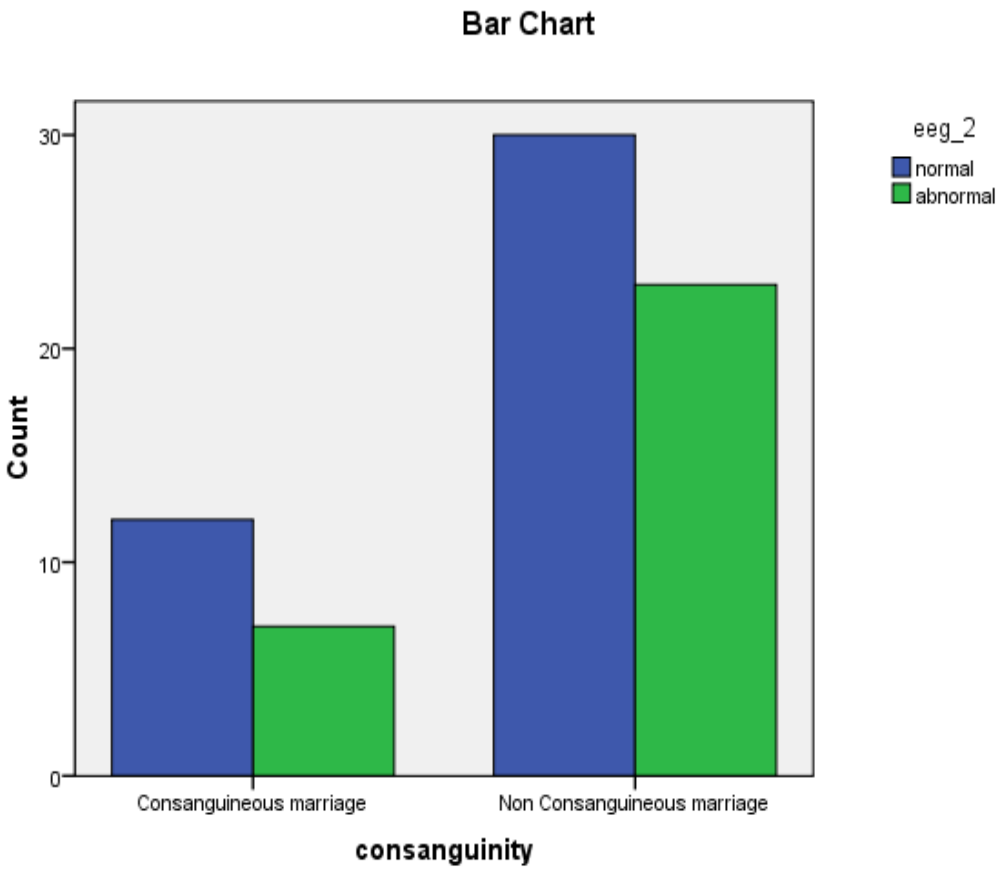
50% (n-36) mothers were 26-30 yrs age at conception, 9.7%(n-7) were above 30 yrs.



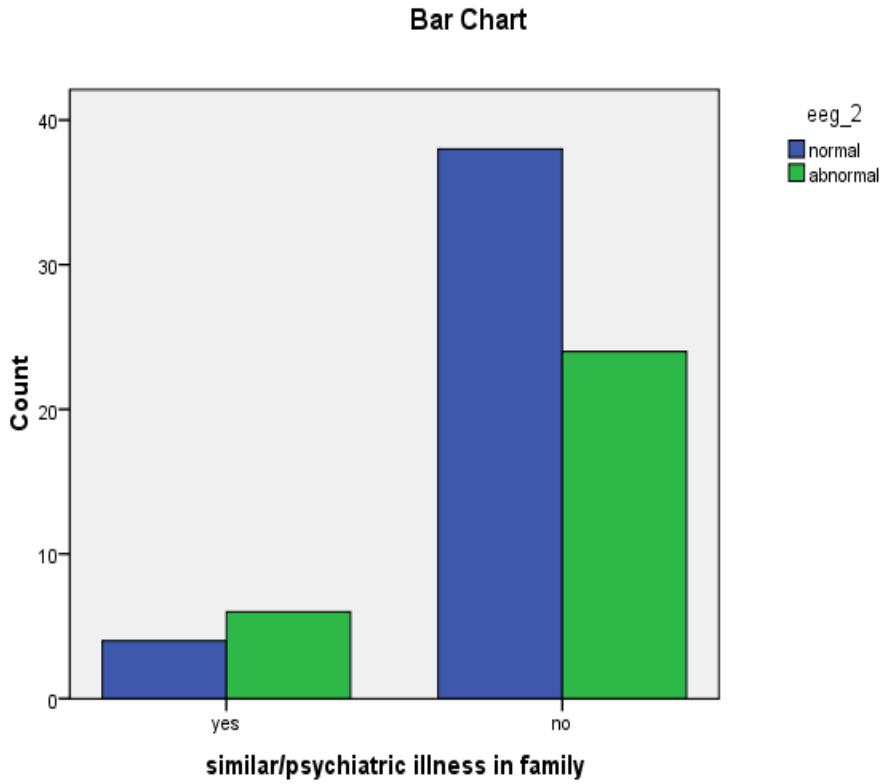
Paternal age at conception above 35 yrs were 29 %(n-21) , 35% (n-25) were 31-35 yrs age .

Chi Square	Value	Df	P Value
Maternal Age	6.465	3	.091
Paternal Age	1.595	4	.810

There is no significant differences in maternal and paternal age between the two EEG groups.



26.4%(n-19) had consanguineous marriage



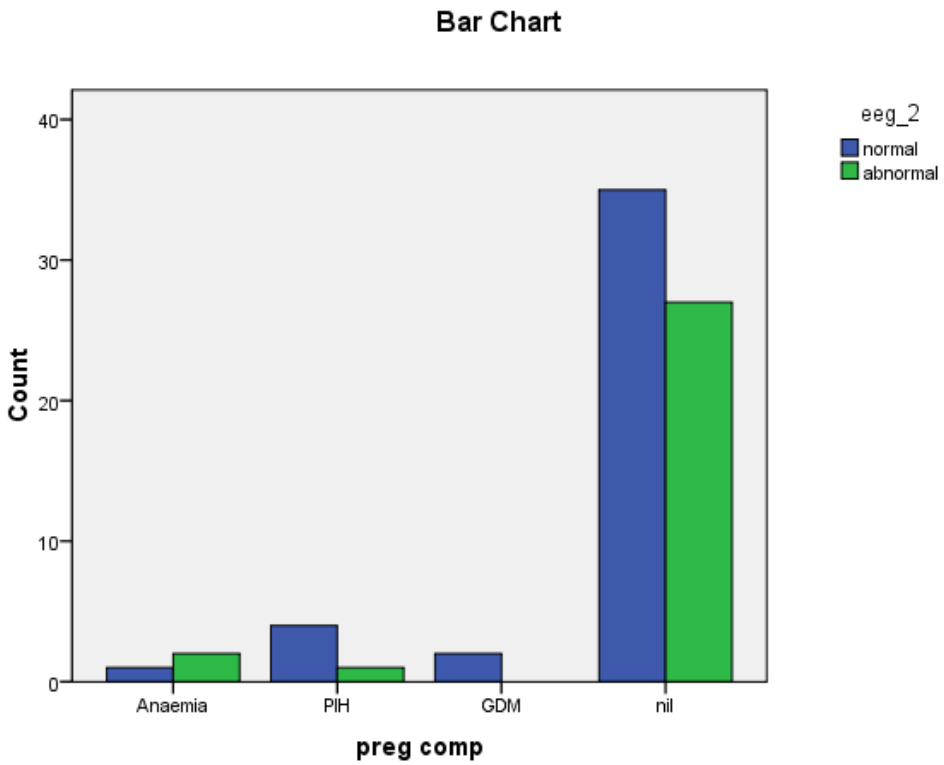
14% (n-10) had positive family history of psychiatric illness.

	Value	Df	P Value
Consanguinity	.247	1	.619
Psychiartic illness in family	1.606	1	.205

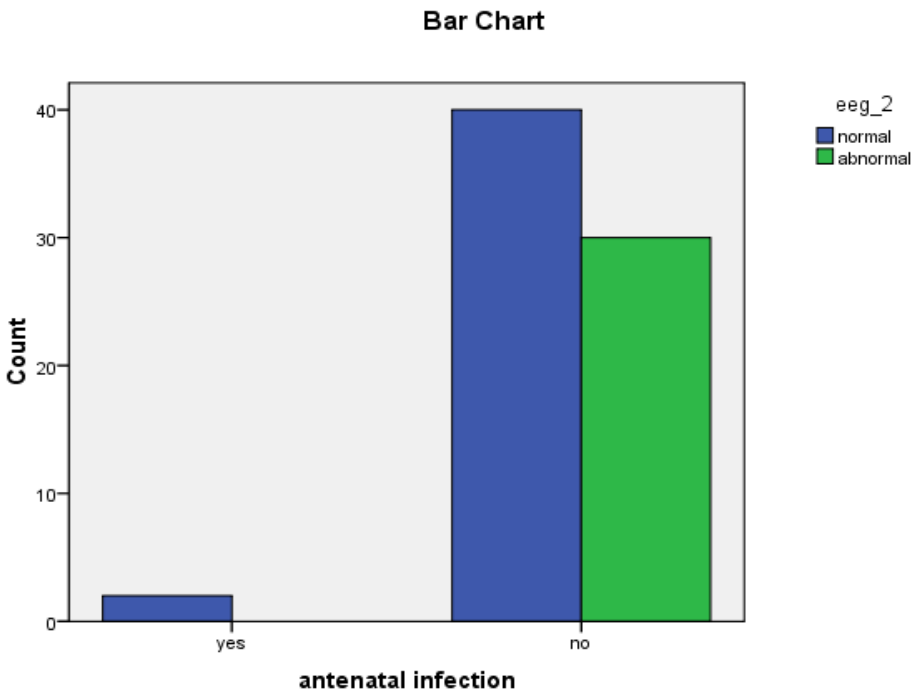
There is no significant differences in psychiatric illness in the family and consanguinity between the two EEG groups.

ASSOCIATION OF PRENATAL RISK FACTORS BETWEEN THE TWO GROUPS

Pregnancy Complications	EEG_2		Total	Percent
	Normal	Abnormal		
Anaemia	1	2	3	4.2
PIH	4	1	5	7
GDM	2	0	2	2.8
Nil	35	27	62	86
Total	**42**	**30**	**72**	**100**
Drug intake yes	0	1	1	1.4
No	42	29	71	98.6
Total	**42**	**30**	**72**	**100**
Antenatal infection yes	2	0	2	2.8
No	40	30	70	97.2
Total	**42**	**30**	**72**	**100**



In the study pregnancy complications such as anaemia was 4.2% (n-3), PIH 7% (n-5), gestational diabetes 2.8% (n-2) .maternal drug intake was only 1.4 %(n-1).



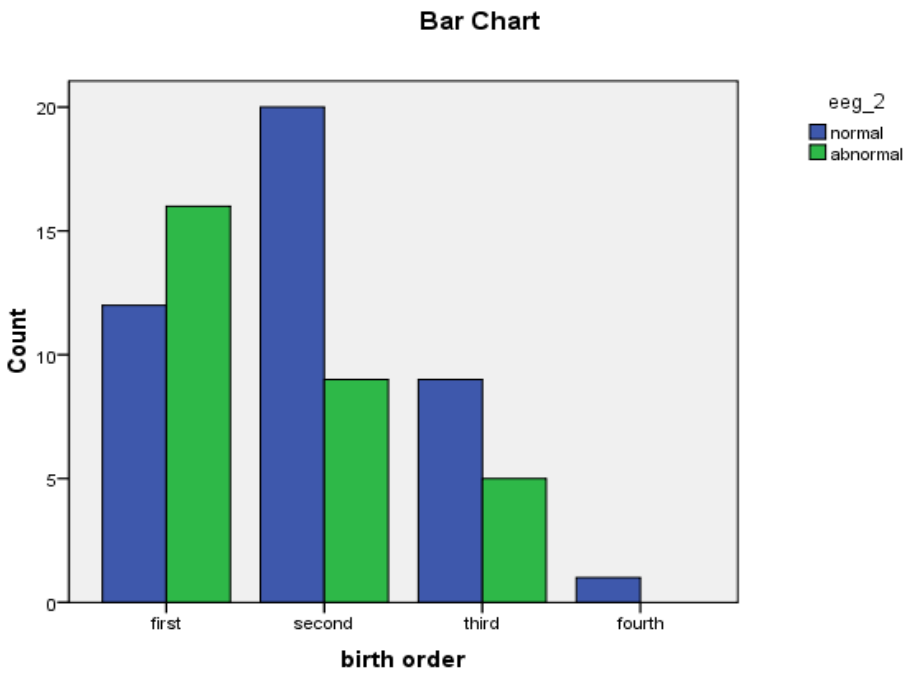
Antenatal infection was 2.8%(n-2).

Chi. Square	Value	Df	P Value
Pregnancy Complication	3.256	3	.354
Drug Intake	2.116	2	.347
Antenatal Infection	1.469	1	.225

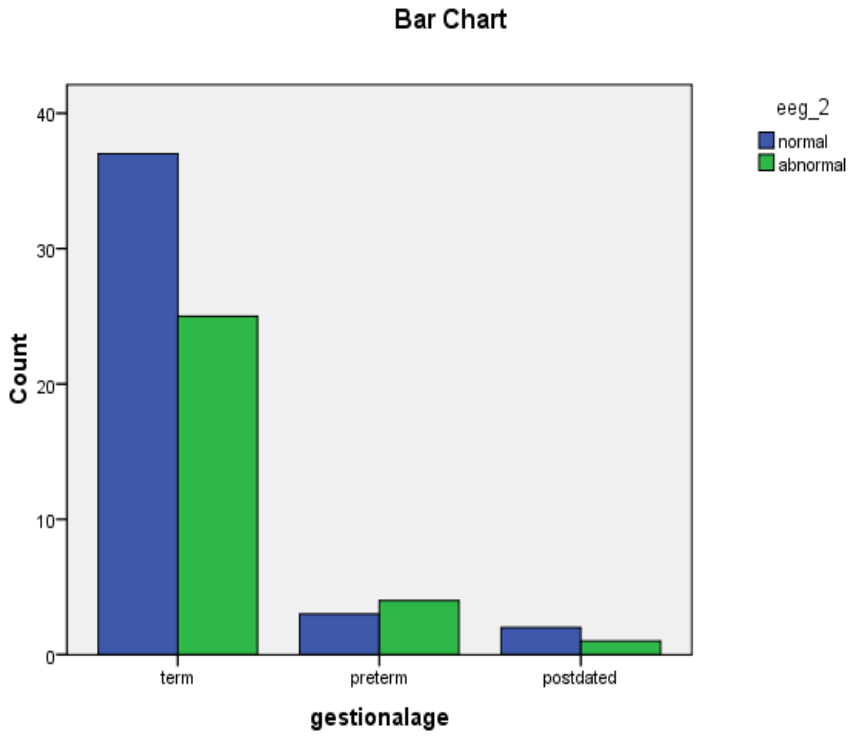
There is no significant differences among pregnancy complications, drug intake and antenatal infection between the two EEG groups.

ASSOCIATION OF PERINATAL RISK FACTORS BETWEEN THE TWO GROUPS

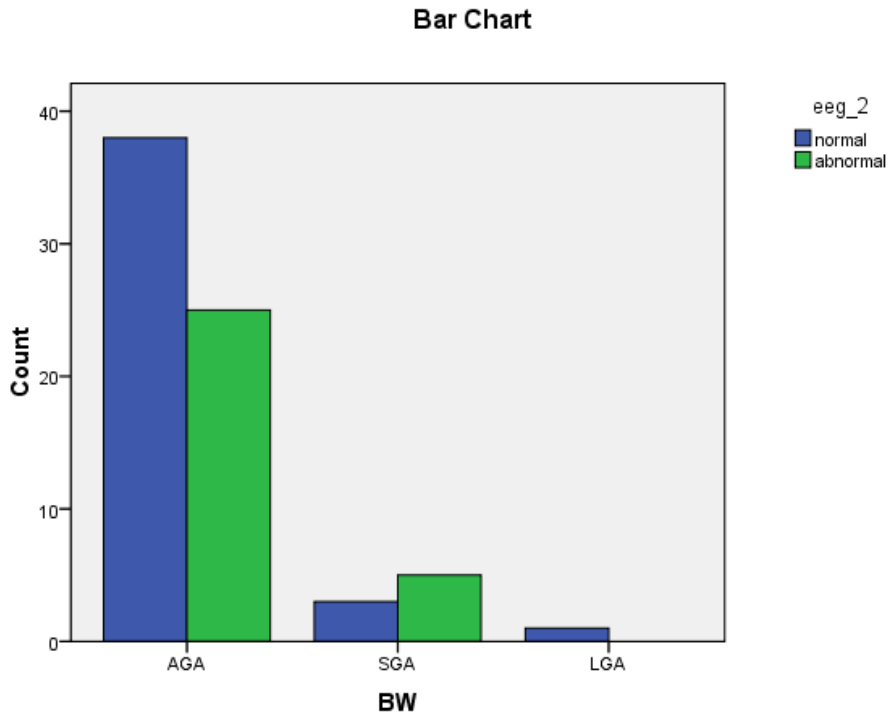
Birth order	EEG_2		Total	Percent
	Normal	Abnormal		
First	12	16	28	39.1
Second	20	9	29	40.2
Third	9	5	14	19.4
Fourth	1	0	1	1.3
Total	**42**	**30**	**72**	**100**
Gestational age term	37	25	62	86
Preterm	3	4	7	9.8
Post term	2	1	3	4.2
Total	**42**	**30**	**72**	**100**
Birth weight AGA	38	25	63	87.5
SGA	3	5	8	11.1
LGA	1	0	1	1.4
Total	**42**	**30**	**72**	**100**



39% (n-28) children were first born, 40.2% (n-29) were second born, 19.4% (n-14) were third born.



86%(n-62) were term born , 9.8%(n-7) were preterms, and 4.2% (n-3) were post term.



AGA- appropriate for gestation

SGA – small for gestation

LGA- large for gestation

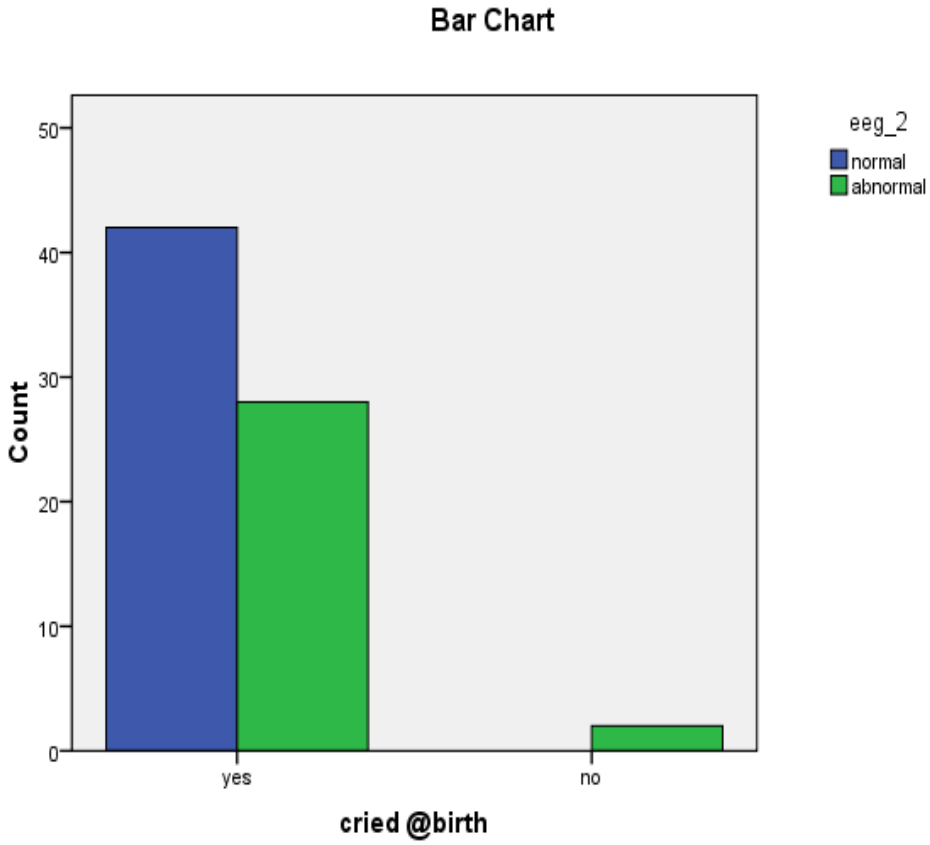
87.5% (n-63) were appropriate for gestation, 11% (n-8) were small for gestation.

Chi. Square	Value	Df	P Value
Birth Order	5.026	3	.170
Gestational Age	.822	2	.663
Birth Weight	2.245	2	.325

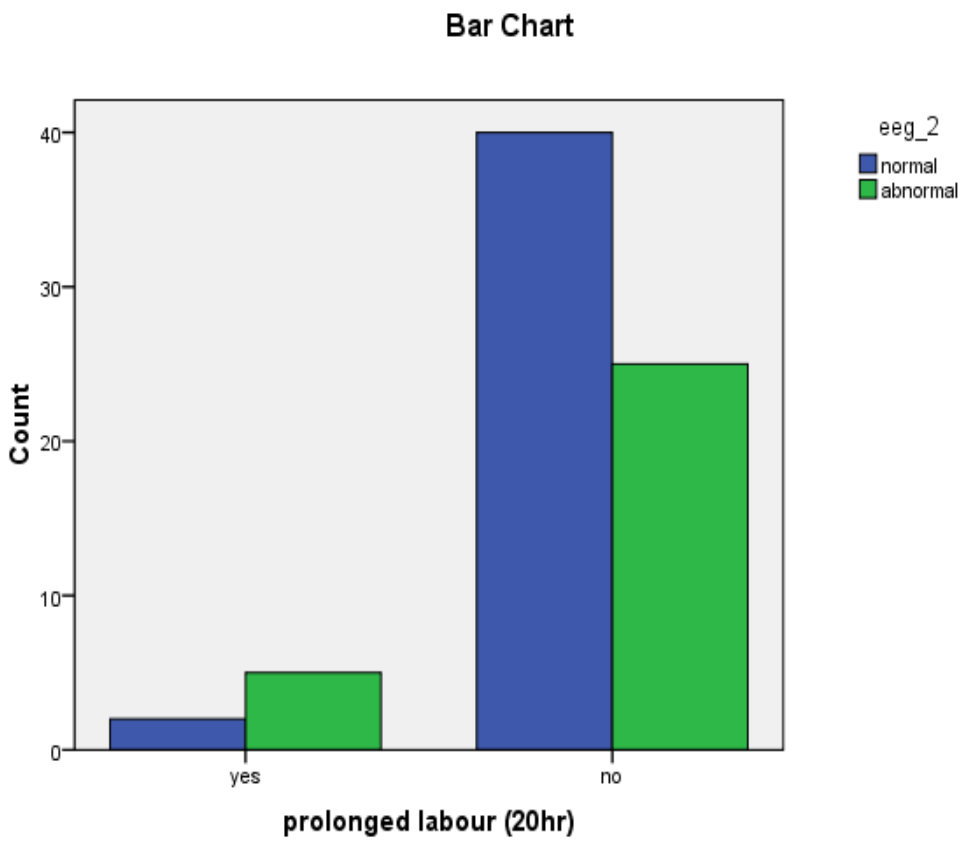
There is no significant differences among birth order, gestational age and birth weight between the two EEG groups.

ASSOCIATION OF PERINATAL RISK FACTORS BETWEEN THE TWO GROUPS

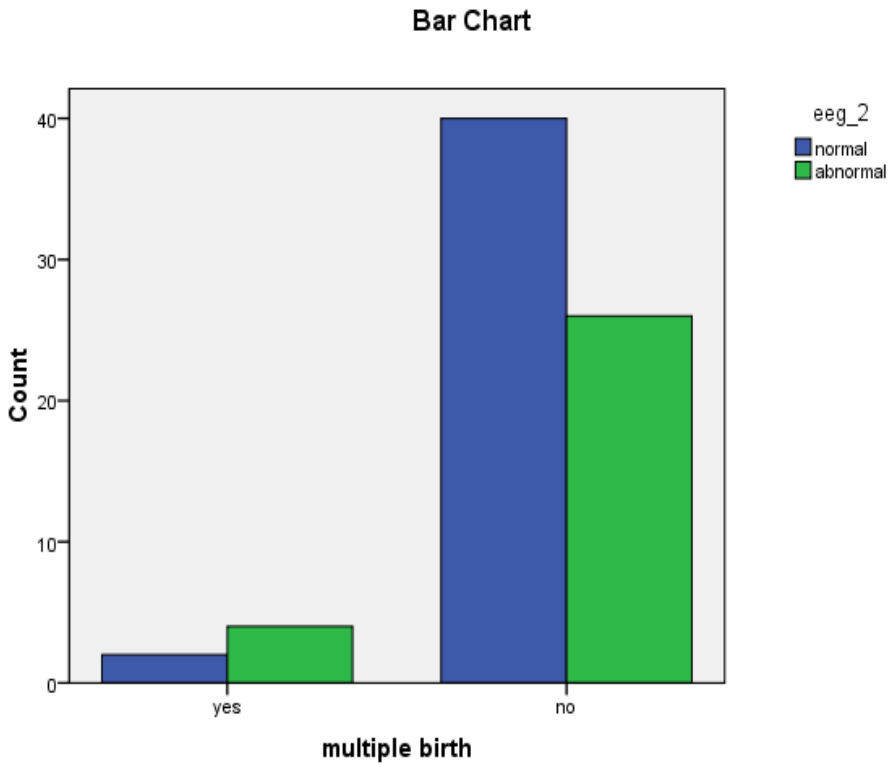
Prolonged labour (20hr)	EEG_2		Total	
	Normal	Abnormal		Percent
Yes	2	5	7	9.7
No	40	25	65	90.3
Total	**42**	**30**	**72**	**100**
Mode of delivery-normal delivery	27	22	49	68
Caesarean delivery	14	7	21	29.2
Assisted delivery	1	1	2	2.8
Total	**42**	**30**	**72**	**100**
Multiple birth Yes	2	4	6	8
No	40	26	66	92
Total	**42**	**30**	**72**	**100**
Cried at birth Yes	42	28	70	97.2
No	0	2	2	2.8
Total	**42**	**30**	**72**	**100**



2.8% (n-2) children had birth asphyxia.



9.7%(n- 7) had prolonged labour.



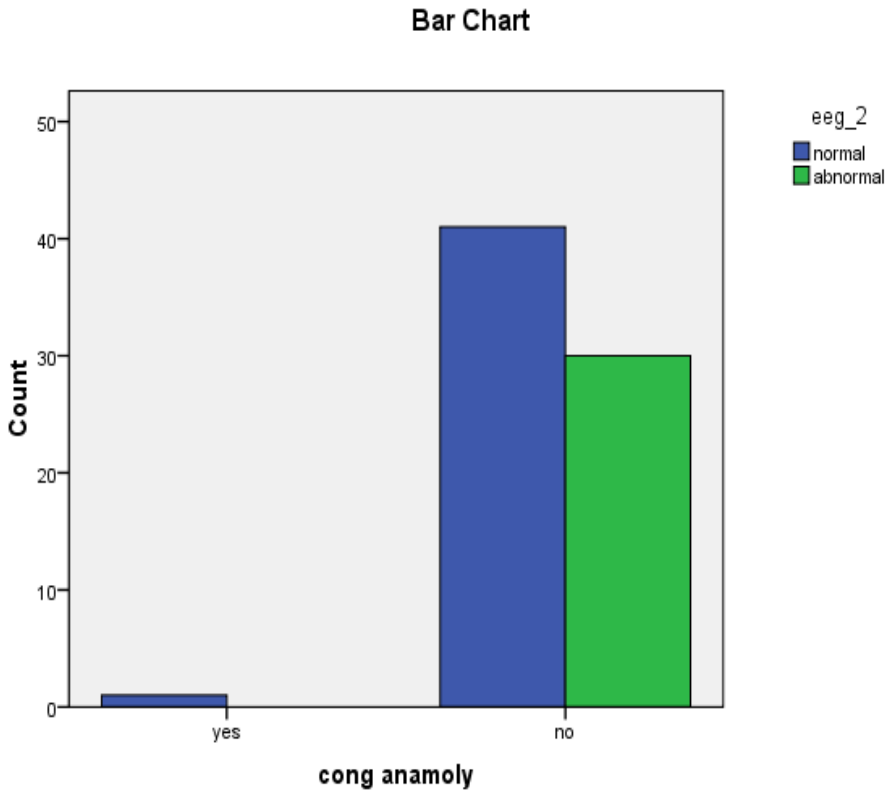
8%(n-6) children had twin delivery

Chi. Square	Value	Df	P Value
Prolonged labour	2.826	1	.093
Mode of delivery	.868	2	.648
Multiple birth	1.683	1	.195
Cried at birth	2.880	1	.090

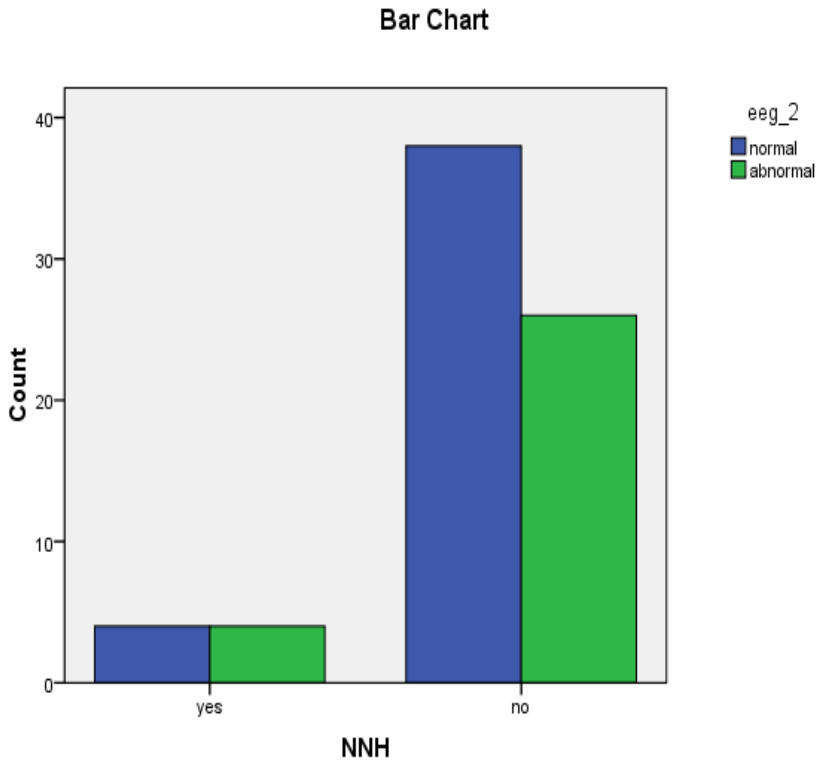
There is no significant differences among prolonged labour, mode of delivery, multiple birth and birth asphyxia between the two EEG groups.

ASSOCIATION OF POSTNATAL RISK FACTORS BETWEEN THE TWO GROUPS

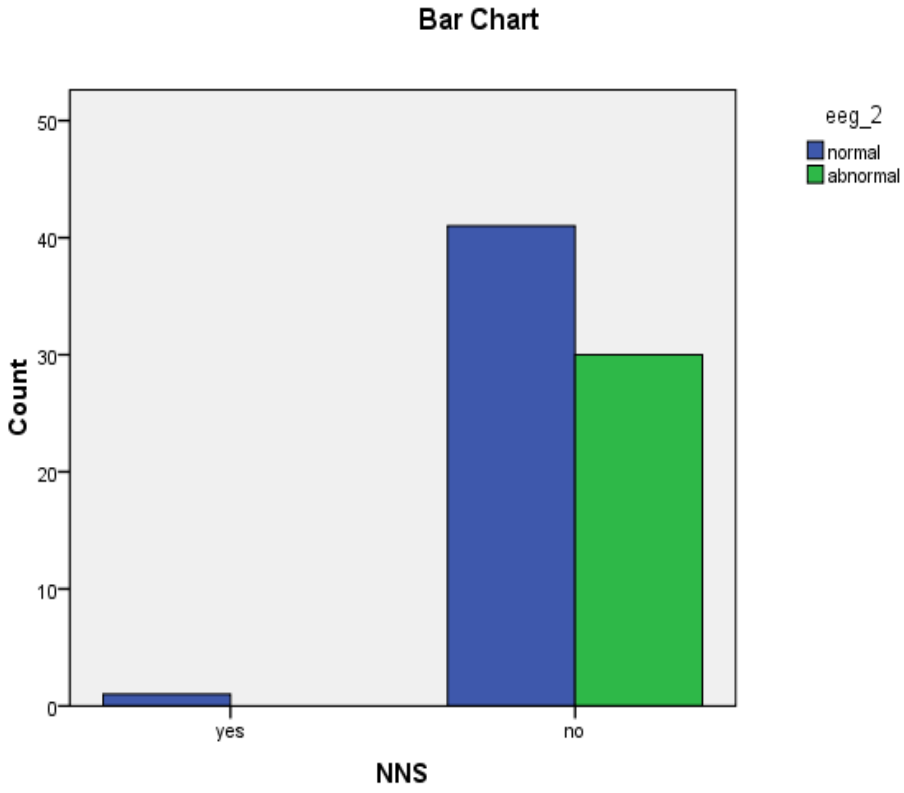
Neonatal Hyperbilirubinemia (NNH)		EEG_2		Total	Percent
		Normal	Abnormal		
	Yes	4	4	8	11
	No	38	26	64	89
Total		**42**	**30**	**72**	**100**
Congenital anomaly	Yes	1	0	1	1.3
	No	41	30	71	98.7
Total		**42**	**30**	**72**	**100**
Neonatal seizures (NNS)	Yes	1	0	1	1.3
	No	41	30	71	98.7
Total		**42**	**30**	**72**	**100**



Only 1 child had congenital anomaly



11% (n-8) children had history of neonatal hyperbilirubinemia.



Only 1 child had history of neonatal seizures

Chi. Square Test	Value	Df	P Value
NNH	.257	1	.612
Congenital anomaly	.724	1	.395
NNS	.724	1	.395

There is no significant differences among neonatal hyperbilirubinemia, neonatal seizures and congenital anomaly between the two EEG groups.

CORRELATION OF PRENATAL RISK FACTORS WITH CARS IN EEG NORMAL GROUP

Spearman's rho correlation

	CARS		
	N	**Correlation Coefficient**	**P value**
Maternal age	42	.295	.058
Paternal age	42	.203	.198
Consanguinity	42	.180	.254
Psychiatric illness in family	42	-.375	.014*
Pregnancy complication	42	-.119	.453
Drug intake	42	-.169	.284
Antenatal infection	42	.075	.639

*Correlation is significant at 0.05 level

Psychiatric illness in family is a significant risk factor which correlates to CARS in EEG normal group.

CORRELATION OF PERINATAL RISK FACTORS WITH CARS IN EEG NORMAL GROUP

Spearman's rho correlation

	CARS		
	N	**Correlation Coefficient**	**P value**
Birth order	42	.344	**.026***
Prolonged labour	42	-.070	.66
Mode of delivery	42	.062	.69
Gestational age	42	.069	.066
Birth weight	42	-.074	.64
Multiple birth	42	.075	.63

*Correlation is significant at 0.05 level

Birth order- first birth is significant risk factors which correlates with CARS in EEG normal group.

CORRELATION OF POSTNATAL RISK FACTORS WITH CARS IN EEG NORMAL GROUP

Spearman's rho correlation

	CARS		
	N	**Correlation Coefficient**	**P value**
Neonatal hyperbilirubinemia	42	.074	.64
Neonatal seizures	42	-.130	.412
Congenital anomaly	42	.169	.284

Post natal risk factors are not statistically significant in EEG normal group.

CORRELATION OF PRENATAL RISK FACTORS WITH CARS IN EEG ABNORMAL GROUP

Spearman's rho correlation

	CARS		
	N	**Correlation Coefficient**	**P value**
Maternal age	30	.286	.126
Paternal age	30	.061	.751
Consanguinity	30	-.100	.597
Pregnancy complication	30	.283	.130
Drug intake	30	.140	.461

Prenatal risk factors are not statistically significant in EEG abnormal group**.**

CORRELATION OF PERINATAL RISK FACTORS WITH CARS IN EEG ABNORMAL GROUP

Spearman's rho correlation

	CARS		
	N	**Correlation Coefficient**	**P value**
Birth order	30	.233	.214
Prolonged labour	30	-.109	.56
Mode of delivery	30	.136	.473
Gestational age	30	.245	.191
Cried at birth	30	-.139	.462
Birth weight	30	.327	.078
Multiple birth	30	.307	.099
Neonatal hyperbilirubinemia	30	-.193	.306

Perinatal and postnatal risk factors are not statistically significant in EEG abnormal group**.**

CORRELATION OF PRENATAL RISK FACTORS WITH CARS IN EEG ABNORMAL WITH SHARP WAVES

Spearman's rho correlation

	CARS		
	N	**Correlation Coefficient**	**P value**
Maternal age	23	.476	**.022***
Paternal age	23	.155	.481
Consanguinity	23	.007	.97
Psychiatric illness in family	23	-.029	0.89
Pregnancy complication	23	.296	.170

*Correlation is significant at 0.05 level

Advanced maternal age is a significant risk factor correlates to CARS in EEG abnormal with sharp wave group.

CORRELATION OF PERINATAL RISK FACTORS WITH CARS IN EEG ABNORMAL WITH SHARP WAVES

Spearman's rho correlation

	CARS		
	N	**Correlation Coefficient**	**P value**
Birth order	23	.297	.168
Prolonged labour	23	.113	.608
Mode of delivery	23	.252	.245
Gestational age	23	.132	.54
Cried at birth	23	.245	.26
Birth weight	23	.303	.160
Multiple birth	23	0.430	**0.041***

*Correlation is significant at 0.05 level

Multiple birth is a significant risk factor which correlates to CARS in EEG abnormal with sharp wave group.

DISCUSSION

Autism is a neurodevelopmental disorder with difficulties in social interaction, social communication and repetitive, restricted or stereotyped behavior, interests or activities.

In this study, out of 72 autistic children 73.6 % (n-53) were in the age group of 3-6 years, 19.4% (n-14) were in the age group of 6-9 years and 7 % (n-5)were in 9-12 years.

In the study population of 72 ,83.3% (n-60) were males and 16.7%(n-12) were females. Male : female ratio is 5:1. Maximum incidence was seen in males, the exact reason for male preponderance is not known.

Speech delay, absence of eye contact and hyperactivity (82%) are the most common behavioural problems noted in this study.

In this study 38.9% (n-28) children were going to special school, 37.5% (n-27) were going to regular school and 20.8% (n-15) were not attending any school.

Out of 72 children, 33.3%(24) children were on drugs and 66.7 %(n-48) were not on any medications. Maximum children were consuming T Risperidone, T Trihexyphenidyl.

Childhood autism rating scale (CARS) was used to assess the severity of autism. The mean CARS for 3-6 yrs age group was 33.3, for 6-9 yrs mean CARS was 33.8 and for 9-12yrs mean CARS was 36.6. In this study correlation of CARS with age is significant at the 0.05 level, as the age increases severity increases.

The mean CARS for males was 33.5 and for females 34.2, there was no significant correlation between CARS and gender.

20 risk factors were studied in all 72 autistic children , they were divided into three groups such as prenatal, perinatal and postnatal risk factors. Out of 20, three risk factors – irradiation during pregnancy, threatened abortion and mode of presentation did not show positivity in 72 children so was not considered for analysis. Rest 17 risk factors were considered for analysis.

Prenatal risk factors	Perinatal risk factors	Postnatal risk factors
Maternal age	Birth order	Neonatal hyperbilirubinemia
Paternal age	Gestational age	Neonatal seizures
Consanguinity	Prolonged labour	Congenital anomaly
Psychiatric illness in family	Mode of presentation	
Pregnancy complication	Mode of delivery	
Threatened abortion	Birth weight	
Drug intake	Cried at birth	
Irradiation during pregnancy	Multiple birth	
Antenatal infection		

Many studies have reported EEG abnormalities mainly epileptiform activity in approximately 30% of autistic children with no clinical seizures (41,42,43). Where as in this study 41.7% (n-30) had abnormal EEG and 58.3% (n-42) children had normal EEG.

Out of 30 abnormal EEG 24 (45.2%) were in the age group 3-6yrs, 5(35.8%) were 6-9 yrs and 1(20%) were 9-12 yrs. Out of 30 abnormal EEG 23 (76.7%) were males and 7 (23.3%) were females. There was no statistical significance was noted between age and gender with EEG.

Most commom EEG abnormality reported in various study in children with autism with no seizures is epileptiform activity(44,45,46). Discharges may be generalized or diffuse, focal or multi-focal , bilateral or unilateral , localized to different areas of brain (47,48,49). Pattern of

epileptiform discharges are sharp wave ,spike wave discharges, sharp slow waves, generalized spike-wave, and generalized polyspike waves.

In this study 41.7%(n-30) children had abnormal EEG ,76.7% (n-23) had bilateral generalised epileptiform activity with Sharp waves, 20% (n-6) had bilateral generalised epileptiform activity with both sharp and spike waves and 3.3% (n-1) had spike wave.

Yasuhara et al have showed in their study that epileptic seizure waves noted from frontal lobe (65.6%). The spike discharges in temporal lobe, parietal lobe, occipital lobe and multifocal spike waves were seen in < 10% children. (37)

EEG was correlated with CARS using spearman's rho correlation test and found to be significant, **P value – 0.005.** Hence EEG abnormality is highly correlated with the severity of autism. This is comparable to the study done by **Riad M .Elsayed et al** has concluded that Subclinical EEG abnormalities were noted at higher incidence in autistic children (51.1%), abnormal EEG were highly correlated to autism severity (p value 0.000).(35)

72 autistic children were divided into two groups for analysis purpose. One group with EEG normal (n-42) and the other with EEG abnormal group (n-30), sociodemographic data and the risk factors were

compared between the two groups and association was tested using pearson chi square test.

There was no significant difference between the two groups in socio demograghic factors like age, gender, mother and father's education and occupation was noted.

In this study 44 (61.2%) children had speech delay, 16/44 had EEG abnormal. 14(19.4%) children had global developmental delay, 8/14 had abnormal EEG. Rest 14(19.4%) children were developmentally normal with 6/14 abnormal EEG. Developmental delay was correlated with severity of autism (CARS) and found to have no statistical significance.

Many risk factors have been implicated in the etiology of autism such as advanced maternal age and paternal age at birth, maternal gestational diabetes, maternal bleeding during pregnancy, maternal drug intake, antenatal infection ,birth order- first born (50) , instrumental delivery, birth asphyxia ,neonatal jaundice, breech presentation, low apgar score, LBW, GA< 35 weeks, family h/o psychiatric disease (25,26).

Prenatal risk factors

50% (n-36) mothers in the study were 26-30 yrs age at conception, 9.7%(n-7) were above 30 yrs. Paternal age at conception above 35 yrs were 29 %(n-21) , 35% (n-25) were 31-35 yrs age .

26.4%(n-19) had consanguineous marriage. 14%(n-10) had positive family history of psychiatric illness. There was no significant difference between the two groups was noted

The above four prenatal risk factors were correlated with CARS, maternal age at conception was found significant, **P value – < 0.05** in EEG abnormal with sharp wave group. Positive family history of psychiatric illness was significant, **p value – < 0.05** in EEG normal group.

Advanced maternal age and psychiatric illness in the family correlates with the severity of autism.

Pregnancy complications such as anaemia was 4.2% (n-3), PIH 7% (n-5), gestational diabetes 2.8% (n-2) .maternal drug intake was only 1.4 %(n-1). Antenatal infection was 2.8% (n-2).

There was no significant difference between the two groups and pregnancy complications, gestational diabetes, antenatal infection.

These prenatal risk factors are not significantly correlated with severity of autism (CARS).

Perinatal risk factors

Birth order	:	39% (n-28) children were first born, 40.2% (n-29) were second born, 19.4% (n-14) were third born.
Gestational age	:	86%(n-62) were term born, 9.8%(n-7) were preterms, and 4.2%(n-3) were post term.
Birth weight	:	87.5%(n-63) were appropriate for gestation, 11% (n-8) were small for gestation.
Prolonged labour	:	9.7%(n- 7) had prolonged labour.
Mode of delivery	:	68%(n-49) delivered normally, 29.2%(n-21) delivered by Caesarean section and 2.8% (n-2) born by assisted delivery.
Multiple birth	:	8%(n-6) children had twin delivery.
Cried at birth	:	2.8%(n-2) children had birth asphyxia.

There was no significant difference between the two groups and perinatal risk factors.

Correlation between perinatal risk factors and CARS was tested using spearman’s rho birth order was found to be significant in EEG normal group.

P value- < 0.05

Correlation of multiple birth was also significant **P value - < 0.05** in EEG abnormal with sharp wave group.

Birth order and multiple birth were highly correlated with the severity of autism. Rest of the perinatal risk factors were not significantly correlated with CARS.

Postnatal risk factors

Neonatal hyperbilirubinemia	:	11% (n-8) children had history of neonatal hyperbilirubinemia.
Neonatal seizures	:	1.3% (n-1) had history of neonatal seizures.
Congenital anomaly	:	1.3% (n-1) had congenital anomaly.

There was no significant difference between the two groups and postnatal risk factors was noted.

The correlation of postnatal risk factor and CARS was not significant.

Advanced maternal age, psychiatric illness in the family, Birth order and multiple birth were highly correlated with the severity of autism (CARS).

Advanced maternal age and multiple birth were significant risk factors associated with the severity in EEG abnormal with sharp wave group and EEG highly correlates with the severity of autism. Hence ideal maternal age for having a child should be emphasised. Multiple birth should be considered as a significant risk factor with such severe level of autism should be taken note of and an appropriate measures should be instituted.

Early anticipation of the diagnosis of autism in children with subtle signs and symptoms should be considered in children with positive family history of psychiatric illness and in first born child which will help us in early diagnosis and intervention.

CONCLUSION

- Autism is more common in males.
- Most common age group in the study is 3-6 years.
- Speech delay, absence of eye contact, hyperactivity are the most common behavioural problems.
- Age correlates with the severity, as the age increases severity increases.
- 40.7% children had EEG abnormality.
- EEG abnormality is more frequently found in males in the age group 3-6 years.
- Most common pattern of EEG abnormality noted in the study is bilateral epileptiform activity with sharp waves.
- EEG significantly correlates with CARS, abnormal EEG highly correlates with the severity of autism.
- Advanced Maternal age at conception, positive family history of psychiatric illness are the prenatal risk factors positively correlated with severity of autism.
- Birth order and multiple births are the perinatal risk factors correlated with the severity of autism.

- Advanced paternal age, pregnancy complications, drug intake, gestational age, prolonged labour, mode of delivery, birth weight, birth asphyxia, neonatal hyperbilirubinemia and neonatal seizures are not correlated to the severity of autism in this study.

LIMITATION OF THIS STUDY

- Assessment of intelligence was not carried out in this study.
- Associated behavioural problems was not considered.
- Large sample size may be needed to decide about the risk factors such as bleeding during pregnancy, irradiation during pregnancy, postnatal risk factors and their role in the severity of the disease.
- Since the study period is short follow up of patients could not be done.
- EEG was done only once during the study.

FUTURE DIRECTION FOR THE FURTHER STUDY

- It is proposed to include neuroimaging (MRI brain) along with quantitative EEG in the future.
- Proposed to follow up children with abnormal EEG and risk of developing seizures in the future.
- Proposed to follow up children with autism without EEG abnormality at current state by serial EEG monitoring.
- To find the role of anti epileptic drugs in treating abnormal EEG in relation to its clinical severity.

BIBLIOGRAPHY

1. American Psychiatric Association. Diagnostic and Statistical

Manual of Mental Disorders, 5th Edition, Arlington, VA : American Psychiatric Publishing; 2013 –Diagnostic criteria for 299.00 Autism spectrum disorder

2. Jon Baio, EdS, National Center on Birth Defects and Developmental Disabilities, CDC, Autism and Developmental Disabilities Monitoring Network Surveillance Year 2010, Surveillance SummariesMarch 28, 2014 / 63(SS02);1-21

3. Minshew NJ,Sweeney JA,Bauman ML, Webb SJ:Neurologic aspects of autism ,in handbook of autism and Pervasive developmental disorders,vol 1 .Volkmar FR, Klin A, Paul R,Cohen DJ.(eds):Hoboken, Wiley, 2005, pp.453-72

4. Werner, E; Dawson, Munson, & Osterling (2005). "Variation in early developmental course in autism and its relation with behavioral outcome at 3-4 years of age". Journal of Autism and Developmental Disorders 35 (3): 337–350.

5. Ballaban-Gil, K; Tuchman (2000). "Epilepsy and epileptiform EEG: Association with autism and language disorders".Mental Retardation and Developmental Disabilities Research Reviews 6 (4): 300–308.

6.Muhle R, Trentacoste SV, Rapin I. The genetics of autism. Pediatrics. 2004;113(5).

7. Kanner L. Autistic disturbances of affective contact. Nerv Child.

1943;2:217–250

8. Piven J, Palmer P, Jacobi D, Childress D, Arndt S. Broader autism phenotype: evidence from a family history study of multiple-incidence autism families [PDF]. Am J Psychiatry. 1997;154(2):185–90. PMID 9016266.

9.Blumberg SJ, Bramlett MD, Kogan MD, et al. Changes in prevalence of parent-reported autism spectrum disorder in school-aged U.S. children: 2007 to 2011–2012. Natl Health Stat Rep 2013;65:1–11.

10.Schieve LA, Rice C, Devine O, et al. Have secular changes in perinatal risk factors contributed to the recent autism prevalence increase? Development and application of a mathematical assessment model. Ann Epidemiol 2011;21:930–45.

11.Kleigman, Stanton, ST. Geme, Schor, Behrman. Nelson Textbook

of Pediatrics. 19th ed. Philadelphia: Elsevier Saunders; 2011. Autistic

Disorder; p. 100-106

12. Risch N, Spiker D, Lotspeich L, et al. A genomic screen of autism: evidence for a multilocus etiology. Am J Hum Genet.1999;65 :493– 507

13. Asherson PJ, Curran S. Approaches to gene mapping in complex disorders and their application in child psychiatry and psychology. Br J Psychiatry.2001;179 :122– 128

14. Rutter M. Genetic influences and autism. In: Volkmar FR, Paul R, Klin A, Cohen D, eds. Handbook of Autism and Pervasive Developmental Disorders. 3rd ed. Vol 1. Hoboken, NJ: John Wiley & Sons; 2005:425–452

15. Bailey A, Le Couteur A, Gottesman I, et al. Autism as a strongly genetic disorder: evidence from a British twin study. Psychol Med 1995;25:63–77.

16. Veenstra-Vanderweele J, Christian SL, Cook EH Jr. Autism as a paradigmatic complex genetic disorder. Annu Rev Genomics Hum Genet.2004;5 :379– 405

17. Buxbaum JD. The genetics of autism spectrum disorders. Medscape Psychiatry Ment Health. 2005;10(2)

18.Korvatska E, Van de Water J, Anders TF, Gershwin ME. Genetic and immunologic considerations in autism [published correction appears in Neurobiol Dis. 2002;10:69]. Neurobiol Dis.2002;9 :107– 125

19. Cook EH Jr, Lindgren V, Leventhal BL, et al. Autism or atypical autism in maternally but not paternally derived proximal 15q duplication. Am J Hum Genet. 1997;60:928–934

20. Croen LA, Najjar DV, Fireman B, Grether JK. Maternal and paternal age and risk of autism spectrum disorders. Arch Pediatr Adolesc Med. 2007;161:334–340

21. Chess S, Korn SJ, Fernandez PB. Psychiatric Disorders of Children With Congenital Rubella. New York, NY: Brunner/Mazel; 1971

22. Fombonne E. The epidemiology of autism: a review. Psychol Med. 1999;29:769–786

23. Arndt T, Stodgell CJ, Rodier PM. The teratology of autism. Int J Dev Neurosci. 2005;23:189 –199

24 . Badawi N, Dixon G, Felix JF, et al. Autism following a history of newborn encephalopathy: more than a coincidence? Dev Med Child Neurol. 2006;48:85– 89

25. Farida El-Baz, Nanees Ahmed Ismael, Sahar M. Nour El-Din : Risk factors for autism, Egyptian Journal of Medical Human Genetics Volume 12, Issue 1, May 2011, Pages 31–38

26. American journal of epidemiology (2005) 161(10): 916-925

To explore the association between perinatal factors, parental psychiatric history and risk of autism

27. Institute of Medicine, Immunization Safety Review Committee. Immunization Safety Review: Measles-Mumps-Rubella Vaccine and

Autism. Stratton K, Gable A, Shetty P, McCormick M, eds. Washington, DC: National Academies Press; 2001

28. Pickett J, London E. The neuropathology of autism: a review. J Neuropathol Exp Neurol. 2005;64:925–935

29. Filipek PA. Neuroimaging in the developmental disorders: the state of the science. J Child Psychol Psychiatry. 1999;40: 113–128

30. Grelotti DJ, Gauthier I, Schultz RT. Social interest and the development of cortical face specialization: what autism teaches us about face processing. Dev Psychobiol 2002;40: 213–25.

31. Azmitia EC. Modern views on an ancient chemical: serotonin effects on cell proliferation, maturation, and apoptosis. Brain Res Bull 2001;56:413–24.

32. Dapretto, M., Davies M.S. et al. (2006). "Understanding emotions in others: mirror neuron dysfunction in children with autism spectrum disorders". Nature Neuroscience 9 (1): 28–30.

33. Miles JH, Hillman RE. Value of a clinical morphology examination in autism. Am J Med Genet. 2000;91:245–253

34. Baron-Cohen S. Mindblindness: An Essay on Autism and Theory of Mind. Cambridge, MA: MIT Press; 1995

35. Riad M .Elsayed and Hala E. Sayyah: Subclinical Epileptiform Dysfunction in Children with Idiopthic Autism, Journal of American Science 2012;8(8)

36. Michael G. Chez, Mina Chang, Valerie Krasne, Carolyn Coughlan, Matthew Kominsky: Frequency of epileptiform EEG abnormalities in a sequential screening of autistic patients with no known clinical epilepsy, Epilepsy & Behaviour ,volume 8, issue1, pages267-271, february2006

37. Yasuhara Children's Clinic and YCC Education Center, Japan : Correlation between EEG abnormalities and symptoms of autism spectrum disorder (ASD), Official journal of the Japanese society of child neurology Brain Dev. 2010 Nov;32(10):791-8. Epub 2010 Sep 9.

38. Hideaki Kanemura, Fumikazu Sano, Tomoko Tando, Kanji Sugita, Masao Aihara : Can EEG characteristics predict development of epilepsy in autistic children?, European Journal Of Paediatric Neurology volume 17, issue 3, pages232-237, may 2013

39.Ahmed I. Kotoury, Ghada Y. El-Kamah, Samira I. Ibrahim and Engy A. Ashaat : EEG changes and neuroimaging abnormalities in relevance to severity of autism, Egypt. J. Med. Hum. Genet. Vol. 10, No. 1, May, 2009

40. Rutter M, Bailey A, Bolton P, Le Couteur A. Autism and known medical conditions: myth and substance. J Child Psychol Psychiatry. 1994;35:311–322

41. Komarek V, Propper L, Kulisek R, Zumrova A, Faladova L, Havlovicova M, Sedlacek Z, Blatny M, Urbanek T. Not EEG abnormalities but epilepsy is associated with autistic regression and mental functioning in childhood autism. Eur Child Adolesc Psychiatry. 2004;13:209–213

42. N, Farid N, Courchesne E, Haas R. Abnormalities on the neurological examination and EEG in young children with pervasive developmental disorders. J Autism Dev Disord. 2007;37:887–893.

43. inson RO, Boyd S, Charman T. Sleep electroencephalograms in young children with autism with and without regression. Dev Med Child Neurol.2006;48:604–608.

44. Donnelly JH, Tournay AE, Book TM, Filipek P. Absence of seizures despite high prevalence of epileptiform EEG abnormalities in children

with autism monitored in a tertiary care center. Epilepsia. 2006;47:394–398.

45. Gabis L, Pomeroy J, Andriola MR. Autism and epilepsy: cause, consequence, comorbidity, or coincidence? Epilepsy Behav. 2005;7:652–656

46. KA, Ballaban-Gil K, Rapin I, Moshe SL, Shinnar S. Epileptiform EEG abnormalities in children with language regression. Neurology. 2005;65:129–131.

47. Hara H. Autism and epilepsy: a retrospective follow-up study. Brain Dev. 2007;29:486–490.

48. Melyn M. EEG and seizures in autistic children and adolescents: further findings with therapeutic implications. Clin EEG Neurosci. 2005;36:15–20.

49. Chang M, Krasne V, Coughlan C, Kominsky M, Schwartz A. Frequency of epileptiform EEG abnormalities in a sequential screening of autistic patients with no known clinical epilepsy from 1996 to 2005. Epilepsy Behav. 2006;8:267–271

50.Hannah Gardener, ScD, Donna Spiegelman, ScD, and Stephen L. Buka, ScD, Prenatal Risk Factors for Autism: A Comprehensive Meta-analysis , Br J Psychiatry .july 2009;195(1):7-14

ABBREVIATIONS

ASD	-	Autism spectrum disorder
AD	-	Autistic disorder
DSM	-	Diagnostic and Statistical Manual of Mental Disorders
PDD	-	Pervasive Developmental Disorder
MR	-	Mental retardation
GDD	-	Global developmental delay
MMR	-	Measles-mumps-rubella
JA	-	Joint attention
CHAT	-	Checklist for Autism in Toddlers
M-CHAT	-	Modified Checklist for Autism in Toddlers
CARS	-	Childhood Autism Rating Scale
EEG	-	Electroencephalogram
AGA	-	Appropriate for gestational age
SGA	-	Small for gestational age
LGA	-	Large for gestational age
LSCS	-	Lower segment caesarian section
PIH	-	Pregnancy induced hypertension
GDM	-	Gestational diabetes mellitus
CGC	-	Child guidance clinic
ADI-R	-	Autism Diagnostic Interview - Revised
ADOS	-	Autism Diagnostic Observation Schedule

ANNEXURE

Diagnostic Criteria for 299.00 Autism Spectrum Disorder

A. **Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history**

1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
3. Deficits in developing, maintaining, and understand relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

B. **Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history**,

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypes, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g. apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

Specify **current severity:**

Severity is based on social communication impairments and restricted, repetitive patterns of behavior.

C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).

D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

PROFORMA

DEMOGRAPHIC DATA

1. Serial No : _____
2. CGC No : _____
3. Age :
4. Sex : a)Male b)Female

5. Father's educational Status :

   a) Primary School

   b) Secondary School

   c) Higher Secondary

   d) Degree holder & Higher

   e) Illiterate

5. Mother's educational Status :

   a) Primary School

   b) Secondary School

   c) Higher Secondary

   d) Degree holder & Higher

   e) Illiterate

7. Father's Occupation : a) unemployed b) unskilled c) skilled

d) Business e) Professional

8.Mother's Occupation : a) unemployed b) unskilled c) skilled

d) Business e) Professional

9. Children's type of education : a) Special School b) Regular School

c) both d) not attending school

II. ILLNESS

10.Age at which the diagnosis of autism :

11.Presenting complaints :

12. Is the Child on Pharmacological therapy :

a) yes if yes _____ (drugname)

b) no

c) Duration of treatment

13. Is the child on :

a) occupational therapy

b) speech therapy

c) special educators help

d) combination of any

III. Risk Factors

14. Age of mother at the time of conception :

15.Age of father at the time of conception:

16. Pregnancy Complications : a) Anemia b) PIH

c) GDM d) Seizure Disorder

17.H/O Threatened abortion : a) yes b) no

18. H/o Drug Intake : a) Yes b) No

If yes _____ (Drug Name)

19. H/o. Irradiation : a) Yes b) No

20. H/o. antenatal Infections : a) Yes b) No

(Fever with rash)

21. Birth Order :

22. Gestational Age : a)Term b) Preterm c) Post – dated

23. Mode of delivery : a) Normal Vaginal delivery b) LSCS

c) Assisted delivery

24. Mode of Presentation : a) Vertex b)breech c) Not known

25. Prolonged labour (>20hrs) : a) Yes b) No

26. Multiple Gestation : a) Yes b) No

27. Birth Weight : a) AGA b) SGA c) LGA kg

28. Whether cried Immediately after birth ? a) Yes b) No

29. Neonatal Jaundice : a) Yes b) No

30. Any Hospitalization required for Jaundice : a) Yes b) No

31. Congenital Anomaly : a) Yes b) No

32. Neonatal Seizures : a) Yes b) No

33. a) Consanguineous Marriage

b) Non – Consanguineous Marriage

34. Similar Illness / Psychiatric illness in Other family members :

a) Yes b) No

IV . DEVELOPMENTAL MILESTONES

Head control

Sitting with out support

Standing with out support

Walking

35. CARS

36. EEG

MASTER CHART

sl no	name	age yrs	sex	father education	mother edu	father occupation	mother occ	pt type of edu	age @ diag	presenting c/o	on drugs	treatment
1	saidarun	6.5	1	4	4	5	5	2	2.5	5	1	4
2	Mugunthan	5	1	2	2	2	1	1	2	8	1	4
3	Tharani	9	2	3	3	3	1	2	3	9	2	1
4	Ajmal	5	1	2	2	3	1	4	3	10	2	2
5	suriya	3	1	2	3	3	1	4	2	1	2	4
6	Vikas	5	1	2	2	2	1	2	3	7	2	4
7	Ezhilarasan	8	1	2	1	2	1	1	2.5	10	1	4
8	Nivas	8	1	2	2	3	1	1	2	10	1	4
9	Saran	5	1	1	2	3	1	1	3	7	1	4
10	Prabhu	5	1	2	3	3	1	2	1.5	7	1	4
11	Kalif	5	1	3	3	3	1	2	3.5	7	2	4
12	Kamaleshwaran	4	1	4	4	3	1	2	2	1	2	2
13	Fazil	6	1	2	4	3	1	2	3.5	5	2	4
14	Logeswari	5	2	2	2	2	1	2	4	1	2	2
15	Muthukumar	9	1	3	3	2	1	1	3	10	1	4
16	Sachin	4.5	1	2	2	3	1	1	3	9	2	4
17	Suriya	5	1	5	5	2	1	1	3	7	1	2
18	Belson	11	1	4	4	5	5	2	3	9	2	3
19	Ragavarshini	3.5	2	2	2	3	3	2	2.5	1	2	1
20	Sivaranjan	9	1	2	4	3	1	2	2.5	11	2	2
21	Narenkarthic	4	1	4	2	5	1	2	3	10	2	4
22	Tamilmani	9.5	1	4	4	4	1	1	3	8	2	4
23	Md fariduddn	8	1	2	2	3	1	1	4	7	1	4
24	Rohith	3.5	1	4	4	3	1	4	2.5	6	2	1
25	Sandhaya	4	2	2	2	3	3	2	3	5	2	2
26	Manikandan	4.5	4	2	3	1	1	3	6	1	1	2
27	Jaibalaji	6	1	4	4	3	3	2	5	11	2	6
28	Poorvaja	3	2	2	2	3	1	2	2.5	5	2	2
29	Ashwin	9	1	2	5	2	1	2	8	5	2	5
30	Nithyashree	9	2	2	2	3	1	2	2.5	7	1	5
31	Mukila	4	2	4	4	3	1	1	2.5	7	2	4
32	Madanraj	5	1	1	2	2	1	1	4	7	1	1
33	Dinesh	4	1	2	2	3	1	4	4	7	2	2
34	Mohanprasad	4	1	1	2	3	2	2	3	1	1	6
35	Jaidev	4	1	3	2	3	1	3	2.5	1	2	4
36	Balaji	3	1	2	1	2	1	4	2.5	8	1	6
37	Harshankar	4	1	2	2	2	1	2	3.5	8	2	6
38	Mahadevan	7	1	4	4	4	1	2	2.5	8	2	1
39	Shakir	4	1	1	1	2	1	1	3	7	2	4
40	Tharun	3	1	2	2	2	1	4	3	5	2	1
41	Prithviraj	4	1	4	3	4	1	2	3	5	2	4
42	Sadhana	3.5	2	2	2	2	1	2	2.5	8	1	6
43	Hema	5	2	2	2	3	1	4	3	5	2	2
44	Vigneshwaran	8	1	4	2	4	1	1	3	7	2	4
45	Praveen	3	1	2	2	3	1	1	2.5	5	2	2
46	Edwin	3	1	3	2	3	1	1	2	7	2	4
47	Praveen	5	1	2	3	4	1	1	3	5	2	2
48	Arjun	4	1	2	2	3	1	1	3	5	2	2
49	Sabarish	5	1	2	2	3	1	4	4	5	2	2
50	Daniel	9	1	2	2	3	3	4	7	5	2	6
51	Jeevanandan	5	1	4	2	5	1	1	3	5	2	4
52	Kishore	4	1	5	1	3	1	1	3	7	2	4
53	Srisanjayraj	8	1	2	2	2	1	1	5	8	2	4
54	Jagan	6	1	4	2	5	1	1	3	7	2	4
55	Ajaykumar	4	1	1	2	2	1	2	3.5	5	2	1
56	Parthiban	4	1	5	2	2	1	1	2.5	5	2	4
57	Joshva	5	1	2	2	2	1	2	4	1	2	2
58	Rishija	8	2	2	2	3	1	1	4	1	1	2
59	Dhanush	4	1	2	3	3	1	4	3	1	2	6
60	AlimaTaskeen	6	2	2	2	4	1	2	3	8	1	6
61	Karan	3	1	2	3	2	1	1	2.5	7	2	4
62	Amuthabarati	4	2	3	2	2	1	4	3	12	2	2
63	Harikumar	11	1	5	5	2	1	4	4	13	1	6
64	Dinesh	4	1	2	2	3	1	4	3.5	8	2	2
65	Mokesh	4	1	2	2	2	1	1	2	8	1	4
66	Prabhu	4	1	2	1	3	1	1	3.5	1	1	4
67	Pranav	3	1	4	3	4	1	4	2	8	2	4
68	Md Yasin	6	1	2	2	2	1	1	2.5	5	1	4
69	Dhilipkumar	12	1	5	5	2	1	2	8	8	1	6
70	Divakar	6	1	3	2	3	1	2	3.5	7	1	4
71	Gopi	4	1	2	2	2	1	4	2	1	2	2
72	Kamal raj	12	1	2	2	3	1	1	4	1	1	2
				primary-1		unemployed-1		specialschool-1		speechdelay-1	yes-1	occp therapy-1
				sec school -2		unskilled-2		regular sch-2		noeyecontact-2	no-2	speechtherapy-2
				higher sec -3		skilled-3		both-3		solitaryplay-3		special edu help-3
				degree/higher4		buisness-4		no school-4		hyperactivity-4		nill-6
				illiterate -5		proffess-5				stereotypies-14		
						others-6						
										1+2-5		1+2-4
										1+2+3-6		1+2+3-5
										1+2+4-7		
										1+4-8		
										1+2+3+4-9		
										1+3+4-10		
										1+3-11		
										1+4+14-12		
										1+14-13		

sl no	maternal age @conception	paternalage	preg comp	drug intake	antenatal infection	birth order	gestionalage	mode of delivery	prolonged labour (20hr)	multiple birth	BW
1	3	3	5	2	2	1	1	2	2	2	1
2	4	3	5	2	2	2	1	1	2	2	1
3	3	4	5	2	2	2	1	1	2	2	1
4	2	1	5	2	2	2	1	1	2	2	1
5	2	3	5	2	2	1	1	1	2	2	1
6	3	4	5	2	2	3	3	2	2	2	1
7	3	4	5	2	2	2	1	1	2	2	1
8	4	4	5	2	2	3	1	1	2	2	1
9	2	3	5	2	2	1	1	1	1	1	1
10	4	4	5	2	2	2	1	2	2	1	1
11	2	4	5	2	2	1	1	3	2	1	1
12	4	3	5	2	1	1	1	2	2	2	1
13	2	1	5	2	2	2	1	1	2	2	1
14	2	2	5	2	2	1	1	1	2	2	1
15	3	4	5	2	2	1	2	2	2	1	2
16	2	1	5	2	2	1	3	1	1	2	1
17	4	4	5	2	2	2	1	2	2	2	1
18	3	4	3	2	2	1	1	2	2	2	3
19	2	3	1	2	2	1	1	2	2	2	1
20	3	4	5	2	2	2	1	2	2	2	1
21	3	4	5	2	2	2	1	2	2	2	1
22	4	4	5	2	2	3	2	1	2	2	1
23	3	4	5	2	2	2	1	1	1	2	1
24	3	3	1	2	2	2	1	1	2	2	1
25	2	2	5	2	2	1	1	1	2	2	1
26	2	2	2	2	1	1	1	1	2	1	1
27	3	4	5	2	2	2	1	1	2	2	1
28	2	3	5	2	2	1	1	1	2	2	1
29	2	3	5	2	2	2	1	2	2	2	1
30	2	2	5	2	2	1	1	1	2	2	2
31	3	3	5	2	2	2	1	2	2	2	1
32	1	1	5	2	2	1	2	1	2	2	1
33	3	2	5	2	2	1	1	2	2	2	1
34	3	2	5	2	2	3	1	1	2	2	1
35	3	4	5	1	2	1	1	2	2	2	1
36	3	3	5	2	2	3	1	1	2	2	1
37	3	2	2	2	2	2	2	1	2	2	2
38	2	3	5	2	2	1	1	1	2	2	1
39	3	2	5	2	2	3	1	1	2	2	1
40	2	3	5	2	2	1	1	1	2	2	1
41	3	3	2	2	2	1	1	2	2	2	1
42	2	2	5	2	2	1	2	1	1	2	2
43	3	2	5	2	2	2	1	1	2	2	1
44	3	3	5	2	2	3	1	2	2	2	1
45	2	2	5	2	2	2	1	1	2	2	1
46	3	2	5	2	2	1	1	1	2	2	1
47	3	3	5	2	2	2	1	1	2	2	1
48	3	2	5	2	2	2	1	1	2	2	1
49	3	3	5	2	2	2	1	1	2	2	1
50	2	2	5	2	2	3	1	1	2	2	1
51	3	3	5	2	2	3	1	1	2	2	1
52	3	2	5	2	2	2	1	2	2	2	1
53	1	2	2	2	2	1	1	2	2	2	1
54	3	3	5	2	2	2	1	1	2	2	1
55	3	4	5	2	2	2	1	1	2	2	1
56	2	3	5	2	2	3	1	1	2	2	1
57	3	3	5	2	2	2	1	1	2	2	1
58	2	2	5	2	2	2	1	1	1	2	1
59	3	4	1	2	2	3	1	1	2	2	2
60	1	3	5	2	2	1	1	1	2	2	1
61	2	2	5	2	2	2	1	2	2	2	1
62	3	4	5	2	2	2	1	3	1	1	2
63	3	3	5	2	2	3	1	1	2	2	1
64	3	4	5	2	2	3	3	1	2	2	1
65	2	1	5	2	2	2	2	1	1	2	2
66	2	2	5	2	2	1	1	1	2	2	1
67	2	3	5	2	2	1	1	1	2	2	1
68	3	4	3	2	2	4	1	1	2	2	1
69	4	4	5	2	2	2	1	1	2	2	1
70	2	2	2	2	2	1	2	2	2	2	2
71	2	2	5	2	2	1	1	1	2	2	1
72	3	3	5	2	2	3	1	2	2	2	1
	<20 years-1	<25y=1	anemia-1	yes-1	yes-1	1st-1	term-1	FTND-1	yes-1	yes-1	AGA-1
	21-25y=2	26-30y=2	pih-2	no-2	no-2	2nd-2	preterm-2	LSCS-2	no-2	no-2	SGA-2
	26-30y=3	31-35y=3	gdm-3			3rd-3	post dated-3	ASSIST DELIVERY-3			LGA-3
	>30y=4	>35y=4	seizure-4			4th-4					
			nil-5								

cl no	cried @birth	NNH	cong anamoly	NNS	consanguinity	similar/psychiatric illness in family	devel delay	head circumferance	CARS	EEG
1	1	2	2	2	2	2	2	1	32	1
2	1	2	2	2	2	2	4	1	34.5	4
3	1	2	2	2	2	2	2	1	32	1
4	1	2	2	2	2	2	2	2	33	2
5	1	2	2	2	1	2	3	1	30	2
6	1	2	2	2	1	2	2	1	34.5	1
7	1	2	2	2	1	1	3	1	33.5	1
8	1	2	2	2	2	2	3	1	38	1
9	1	2	2	2	2	1	4	1	33.5	3
10	1	2	2	2	2	2	3	1	35.5	2
11	1	2	2	2	2	2	2	1	30	1
12	1	2	2	2	2	2	2	1	30	1
13	1	2	2	2	2	2	4	1	30	1
14	1	2	2	2	2	2	4	1	31	1
15	1	2	2	2	2	2	3	1	38	2
16	1	2	2	2	2	2	2	1	31.5	1
17	1	2	2	2	2	2	2	1	34.5	1
18	1	2	2	2	2	2	2	1	30	1
19	1	2	2	2	2	1	2	1	32	4
20	1	1	2	2	2	2	2	1	30	1
21	1	2	2	2	2	2	2	1	32	2
22	1	2	2	2	2	2	2	1	33	1
23	1	2	2	2	2	1	3	1	36	2
24	1	2	2	2	2	2	2	1	32	2
25	1	2	2	2	1	1	2	1	35	2
26	1	2	2	2	1	2	4	1	34	1
27	1	2	2	2	2	2	4	1	34	1
28	1	2	2	2	2	2	4	1	30	4
29	1	2	2	2	2	2	2	1	30	1
30	1	2	2	2	1	2	4	1	37.5	2
31	1	2	2	2	2	1	4	1	38	1
32	1	2	2	2	2	1	4	1	36	4
33	1	1	2	2	2	2	2	1	37	2
34	1	2	2	2	2	2	3	1	30	4
35	1	2	2	2	2	2	4	1	33	4
36	1	2	2	2	2	2	3	1	32.5	1
37	1	1	1	2	2	2	2	1	31	1
38	1	2	2	2	2	2	2	1	31.5	2
39	1	2	2	2	1	2	2	1	37.5	2
40	1	2	2	2	2	2	3	1	34	2
41	1	2	2	2	2	2	2	1	35	1
42	2	1	2	2	1	2	3	1	33	2
43	1	2	2	2	2	2	2	1	32	1
44	1	2	2	2	1	2	2	1	33	1
45	1	2	2	2	2	2	2	1	32	1
46	1	2	2	2	1	2	2	1	32	1
47	1	2	2	2	2	2	2	1	32	1
48	1	2	2	2	1	2	2	1	33	1
49	1	2	2	2	1	2	2	1	32	1
50	1	2	2	2	2	2	3	1	32	1
51	1	2	2	2	1	2	2	1	33	1
52	1	2	2	2	2	2	2	1	34.5	1
53	1	2	2	2	2	2	2	1	34	2
54	1	2	2	2	2	2	2	1	33	1
55	1	2	2	2	2	2	2	1	34.5	2
56	1	2	2	2	1	2	2	1	34.5	2
57	1	2	2	2	2	2	4	1	32	1
58	1	2	2	2	2	1	2	1	36.5	1
59	1	2	2	2	1	2	2	1	33	1
60	2	2	2	2	2	1	2	1	34	2
61	1	1	2	1	2	1	2	1	34	1
62	1	1	2	2	2	2	2	1	40	2
63	1	2	2	2	2	2	2	1	50	2
64	1	2	2	2	2	2	2	1	37	2
65	1	1	2	2	2	2	2	1	34.5	2
66	1	2	2	2	1	2	3	1	31	1
67	1	2	2	2	2	2	4	1	31	1
68	1	2	2	2	1	2	2	2	33	1
69	1	2	2	2	1	2	4	1	36	1
70	1	2	2	2	2	2	2	1	36.5	1
71	1	2	2	2	1	2	3	2	35	2
72	1	1	2	2	2	2	3	1	34	1
	cried-1	yes-1	yes-1	yes-1	consang-1	yes-1	motar delay-1	normal-1		normal-1
	asphyxia-2	no-2	no-2	no-2	nonconsang-2	no-2	speechdelay-2	microcephaly-2		Abn + sharp wave-2
							GDD-3	macrocephaly-3		abn +spike-3
							nill-4			both-4