Congenital anomalies in rural black South African neonates — a silent epidemic?

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Study objective. To ascertain the incidence and spectrum of congenital anomalies in neonates born in a rural hospital.

Design. This was a prospective, hospital-based study, undertaken on liveborn neonates over the period 12 June 1989 - 31 December 1992.

Setting. Mankweng Hospital, Sovenga, Northern Transvaal.

Main results. Of a total of 10 380 neonates born during this period, 7 617 (73,4%) were examined within the first 24 hours of life. On the basis of published observations, only 26,2% of severe congenital anomalies diagnosable by age 5 years are diagnosable at birth. In this South African study the finding at birth of severe, externally visible congenital anomalies in 14,97 per 1 000 livebirths could mean that by age 5 years the minimum cumulative incidence of severe congenital anomalies may involve 57,14 per 1 000 children. Extrapolating from other Third-World studies, the cumulative incidence of severe congenital anomalies in such communities may affect up to 84,85 per 1 000 children by the age of 5 years.

High incidences of neural tube defects (3,55 per 1 000 livebirths) and Down syndrome (2,10 per 1 000 livebirths), both conditions which can be prevented by prenatal screening, were recorded.

Conclusions. These figures indicate the necessity for inclusion of appropriate prenatal, genetic, family planning and paediatric facilities into the primary health care delivery system of rural areas, to manage such problems and to initiate programmes to reduce the incidence of selected congenital anomalies such as Down syndrome and neural tube defects.

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Congenital anomalies have recently been demonstrated to represent an increasingly significant component of child health care and the right to be healthy.[1] The World Health Organisation has indicated the necessity to evaluate the potential burden of congenital anomalies in every country, at whatever stage of development, with a view to introducing preventive measures at the appropriate time.[2]

Congenital anomalies affect 1 - 5% of liveborn infants. Major malformations resulting in chronic handicap or requiring surgery are present in approximately 2%.[3] It is accepted that the incidence of birth defects varies according to the geographical, socio-economic and ethnic characteristics of the population.[4,5]

Although the black people of South Africa constitute 74% of the total population,[6] limited information is available regarding the incidence of congenital anomalies in this population group. Reported studies were retrospective, restricted to one or a few specific congenital anomalies, or undertaken in urban populations.[7-9] Studies on black African populations in other countries south of the Sahara are also limited, owing to small sample sizes.[10,11] A more comprehensive 3-year prospective study on congenital anomalies in urban black South African neonates has recently been completed by Delport *et al.*[12]

To our knowledge, no data exist on the incidence of congenital anomalies in a black African rural population. We report the results of a study initiated to evaluate the potential burden of congenital anomalies in a rural area. Such information would be required for the planning of future prenatal, genetic and paediatric services and to compare the South African rural situation with findings of other First- and Third-World studies.

Patients and methods

This study was carried out in the newborn nursery and the postnatal wards of the hospital, between 12 June 1989 and 31 December 1992. Mankweng Hospital has 800 beds and serves a large rural black community; it is situated 30 km to the east of Pietersburg, the nearest city, in the north of South Africa. Only 400 of the available beds are utilised owing to lack of both financial resources and medical manpower. No medical specialists are employed full-time at the hospital, which is run entirely by medical officers and nursing staff. The maternity unit is open to all women who wish to deliver there, and there are no restrictions regarding admission. Because of the location of the hospital, almost all the women who deliver at the hospital are indigenous Northern Sotho. The Mankweng district is in one of the poorer areas of South Africa.

Of the 10 380 liveborn infants delivered at the hospital during the study period, 7 617 (73,4%) were examined by a senior nursing sister in the maternity unit (C.M.H. or M.P.M.), in conjunction with P.A.V., a medical genetic scientist. On a daily basis all liveborn infants, including neonatal deaths, delivered in the hospital during the preceding 24 hours were examined. The nursing staff had been trained by the Genetic Services Division, Department of National Health and Population Development (DNHPD). The examinations were undertaken by observation, palpation and measurement of the newborns, in accordance with the guidelines for assessment of infants and children taught by the Genetic Services Division, DNHPD, and outlined in a document prepared by the Division (M. M. Nelson — personal communication). The remaining 2 763 infants (26,6%) were not examined because the examiners were not available during their first 24 hours of life. All infants considered to have an abnormality were reviewed by the paediatric medical officer on duty, appropriate investigations and management were undertaken, and the diagnosis was recorded.

In cases in which a diagnosis could not be made, the clinical details and results of investigations, including biological specimens, radiographs and photographs, were referred to two of the authors (G.S.G. and A.L.C., both clinical geneticists working in the Human Genetics Department at the University of Pretoria, 250 km distant from the site of survey) for evaluation and diagnosis. Diagnoses were further recorded and confirmed whenever possible at genetics outreach clinics conducted by one or both of these authors at Mankweng Hospital. Alternatively, if more immediate management was required the infant was referred to GaRankuwa Hospital, the academic hospital attached to the Medical University of South Africa (MEDUNSA). The genetics clinic at this institution had been managed by G.S.G. or A.L.C. during this period. Wherever possible, diagnoses from these infants were obtained and incorporated into the results.

The number of infants delivered at Mankweng Hospital during the period of the survey was confirmed by examination of the maternity ward register, and the number of infants examined (7 617) was derived from the total of infants examined and recorded daily by one of the authors (P.A.V.) and the examining nursing sister. Infants, including abnormal neonates, born on the days when no infants were examined were not included in the study results. Similarly, those born before arrival at the hospital were excluded.

For the purposes of this study, a congenital anomaly was defined as any gross developmental defect apparent on inspection at the time of birth, or within the first few weeks of life.[13] If more than one system was affected with a congenital anomaly a composite diagnosis was made where possible; if not, the infant was classified as having a multiple congenital abnormality (MCA). Thus each affected infant was recorded only once.

Results

During the 3½-year study period, a total of 10 380 liveborn infants were delivered at the hospital and 7 617 (73,4%) were examined. In 234 infants congenital anomalies were recorded, giving a total incidence of congenital anomalies in the infants examined of 30,72 per 1 000 livebirths. However, 118 of these anomalies (15,49 per 1 000 livebirths) were postminimus polydactyly, a condition of no clinical significance to the patient. When postminimus polydactyly was excluded from the results, 116 infants (15,23 per 1 000 livebirths) with congenital anomalies were examined.

The individual conditions recorded, and their incidence per 1 000 livebirths, are listed in Table I.

Table I. Birth defects in systems with incidence per 1 000 livebirths in 7 617 neonates

System/condition	No.	Incidence per 1 000 livebirths
Musculoskeletal system	142	18,64
Polydactyly (postminimus)	118	15,49
Talipes equinovarus	19	2,50
Limb reduction anomalies	2	0,26
Klippel-Trenaunay-Weber syndrome	2	0,26
Torticollis	1	0,13
Central nervous system	33	4,33
Anencephaly	13	1,71
Spina bifida (with and without hydrocephalus)	12	1,58
Encephalocele	2	0,26
(Combined neural tube defects)	(27)	(3,55)
Hydrocephalus	4	0,53
Microcephalus	2	0,26
Chromosomal	21	2,75
Down syndrome	16	2,10
Trisomy 18 translocation	1	0,13
Trisomy 13	1	0,13
Other chromosomal abnormalities	3	0,39
Urogenital system	10	1,31
Hypospadias	6	0,79
Undescended testes	4	0,52
Gastro-intestinal system	9	1,18
Exomphalos	3	0,39
Cleft lip/palate	3	0,39
Anorectal stenosis/atresia	2	0,26
Oesophageal stenosis/atresia	1	0,13
Multiple congenital abnormalities	9	1,18
Mendelian inheritance	5	0,66
Albinism	5	0,66
Integument	2	0,26
Ichthyosis	1	0,13
Neurocutaneous melanosis	1	0,13
Other	3	0,39
Cystic hygroma	2	0,26
Cyst in neck	1	0,13
Total	234	30,72

The central nervous system (CNS) was the system most frequently affected. Thirty-three infants (4,33 per 1 000 livebirths) were recorded and these included 13 (1,71 per 1 000 livebirths) with anencephaly, 12 (1,58 per 1 000 livebirths) with spina bifida, with or without hydrocephalus, and 2 (0,26 per 1 000 livebirths) with encephaloceles. The combined number of neural tube defects (NTDs) was 27 (3,55 per 1 000 livebirths). Hydrocephalus in isolation (0,53 per 1 000 livebirths) and microcephalus (0,26 per 1 000 livebirths) were the other CNS conditions recorded.

Congenital anomalies of the musculoskeletal system, postminimus polydactyly excluded, were the second most common recorded. These accounted for 24 cases (3,14 per 1 000 livebirths), the most frequent of which were 19 cases (2,50 per 1 000 livebirths) of talipes equinovarus, the second-commonest of all individual diagnoses.

There were 21 proven chromosomal disorders (2,75 per 1 000 livebirths), of which Down syndrome was the diagnosis in 16 cases (2,10 per 1 000 livebirths). The other chromosomal disorders included a trisomy 13, a trisomy 18 translocation and 3 cases of complex chromosomal rearrangement in infants with congenital anomalies. Fifteen of the infants with Down syndrome had trisomy 21 and the 16th had a 21:21 translocation. The ages of the mothers of the Down syndrome infants ranged from 18 years to 44 years, with a mean of 36 years; 9 of the mothers (56,25%) were 35 years of age or older, and 7 (43,75%) were 40 years of age or older.

Malformations of the urogenital and gastro-intestinal systems affected 10 (1,31 per 1 000 livebirths) and 9 (1,18 per 1 000 livebirths) infants respectively. There were 9 (1,18 per 1 000 livebirths) MCAs including 2 in which diagnoses of trisomy 13 and trisomy 18 were suspected clinically but not confirmed cytogenetically because the lymphocyte culture failed to show growth. Follow-up chromosomal analyses could not be obtained. Albinism represented the second most common condition after postminimus polydactyly, with a clear Mendelian pattern of inheritance. There were 5 cases, giving an incidence of 0,66 per 1 000 livebirths.

Postminimus polydactyly was the commonest individual anomaly recorded, with 118 cases (15,49 per 1 000 livebirths) reported. It was seen in 36 (30,5%) cases on the left hand, in 9 (7,6%) on the right hand and in 73 (61%) on both hands. These cases were all considered trivial according to the definition of Christianson *et al.*[4]

Discussion

The total incidence of congenital anomalies in the infants examined in this study was 30,72 per 1 000 livebirths. When postminimus polydactyly was excluded, the incidence of those anomalies remaining was 15,23 per 1 000 livebirths. All but 2 of these diagnoses could be regarded as severe according to the definition of Christianson *et al.*,[4] giving an incidence of severe congenital anomalies of 14,97 per 1 000 livebirths.

Comparison of the incidences of congenital anomalies in different reports is fraught with problems. This is particularly true when considering our study, in which the infants were examined by a nursing sister (C.M.H. or M.P.H.) with basic training in clinical genetic examination, in conjunction with a medical genetic scientist (P.A.V.). The examinations were by measurement, palpation and observation of the infant. The examiners saw only those liveborn infants present on the wards (and the neonatal deaths) delivered in the preceding 24 hours; infants not examined during that period because a sister or P.A.V. was not available were excluded. All infants and their mothers considered to be well 24 hours after delivery were discharged according to hospital policy. Given

these circumstances, it can be appreciated that mainly severe congenital anomalies were diagnosed.

The incidence of severe congenital anomalies (14,97 per 1 000 livebirths) was based on 114 patients. However, only 23 individual diagnoses constituted these 114 cases.

The incidences of severe congenital anomalies diagnosed at birth in a First-World study from the USA[4] were 12,0 and 10,2 per 1 000 livebirths for white and black children, respectively. Third-World studies report an incidence of severe congenital anomalies in Abu Dhabi of 12,95 per 1 000 livebirths[14] and in Nairobi of 11,60 per 1 000 livebirths.[10] The latter figure was derived from the results reported in that paper by identification of the severe congenital anomalies in liveborn infants. In Singapore[15] the incidence of moderate and severe congenital anomalies was shown to be 15,13 per 1 000 livebirths. If the figures from Uganda reported by Simpkiss and Lowe[11] are revised to ensure that only severe congenital anomalies in liveborn infants are considered, their recorded incidence of 14,5 per 1 000 livebirths is similar to our findings. The incidence of severe congenital anomalies diagnosed from a study in rural India[16] was 20,6 per 1 000 births, and that in Tunis 22,23 per 1 000 livebirths (calculated from the results of a study documented by Khrouf *et al.*[17]). Only one comparable study in an urban academic hospital[12] has been reported in South Africa; the total incidence of congenital anomalies reported was 11,87 per 1 000 livebirths.

All the above investigations, in both First- and Third-World countries, were performed in hospitals by specialists. This would ensure greater ascertainment of cases than was possible in the Mankweng Hospital survey. Our figure of 14,97 per 1 000 livebirths is therefore considered to be the minimum incidence of severe congenital anomalies diagnosable within the first 24 hours of life.

In their study, Christianson *et al.*[4] showed that the severe congenital anomalies diagnosable at birth in black infants represented 40% of the total severe congenital anomalies diagnosable by 1 year of age and 26,2% of those diagnosable by 5 years of age. The figures for white infants in the same study were comparable, being 46,3% and 28,9% by 1 and 5 years of age, respectively.

The concept that congenital anomalies diagnosable at birth represent the 'tip of the iceberg' has been validated further by the studies of Lumley *et al.*[18] and Van Regemorter *et al.*[19] If the iceberg concept is accepted and the figures for severe congenital anomalies in black infants published by Christianson *et al.*[4] are utilised, it can be calculated, extrapolating from the figure of 14,97 severe congenital anomalies per 1 000 livebirths recorded in our study, that 37,43 severe congenital anomalies per 1 000 livebirths could be diagnosed by 1 year of age and 57,14 per 1 000 livebirths by 5 years of age (Fig. 1). If the same extrapolation is calculated using the incidence of severe congenital anomalies documented in the first 24 hours of life in Tunis (22,23 per 1 000 livebirths) by Khrouf *et al.*,[17] a cumulative incidence of 84,85 per 1 000 livebirths could be expected by 5 years of age (Fig. 1). From the description given, the population studied in Tunis[17] was similar to that in the Mankweng area, in that they were both underdeveloped Third-World communities in which consanguinity was practised.

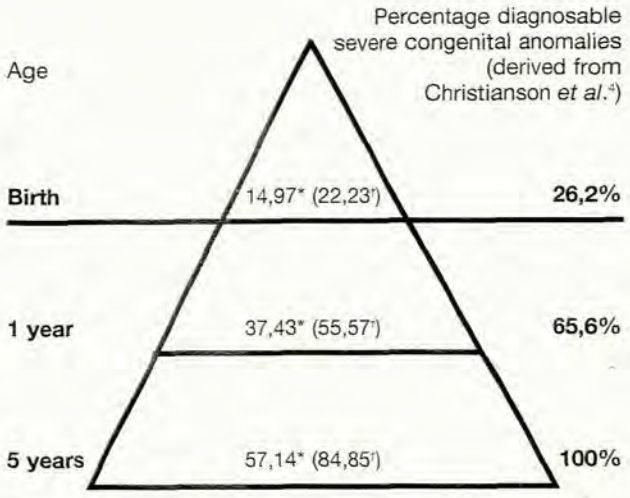

Fig. 1. Congenital anomalies iceberg (* = derived from present study; † = derived from Khrouf *et al.*[17]).

For the reasons described above, the incidence of congenital anomalies in the Mankweng rural area could be considered significantly higher than in many other First- and Third-World countries,[4,10-12,14,15] except India[16] and Tunisia[17] where the findings derive from similarly poor socio-economic communities. The existence of a high incidence of severe congenital anomalies in rural black neonates (14,97 per 1 000 livebirths) and not in urban black neonates (11,87 per 1 000 livebirths)[12] has hitherto not been recognised in South Africa. Furthermore, the cumulative incidence of severe congenital anomalies may be much higher than previously described in the First World.[4] This cumulative incidence of severe congenital anomalies may not have been recognised previously because the prevalence of congenital anomalies in this situation has not been researched, medical expertise and facilities for diagnosing the conditions are not available, and many of the afflicted individuals die as a consequence of their congenital anomalies; however their deaths are absorbed into the general statistics related to infectious diseases and malnutrition, and therefore remain unrecognised for what they truly represent.[20]

According to the Mankweng Hospital survey, the greatest number of congenital anomalies occurred within the central nervous system. This was similar to the Pretoria urban study.[12] The incidence of NTDs was 3,55 per 1 000 (or 1 in 282) livebirths; this figure is higher than previously recorded incidences of NTDs in urban black populations in South Africa.[7] However, an even higher incidence of NTDs, 6,13 per 1 000 livebirths, has been reported in a rural black Xhosa population in Transkei.[8] In contrast, the incidence of NTDs in the Cape Town black population, which mainly consists of Xhosa people from Transkei, was reported in two previous papers[21,22] to be 0,55 and 1,03 per 1 000 livebirths. The difference is of major interest. The same discrepancy emerges when comparing our rural study and the urban findings from Pretoria[12] and from Johannesburg.[7]

The high incidence of NTDs in the rural areas is possibly related to environmental factors. Sixty per cent of pregnant women living approximately 150 km from Mankweng Hospital in circumstances similar to the mothers in the present study have been shown to be folate-deficient.[23] Folate deficiency may therefore in part be responsible for the high NTD incidence in the Mankweng area. Further investigation is required to confirm the high NTD incidence in this and other rural areas of South Africa, to reveal the underlying aetiological factors, and to determine practical solutions to the problem. Evidence that folic acid supplementation can significantly reduce NTD recurrence and occurrence[24,25] gives renewed impetus to the previous recommendation that maize meal, the staple diet of the majority of people in South Africa, be supplemented with folic acid.[23]

Penrose[26] noted that anencephaly appeared to be uncommon in black African populations. At Mankweng Hospital, anencephaly was the most frequently observed NTD (1,71 per 1 000 livebirths), ahead of spina bifida (1,58 per 1 000 livebirths). In rural Transkei the incidence of anencephaly was similarly high, but spina bifida was more common than anencephaly.[6]

Hydrocephalus, a problem previously reported as common in the black population of South Africa,[7] was seen in 4 cases (0,53 per 1 000 livebirths). This figure is comparable to that reported by Delport *et al.*[12] However, it is accepted that the ascertainment of these cases could have been limited, because diagnosis was based only on observation and skull circumference measurement.

Talipes equinovarus was the commonest severe individual condition recorded (2,50 per 1 000 livebirths). This figure is higher than that reported by Delport *et al.*[12] and Kromberg and Jenkins,[7] but is comparable to a figure reported by Pompe van Meerdervoort[9] (3,50 per 1 000 livebirths) in a study of musculoskeletal malformations in black South Africans.

Down syndrome has in the past been considered uncommon in the black population in Africa. More recently Delport *et al.*[12] reported a figure of 1,33 per 1 000 livebirths and Kromberg *et al.*[27] 1,67 per 1 000 livebirths. The incidence in our study (2,10 per 1 000 livebirths) is high, but an incidence of 2,4 per 1 000 has been recorded previously.[28] The high incidence in our study (2,10 per 1 000 livebirths) is possibly due to a high ascertainment of cases, and the relatively high number of childbearing women of advanced maternal age in this area.

Since Down syndrome has not previously been recognised as a problem in the black population in South Africa, there are a limited number of designated facilities in the country for counselling black women of advanced maternal age, and similarly limited facilities for prenatal diagnosis and management. This is confirmed by Kromberg *et al.*[27] who recorded that in 1990 only 5% of amniocenteses performed in Johannesburg were on black women, who, however, comprised 90% of the pregnant population. These statistics highlight the urgent need for establishment of appropriate family planning, prenatal, genetic and paediatric services to address the problem.

The 9 MCA cases (1,18 per 1 000 livebirths) were possibly a reflection of the nursing and medical staff's inexperience in assessing infants with genetic syndromes.

Five patients with oculocutaneous albinism were diagnosed, giving an incidence of 0,66 per 1 000 livebirths (1 in 1 515 births). This figure is significantly higher than the national prevalence of 1 in 3 900 for oculocutaneous albinism reported by Kromberg *et al.*[29] However, it is comparable to the 1 in 2 041 prevalence documented in the Southern Sotho people.[29]

No cases of congenital heart disease were diagnosed in this study, since the examinations were only by measurement, observation and palpation of the infants. Delport *et al.*[12] reported an incidence of congenital heart disease of 1,79 per 1 000 livebirths in black neonates in Pretoria. Congenital heart anomalies were one group of conditions which, because they were not diagnosable, ensured reduced ascertainment of all severe congenital anomalies in our study. This was one of the limitations imposed on this study by the limited medical and nursing staff and facilities at Mankweng Hospital. The authors are cognisant of the fact that the study has several other limitations that may have caused bias in the results obtained. These include the fact that the study was hospital-based, the relatively small number of neonates examined (7 617), and the fact that these represented only 73,4% of all neonates delivered in the hospital during the study period. By ensuring that only liveborn infants and neonatal deaths delivered in the hospital in the preceding 24 hours were examined and included in the statistics it was hoped that bias from the latter source would be reduced to a minimum.

Conclusion

The high incidence (14,97 per 1 000 livebirths) of a relatively few severe congenital anomalies recorded in this study, and the estimation that by 5 years of age the cumulative burden of severe congenital anomalies could be from 57,14 to 84,85 per 1 000 livebirths, suggest a hitherto unrecognised silent congenital epidemic in this rural area. However, we propose that this situation may be common to other rural areas of South Africa and Africa south of the Sahara. Czeizel[30] has recently established that the incidence of major congenital anomalies is significantly reduced in women who take periconceptual multivitamin supplements. The converse of this finding could be that women who are malnourished are at greater risk of having an infant with a major congenital anomaly; our study appears to indicate this, most markedly in respect of neural tube defects. We therefore propose that the underlying cause for this silent epidemic of congenital anomalies, could in part be the poor socio-economic status of the population and the deficient health care facilities available in this area.

The consequences for infant mortality and morbidity of the recorded high incidence of congenital anomalies in this rural South African environment have still to be elucidated by ongoing research. The economic sequelae of this situation can be extrapolated from figures published in 1983 by the Committee for the Year of the Disabled.[31] It was estimated in 1983 that R1 billion was spent on the

management of congenital/genetic conditions. In the same year only R112 million was spent on tuberculosis. Since 1983, these figures will have quadrupled owing to the effects of inflation.

This study helped expedite the establishment of a clinical genetics outreach programme in the area. It is hoped that the information derived from the study will stimulate further research in this field, and that it could be utilised for the planning and provision of future family planning, genetic, paediatric and prenatal services, and give impetus to the initiation of specific programmes to reduce selected common congenital anomalies such as Down syndrome, NTDs and congenital hydrocephalus.

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