Research article Anatomical variations of sulci in human fetal cerebrum and its clinical significance

Muthuchitra Pandian¹, Sabnis Anjali², Shroff Gautam³

¹PhD Scholar, MGM Institute of Health Sciences India

²Professor and Head, Department of Anatomy, MGM Medical College, Navi Mumbai, Maharashtra, India ³Professor and Head, Department of Anatomy, MGM Medical College, Aurangabad, Maharashtra, India

(Received: May 2021 Revised: August 2021 Accepted: September 2021)

Corresponding author: Sabnis Anjali. Email: dranjus2003@yahoo.com

ABSTRACT

Introduction and Aim: Appearance of sulci and its number in the fetal cerebrum is a signal of growth and development. Chronological appearance and symmetrical development of sulci corresponds to gestational age of fetus. Few sulci can be visualized in the prenatal period to judge the growth of fetus. Any change in chronological appearance, symmetry and number of sulci in fetal cerebrum is of prime importance.

Materials and Methods: Hundred and six cerebral hemispheres of 53 fetal brains of different gestational ages were collected from MGM Hospital Kalamboli and Aurangabad after institutional ethical approval to study the pattern of sulci on both sides after fixing in 10% formalin.

Results: In 6 (5.6 %) cerebral hemispheres variation in appearance of sulci was observed. It was noted that there is change in number of superior temporal sulcus (STS), superior frontal sulcus (SFS), parieto-occipital sulcus (POS), calcarine sulcus (CS) and occipitotemporal sulcus (OTS) on both the sides in 6 cerebral hemispheres. Remaining 100 cerebral hemisphere showed normal, symmetrical appearance and number of sulci.

Conclusion: It was observed that the fetal cerebral hemispheres which showed variations in appearance and number of sulci were associated with mother having eclampsia.

Keywords: Human fetus; cerebral hemisphere; sulci; intra uterine growth retardation; eclampsia.

INTRODUCTION

he development of cerebral hemisphere initiates in 5th week of intrauterine life from prosencephalon. Continuous and programmed growth marches to develop cerebral hemisphere with three surfaces, five lobes having depressions called sulci and elevations called gyri. The cerebral sulci are known as main micro-anatomical borders that serve as a gateway and surgical passage to reach the ventricles or to the deeper lesions (1). The development in both the cerebral hemispheres occurs simultaneously and symmetrical. The phenomenon of sequential appearance of sulci and gestational age of the fetus goes hand in hand. Maternal and fetal factors contribute in achieving normal and symmetrical development of cerebral hemisphere. Sulcal morphology is influenced by genetic, developmental, and environmental factors (2, 3). Identification of particular sulci may assist to predict the gestational age of fetus if anatomical appearance of sulci is well known. Asymmetry sulci pattern may lead to speech defect or language problem as the child matures (4). Cerebral cortical malformations are common causes of neurological developmental delay and epilepsy and include a wide range of antenatal neurogenesis disorders (5). The absence or abnormal appearance of a particular sulcus at the expected gestational age should raise the suspicion of abnormal or delayed cortical development. This can be seen in a wide spectrum of central nervous system malformations

(6).The sonographic recognition of the fissures, gyri and sulci lagged behind the observations by anatomical studies (7). Early identification of alteration in number, appearance and symmetry of various sulci in both fetal cerebral hemispheres is of paramount importance. In the current study variations in different sulci in term of their number, appearance and symmetry is studied on fetal cerebrum.

METHODOLOGY

Hundred and six cerebral hemispheres from 53 fetuses of 17th- 40th gestational week were collected from Kalamboli MGM hospital and Aurangabad hospital after ethical approval and fixed with formalin. All the fetuses were from spontaneous abortions. Those parents who gave written consent were included in the study. Macerated, decomposed fetuses and fetuses with other congenital anomalies and those who did not give consent were not included in the study.

Fetal cerebrum was removed after fixation by taking median incision form root of the nose to external occipital protuberance and a coronal incision between both mastoid processes. The scalp and skull bone was reflected in four flaps. Cerebrum was carefully removed from anterior to posterior by cutting the cranial nerves and medulla and spinal cord. Meninges were removed to study the sulci on the supero- lateral, medial and inferior surface of cerebrum and number, appearance and symmetry of sulci were noted. Photographs were taken.

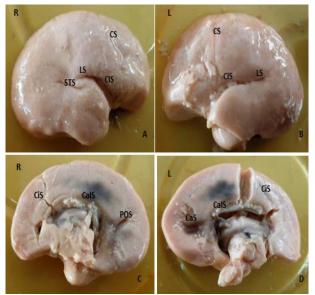


Fig. 1: Variations in sulci on both sides of supero-lateral surface of fetal cerebrum of fetus of 25th gestational week. CS-Central sulcus, LS-lateral sulcus, CIS-circular insular sulcus and STS-superior temporal sulcus, POS-Parieto-occipital sulcus, CaS- callosal sulcus, CiS-cingulate sulcus.

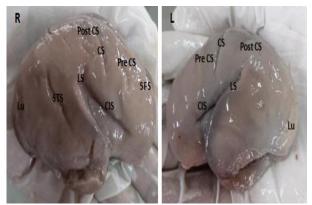


Fig. 2: Variations in sulci on both sides of supero-lateral surface of fetal cerebrum of fetus of 26th gestational week. CS- central sulcus; Pre CS- pre-central sulcus; Post CS-Post central sulcus; LS- lateral sulcus; CIS circular insular sulcus; Lu- lunate sulcus; SFS- superior frontal sulcus and STS- superior temporal sulcus.

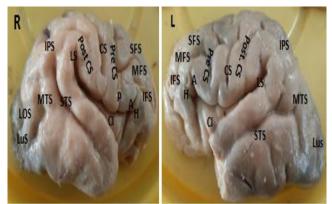


Fig. 3: Variations in sulci on both sides of supero-lateral surface of fetal cerebrum of fetus of 30th gestational week. CS-Central sulcus, Pre CS-Precentral sulcus, Post CS-Postcentral sulcus, LS-Lateral sulcus, CIS-Circular insular, LuS-Lunate sulcus, SFS-Superior frontal sulcus, IFS-Inferior frontal sulcus, IPS-Intra-parietal sulcus, STS-Superior temporal sulcus, ITS-Inferior temporal sulcus, LOS-Lateral occipital sulcus, P-Posterior, A-ascending and H-horizontal ramus of lateral.

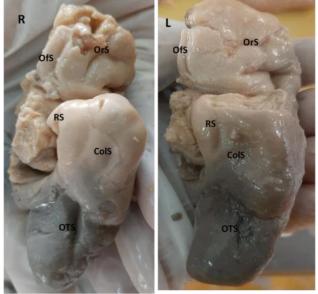


Fig. 4: Variations in sulci on both sides of inferior surface of fetal cerebrum of fetus of 30th gestational week OS-Olfactory, OrS-Orbital, ColS-Collateral, OTS-Occipitotemporal and RS-Rhinal.

RESULTS

- 100 cerebral hemispheres showed normal number, appearance, and symmetrical development of sulci on both sides and anatomical variations were observed in appearance of fetal cerebral sulci in 6 (5.6%) cerebral hemispheres.
- It was noticed that 3 fetal cerebrums which showed variations were associated with mothers having eclampsia
- Out of 3 fetal cerebrums, Superior temporal and parieto- occipital sulcus was developed on right cerebral hemisphere and it was absent on left side of supero-lateral surface cerebral hemisphere of one fetus of 25th week of gestation (Fig. 1).
- Superior temporal and superior frontal sulcus were developed on right cerebral hemisphere and it was absent on left side of supero-lateral surface of cerebral hemisphere of one fetus of 26th week of gestation (Fig. 2).
- Lateral occipital sulcus and posterior ramus of lateral sulcus was developed on right cerebral hemisphere and it was absent on left side of supero-lateral surface of cerebral hemisphere of one fetus of 30th week of gestation (Fig. 3) and orbital and occipito-temporal sulcus was well developed on right side than left side of inferior surface of cerebral hemisphere of same fetus (Fig. 4).

DISCUSSION

Progressive and sequential development of various sulci in cerebral hemisphere is an exceptional phenomenon which indicates an appropriate growth of cerebrum. Accurate parcellation and labeling of primary cortical sulci in the human fetal brain is useful for regional analysis of brain development (8). Constant and congruous development of cerebrum begins in 5th week of gestation where transformation from smooth surface to multiple sulci on all surfaces of cerebral hemispheres takes place. Left-right symmetry of time of appearance of sulci is the rule in anatomical studies (9). The whole process of appearance of sulci, its progression and maturation goes along with gestational age of fetus. In the initial three months of gestational age the fetal cerebrum is smooth and later in 2nd trimester the development of sulci begins. Knowledge of anatomical appearance of different sulci in specific gestational age would be valuable while doing fetal anomaly scan. This may be useful to recognize any variation or abnormality in appearance, number and symmetry of sulci and to predict gestational age. Familiarity with normal pattern of sulcal development and discriminating gestational ages for appearance of different sulci may allow early suspicion of lissencephaly (10). In the current study hundred and six cerebral hemispheres from 53 fetuses of 17th - 40thgestational week were studied in connection with number, appearance and symmetrical growth of various sulci. It was observed longitudinal cerebral that fissure, callosal, hippocampal, lateral, central, circular insular, calcarine, parieto-occipital sulci were visible in 17th week, lunate, cingulate in 22nd week, collateral, olfactory in 23rd week, superior frontal in 24th week, pre-central, post-central, superior temporal, rhinal 24th week, intra-parietal, para-olfactory in 27th week, inferior frontal, inferior temporal, lateral occipital, occipito-temporal, orbital in 28th week, cingulate, paracentral, central insular in 29th week, posterior, horizontal, ascending ramus of lateral, transverse transverse temporal, occipital. supra-splenial. subparietal in 31st week. All the sulci on both sides of cerebrum showed resemblance in number, appearance symmetrical growth except 6 cerebral and hemispheres of 3 fetal brains. Our observations related to number, appearance and symmetrical growth of sulci were close to other study (11).

In 6 cerebral hemispheres of 3 fetal brains of third trimester, asymmetrical growth of superior temporal, parieto-occipital, lateral occipital, superior frontal, orbital and occipito-temporal sulcus was observed (Fig. 1-4). After co-relating with the history it was found that all three fetuses were aborted from mother having eclampsia. Eclampsia is an acute neurological complication of preeclampsia characterized by seizures and/or consciousness disorders which cannot be related to another neurological disease (12). Preeclampsia (PE) is a significant gestational disorder that causes complications in 3- 5% of all human pregnancies (13). It is associated with decreased cognitive function (14), memory, visuospatial processing (15) and increased risk of intellectual disability (16) which is explained by mechanism where brain derived neurotrophin (17) and placental growth factor (18) is reduced. Reduction in placental growth factor causes alteration in neurological

development (18) and it is documented that preeclampsia might be associated with defective neurogenesis in rat (19). Eclampsia and alteration in fetal brain development is proved with disturbed physiological and biochemical factors (14-19). We came across asymmetrical development in 6 cerebral hemispheres of 3 fetuses which were associated with mothers with eclampsia. Alteration in blood flow in eclampsia might have caused neurological changes (20) on the other hand in circumstances of maternal stress and uteroplacental nutrient deprivation, human fetal brain development takes priority over other tissues, with evidence of head sparing effects (21). In eclampsia narrowing of lumen may cause micro ischemia leading to less cortical growth. In an autopsy study of 23 fetuses from 27 to 34 weeks' gestation, found gyral maturation accelerated by 2 to 11 weeks in 19/23 fetuses in which growth restriction or maternal hypertension were present (22). Abnormal sulcus development could be an early warning sign of an underlying fetal neurodevelopment migration disorder (23) which may present clinically with cognitive deficits, epilepsy, and/or motor deficits (24).

It was observed that superior temporal sulcus was developed on right side in 25th and 26th week of gestation in fetuses of mothers with eclampsia. Presence of areas involved in voice and face recognition, gaze perception, and theory of mind confirms the importance of the right superior temporal cortex in social cognition (25). Right hemispheric dominance for language and autistic children who previously have been reported to show anatomical and functional abnormalities in the STS (26). Asymmetry in the development of the temporal lobe has been demonstrated anatomically and with MRI, with the right side developing earlier than the left (27). In humans, the CS and STS emerge earlier on the right side compared to the left side during fetal development which suggests a large influence of genetic factors on the asymmetric sulcal emergence (28). Our observations regarding asymmetrical development of STS were similar to other studies. Data regarding other sulci available is based on sonography and MRI Scanning. Our observations regarding development of sulci cannot be compared as there is disparity between anatomical and sonological findings of sulcal development. We have observed asymmetry in development of sulci in all fetuses of eclamptic mothers and symmetrical development of sulci in fetuses of normal mothers which made us curious to find out its significance and authenticity. To confirm the association between eclampsia in mother and asymmetrical development of sulci in fetal cerebrum, large sample size is needed but the chances of abortions in eclampsia are very rare which a limitation for sample collection. Appearance of specific sulcus in specific gestational age may become a guideline while doing fetal anomaly scan. Observation of any asymmetrical appearance of sulcus should be paid

attention, it demands alertness to carry out further mode of action.

CONCLUSION

Knowledge regarding appearance of specific sulcus in particular gestational week can be used while doing fetal anomaly scan to predict wellbeing of fetus or intra uterine growth retardation. Asymmetrical appearance of sulci while doing fetal anomaly scan should not be ignored.

ACKNOWLEDGEMENT

- Dr. Sushil Kumar, Professor and head, OBGY Department, MGM Medical College for permitting to collect fetuses from MGM Kalamboli Hospital.
- Dr. Atul Deshmukh for helping us with using Image J software for measuring the cortical thickness.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

REFERENCES

- Gonul, Y., Songur, A., Uzun, I., Uygur, R., Alkoc, O. A., Kucuker, V. C. H. Morphometry, asymmetry, and variations of cerebral sulci on superolateral surface of cerebrum in autopsy cases Surg Radiol Anat. 2014 Sep; 36 (7): 651-661.
- Clark, G. M., Mackay, C. E., Davidson, M. E., Iversen, S. D., Collinson, S. L., James, A. C., *et al.*, Paracingulate sulcus asymmetry; sex difference, correlation with semantic fluency and change over time in adolescent onset psychosis. Psychiatry Res. 2010; 184(1): 10-15.
- Bonan, I., Argenti, A. M., Duyme, M., Hasboun, D., Dorion, A., Marsault, C., *et al.*, Magnetic resonance imaging of cerebral central sulci: A study of monozygotic twins. Acta Genet. Med. Gemellol. (Roma) 1998; 47 (2): 89-100.
- 4. Minagawa-Kawai, Y., Cristià, A., Dupoux, E. Cerebral lateralization and early speech acquisition: A developmental scenario. Dev Cog Neurosci. 2011; 1(3): 217-232.
- Pasquale, C., Mariangela, Vincenzo, D. A. Malformations of Cortical Development Donald School Journal of Ultrasound in Obstetrics and Gynecology. 2017; 11(4): 308-313.
- 6. Fong, K. W., Ghai, S., Toi, A., Blaser, S., Winsor, E. J. T., Chitayat, D. Prenatal ultrasound findings of lissencephaly associated with Miller–Dieker syndrome and comparison with pre- and postnatal magnetic resonance imaging Ultrasound Obstet Gynecol 2004; 24(7): 716-723.
- 7. Monteagudo, A., Timor-Tritsch, I. E. Development of fetal gyri, sulci and fissures: a transvaginal sonographic study. Ultrasound Obstet Gynecol 1997; 9(4): 222-228.
- Yun, N. H. J, Chung, A. W., Vasung, L., Tarui, E. Y. T., Rollins, C. K., Ortinau, C. M., *et al.*, Automatic labeling of cortical sulci for the human fetal brain based on spatiotemporal information of gyrification. Neuroimage. 2019; 88: 473-482.
- 9. Chi, J. G., Dooling, E. C., Gilles, F. H. Gyral development of the human brain. Ann Neurol. 1977; 1(1): 86-93.
- Toi, A., Lister, W. S., Fong, K. W. How early are fetal cerebral sulci visible at prenatal ultrasound and what is the normal pattern of early fetal sulcal development? Ultrasound Obstet Gynecol. 2004; 24(7): 706-715.
- 11. Nishikuni, K., Ribas, G. C. Study of fetal and postnatal morphological development of the brain sulci. J Neurosurg Pediatrics 2013; 11(1): 11.
- 12. Bushnell, C., Chireau, M. Preeclampsia and Stroke: Risks during and after Pregnancy. Stroke Res Treat 2011.

- Dang, F., Croy, B. A., Stroman, P. W., Figueiró-Filho, E. A. Impacts of Preeclampsia on the Brain of the Off spring, Rev. Bras. Gynecol. Obstet. 2016; 38(8): 416-422.
- 14. Eide, M. G., Moster, D., Irgens, L. M., Reichborn, T., Kjennerud, C., Stoltenberg, R., *et al.*, Degree of fetal growth restriction associated with schizophrenia risk in a national cohort. Psychol Med. 2013; 43(10): 2057-2066.
- Rätsep, M. T., Hickman, A. F., Maser, B., Pudwell, J., Smith, G. N., Brien, D., *et al.* Impact of preeclampsia on cognitive function in the offspring. Behav Brain Res. 2016; 302: 175-181.
- Ehrenstein, V., Rothman, K. J., Pedersen, L., Hatch, E., Sørensen, H. T. Pregnancy-associated hypertensive disorders and adult cognitive function among Danish conscripts. Am J Epidemiol. 2009; 170(08): 1025-1031.
- 17. Qing, H., Hu, L. R. Lasting Effects of Intrauterine Exposure to Preeclampsia on Offspring and the Underlying Mechanism, AJP Rep. 2019; 9(3): e275–e291.
- Carmeliet, P., Ferreira, V., Breier, G. Pollefeyt, S., Kieckens, L., Gertsenstein, M., *et al.*, Abnormal blood vessel development and lethality in embryos lacking a single VEGF allele Nature. 1996; 380(6573): 435-439.
- Liu, X., Zhao, W., Liu, H., Kang, Y., Ye, C., Gu, W., *et al.*, Developmental and functional brain impairment in offspring from preeclampsia-like rats. Mol Neurobiol. 2016; 53(02): 1009-1019.
- Luna, R. L., Kay, V. R., Rätsep, M. T., Khalaj, K., Bidarimath, M., Peterson, N., *et al.*, Placental growth factor deficiency is associated with impaired cerebral vascular development in mice. Mol Hum Reprod. 2016; 22(2): 130-142.
- Baker, J., Workman, M., Bedrick, E., Frey, M. A., Hurtado, M., Pearson, O. Brains versus brawn: An empirical test of Barker's brain sparing model. Am J Hum Biol. 2010; 22(2): 206-215.
- 22. Hadi, H. A. Fetal cerebral maturation in hypertensive disorders of pregnancy. Obstet Gynecol. 1984; 63: 214-219.
- 23. Malinger, G., Lev, D., Lerman-Sagie, T. Abnormal sulcation as an early sign for migration disorders. Ultrasound Obstet Gynecol. 2004; 24(7): 704-705.
- 24. Semin, G. P. Sonographic stroke templates. Fetal Neonatal Med. 2009; 14(5): 284-298.
- 25. Hein, G., Knight, R. T. Superior temporal sulcus—it's my area: Or is it? J Cogn Neurosci. 2008; 20(12): 2125-2136.
- Zilbovicius, M., Saitovitch, A., Popa, T., Elza Rechtman, E., Diamandis, L., Chabane, N., *et al.*, Autism, social cognition and superior temporal sulcus. Open J Psychiatry. 2013; 3 (2A): 46-55.
- 27. Bossy, J., Godlewski, G., Maurel, J.C. Study of right-left asymmetry of the temporal planum in the fetus]. Bull Assoc Anat Nancy, 1976; 60 (169): 253-258.
- Kasprian, K., Langs, G., Brugger, P. C., Bittner, M., Weber, M. Arantes, M., *et al.*, The prenatal origin of hemispheric asymmetry: An *in utero* neuroimaging study. Cereb. Cortex 2011; 21(5): 1076-1083.