International Journal of Contemporary Pediatrics
Malik N et al. Int J Contemp Pediatr. 2020 Oct;7(10):2010-2014
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20204044

Original Research Article

Spectrum of prenatally diagnosed neural tube defects at a tertiary referral hospital in North India: a retrospective cohort study

Nisha Malik*, Savita Rani Singhal, Smiti Nanda, Daya Sirohiwal, Pushpa Dahiya, Anita Bharti

Department of Obstetrics and Gynaecology, Pt. BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India

Received: 09 August 2020
Accepted: 05 September 2020

***Correspondence:**
Dr. Nisha Malik,
E-mail: dr.maliknisha@gmail.com

ABSTRACT

Background: Neural tube defects, although largely preventable, constitute an important cause of neonatal mortality and morbidity. The study aimed to identify incidence rate, demographic profile, risk factors, and pregnancy outcomes of women with prenatally diagnosed NTDs.
Methods: This retrospective cohort study reviewed the case records of all antenatal women admitted in labour ward of Pt. B.D Sharma postgraduate institute of medical sciences, Rohtak, India with the prenatal diagnosis of NTDs on ultrasound from August 2018 to January 2020. The sociodemographic details, risk factors, obstetric history and pregnancy outcomes were noted. The mean, standard deviation and range values were calculated for normally distributed data. Categorical data were presented as frequency and percentage values.
Results: From a total of 21,187 births, 90 had neural tube defects, making an incidence rate of 4.3 per 1000 births. Out of the 86 included cases of NTDs, 46.5% (n=40) had anencephaly, 45.3% (n=39) spina bifida, 5.8% (n=5) encephalocele and 2.3% (n=2) had mixed defects. Majority (69.7%, n=60) of the women were multigravida with a mean age of 24.9±4.2 years. Preconceptional folic acid intake was found in merely 2.3% (n=2) cases and during first trimester of pregnancy in 39.5% (n=40) cases. About 61.6% (n=53) cases who presented at ≤20 weeks gestation underwent pregnancy termination while 38.3% (n=33) had vaginal delivery, of which majority (90.7%) were still births.
Conclusions: NTDs are one of the commonest preventable congenital anomalies. Ensuring periconceptional folate supplementation to women-either by food fortification, dietary modification and public awareness is urgently required.

Keywords: Folic acid, Neural tube defects, Pregnancy

INTRODUCTION

Despite the widespread implementation of folic acid supplementation recommendations and fortification programmes, a significant number of cases of neural tube defects (NTDs) still exist. The global estimates suggest that more than 300,000 babies each year are born with NTDs.[1] The incidence of these birth defects in developing nations is about four times higher than in developed ones.[2] NTDs are among the major congenital anomalies which consists mainly of anencephaly, spina bifida and encephalocele, the first two being most common.[3] NTDs, although largely preventable, constitute an important cause of neonatal mortality and morbidity. These birth defects constitute 10% of the burden of all congenital anomalies and accounts for 10% of all neonatal mortality worldwide.[4] The health care of a child with NTD imposes a great financial, emotional and social burden on such families.

It has been known since long that daily folic acid supplementation in the periconceptional period reduces the risk of NTDs.[5] The recent US preventive services task force (USPSTF) recommends a daily intake of 400-800µg of folic acid supplement for all women who are planning pregnancy for prevention of NTDs.[6] But it was alarming to see the results of a US National health and nutrition examination survey based on 2003-2006 data which suggests that 75% of women aged 15-44 years don't take the recommended amount of folic acid around the conception for prevention of NTDs.[7]

Although there is a risk of occurrence of NTDs in pregnancy to all women capable of childbearing but certain factors increase this risk which includes micronutrient deficiency including folic acid, personal or family history of NTDs, maternal diabetes, obesity, use of some antiepileptic medications and mutations in folate related enzymes.[2] This study aimed to identify demographic profile, risk factors, periconceptional folic acid usage and pregnancy outcomes of women with NTDs.

METHODS

This is a retrospective, single centre, cross sectional study carried out at the department of Obstetrics and Gynaecology, Pt. B.D Sharma postgraduate institute of medical sciences, Rohtak, India during the period from August 2018 to January 2020. The medical case records of all antenatal women admitted in labour ward during the study period with prenatal diagnosis of congenital anomalies on ultrasound were reviewed. The confirmation of congenital anomaly was done by ultrasound examination by radiologist from our institute. All those with NTDs were included in the study whereas those with other anomalies were excluded. From the records, the sociodemographic details of women, risk factors, obstetric history, pattern of congenital anomaly and obstetric outcomes were noted. Informed consent: All individual participants included in the study gave their informed consent to the anonymous use of their data for scientific purposes at the time of admission.

Statistical analysis

Data analysis was carried out using statistical software STATA version 14.0. Descriptive statistics such as mean, standard deviation and range values were calculated for normally distributed data. categorical data were presented as frequency and percentage values.

RESULTS

There were a total of 21,187 births during the study period of 18 months. Women admitted in labour ward with the prenatal diagnosis of congenital anomalies were 514, of which 90 (17.5%) had neural tube defects, making an incident rate of 4.3 per 1000 births. Out of the 90 cases, four were excluded from the study due to lack of medical records. Out of the 86 included cases of NTDs, 46.5% (n=40) were diagnosed with anencephaly, 45.3% (n=39) with spina bifida, 5.8% (n=5) with encephalocele and 2.3% (n=2) with mixed defects. within the spina bifida cases, 58.9% (n=23) had meningomyelocele and 41.0% (n=16) had meningocele. Photographs of some of these cases are shown in (Figure 1). Out of the total cases of NTDs, five women (5.8%) had associated malformations including gross hydrocephalus, omphalocele, gastroschisis and hydronephrosis.

Figure 1: Three cases with (A) anencephaly, (B) myelomeningocoele and (C) encephalocele.

The sociodemographic profile of patients is illustrated in (Table 1). Majority (69.7%, N=60) of the mothers were multigravida with a mean age of 24.9±4.2 years. About 74.4% women had a rural background and 25.6% were uneducated. Nearly 60% (N=53) of women were admitted at or below 20 weeks of gestation, of whom only 5 were in first trimester of pregnancy.

Table 1: Social demographics and obstetric characteristics (n=86).

Characteristics	Mean±SD/N (%)
Women age (years)	24.9±4.2 (18-36)
Husbands age (years)	27.7±3.6 (21-38)
Residence	
Rural	64 (74.4)
Urban	22 (25.6)
Education level	
Uneducated	22 (25.6)
Up to matric	52 (60.4)
Up to graduate	11 (12.8)
Postgraduate	1 (1.1)
Parity	
P1	26 (30.2)
P2	28 (32.5)
≥P3	32 (37.2)
Previous abortions	27 (31.4)
Previous caesarean	12 (13.9)
Chronic illness	4 (4.6)

The risk factors among women with NTDs is enumerated in (Table 2). Out of the 86 NTD cases, history of pre-conceptional folic acid intake was found in only 2 (2.3%) women. Three women had a history of congenital anomaly in previous pregnancy. No cases had history of teratogen exposure before or after conception. Details about consanguineous marriage could not be found from records.

Table 2: Risk factors (n=86).

Factors	N (%)
Congenital anomaly in previous pregnancy	3 (3.4)
Pre-conceptional folic acid intake	2 (2.3)
Folic acid intake during first trimester	34 (39.5)
Diabetes mellitus	1 (1.1)

The data related to pregnancy and neonatal outcome is outlined in (Table 3). Out of the 86 cases, termination of pregnancy was done at ≤20 weeks gestation in 61.6% (N=53) cases while 38.3% (N=33) underwent vaginal delivery. Among the neonatal characteristics, the mean birth weight was 1064.4±1059.4 grams. Majority (56.9%) were females. Among women who delivered at or beyond 28 weeks period of gestation, the mean birth weight was 2338.1±620.7grams. Majority (90.7%) were still births and only 8 were live born who eventually succumbed to death after a few hours or days.

Table 3: Pregnancy and neonatal outcome (n=86).

	Mean ±SD/N (%)
Gestational age at delivery (weeks)	24.5±9.6
Mode of delivery	
Abortion	53 (61.6)
Vaginal delivery	33 (38.3)
LSCS	0 (0)
Live births	8 (9.3)
Still births	78 (90.7)
Birth weight (grams)	1064.4±1059.4
Fetal sex	
Male	30 (34.8)
Female	51 (59.3)
Unidentified	5 (5.8)

DISCUSSION

NTDs are major congenital anomalies involving brain and spine occurring as a result of improper closure of embryonic neural tube. There are three major subtypes: first is anencephaly, in which a major part of brain, skull and scalp is absent. The second subtype is spina bifida, in which there is mal-development of vertebrae of spine. It can be further classified into closed or open spina bifida. In the open type, if both spinal cord and meninges protrude through a defect in spine, it is called as myelomeningocele and if only meninges protrude through the defect, it is known as meningocele. The third subtype is encephalocele in which brain tissue and/or its covering membrane protrudes through a skull defect.[8] These defects may lead to a range of disabilities or death.

The worldwide prevalence rate of NTDs ranges from 1 to 10 per 1000 births.[9] A systematic review by Bhide et al has reported an overall birth prevalence rate of 4.1 per 1000 births (95% confidence interval, 3.1-5.4) for NTDs in India.[10] Our study observed an incidence rate of 4.2 per 1000 births for NTDs and the most common subtype was anencephaly (46.5%) followed closely by spina bifida (45.3%). Our findings were similar to a study among Iraq families by Zlotogora et al where anencephaly was the most prevalent NTD subtype.[11] The published studies by Nasri et al and Sharma et al has found spina bifida as the most common defect in Tunisia and India respectively.[8,12] The relationship between age and incidence of NTDs, if any, is unclear. The mean age of the women in the present study was 24.9±4.2 years. The findings of Nasri et al has not found any significant association between age and incidence of NTDs whereas the study by Own et al has demonstrated a decreasing incidence of NTDs with advancing maternal age.[8,13] Nearly three-fourth of women in our study had a rural background and one fourth were uneducated. This seems to be clearly understandable as the lack of education, awareness and poor health services has a direct implication on poor maternal nutritional status and chances of missing opportunities for early detection of major anomalies in pregnancy. The findings from Wasserman et al also demonstrated that lower socioeconomic status (SES) and residence in a lower SES neighbourhood increased the likelihood of occurrence of NTDs in pregnancy.[14]Although parity has not been linked directly to the occurrence of NTDs, majority of women in the present study had parity equal to or more than three. Similar results were obtained from study by Vieira et al who found that spina bifida was more commonly observed in women with higher parity.[15] The data from two other studies show conflicting results reflecting reduced risk of NTDs with increasing parity.[16,17]

The etiology of NTDs is not properly understood. The risk factors associated with occurrence of NTDs include many genetic, environmental and nutritional factors. There is a recurrence rate of approximately 2-5% in cases of previous child with NTD.[2] Indian babies are particularly vulnerable to NTDs due to several factors like poverty, low standard of living, poor maternal nutrition, high rate of unplanned pregnancies, poor periconceptional and antenatal care, inadequate access to health services, practice of self-medication and intake of non-prescribed drugs and high rate of consanguineous marriages.[18]The author opines that maternal malnutrition, which includes folic acid deficiency, may be the leading cause for occurrence of NTDs in our study. It was really unfortunate to see a very low rate of pre-conceptional folic acid consumption among women in our study. Even during first trimester of pregnancy, only around 40% women took the recommended folic acid supplementation. The available evidence clearly demonstrates that 50-70% of NTDs can be prevented by adequate folic acid intake during periconception period.[19]

It was alarming to see that nearly 40% of women had presented with NTDs after 20 weeks period of gestation in the present study. In a country like India with strict abortion laws where termination of pregnancy is not allowed after 20 weeks, delayed detection of such severe and lethal birth defects imposes a significant mental and financial toll for the families. It has been observed that ultrasound has a sensitivity and specificity of around 97% (95% confidence interval, 0.898,0.996) and 100% (CI 0.998, 1.0) for detection of open NTDs.[20] Proper antenatal care and screening can help in timely detection of such major birth defects and thus can allow the option of termination of pregnancy for the parents.

The management of prenatally diagnosed NTDs is an enormous challenge. There may be three options depending upon the gestation at diagnosis and type of anomaly: first, to continue with pregnancy, second, fetal treatment where feasible and third, termination of pregnancy. Even after diagnosis at an appropriate gestation, the option of pregnancy termination involves cultural and ethical issues. Therefore, the key for management is prevention by simple measures such as folic acid supplementation, adequate antenatal care and genetic counselling where appropriate. Although the study was limited by its retrospective design, it highlights the urgent need to focus on primary prevention strategies to reduce the burden of NTDs in India. The health policy makers should take initiatives to extend coverage of periconceptional folate supplementation among eligible women on a mass level.

CONCLUSION

To conclude, NTDs are one of the commonest preventable congenital anomalies. Ensuring periconceptional folate supplementation to women either by food fortification, dietary modification and public awareness is urgently required.

ACKNOWLEDGEMENTS

The authors would like to thank the trainees who helped in collection of data.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Christianson A, Howson CP, Modell B. The hidden toll of dying and disabled children, March of Dimes, Global report on birth defects 2006. Available at: https://www.marchofdimes.org/global-report-on-birth-defects-the-hidden-toll-of-dying-and-disabled-children-full-report.pdf. Accessed on 20 April 2020.
2. Lawal TA, Adeleye AO. Determinants of folic acid intake during preconception and in early pregnancy by mothers in Ibadan, Nigeria. Pan Afri Med J. 2014; 19:113.
3. Viswanathan M, Treiman KA, Doto JK, Middleton JC, Coker-Schwimmer EJL, Nicholson WK. Folic Acid Supplementation: An evidence review for the U.S. preventive services task force. Rockville (MD): Agency for Healthcare Research and Quality (US); 2017.
4. Nelson AL. Folates for reduction of risk of neural tube defects: using oral contraceptives as a source of Folate. J Contracept. 2011;2:137-50.
5. De Wals P, Tairou F, Van AMI, Uh SH, Lowry RB, Sibbald B, et al. Reduction in neural-tube defects after folic acid fortification in Canada. N Engl J Med. 2007;357:135-42.
6. Bibbins-Domingo K, Grossman DC, Curry SJ, Davidson KW, Epling JW, Garcia FA, et al. Folic Acid Supplementation for the prevention of neural tube defects: US preventive services task force recommendation statement. JAMA. 2017;317(2): 183-9.
7. Tinker SC, Cogswell ME, Devine O, Berry RJ. Folic acid intake among U.S. women aged 15-44years, National Health and Nutrition Examination Survey, 2003-2006. Am J Prev Med. 2010;38(5):534-42.
8. Nasri K, Ben FMK, Hamdi T, Aloui M, Jeema MB, Nahdi S, et al. Epidemiology of neural tube defect subtypes in Tunisia, 1991-2011. Pathol Res Pract. 2014;210(12):944-52.
9. Au KS, Ashley-Koch A, Northrup H. Epidemiologic and genetic aspects of spina bifida and other neural tube defects. Dev Disabil Res Rev. 2010;16(1):6-15.
10. Bhide P, Sagoo GS, Moorthie S, Burton H, Kar A. Systematic review of birth prevalence of neural tube defects in India. Birth Defects Res A Clin Mol Teratol. 2013;97(7):437-43.
11. Sharma JB, Gulati N. Potential relationship between dengue fever and neural tube defects in a northern district of India. Int J Gynaecol Obstet. 1992;39:291-5.
12. Zlotogora J. Hereditary disorders among Iranian Jew s. Am J Med Genet. 1995;58:32-7.
13. Owen TJ, Halliday JL, Stone CA. Neural tube defects in Victoria, Australia: potential contributing factors and public health implications. Aust N Z J Public Health. 2000;24(6):584-9.
14. Wasserman CR, Shaw GM, Selvin S, Gould JB, Syme SL. Socioeconomic status, neighbourhood social conditions and neural tube defects. Am J Public Health. 1998;88(11):1674-80.
15. Vieira AR. Birth order and neural tube defects: a reappraisal. J Neurol Sci. 2004;217(1):65-72.
16. Obeidat AZ, Amarin Z. Neural tube defects in the north of Jordan: is there a seasonal variation?. J Child Neurol. 2010;25(7):864-6.

17. Obeidat AZ, Amarin Z. Neural Tube Defects in the North of Jordan: Is There a Seasonal Variation? Journal of Child Neurology. 2010;25(7):864-6.
18. Sharma R. Birth defects in India: Hidden truth, need for urgent attention. Indian J Hum Genet. 2013;19(2):125-9.
19. Blencowe H, Cousens S, Modell B, Lawn J. Folic acid to reduce neonatal mortality from neural tube disorders. Int J Epidemiol. 2010;39(Suppl 1):i110-21.
20. Lennon CA, Gray DL. Sensitivity and specificity of ultrasound for the detection of neural tube and ventral wall defects in a high-risk population. Obstet Gynecol. 1999;94:562-6.

Cite this article as: Malik N, Singhal SR, Nanda S, Sirohiwal D, Dahiya P, Bharti A. Spectrum of prenatally diagnosed neural tube defects at a tertiary referral hospital in North India: a retrospective cohort study. Int J Contemp Pediatr 2020;7:2010-4.