

ORIGINAL RESEARCH**A study to assess the associations between fetal growth rate in various trimester of pregnancy with the incidence of febrile seizures****¹Dr Vijay Bhardwaj, ²Dr Ranjana Bhardwaj, ³Dr. Meeta Agnihotri, ⁴Dr. S.K.Pathak**¹Associated Professor, Department of Paediatrics, Career Institute of Medical Sciences, Lucknow, Uttar Pradesh, India²Associated Professor, Department of Gynecology, Career Institute of Medical Sciences, Lucknow, Uttar Pradesh, India³Professor, Department of Pathology, Career Institute of Medical Sciences, Lucknow, Uttar Pradesh, India⁴Professor, Department of Orthopaedics, Career Institute of Medical Sciences Lucknow, Uttar Pradesh, India**Correspondence:**

Dr Vijay Bhardwaj

Associated Professor, Department of Paediatrics, Career Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

Abstract

Background: Febrile seizures are the most common seizure of childhood. They are seizure events occurring in young febrile children, where the fever is not due to infection of the central nervous system (CNS). The present study was designed to assess the associations between fetal growth rate in various trimester of pregnancy with the incidence of febrile seizures.

Material and methods: In total, 1200 mothers were enrolled in the study. Assessments were planned in first-, second-, and third-trimester, respectively. Postnatal information on growth and development of the participating children was obtained through questionnaires and hands-on measurements. Fetal growth measurements used for the present study included the biparietal diameter from outer to outer skull, transverse cerebellar diameter (TCD), head circumference, abdominal circumference, and femur length in the second and third trimesters. Statistical analyses were performed by using SPSS 15.0 for Windows (SPSS, Chicago, IL) and SAS 9.2 (SAS Institute, Cary, NC).1336

Results: General growth parameters in the second trimester were not associated with the risk of febrile seizures. In the third trimester, children in the lowest tertile of femur length, abdominal circumference, and estimated fetal weight were at increased risk of febrile seizures, compared with children in the highest tertile. Regarding the growth characteristics of the head and brain, smaller TCDs in the second trimester were associated with increased risk of febrile seizures. In the third trimester, small biparietal diameters were associated with the development of febrile seizures. Similar tendencies were observed for third-trimester head circumferences and TCDs.

Conclusion:The present study concluded that fetal growth retardation is associated with increased risk of febrile seizures. Febrile seizures were most evident for estimated fetal weight, femur length, and TCD.

Keywords: febrile seizures, third trimester, second trimester.

Introduction

Febrile seizure (FS) is the most common type of seizure in children. It is defined as a seizure accompanied by a fever of ≥ 38 °C without other seizure-provoking causes.^{1,2} Febrile seizures are classified as either simple or complex based on their clinical features. Simple febrile seizures are single, generalised convulsions lasting < 15 min. Complex febrile seizures present with focal features, occur as clusters of episodes during the same 24-h period (multiple seizures) or are prolonged with a duration longer than 15 min.³ Approximately 20–35% of febrile seizures are complex.^{4,5} Febrile seizures are the most common type of seizures in childhood, affecting 2% to 5% of all children between the ages of 3 months and 5 years. The highest incidence has been observed during the first 2 years of life. The cause of febrile seizures remains largely unknown. Genetic factors and environmental factors may be important.⁶ Although genetic factors are considered to play the most important role in whether a child develops FS, the cause of FS remains unclear and is likely to be multifactorial. It is generally believed that FS is caused by a vulnerability of the developing central nervous system to the effects of fever, in combination with a genetic predisposition and environmental factors.⁷ Several studies have investigated the association of environmental factors, such as maternal smoking or alcohol intake during pregnancy, or of birth outcomes such as low birth weight or preterm birth, with the risk of FS; the results, however, are inconsistent.^{2,7-10} The present study was designed to assess the associations between fetal growth rate in various trimester of pregnancy with the incidence of febrile seizures.

Material and methods

The present prospective, cohort study was designed to assess the associations between fetal growth rate in various trimester of pregnancy with the incidence of febrile seizures over a period of 1 year. In total, 1200 mothers were enrolled in the study. Before the commencement of the study ethical approval was taken from the ethical committee of the institute and informed consent was taken from the patient. Assessments were planned in early pregnancy (gestational age of < 18 weeks), middle pregnancy (gestational age of 18–25 weeks), and late pregnancy (gestational age of 25 weeks) and included questionnaires, physical examinations, and fetal ultrasound examinations. These measurements were considered as first-, second-, and third-trimester measurements, respectively. Postnatal information on growth and development of the participating children was obtained through questionnaires and hands-on measurements. For this study on fetal growth and febrile seizures, participants who were included during pregnancy and who gave full consent for postnatal follow-up evaluations were selected. Twins and children who were not born at term were excluded. Ultrasound examinations were performed in the first, second, and third trimesters of pregnancy. First-trimester measurements were not included because these fetal ultrasound examinations were used primarily to establish gestational age. Fetal growth measurements used for the present study included the biparietal diameter from outer to outer skull, transverse cerebellar diameter (TCD), head circumference, abdominal circumference, and femur length in the second and third trimesters. Estimated fetal weight was calculated by using the formula described by Hadlock et al. Information about the occurrence of febrile seizures was collected with questionnaires at the ages of 12 and 24 months. In addition to direct questions regarding febrile seizures, the parents were asked about symptoms that might have been caused by a seizure. If ≥ 1 of these questions was answered positively, then an extended questionnaire concerning this episode was sent to collect detailed information about the event. If a physician was consulted, then the medical records for the visit were obtained. Maternal smoking habits were assessed with questionnaires in each trimester and were categorized as no smoking during pregnancy (never smoked or quit smoking before pregnancy or in the first

trimester) or smoking during pregnancy (continued smoking after the pregnancy was known). Statistical analyses were performed by using SPSS 15.0 for Windows (SPSS, Chicago, IL) and SAS 9.2 (SAS Institute, Cary, NC).1338

Results

Mean age of mothers without febrile seizures was 32.4yrs and with seizures were 31.8yrs. Mean height of mothers without seizures was more than mothers with febrile seizures. Mean weight, BMI was more of mothers with febrile seizures than mothers without febrile seizures. Nulliparous, preeclampsia, Smoking during pregnancy, Febrile seizures in mother was more in mothers with febrile seizures. Males were in group without febrile seizures than with febrile seizures. Child Birth weight was more in group without febrile seizures than with febrile seizures. General growth parameters in the second trimester were not associated with the risk of febrile seizures. In the third trimester, children in the lowest tertile of femur length, abdominal circumference, and estimated fetal weight were at increased risk of febrile seizures, compared with children in the highest tertile. Regarding the growth characteristics of the head and brain, smaller TCDs in the second trimester were associated with increased risk of febrile seizures. In the third trimester, small biparietal diameters were associated with the development of febrile seizures. Similar tendencies were observed for third-trimester head circumferences and TCDs.

Table 1: Subject characteristics

	No Febrile Seizures (N=1160)	Febrile Seizures(N=40)
Maternal characteristics		
Age, mean \pm SD (year)	32.4 \pm 5.4	31.8 \pm 3.8
Height, mean \pm SD (cm)	170.7 \pm 6.1	169.8 \pm 7.2
Weight, mean \pm SD(kg)	69.5 \pm 10.4	70.6 \pm 12.4
BMI, mean \pm SD, (kg/m) ²	24.5 \pm 4.3	25.5 \pm 4.6
Nulliparous, %	60	65
Preeclampsia %	2	3
Smoking during pregnancy, %	14	18
Febrile seizures in mother, %		
Yes	3	4
No	92	93
Do not know	5	3
Child characteristics		
Male, %	48	47
Birth weight, mean \pm SD, g	3504 \pm 445	3442 \pm 467

Table 2: Associations of General Second- and Third-Trimester Fetal Growth Characteristics With Risk of Febrile Seizures

	Febrile Seizure OR (95% CI)	
	Second Trimester	Third Trimester
Estimated fetal weight		
Lowest tertile	1.05	2.56
Middle tertile	1.17	1.25
Highest tertile	1.00	1.00
P for trend.	0.497	0.006
Abdominal circumference		
Lowest tertile	1.12	2.03
Middle tertile	1.51	1.14

Highest tertile	1.00	1.00
P for trend.	0.826	0.26
Femur length		
Lowest tertile	1.25	2.32
Middle tertile	1.41	1.29
Highest tertile	1.00	1.00
P for trend	0.367	0.08

Table 3: Associations of Second- and Third-Trimester Fetal Growth Characteristics of Head With Risk of Febrile Seizures

	Febrile Seizure OR (95% CI)	
	Second Trimester	Third Trimester
Head circumference		
Lowest tertile	1.05	1.42
Middle tertile	0.95	1.06
Highest tertile	0.98	0.78
P for trend	0.832	0.081
Biparietal diameter		
Lowest tertile	1.36	1.92
Middle tertile	1.56	1.22
Highest tertile	1.00	1.00
P for trend	0.431	0.087
TCD Lowest tertile		
Lowest tertile	2.86	1.66
Middle tertile	2.33	1.07
Highest tertile	1.00	1.00
P for trend	0.009	0.08

Discussion

Febrile seizures represent a heterogeneous condition with currently unclear pathophysiological and genetic bases. The importance of genetic factors has long been recognized. A family history of febrile seizures is the most consistently identified risk factor for febrile seizures.¹¹⁻¹³

Mean age of mothers without febrile seizures was 32.4yrs and with seizures were 31.8yrs. Mean height of mothers without seizures was more than mothers with febrile seizures. Mean weight, BMI was more of mothers with febrile seizures than mothers without febrile seizures. Nulliparous, preeclampsia, Smoking during pregnancy, Febrile seizures in mother was more in mothers with febrile seizures. Males were in group without febrile seizures than with febrile seizures. Child Birth weight was more in group without febrile seizures than with febrile seizures. General growth parameters in the second trimester were not associated with the risk of febrile seizures. In the third trimester, children in the lowest tertile of femur length, abdominal circumference, and estimated fetal weight were at increased risk of febrile seizures, compared with children in the highest tertile. Regarding the growth characteristics of the head and brain, smaller TCDs in the second trimester were associated with increased risk of febrile seizures. In the third trimester, small biparietal diameters were associated with the development of febrile seizures. Similar tendencies were observed for third-trimester head circumferences and TCDs.

Another study reported that the prevalence of FS was 1.0% in children under 1 year of age, 6.8% in those under 2 years of age, and 8.0% in those under 3 years of age among all nursery school children in one city near Tokyo in 2003.¹⁴

Total brain tissue volume increases linearly in the third trimester of fetal life, with a four-fold increase in cortical grey matter between 29 and 41 weeks and a five-fold increase in myelinated white matter between 35 and 41 weeks.¹⁵ Premature birth itself may lead to subtle neuropathologies, including cerebral white matter gliosis, hippocampal sclerosis and subarachnoid haemorrhage, as shown in non-human primates.^{15,16} Furthermore, children born preterm are more often exposed to infections, pre-eclampsia, eclampsia, and smoking which may increase the risk of epilepsy.¹⁷

A study by Adab and coworkers was one of the first to associate a developmental risk with the occurrence of seizures during pregnancy.¹⁸

Conclusion

The present study concluded that fetal growth retardation is associated with increased risk of febrile seizures. Febrile seizures were most evident for estimated fetal weight, femur length, and TCD.

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