Down syndrome in black South African infants and children — clinical features and delayed diagnosis

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Study objective. Down syndrome (DS), the commonest cause of congenital developmental disability in developed countries, has only recently been shown to have an incidence in black South African neonates as high, and in some studies higher, than currently seen in First-World nations. It has also been reported that the mothers of black African DS newborns and medical and nursing staff have difficulty recognising and diagnosing DS in black neonates. The aims of this study were to document the clinical features of black DS infants and children, compare these to the features of previously documented DS infants and children from other ethnic groups, and finally to ascertain if and for how long the difficulties recorded in diagnosing DS in blacks extended into infancy or childhood.

Design. This was a prospective, genetic clinic-based study, entailing clinical evaluation of black DS infants and children 3 months of age and older, and the administration of a questionnaire to the mothers of these patients.

Setting. Genetics clinics at Kalafong and Ga-Rankuwa hospitals, Pretoria, and at Mankweng, Siloam, Groothoek, Nkhensani and Elim hospitals in the Northern Province.

Main results. Fifty-five DS infants and children were assessed. Their clinical features were comparable to those of children from other ethnic groups. Congenital heart disease (CHD) was recorded in a significantly higher percentage of infants under 12 months of age (51.9%) than children 13 months of age or older (25%). Only 9 (16.4%) of these DS patients were clinically diagnosed in the neonatal period, and a further 18 (32.7%) at between 1 and 6 months of age. More than half (28 or 50.9%) were 7 months of age or older when initially clinically diagnosed. Maternal self-initiated awareness of a problem with their infant or child preceded clinical diagnosis in 32 (58.2%) patients.

Conclusions. The difficulties experienced by medical and nursing staff in diagnosing DS in black neonates extends into infancy and childhood, despite the fact that the clinical features of black DS infants and children do not differ from those seen in DS patients in other ethnic groups. The prevalences of CHD in black DS infants and children suggest that CHD is a significant cause of mortality in black DS patients.

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Down syndrome (DS), the commonest cause of congenital developmental disability in First-World nations, had until 1982 been considered rare in black African populations.[1,2] Prior to Adeyokunnu's[2] documentation in a retrospective study of an incidence of DS in Nigerian neonates of 1.16 per 1 000 births, reports of DS in sub-Saharan Africa had largely been limited to case reports and observations of cases of DS in studies of the incidence of congenital anomalies. Indeed, before Luder and Musoke's[3] first documentation of DS in black children in 1955, no less an authority than Jelliffe[4] had commented on the apparent rarity of DS in black people. The incidence of DS in black South African neonates has recently been shown to be as high as, and in some circumstances higher than, that occurring in other populations.[5-7]

In 1983 Mgone[8] documented the clinical features of black children with DS. More recently Christianson *et al.*[9] documented the features of black DS neonates in 1995, and after comparing these with those of normal black neonates and white normal and DS neonates, suggested reasons why the clinical diagnosis of DS in black neonates may be more difficult than in other ethnic groups. In addition, they observed that DS was not recognised as a specific entity in the black community they studied and that black mothers did not recognise that their DS newborn infants were different from their other infants.[10]

The aim of this study was to document the clinical features of black DS infants and children older than 3 months of age, and to compare these features to those of DS infants and children previously documented to ascertain whether these features differed significantly from black DS neonates and DS children of other ethnic groups. In order to ascertain if and for how long the difficulties in diagnosing black DS children continued, mothers of the DS infants and children were questioned as to how and when their child's diagnosis had been made.

Materials and methods

The subjects were 55 black African children and infants over 3 months of age with cytogenetically confirmed DS, and their mothers, seen between February 1993 and February 1995 at genetics clinics and in the paediatric wards at Kalafong and Ga-Rankuwa hospitals, Pretoria, and at genetic outreach clinics in hospitals in the rural Northern Province. All infants had been referred for clinical assessment and counselling of the parents.

As part of the clinical evaluation the patients' mothers were questioned by the author using a structured interview to collect biographical information, establish the infants' birth order, and ascertain when the mother first became

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aware that her child had a problem, who or what had alerted her to this, and if she considered her child's facial features to be different from those of other children. Furthermore, the mothers were questioned as to when the diagnosis of DS had first been confirmed and whether any counselling had been given. These interviews were carried out in the language of the mother's choice, either directly with the author in English or Afrikaans, or in her home language via an interpreter who was usually a nursing sister with specialised training in genetics.

A full history and examination of the patient were then undertaken. The presence of 20 clinical features of DS derived from Jones[11] were documented, as well as other clinical features considered to be significant. Thereafter, full genetic counselling of the parent(s) was undertaken if chromosomal confirmation of the diagnosis was available. Alternatively, the parent(s) were counselled about the clinical concern involving their infant or child and were then seen for follow-up counselling once the diagnosis had been cytogenetically confirmed.

The data on the subjects were tabulated, and the results obtained from an analysis of these.

Results

There were 55 DS infants and children, 30 (55%) boys and 25 (45%) girls, in the sample. The ages of the subjects ranged from 3 months to 12 years and 1 month, with 27 (49.1%) of the patients being infants (12 months of age or younger), and 28 (50.9%) being children (13 months of age or older). Cytogenetic analysis showed that in 52 (94.6%) patients the diagnosis was trisomy 21, in 2 (3.6%) patients a translocation involving chromosome 21 was present, and 1 (1.8%) patient had mosaic DS.

The maternal age at birth of their DS infant was known by 54 mothers. Thirty (54.5%) of the mothers were 35 years of age or older (of advanced maternal age (AMA)). The majority of the DS infants and children assessed were their mother's last-born child (48 or 87.3%), with 6 (10.9%) being the penultimate child born, and 1 (1.8%) the third child in a family of 6 children. Of the 7 patients who were not the last born, 5 were born to mothers of AMA. Only 8 (14.5%) of the DS infants and children were born to primiparous mothers, while 30 (54.5%) were the fourth child or more in birth order. Of the 30 DS infants and children who were fourth or more in birth order, 23 (76.6%) were born to mothers of AMA.

During the patients' post-delivery hospital stay, 15 (27.3%) of the DS infants' mothers became aware of a problem with their newborn. Nine (16.4%) were clinically diagnosed as having DS and the mothers were counselled. In the remaining 6, although the diagnosis of DS had not been contemplated, there was maternal self-initiated awareness of a possible problem. Three mothers noted that their infants looked different from other newborns, and 3 individual mothers were concerned as their infant had either a soft cry, a floppy neck or sucked poorly. Between 1 and 6 months of age a further 26 (47.3%) of the mothers became aware of a problem with their infant. Maternal self-initiated awareness of a problem preceded clinical diagnosis of DS in 18 cases. This awareness had been stimulated by the presence of floppiness, in particular head lag, and developmental delay in 14 patients, and the infant's recurrent infections (associated with congenital heart disease (CHD)) in 2 patients; 1 DS infant had nystagmus, and poor feeding with sucking difficulties were present in another. During the period 1 - 6 months of age, a clinical diagnosis was confirmed and the mother counselled in 18 (32.7%) cases. A further 14 DS patients were all 7 months or older when the mother first became aware that there was a problem. This was self-initiated and preceded clinical diagnosis in 8 mothers, with 6 patients being noted by the mother to have developmental delay; 1 infant had recurrent symptoms related to congestive cardiac failure (CCF), and 1 mother sought advice for her child's squint and associated poor vision. Initial clinical diagnosis of DS and maternal counselling thus occurred in 28 (50.9%) infants and children at 7 months of age or older.

Maternal self-initiated awareness of a problem with their infant or child preceded clinical diagnosis in 32 (58.2%) patients. This self-awareness was initiated by hypotonia (particularly head lag) and developmental delay in 21 (38.2%) patients, the child's appearance being different in 3 (5.5%) patients and symptoms related to CHD in 3 (5.5%) patients. Two (3.6%) patients had feeding difficulties, 2 patients (3.6%) had ocular signs (nystagmus and strabismus), and 1 patient had a soft cry.

On questioning, 31 (56.4%) of the mothers did not consider their DS infant or child's facies to look different from those of normal infants or children. Knowledge of the existence of DS as an entity prior to the diagnosis of DS in their child was confined to 4 (7.2%) parents in this study, a registered nursing sister, a nursing assistant, a hospital children's ward aid and a teacher. Frank denial of the diagnosis of DS post-examination and counselling was recorded in 7 (12.7%) mothers. Only 1 of these mothers, a nursing assistant, had any knowledge of DS prior to the birth of her affected infant.

The frequency of 20 clinical features of DS, derived from Jones,[11] are recorded in Table I and compared with the frequency of DS features previously documented in black neonates and neonates and children from other ethnic groups.[8,9,12,13]

There were 21 (38.2%) patients with clinical evidence of CHD, and 13 underwent full cardiological assessment including radiographs, ECG and ultrasonography. In the 8 patients in whom these investigations were not undertaken, a clinical cardiological diagnosis was made in 7 cases; the eighth was a boy who had previously undergone cardiac surgery and on whom no clinical information was available with regard to his cardiac diagnosis.

Of the 27 infants, 14 (51.9%) had CHD, including 6 who were in CCF. The heart defect was considered clinically significant and a cause of symptoms in 11 of these affected infants. By comparison, 7 (25%) of the 28 DS children had CHD, of whom only 1 (3.6%), aged 13 months, had CCF. One 10-year-old boy, who was asymptomatic, was the only infant or child to have undergone cardiac surgery. Three of the DS children had clinically significant CHD: 2 had endocardial cushion defects and 1 an atrial septal defect, ventricular septal defect and pulmonary hypertension. (Table II).

Other clinical features documented included a small penis in 16 (53.3%) and undescended testes in 3 (10%) of the boys, sparse hair in 16 (29.1%) patients, squint in 3 (5.5%)

Table I. Clinical features of DS infants and children, derived from Jones,[11] compared with other reported studies (%)

Clinical features	Present study Infants and children	Black children[5]	Black neonates[9]	Oriental children[12]	White neonates[13]
Craniofacial					
Flat facial profile	92.7	-	95.0	91.0	89.2
Flat nasal bridge	87.3	100.0	95.0	91.0	75.5
Brachycephaly	63.6	48.0	-	-	-
Flat occiput	72.7	-	30.0	59.0	-
Oblique palpebral fissures	81.8	100.0	82.5	61.0	73.0
Epicanthic folds	94.5	98.0	82.5	46.0	70.3
Dysplastic ears	43.6	40.0	55.0	-	62.2
Protruding tongue	45.5	84.0	37.5	21.0	80.1
Short neck	58.2	-	32.5	45.0	-
Excess neck skin	25.5	46.0	47.5	-	75.5
Speckled irides	0	0	0	02.0	5.0
Musculoskeletal					
Brachydactyly	83.6	78.0	-	60.0	-
Single palmar crease(s)	49.1	63.4	50.0	39.0	45.9
Single crease, 5th finger(s)	20.0	14.6	15.0	34.0	13.5
Clinodactyly	54.5	16.0	32.5	54.0	29.7
Sandal gap	41.8	66.0	55.0	55.0	32.4
Plantar crease	54.5	-	75.0	64.0	-
Central nervous system					
Developmental delay	100.0	?	-	?	-
Hypotonia	94.5	88.0	85.8	68.0	83.3
Hyperextensibility	94.5	-	90.0	80.0	-

Table II. Congenital heart defects seen in the DS infants and children

	Infants (*N* = 27), 3 - 12 months		Children (*N* = 28), 13+ months		Total (*N* = 55)	
Cardiac defect	No.	(%)	No.	(%)	No.	(%)
Confirmed ventricular septal defect	1	(3.7)	1	(3.6)	2	(3.6)
Clinical ventricular septal defect	5	(18.5)	2	(7.1)	7	(12.7)
Atrial septal defect	4	(14.8)	0	(0)	4	(7.3)
Endocardial cushion defect	3	(11.1)	2	(7.1)	5	(9.1)
Other	1	(3.7)	2	(7.1)	3	(5.5)
Total	14	(51.9)	7	(25)	21	(38.2)

patients, nystagmus in 1 (1.8%) patient and a cystic hygroma in the cheek of 1 (1.8%) patient. Five (9.1%) patients were seen while hospitalised with pneumonia, 3 of whom had concomitant CCF.

Discussion

A high incidence of DS has only recently been documented in black South African neonates. Despite this high incidence, DS has been shown not to be a recognised entity in the community studied, and a majority of the mothers of afflicted DS newborns did not distinguish their infants as looking or being different from normal newborns.[10] This inability of black African mothers to differentiate between DS neonates and normal neonates is also true for medical personnel. It is due partly to the overlap in craniofacial features between black DS and normal neonates, making the diagnosis of DS more difficult, and partly due to the lack of awareness of DS, its significance and features. The lack of awareness of DS is considered consequent on the observed low prevalence of older DS children in the population, the majority of DS infants being thought to have died early in life as a consequence of CHD and/or infection.[9,14]

The difficulty medical personnel have distinguishing the features of DS neonates and infants is confirmed in this study by the fact that only 9 (16.4%) patients were diagnosed during the infants' postnatal stay in the hospital or clinic. One reason for this is that most mothers and their infants are discharged from hospitals or clinics on the second day after delivery if both are considered well. However, at 1 - 6 months of age, during which time the infants would have attended clinics for weighing and immunisations, or hospitals and clinics for ill health, only a further 18 (32.7%) cases were diagnosed. Thus more than half the DS infants and children (28 (50.9%)) were 7 months of age or older when the clinical diagnosis of DS was confirmed and the mothers counselled. In total, maternal first awareness of a problem with their infant or child preceded clinical diagnosis in 32 (58.2%) cases, with the majority of cases (46 (83.6%)) being diagnosed after 1 month of age. By comparison, in a British study published in 1977, over one-third of the mothers interviewed realised something was wrong with their newborn when they first saw it, and others were concerned by the extra attention given to the infant by doctors and nursing staff.[15]

The above figures, in addition to the statement of 31 (56.4%) of the mothers that they did not think their DS infant or child's facial features differed from those of other children, and the fact that only 4 (7.2%) parents (including two nursing staff and one hospital worker) were aware of the existence of DS prior to the diagnosis's being made in their child, confirm the previous documentation that DS is an unrecognised entity in this community, and highlight that the mothers of the afflicted infants and medical personnel have difficulty recognising black African DS well into infancy and childhood.

As in previous studies,[5-7] the maternal age at the birth of the DS infant was 35 years or older in the majority (54.5%) of cases. In addition, 30 of the DS patients were the fourth child or more in birth order, with 23 (76.6%) of these DS infants and children having been born to mothers of AMA. Furthermore, 7 of the mothers had had other children after their DS child; 5 (71.4%) of these were of AMA. None of these 7 women was offered prenatal diagnosis.

My observation that mothers of black DS infants tend to seek medical advice when they recognise delayed development in their infant is highlighted in this study by the fact that 21 of the 32 mothers whose first awareness of a problem was self-initiated had become concerned as a result of their infant's head lag and associated developmental delay. I have also observed that black mothers in this region have their own system of developmentally assessing their infants. Head control is observed carefully, as it must be adequate by 4 months of age to allow the baby to be carried on the mother's back in the traditional manner. Furthermore, at 4 months of age infants are expected to have begun bearing weight on their legs and to be able to maintain a sitting position while propped up. Poor head control, in association with inability to perform these functions, was repeatedly the mother's initial reason for concern about her infant.

Frank denial of the diagnosis of DS after observing their child being examined and counselled, was recorded in only 7 (12.7%) of the mothers. This is in contrast to the 40% of mothers of DS neonates who denied the diagnosis in similar circumstances.[10] I propose that this can be ascribed to these infants and children being older when diagnosed and therefore having already exhibited signs and symptoms of developmental delay and/or CHD. The diagnosis and its associated prognosis were therefore more readily accepted by the mothers.

Comparison of the craniofacial, central nervous system and musculoskeletal system features of the DS infants and children in this study with similar studies in black African, Oriental and white neonates and children showed few major differences in the features between these groups (Table I). The most notable difference was the absence of speckled irides in the black children, who do not elicit this sign in their brown irides.[8] Sparse hair, seen in 16 (29.1%) of the patients, should also be included as a feature of black DS infants and children.

CHD was recorded in 38.2% of the DS patients. However, there was a marked discrepancy between the prevalence of CHD in infants under 12 months of age (51.9%) and those children 13 months of age and older (25%). In addition, 11 of the 14 (78.6%) infants had clinically significant CHD, compared with 3 (42.9%) of the afflicted DS children; and 1 of these was only 13 months old. CHD is recognised as a major cause of mortality in DS, especially where medical facilities are limited.[16] Facilities for cardiac surgery on DS patients are limited in South Africa, as evinced by the fact that only 1 individual with CHD in this study had undergone corrective cardiac surgery. These figures strongly suggest that CHD is a significant cause of mortality in black DS infants and children, with the majority of DS children who survive being those without CHD or without clinically significant CHD. Obviously infection, in association with malnutrition and/or CHD, is another significant cause of mortality. The observed low prevalence of DS in the black population has been ascribed to these factors.[14]

The figures documented in this paper further highlight the need for education in Africa to enlighten the public, especially women, and the medical and paramedical professions about DS in the black population. This would hopefully lead to earlier diagnosis of black African DS neonates and infants, as well as alert black women to their increased risk of an affected infant with advancing maternal age, and the possibility of prenatal diagnosis. The figures also preface the need to develop prenatal diagnostic services in a manner that is applicable to the African situation.[14,17]

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