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The Spectrum of Congenital Central Nervous System Anomalies Among Stillborn: An Autopsy Based Study

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Abstract

Background: Congenital central nervous system (CNS) anomalies are the structural or functional abnormalities of the brain and spinal cord that occur during the intrauterine developmental process.

Purpose: The present study aims to detect the prevalence of congenital CNS anomalies among stillborn fetuses, the association between congenital anomalies and maternal factors, and also the association between autopsy and ultrasound findings.

Methods: This study was conducted on 50 stillborn fetuses, obtained from the Department of Obstetrics and Gynecology at JSS Medical College and Hospital, Mysuru. The fetuses were fixed in 10% formalin and autopsies were performed as per the standard fetal autopsy protocol. The congenital CNS anomalies were studied in detail.

Results: CNS anomalies were the most common congenital anomalies observed. Out of the total 50 stillborn fetuses studied, CNS anomalies were found in 17 fetuses and their occurrence was more common among male stillborn than females. Meningomyelocele was the most common anomaly, followed by anencephaly. The other anomalies documented were meningocele, encephalocele, meningoencephalocele, agenesis of the corpus callosum, craniorachischisis, bifid cerebellum with hypoplastic vermis, holoprosencephaly, and sirenomelia.

Fisher's exact test showed a significant association between maternal hypothyroidism and congenital CNS anomalies ($P < .05$). The autopsy confirmed the ultrasound findings in 40 (80%) fetuses. There were significant additional findings observed in seven (14%) fetal autopsies and ultrasound diagnosis completely changed in three (6%) cases, after the final autopsy procedure.

Conclusion: The fetal autopsy is the single most directly evident investigation, which gives information that changes or significantly improves the clinical diagnosis. A multidisciplinary holistic approach toward pregnancy will help to detect any kind of abnormality in the fetus and thus to take a timely decision toward the management.

Keywords

Congenital anomalies, central nervous system, fetal autopsy, stillborn, ultrasonography

Introduction

Congenital central nervous system (CNS) anomalies are the structural or functional abnormalities of the brain and spinal cord that occur during the intrauterine developmental process. The prevalence of congenital anomalies differs significantly across the globe, which varies from 1.07% in Japan to 4.3% in Taiwan. This variation in prevalence may be because of the complex interaction of genetic and environmental factors.[1]

The prevalence of CNS anomalies was maximum among stillborn, whereas anomalies of the musculoskeletal system

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were maximum among live births.[2] Neural tube defects (NTDs) contribute to the majority of CNS anomalies and result from the inability of the neural tube to close between the third and fourth weeks of intrauterine development. Spina bifida occulta, meningocele, myelomeningocele, and encephalocele are included in the major NTDs.[3]

Spina bifida is a common term for NTDs affecting the spinal region. There are two types of spina bifida: spina bifida occulta and spina bifida cystica. Spina bifida occulta is a defect of the vertebral arches without protrusion of the spinal cord or meninges. Spina bifida cystica is also a defect of the vertebral arches, in which the neural tissue or meninges protrude and form a cyst-like sac.

When the meninges protrude the defect in the posterior vertebral arches, it results in meningocele. When the meninges herniate along with neural tissue, it results in meningomyelocele, and the lumbosacral region is the most common location. Encephalocele is a protrusion of meninges, cerebral cortex, cerebellum, or portions of the brainstem, which affects the skull. Agenesis of the corpus callosum is also an important CNS malformation.[3]

Anencephaly occurs as a result of the failure of closure of the cranial neural folds. The neural tube fails to close in cranial and upper spinal cord regions, thus exposing the brain and the spinal cord, and this condition is called craniorachischisis.[4]

Holoprosencephaly occurs as a result of incomplete midline cleavage of the prosencephalon, often associated with neurological damage, and dysmorphism of the brain and face.[5] Sirenomelia, also known as mermaid syndrome, is characterized by a partial or complete fusion of lower limbs, and may include anomalies of the lumbosacral spine and pelvis, genitourinary, and gastrointestinal anomalies.[6]

The World Health Organization defines stillborn as the death of a fetus when the birth weight of 500 g is attained, and suppose if the birth weight is not known, the gestational age of 22 weeks or crown-to-heel length of 25 cm may be considered.[7] Congenital malformations frequently cause psychological disturbance to the parents, because it puts the entire life of a child into complexities. Prenatal diagnosis of congenital anomalies has become an essential part of modern obstetrics.[8]

Antenatal ultrasonography (USG) is a very efficient detector of important congenital anomalies, but it lacks specificity, which is essential for syndrome diagnosis. It offers an opportunity to study the abnormal fetus at an earlier stage in development, which improves the treatment of affected live-born babies. Despite antenatal diagnostic modality, fetal autopsy still plays a vital role in the confirmation as well as identification of congenital anomalies. Fetal autopsy along with USG helps in the counseling of the parents to prevent congenital anomalies in future pregnancies.[9]

Etiological diagnosis in unexplained fetal deaths is possible with a detailed evaluation of the fetus. The fetal autopsy is confirmed in 28.6% to 89%, diagnostic in 10% to 38%; it provides additional information in 3.9% to 24% cases and changed the predicted probability in 18% cases. Also, data about demography, socioeconomic status, and maternal health is helpful to pinpoint the factors behind the occurrence of fetal loss.[10] Ultrasound examination with autopsy will help to compensate for the reduced specificity in the previous investigation.

The present study intends to identify the prevalence of congenital CNS anomalies among the stillborn fetuses, also an association between maternal factors and congenital anomalies, and an association between the autopsy and ultrasound findings.

Methods

Sampling Technique

Nonprobability sampling (simple random) was done to recruit the stillborn fetuses.

Sampling: Thirty-eight fetuses (based on the reported incidence of congenital anomalies to be 69%, article reference no. 10, absolute allowable error of 15%).

Sample Size = 4 PQr^2, where $P = 69$, $Q = 100 - 69 = 31$ and $r = 15$

$$= 4 \times 69 \times 31/ (15)^2$$
$$= 38$$

For convenience, the sample size was rounded to the next higher number 50. A descriptive and cross-sectional study was conducted on 50 stillborn fetuses, which were obtained from the Department of Obstetrics and Gynecology at JSS Medical College and Hospital, Mysuru. The duration of the study was two years. This study was approved by the Institutional Ethics Committee with the approval number JSS/MC/IEC/02/660/2015-16.

Inclusion Criteria: All stillborn fetuses at or above 22 weeks and fetuses whose parents gave informed consent were included.

Exclusion Criteria: Fetuses with gestational age less than 22 weeks and autolyzed fetuses were excluded.

Written consents were obtained from either of the parents for all the stillborn fetuses before conducting the autopsy. A study pro forma was prepared to obtain a detailed history of a mother in terms of consanguinity, obstetric history, history of medical disorders, socioeconomic status, the possible cause of fetal death, mode of termination, and antenatal USG report. The experts validated the study pro forma details regarding fetal and maternal factors, autopsy, and antenatal ultrasound findings. The radiological examination of the fetus was done in suspected cases with musculoskeletal abnormalities.

Fetal Autopsy Procedure

Stillborn fetuses were fixed in 10% formalin. The formalin was injected into the thoracic, abdominal, and cranial cavities

for the fixation of the organs. An autopsy was performed by the standard procedure adopted by Edith L Potter.[11] The various morphometric parameters including birth weight, crown–rump length, and rump heel length, head, chest, and abdominal circumferences were measured. The placenta and umbilical cord were also examined. The external anomalies of the stillborn fetus were noted.

The cranial cavity was opened by giving coronal incision on the scalp, starting behind one ear toward the other ear posterior to the vertex. The scalp was reflected and the surface of the brain was inspected on each side. The brain was studied in detail to look for any malformations present. Each fetus was coded with the unique autopsy number for the identification of congenital anomalies.

Statistical Analysis

Data collected were entered in MS Excel 2010 and analyzed using Statistical Package for the Social Sciences (SPSS) version 22 in (Mysuru) to obtain relevant statistics. Descriptive measures such as percentages, mean, and standard deviation (SD) were calculated. Fisher's exact test was done to find out the association between hypothyroidism and congenital CNS anomalies. The results were interpreted as statistically significant at $P < 0.05$.

Results

Out of the total 50 fetuses studied, congenital CNS anomalies were present in 17 fetuses (34%). Among the 17 fetuses, 11 were males and 6 were females. The descriptive statistics of fetal and maternal factors of this study are presented in Table 1 and Table 2.

Table 1. Descriptive Statistics of Fetal and Maternal Factors in the Present Study (n = 50)

Fetal and Maternal Factors	Number (n)	Percentage (%)
Gender of Stillborn Fetuses		
Male	28	56%
Female	22	44%
Mode of Delivery		
NVD	27	54%
LSCS	23	46%
Association With Ultrasound		
Autopsy confirmed USG findings	40	80%
Additional findings noted in the autopsy	7	14%
Autopsy changed the primary diagnosis	3	6%
External Anomalies		
Present	25	50%
Absent	25	50%
Consanguinity		
Present	10	20%
Absent	40	80%
Gravida		
Primi	22	44%
Second	17	34%
Third	8	16%
Fourth	2	4%
Fifth	1	2%
Socioeconomic Status		
Upper	1	2%
Upper middle	15	30%
Lower middle	25	50%
Upper lower	7	14%
Lower	2	4%

Abbreviations: NVD, normal vaginal delivery; LSCS, lower segment cesarean section; USG, ultrasonography.

Table 2. Descriptive Statistics of Fetal and Maternal Factors in the Present Study (n = 50)

Birth Parameters	Mean	SD	SE of Mean	Median	Min	Max	Range
Birth weight (g)	1128.20	679.01	96.03	965	500	2800	2300
Gestational age (weeks)	28.50	4.35	0.62	28	22	40	18
Maternal age (years)	25.82	3.62	0.51	26	19	34	15

Abbreviations: SD, standard deviation; SE, standard error; Min, minimum; Max, maximum.

Each stillborn fetus was classified, based on birth weight, gestational age, maternal age, gravidity of the mother, and socioeconomic status of parents. Maximum fetuses 29 (58%) were having a birth weight between 500 and 1000 g. Maximum fetuses 20 (40%) were from the gestational age group of 22 to 26 weeks. The maximum number of fetuses 24 (48%) were born to mothers in the age group of 26 to 30 years and 22 (44%) mothers were primigravida. The socioeconomic status was calculated according to modified Kuppuswamy's socioeconomic scale.[12] The maximum number of stillborn, i.e., 25 (50%), belonged to the lower middle class of socioeconomic status. The history of consanguinity was present in ten (20%) mothers. The external anomalies were present in 25 cases (50%). The distribution of various congenital CNS anomalies is presented in Table 3.

Table 3. The Number and Percentages of Various Types of Congenital CNS Anomalies Among Stillborn Fetuses Studied

S. No.	Type of Congenital CNS Anomalies	Number	Percentages (%)
1.	Anencephaly	4	23
2.	Anencephaly with craniorachischisis	1	6
3.	Meningomyelocele	5	29
4.	Meningocele	1	6
5.	Encephalocele	1	6
6.	Meningoencephalocele	1	6
7.	Agenesis of the corpus callosum	1	6
8.	Holoprosencephaly	1	6
9.	Bifid cerebellum with hypoplastic vermis	1	6
10.	Mermaid syndrome	1	6
	Total	**17**	**100**

Meningomyelocele (29%) was the most common anomaly, followed by anencephaly (23%).A small proboscis, hypotelorism, and flat nasal bridge were observed in the fetus with holoprosencephaly (Figure 1 A). Antenatal ultrasound showed a large monoventricle with fused thalami and thinned out at cerebral parenchyma in the same fetus (Figure 1 B). The other anomalies observed in stillborn fetuses were bifid cerebellum with hypoplastic vermis (Figure 2), agenesis of thecorpuscallosum(Figure3),occipitalmeningoencephalocele (Figure 4), meningomyelocele (Figure 5), anterior view of fetus showing anencephaly with craniorachischisis (Figure 6 A), posterior view of fetus showing anencephaly with craniorachischisis (Figure 6 B), mermaid syndrome (Figure 7 A), and radiograph of the fetus with mermaid syndrome (Figure 7 B).

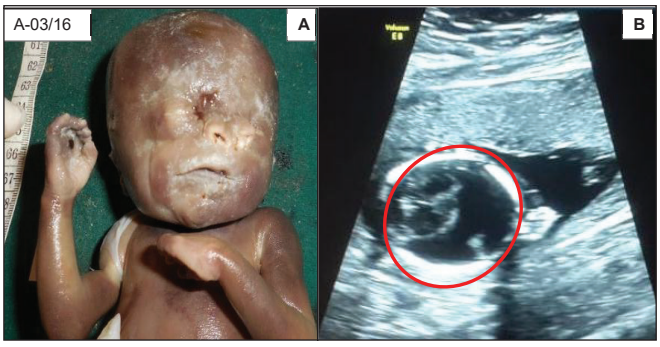

Figure 1. (A) Holoprosencephaly With a Small Proboscis, Hypotelorism, Flat Nasal Bridge and **(B)** Antenatal Ultrasound Image Showing Single Large Monoventricle

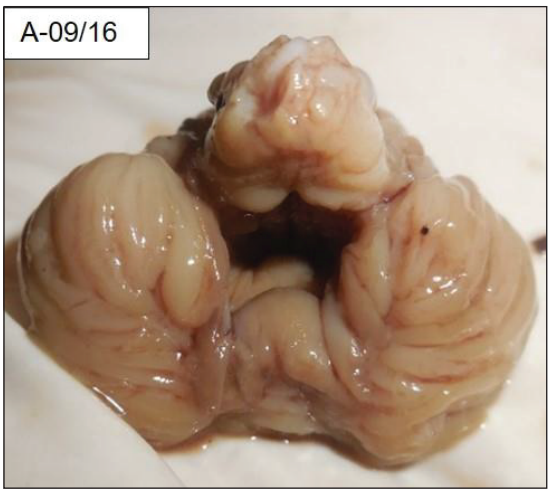

Figure 2. Bifid Cerebellum With Hypoplastic Vermis

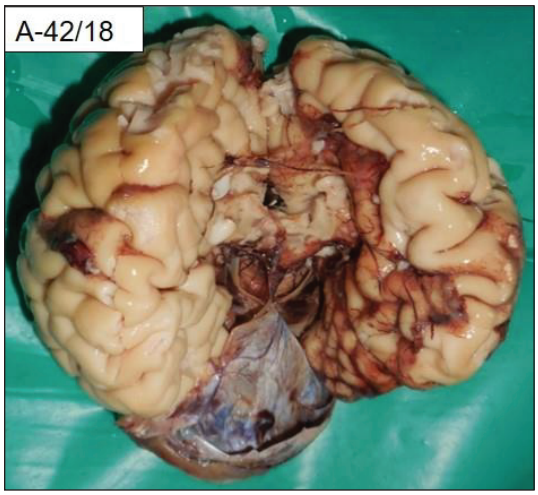

Figure 3. Agenesis of Corpus Callosum

Figure 4. Occipital Meningoencephalocele

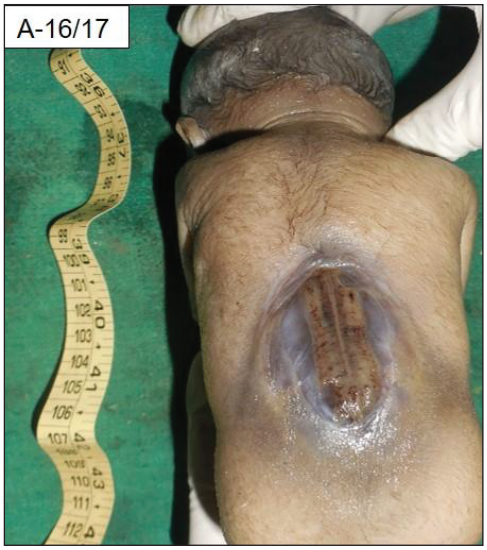

Figure 5. Meningomyelocele

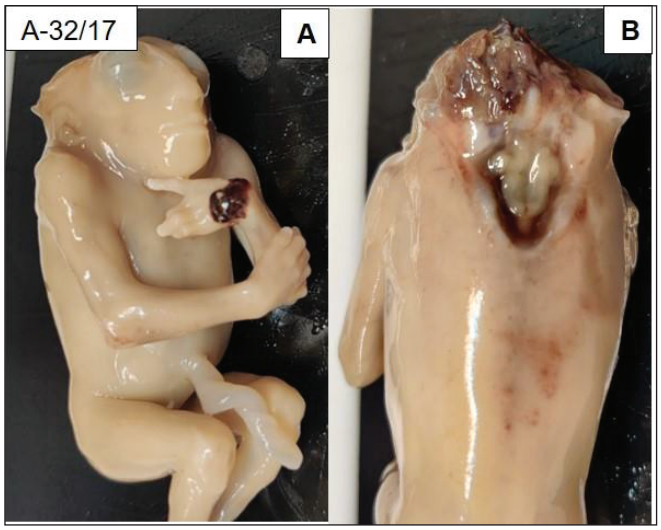

Figure 6. (A) Anencephaly With Craniorachischisis (Anterior View) and (B) Anencephaly With Craniorachischisis (Posterior View)

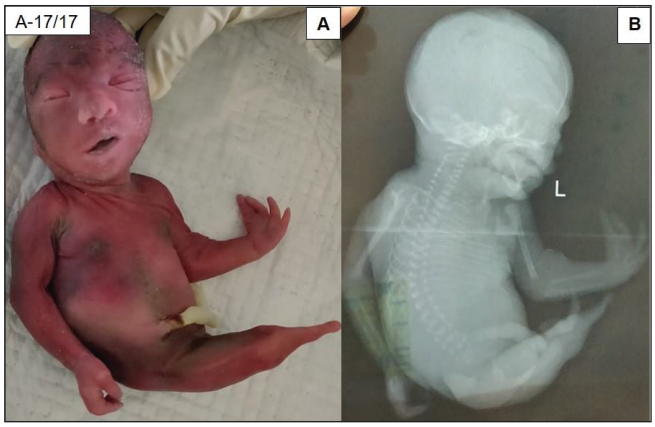

Figure 7. (A) Mermaid Syndrome and (B) Radiograph of the Fetus With Mermaid Syndrome

The risk factors for NTD such as hypothyroidism in mother was observed in 11 out of 17 stillborn fetuses in the present study. Fisher's exact test showed a significant association between hypothyroidism in mother and CNS anomaly in the stillborn fetus (Table 4).

The autopsy confirmed the ultrasound findings in 40 (80%) fetuses. There were significant additional findings observed in seven (14%) fetal autopsies and ultrasound diagnosis completely changed in three (6%) cases, after the final autopsy procedure. In one stillborn fetus with holoprosencephaly, low set ears, amniotic band on the right arm, and syndactyl were the additional findings. Ultrasound showed an encephalocele in another fetus, but there were no such findings after performing the autopsy.

Discussion

Factors such as genetic, environmental, teratogenic, and infectious agents play a vital role in the etiology of congenital malformations during the most delicate period of embryogenesis, i.e., the third to eighth weeks of intrauterine life.[11] Despite routine antenatal folic acid (5 mg) supplementation, a reduction in the incidence of congenital CNS anomalies is not regularly observed. Hence, interplay of risk factors such as hypothyroidism, diabetes, maternal infections, and genetic causes might also play a significant role. The occurrence of CNS anomalies among hypothyroid mothers was a significant observation. The details of the fetal and maternal factors observed in the present study were compared with the available literature (Table 5).

Meningomyelocele (29%) was the most common anomaly, followed by anencephaly (23%) in the present study. Kapoor et al. have found that anencephaly was the most prevalent anomaly in CNS (28.5%) and it was frequently associated with meningocele or meningomyelocele. The incidence of rachischisis (spina bifida) was noted in 22.4% of cases. Hydrocephalus was observed in 20.4% of cases, and there was an abnormal flexion of the vertebral column in 18% of fetuses. The reason may be that most of the fetuses affected with NTDs were aborted very early in the gestational period.[10]

Kale et al. have reported nine cases (15.79%), which is slightly lower as compared to the present study.[11] Padma et al. have found 12 cases (44%) of CNS anomalies in their study.[13] Andola et al. have found 15 cases (34.09) of CNS defects.[14]

Table 4. Association Between Maternal Hypothyroidism and Congenital CNS Anomalies

Major System Involved	Maternal Hypothyroidism			Fisher's Exact Test	
	Present	Absent	Total	χ^2	*P*-Value
Central nervous system	11 (64.7%)	6 (35.3%)	17 (100.0%)	17.962	$P < .05$

*Significant at $P < .05$

Table 5. Comparison of Fetal and Maternal Factors With the Available Literature

S. No.	Authors	No. of CNS Anomalies	Sex Ratio (Male: Female)	Birth Weight in Grams	Gestational Age in Weeks	Maternal Age in Years	Gravida	Socioeconomic Status	Consanguinity
1.	Padma et al.[13] (2011)	12 (44%)	1.7:1	–	29–32	19–28 (23.5)	–	No	–
2.	Andola et al.[14] (2012)	15 (34.09%)	1:1.5	350–1000 g	35–39	–	–	–	–
3.	Kapoor et al.[10] (2013)	49 (33%)	1:1	–	18–20	20–25	50% primi	Upper lower	Nil
4.	Kale et al.[11] (2017)	9 (15.79%)	1.25:1	350–1000 g	20–24	20–24	50.8%primi	No	4 (7.02%)
5.	Present study (2020)	17 (34%)	1.27:1	500–1000 g	22–26	26–30	44% primi	Lower middle	10 (20%)

Taksande et al. have found 15 cases of CNS anomalies in their study. The CNS defects were most commonly seen in stillborn.[15] Siddesh et al. have reported that 243 (31.63%) fetuses had CNS malformations in their study. NTDs accounted for 16.5% of all malformations and 52% of CNS malformations.[16]

Gole et al. also found that CNS anomalies (36%) were the most common in their study. Anencephaly associated with spina bifida was seen in two cases. Anencephaly was more commonly noted in female fetuses.[17] The results obtained in the present study are similar to that of Andola et al.,[14] Kapoor et al.,[10] and Gole et al.[17] Hydrocephalus and spina bifida were the most frequent congenital CNS anomalies, and hydrocephalus may be associated with spina bifida and myelomeningocele. Genetic factors, low birth weight, prematurity, both extremes of maternal age, and the deficiency of maternal folic acid intake may be linked to NTDs.[18]

On analyzing the sex ratio, the congenital malformations were slightly more in males (56%) than females (44%) with the male-to-female (M:F) ratio being 1.27:1 in the present study. Kale et al. have found a similar incidence to be more in males (52.63%) with a ratio of 1.25:1.[11] The incidence of congenital anomalies was observed more in male fetuses than females ($P < .01$), and the sex ratio was 1.7:1.[13] Andola et al. have found the M:F ratio of 1:1.5 with female preponderance in their study.[14] Sexual preponderance was not statistically significant, as 83% of female fetuses had congenital anomalies as compared to 75% male fetuses.[10] The M:F ratio was 1.63:1 by a sex-wise distribution of 62% males and 38% females. Congenital anomalies were significantly observed in stillbirths ($P < .01$) when compared to live births, with a frequency of 4.68% and 1.84%, respectively.[15]

The birth weight of stillborn fetuses ranged from 500 to 2800 g. Similar to the other studies, maximum fetuses 29 (58%) were having a birth weight between 500 and 1000 g. The association between congenital anomalies and low birth weight is well known.[11] The gestational age of most of the stillborn fetuses ranged from 22 to 26 weeks (40%) in the present study. This could be because the termination of pregnancy is immediately done after detecting congenital anomaly on USG. Kale et al. have found that maximum fetuses were having a gestational age of 20 to 24 weeks (63.15%) in their study.[11]

The maternal factors considered in the present study are the age of the mother, gravida, socioeconomic status, consanguinity, and history of medical disorders. The maximum number of fetuses, 24 (48%), were born to mothers in the age group of 26 to 30 years, followed by 19 fetuses (38%) to mothers in the age group 21 to 25 years. 22 (44%) were born to primigravida, followed by the second gravida in 17 fetuses (34%). The number of stillborn fetuses was observed maximum in the lower middle class 25 stillborn (50%), followed by the upper middle class in 15 stillborn (30%), according to modified Kuppuswamy's socioeconomic scale. Kapoor et al. have found 34% of cases belonging to the upper lower class.[10]

The history of consanguinity was observed in ten mothers (20%) in the present study. Consanguinity was present in four mothers (7.02%) out of all congenitally malformed cases.[11] There was not even a single case of consanguineous marriage in north-west India. Consanguinity has a damaging effect on fetal growth, and it increases the risk of congenital anomalies and fetal loss. A few authors have related low socioeconomic status with consanguineous marriages, and thereby increase in the percentage of congenital anomalies is the result of both the abovementioned factors.[10] The consanguinity of parents was noted in 14 cases of congenital anomalies.[15]

In the present study, there was a history of hepatitis E virus Immunoglobulin M antibodies positive in the mother in a fetus with holoprosencephaly. There was a history of chickenpox in the mother in a fetus with bifid cerebellum and hypoplastic vermis. There was a history of hypertension in the mother in one fetus with anencephaly. There was a history of diabetes in the mother in a fetus with mermaid syndrome.

The risk factors for congenital malformations are the presence of hydramnios, first-trimester febrile illness,

Table 6. Association Between the Autopsy Findings and Ultrasound Findings

			Autopsy Confirmed USG Findings		
S. No.	Authors	Year	No Change in Diagnosis	Additional Findings Noted in the Autopsy	Autopsy Changed the Primary Diagnosis
1.	Yeo et al.21	2002	27/88 (30.68%)	30/88 (34.09%)	31/88 (35.22%)
2.	Shankar et al.19	2006	55/134 (41.04%)	77/134 (57.46%)	2/134 (1.49%)
3.	Pradhan et al.20	2013	44/70 (62.86%)	18/70 (25.71%)	8/70 (11.43%)
4	Kale et al.11	2017	27/57 (47.37 %)	27/57 (47.37 %)	3/57 (5.26%)
5.	Present study	2020	40/50 (80%)	7/50 (14%)	3/50 (6%)

previous abortions, eclampsia, and history of congenital heart disease or malformed babies. Maternal diabetes, hypertension, and hypothyroidism show a positive correlation with congenital anomalies.[15] A significant association between maternal hypothyroidism and CNS anomaly in the stillborn fetus was observed in this study.

The association between the autopsy and ultrasound findings is compared with that of previous studies in Table 6.

With the current advanced ultrasound techniques, the false-positive diagnosis is very rare. However, poor visibility because of oligohydramnios or obesity is an important cause of errors in ultrasound diagnosis. Sometimes USG may fail to detect associated malformations, which may lead to alteration in etiological diagnosis. Fetal autopsy provided significant additional information in 38% of cases and the change in recurrence risk in 18% of cases.[19]

When postmortem examinations were compared with USG findings, in eight cases (11.43%) the USG findings were incorrect. In 18 cases (25.71%), additional information was obtained on autopsy.[20] Only a few studies have shown a comparison of antenatal ultrasonographic findings and autopsy findings. Autopsy diagnosis confirmed USG findings in 54 cases (94.74%), it provided additional information in 27 cases (47.37%), whereas the primary diagnosis provided by USG was changed in three cases (5.26%).[11]

When a major anomaly has already been detected, the error in prenatal diagnosis is a failure to conduct a complete examination of the fetus. It is avoided by using a systematic approach to perform a comprehensive anatomic evaluation of the fetus. Accurate prenatal diagnosis of all associated anomalies is not possible every time, even in the ideal situation.[21] There is an alarming decrease of autopsy procedures, because of the centralization of pathology facilities or changes in clinician's perception of autopsy importance or improvements in ultrasound diagnostics, or poor counseling provided by inexperienced personnel. As a result, parents are refusing to give consent to a fetal autopsy procedure.[22]

Future Implications of Experimental Research in Animal Models

Neural stem cells are originated from the embryonic ectoderm, which produces the neuroepithelial cells. A large number of neural stem cells are required for the basic research as well as for the development of novel approaches, needed for the treatment of various neurological disorders. Human embryonic stem cell that is derived from retinal pigment epithelium is known to protect the visual function in an animal model of retinal disease. When fetal neurons were evaluated, they are known to survive the transplantation surgery much better than adult neurons, which reflects the value of fetal-derived neural stem cells.[23]

Hematopoietic, mesenchymal, embryonic, neural, and retinal stem cells are known to differentiate into neuronal lineages, and they may be able to regenerate neural retinal tissue.[24]

Neural stem cells are localized in the highly vascularized regions of the CNS, instead of being distributed throughout the brain.[25]

Anand et al. have stated that the potential use of traditional herbs such as Brahmi (Bacopa monniera) needs deeper investigation.[26] Brahmi appears to perform very important functions in the CNS. A better understanding of the physiopathological nature of different neurological diseases at various levels (systemic, organ, tissue, and cell) is of paramount importance for further progress, and the mechanisms underlying the effects of Brahmi need to be elucidated in animal models.[27]

Conclusion

Congenital CNS anomalies are the most commonly observed anomalies in the present study. Meningomyelocele was the most common CNS anomaly, followed by anencephaly. There was a significant association between maternal hypothyroidism and CNS anomalies. It is mandatory to have an autopsy study for all the

stillborn fetuses to predict and counsel for safe future pregnancy outcomes. Hence, this study focuses on the importance of concomitant fetal autopsy and antenatal USG in providing accurate genetic counseling. Future studies are required to evaluate the cause of fetal loss as a multidisciplinary holistic approach.

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Ethical Statement

This study was approved by the Institutional Ethics Committee of JSS Medical College, Mysuru with the approval number JSS/MC/IEC/02/660/2015-16. The written informed consent was obtained from the participants in the study.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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References

1. Ameen, SK Alalaf, SK Shabila, NP. Pattern of congenital anomalies at birth and their correlations with maternal characteristics in the maternity teaching hospital, Erbil city, Iraq. BMC Pregnancy Childbirth 2018; 18: 501.
2. Bhide, P Kar, A. A national estimate of the birth prevalence of congenital anomalies in India: Systematic review and meta-analysis. BMC Pediatr 2018; 18:175.
3. Catibusic, FH Maksic, H Uzicanin, S Congenital malformations of the central nervous system: Clinical approach. Bosn J Basic Med Sci 2008; 8(4): 356–360.
4. Sadler, TW. *Langman's Medical Embryology*. 12th ed. Philadelphia: Lippincott Williams and Wilkins, 2012: p.311.
5. Raam, MS Solomon, BD Holoprosencephaly:, Muenke M. A guide to diagnosis and clinical management. Indian Pediatr 2011; 48(6): 457–466.
6. Samal, SK Sirenomelia:, Rathod S. The mermaid syndrome: Report of two cases. J Nat Sci Biol Med 2015; 6(1): 264–266.
7. Silva, FTD Gonik, B McMillan, M Stillbirth: Case definition and guidelines for data collection, analysis, and presentation of maternal immunization safety data. Vaccine 2016; 34: 6057–6068.
8. Gupta, S Gupta, P Soni, JS. A study on incidence of various systemic congenital malformations and their association with maternal factors. *Natl J Med Res* 2012; 2(1): 19–21.
9. Pushpa, B Subitha, S Lokesh Kumar, V. Study on various congenital anomalies in fetal autopsy. *Int J Med Res Rev* 2016; 4(9): 1667–1674.
10. Kapoor, K Singh, K Sharma, A Congenital anomalies in North Western Indian population: A fetal autopsy study. *Eur J Anat* 2013; 17(3): 166–175.
11. Kale, PP Kanetkar, SR Shukla, DB Study of congenital malformations in fetal and early neonatal autopsies. *Ann Pathol Lab Med* 2017; 4(4): 433–441.
12. Bairwa, M Rajput, M Kuppuswamy's, Sachdeva S. Modified socioeconomic scale: Social researcher should include updated income criteria, 2012. *Indian J Community Med* 2013; 38(3): 185–186.
13. Padma, S Ramakrishna, D Jijiya, BP Pattern of distribution of congenital anomalies in stillborn: A hospital based prospective study. *Int J Pharm Bio Sci* 2011; 2(2): 604–610.
14. Andola, US Anita, AM Ahuja, M Congenital malformations in perinatal autopsies: A study of 100 cases. *J Clin Diagn Res* 2012; 6(10): 1726–1730.
15. Taksande, A Vilhekar, K Chaturvedi, P Congenital malformations at birth in Central India: A rural medical college hospital based data. *Indian J Hum Genet* 2010; 16(3): 159–163.
16. Siddesh, A Gupta, G Sharan, R Spectrum of prenatally detected central nervous system malformations: Neural tube defects continue to be the leading fetal malformation. *Indian J Med Res* 2017; 145: 471–478.
17. Gole, RA Meshram, PM Hattangdi, SS. Congenital malformations in stillborn fetuses. *Int J Recent Trends Sci Technol* 2014; 11(3): 412–414.
18. Cosmea, HW Limaa, LS Barbosaa, LG. Prevalence of congenital anomalies and their associated factors in newborns in the city of Sao Paulo from 2010 to 2014. *Rev Paul Pediatr* 2017; 35(1): 33–38.
19. Shankar, VH Phadke, SR. Clinical utility of fetal autopsy and comparison with prenatal ultrasound findings. J Perinatol 2006; 26: 224–229.
20. Pradhan, R Mondal, S Adhya, S Perinatal autopsy: A study from India. *J Indian Acad Forensic Med* 2013; 35(1): 10–13.
21. Yeo, L Guzman, ER Shen-Schwarz, S Value of a complete sonographic survey in detecting fetal abnormalities. *J Ultrasound Med* 2002; 21: 501–510.
22. Sorop Florea, M Ciurea, RN Ioana, M The importance of perinatal autopsy. Review of the literature and series of cases. *Rom J Morphol Embryol* 2017; 58(2): 323–337.
23. English, D Sharma, NK Sharma, K Neural stem cells: trends and advances. *J Cell Biochem* 2013; 114(4): 764–772.
24. Singh, T Prabhakar, S Gupta, A Recruitment of stem cells into the injured retina after laser injury. *Stem Cells Dev* 2012; 21(3): 448–454.
25. Abburi, C Anand, A. Ciliary epithelium: An underevaluated Target for Therapeutic Regeneration. *Critl Rev Eukaryot Gene Expr* 2012; 22(2): 87–95.
26. Anand, A Saraf, MK Prabhakar, S. Antiamnesic effect of B. monniera on L-NNA induced amnesia involves calmodulin. *Neurochem Res* 2010; 35(8): 1172–1181.
27. Mathur, D Goyal, K Koul, V The molecular links of re-emerging therapy: A review of evidence of Brahmi (Bacopa monniera). *Front Pharmacol* 2016; 7: 44.