The range of neural tube defects in southern India

M L KULKARNI, M A MATHEW, AND V REDDY

Department of Paediatrics, Jagadguru Jayadeva Murughranjendra Medical College, Davangere, Karnataka, India

SUMMARY During a prospective study of 3500 consecutive births from November 1985 to January 1987 at three hospitals, 40 babies were found to have neural tube defects, an extremely high incidence (11.4/1000 births). The defects comprised anencephaly (n=18), meningomyelocele (n=11), Arnold-Chiari deformity (n=3), encephalocele (n=3), iniencephaly (n=2), and one each of occipital meningocele, spina bifida occulta, and anencephaly with rachischisis. There were significant differences in incidence between those with consanguineous and non-consanguineous parents and those whose mothers had previously given birth to malformed infants or who had had miscarriages, and those who had not. Significantly more defects were found among stillborn and low birthweight babies, among girls, and among those whose mothers were aged between 20 and 30 years. Just over a third (14) were breech presentations, and hydramnios was present in 16 (40%).

The incidence of neural tube defects varies not only from country to country but also from region to region within a country.¹ We showed in a preliminary study that the incidence in this area was 11/1000 births, an extremely high figure.² We therefore undertook the present larger study to find out the incidence and type of neural tube defects found in the area served by our three hospitals, and to look for possible aetiological factors.

Patients and methods

Three thousand five hundred consecutive live and stillbirths took place at three hospitals between November 1985 and January 1987. They were

examined within 24 hours of birth for evidence of neural tube defects. Mothers were questioned about their obstetric history, parental consanguinity, and socioeconomic class. Social class was graded according to the classification of Prosod³; classes I and II were upper class, class III middle class, and classes IV and V lower class. Nearly half the births in the area took place at these three hospitals, and the socioeconomic and religious groupings were comparable with those of the total population of the area.

Necropsies were carried out on all babies who were stillborn with neural tube defects, and on those that were born alive but subsequently died.

The χ^2 test was used for statistical analysis.

Table 1 *Number and incidence of neural tube defects*

Defect	No of boys	No of girls	Total No (%)	Incidence/1000 births
Anencephaly	8	10	18 (45.0)	5.10
Meningomyelocele	4	7	11 (27.5)	3.12
Iniencephaly	2	0	2 (5.0)	0.57
Encephalocele	0	3	3 (7.5)	0.85
Arnold-Chiari deformity	2	1	3 (7.5)	0.85
Occipital meningocele	1	0	1 (2.5)	0.28
Spina bifida occulta	0	1	1 (2.5)	0.28
Anencephaly with rachischisis	0	1	1 (2.5)	0.28
Total	17	23	40 (100.0)	11.4

Results

A total of 40 babies were born with neural tube defects (table 1). Thirty three of the babies were born to the group of 2685 Hindu mothers and seven to the 815 Moslem mothers (incidence 11.5/1000 compared with 8.1/1000, NS). The differences in incidences among the social classes were not significant (26 of 2068, 11.2/1000 being in the lower class, 14 of 1326, 10.5/1000 in the middle class, and none in 106 in the upper class). To find out if there was any seasonal variation we analysed only those births in the calendar year 1986; no significant differences were found. The association between consanguinity and incidence is shown in table 2. The incidence was 20.6/1000 among consanguineous parents compared with 8.4/1000 among non-consanguineous parents ($p<0.01$), but there were no significant differences among the types of consanguineous marriage. The associations between incidence and maternal age and parity are shown in tables 3 and 4, respectively.

Sixteen (40%) of the babies with neural tube defects had a history of hydramnios, including 13 (72%) of those with anencephaly. Seven of the 40 mothers (17.5%) had had previous miscarriages compared with 291 of 3460 mothers (8.4%) who had babies who did not have neural tube defects ($p<0.05$). Ten of the 40 had previously given birth to malformed babies compared with 258 of the remaining 3202 ($p<0.001$).

Fourteen (35%) were breech presentations; these were all anencephalic. Two babies were delivered by caesarean section (one with iniencephaly and one with spina bifida); the remainder were vertex presentations. Twenty three of the 40 were girls but the difference between the sexes was not significant; there were, however, more girls with both anencephaly and spina bifida (table 1). Four of the babies weighed less than 1000 g (incidence 95.2/1000), 27 weighed between 1000 and 2500 g (incidence 30.4/1000), and only nine weighed more than 2500 g (incidence 3.5/1000) ($p<0.001$).

Thirty babies with neural tube defects (75%) died in the perinatal period, which included all those with

Table 3 Association between maternal age and incidence of neural tube defects

Age of mother (years)	No of mothers	No of neural tube defects	Incidence/1000 births
<20*	824	4	4.8
20-30*	2152	33	10.6
>30	524	3	5.5
Total	3500	40	11.4

* $p<0.05$.

Table 4 Association between parity and incidence of neural tube defects

Parity	No of mothers	No of neural tube defects	Incidence/1000 births
One	1258	15	11.9
Two	986	10	10.1
Three	644	7	10.8
Four	426	5	11.2
Five or more	186	3	16.1
Total	3500	40	11.4

anencephalus, encephalocele, iniencephaly, and Arnold-Chiari deformity, as well as two of the 11 with meningomyeloceles. The perinatal mortality from other causes could not be ascertained because of our practice of early discharge. In addition, follow up facilities were poor.

Discussion

The incidence of neural tube defects of 11.4/1000 births is higher than previously reported from India.⁴⁻⁶ In Delhi the incidence was 8.7/1000,⁴ in Agra 6.25/1000,⁵ and in Chandigarh 8.8/1000.⁶ These figures are comparable with those reported from Belfast and south Wales in 1966.⁷ In contrast to the high incidence in India, however, many

Table 2 Association between consanguinity and incidence of neural tube defects

	Consanguineous				Non-consanguineous	Total births
	Uncle/niece	First cousin	Beyond first cousin	Total		
No of mothers	486	325	61	872	2628	3500
No of neural tube defects	10	7	1	18	22	40
Incidence/1000 births	20.6	21.5	16.4	20.6	8.4	11.4

western countries (for example, the United States and Scotland) are reporting downward trends.^{8,9} The reasons for this are probably the difference in the general health of the populations, and the widespread prenatal screening and termination of affected pregnancies in those countries.¹⁰

The significantly higher incidence in consanguineous families suggests that there may be a genetic component to the aetiology; similar observations have been reported from Bombay,⁷ Iran,¹¹ and Alexandria⁷ where the incidence was 14.2 when the parents were first cousins or closer, 8.6/1000 when they were related to a lesser degree than first cousin, and 5.7/1000 when they were not related. The incidence in our series is shown in table 2, but the differences between the consanguineous groups was not significant. In three states in southern India (including Karnataka) inbreeding has been practised for more than 2000 years¹² and so genetic factors may also be important among non-consanguineous couples.

Previous miscarriages, stillbirths, and births of malformed babies were significantly commoner in our series among mothers who gave birth to babies with neural tube defects. Previous reports have shown similar findings.^{13,14} It has been suggested that neural tube defects are more common if miscarriages or stillbirths occur just before the proband, but we have no data about this in our study.¹⁵ Again genetic factors have been mentioned as causing repeated pregnancy losses in both animals and humans, though their exact nature has not been specified.^{16,17}

Reports from Britain have mentioned associations between the occurrence of neural tube defects and season of the year and social class,¹⁸⁻²¹ but we found no such associations. Reports concerning the incidence of such defects and maternal age and parity are conflicting¹⁵; we found significantly more defects in babies whose mothers were in the age group 20 to 30 years; parity however, did not exert a significant effect in our series. In addition, and contrary to accepted teaching, we found that babies with anencephaly tended to have low birth weights.

There was a wide range of associated defects, the most common being talipes equinus, which was present in eight babies (20%). Other reported defects include club foot; congenital dislocation of the hips; flexion contractures; arthrogryposis; abnormalities of the spine, ribs, and sternum; and adrenal and lung hypoplasia.²² The incidence of these varies among series from as low as 6.5% to as high as 40% depending on the method of diagnosis.¹⁵ Other associated deformities may include omphoceles, diaphragmatic hernias, and facial clefts, as well as renal agenesis and cardiovascular abnor-

malities.²³ Five of our babies had cleft palates (12.5%), which is lower than the figure quoted by Martin *et al.*²⁴

There is obviously a complex interaction of genetic and other factors in the aetiology of neural tube defects,²⁵ and our results suggest that in our highly inbred population the genetic factors are probably the most important.

References

- 1 Verma IC. High frequency of neural tube defects in North India. *Lancet* 1978;i:879.
- 2 Kulkarni ML, Mathew MA, Ramchandran B. High incidence of neural tube defects in South India. *Lancet* 1987;i:1260.
- 3 Prosad BG. Changes proposed in the social classification of Indian families. *J Indian Med Assoc* 1970;55:198-9.
- 4 Ghosh S, Bali L. Congenital malformations in the newborn. *Indian Journal of Child Health* 1963;12:448-52.
- 5 Kalra A, Kalra K, Sharma U, Singh M, Dayal RS. Congenital malformations. *Indian Pediatr* 1984;21:945-50.
- 6 Saifullah S, Chandra RK, Pathak IC, Dhali GI. Congenital malformations in new born—a prospective longitudinal study. *Indian Pediatr* 1967;4:251-61.
- 7 Stevenson AC, Johnston HA, Steward MIP, Golding DR. Congenital malformations—a report of a study of series of consecutive births in 24 centres. *Bull WHO* 1966;34 (suppl): 1-127.
- 8 Windham GC, Edmonds LD. Current trends in the incidence of neural tube defects. *Pediatrics* 1982;70:333-7.
- 9 Carstairs V, Cole S. Spina bifida and anencephaly in Scotland. *Br Med J* 1984;289:1182-4.
- 10 Seller MJ. Unanswered questions on neural tube defects. *Br Med J* 1987;294:1-2.
- 11 Naderi S. Congenital abnormalities in newborns of consanguineous and nonconsanguineous parents. *Obstet Gynecol* 1979; 53:195-9.
- 12 Sastri KAN. *A history of South India from prehistorical time to the fall of Vijayanagar*. Madras: Oxford University Press, 1955.
- 13 WHO Scientific group on genetic factors in congenital malformations. Genetic factors in congenital malformations. *WHO Tech Rep Ser* 1970;438:17-27.
- 14 Clarke C, Hobson D, McKendrick OM, Rogers SC, Sheppard PM. Spina bifida and anencephaly: miscarriage as possible cause. *Br Med J* 1975;iv:743-6.
- 15 Alasdair-Hunter GW. Neural tube defects in eastern Ontario and western Quebec. Demography and family data. *Am J Med Genet* 1984;19:45-63.
- 16 Simmons JF, Tunis S, Jackson D, Wapner RJ, Jackson L. Factors related to subsequent reproductive outcome in couples with repeated pregnancy loss. *Am J Med Genet* 1984;18:407-11.
- 17 Reame NE, Hafez ESE. Hereditary defects affecting fertility. *N Engl J Med* 1975;292:675-81.
- 18 Renwick JH. Hypothesis: anencephaly and spina bifida are usually preventable by avoidance of a specific but unidentified substance present in certain potato tubers. *British Journal of Preventive and Social Medicine* 1972;26:67-88.
- 19 Granroth G, Hakma M, Saxon L. Defects of the central nervous system in Finland. I. Variations in time and space, sex distribution and parental age. *British Journal of Preventive and Social Medicine* 1977;31:164-70.
- 20 Fredrick J. Anencephaly in Scotland 1961-72. *British Journal of Preventive and Social Medicine* 1976;30:132-7.
- 21 Elwood JH, Navin NC. Factors associated with anencephalus and spina bifida in Belfast. *British Journal of Preventive and Social Medicine* 1973;27:73-80.

- ²² Khoury MJ, Erickson JD, James LM. Etiologic heterogeneity of neural tube defects: clues from epidemiology. *Am J Epidemiol* 1982;**115**:538-48.
- ²³ Czeizel A. Schisis association. *Am J Med Genet* 1981;**10**:25-35.
- ²⁴ Martin RA, Fineman RM, Jorde LB. Phenotypic heterogeneity in neural tube defects—a clue to causal heterogeneity. *Am J Med Genet* 1983;**16**:519-25.
- ²⁵ Borman BG, Howard KJ, Chapman CJ. Secular trends in anencephalus prevalence in New Zealand. *NZ Med J* 1986;**99**: 183-5.

Correspondence and requests for reprints to Dr M L Kulkarni, Sriram Prasad, P J Extension, Davangere 577004, Karnataka, India.

Accepted 26 August 1988