PREVALENCE OF DEVELOPMENTAL DELAY IN INFANTS WHO ARE HIV POSITIVE

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ABSTRACT: *The presence of developmental delay in children who are HIV positive has been well described. International studies have identified 25 - 40% of HIV infected infants to have developmental delay. This study aimed to establish the prevalence of developmental delay in HIV positive infants in South Africa.*

The study was conducted at Coronation Hospital, Gauteng, South Africa. Infants under 12 months of age attending an out-patient follow-up clinic were assessed for developmental delay using the Neurodevelopment Assessment Score. Informed written consent was obtained from the caregivers prior to assessment. The results from 30 HIV positive and 30 HIV negative infants were analysed. Descriptive analyses were used to analyse most of the data. Data were summarised using means for continuous variables and frequencies and proportions for categorical variables.

The two groups were well matched for age, weight and socio-economic status. Forty percent of the HIV positive sample presented with developmental delay compared to 13% of the HIV negative sample. The caregivers of the HIV infected children expressed a need for support groups and education on HIV and how to care for their infants.

The results of this study support the findings of international studies on developmental delay in HIV infected infants. Furthermore this study identifies the need for cost effective, innovative programmes to address the long term needs of HIV infected infants and their caregivers.

KEY WORDS: NEURODEVELOPMENTAL DELAY, HIV POSITIVE, INFANTS.

INTRODUCTION

At present there are approximately one million children in Sub-Saharan Africa infected with HIV (UNAIDS Report, 2000). In South Africa young women between 20 and 30 have the highest prevalence rates of HIV infection in the country (HIV/AIDS/STD Strategic Plan for South Africa 2000 - 2005, 2000). As more young women of child-bearing age become infected with HIV, so the number of infants born with vertically transmitted HIV will continue to rise. The health care costs for these children are largely borne by the state as the majority are unable to afford private health care.

Despite the fact that the number of HIV infected infants in South Africa continues to grow, no research on the prevalence of neurological complications in HIV infected children in South Africa could be found. Unless an effort is made to identify the magnitude of this particular aspect of paediatric HIV in South Africa we are not going to be able to plan appropriate and affordable intervention programmes for the patients in our care.

The purpose of this study was to establish whether developmental delay presented in the first 12 months in infants with vertically transmitted HIV infection and, to ascertain the prevalence of developmental delay in HIV infected infants under 12 months of age. This study further undertook to establish whether a need exists for regular developmental screening and the development of a home programme for HIV infected infants.

Many questions remain as to how and when mother to child transmission of HIV occurs, the rate of the vertical transmission ranges from 14% - 40% (Quinn et al, 1994). The timing of infection of a foetus varies and depends on a number of factors largely related to the mother's disease status (Tardieu, 1998). In contrast to what was originally believed, international trials have shown no significant difference in transmission rates between infants delivered by caesarian section and those delivered vaginally (Falloon et al, 1989; Quinn et al, 1994).

The diagnosis of HIV in infants under 15 - 18 months of age is complicated by the possible presence of maternal antibodies in infants' bloodstreams which may lead to false positive results if serologic testing is done, this includes the ELISA and Western Blot tests which are commonly used in developing countries (Falloon et al, 1989). A more accurate test is the Polymerase Chain Reaction which tests the infants leucocytes for the presence of HIV DNA (Falloon et al, 1989). The PCR is a specialised and expensive test and is therefore not routinely used in South African hospitals.

Central nervous system involvement was recognized in children infected with HIV soon after AIDS was first identified in the early 1980s (Belman, 1992). The neurological syndrome described,

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together with the neuropathological findings, confirmed the hypothesis that HIV was a neurotropic retrovirus (Belman, 1992). The most frequently infected cells within the brain are the macrophages (Tardieu, 1998). Macrophages in the white matter, the basal ganglia and around the blood vessels are the most vulnerable to infection. Monocytes, lymphocytes and astrocytes may also become infected but to a lesser degree (Tardieu, 1998).

The discrepancy between the severity of the ensuing encephalopathy and the relatively small viral load in the CNS suggest that factors other than direct cellular damage may play a role. Falloon et al (1989) suggest that this allows for hope that antiretrovirals may reverse the encephalopathy to a certain extent, while Tardieu (1998) takes a more pessimistic view that much of the damage may in fact take place prenatally and be irreversible.

A characteristic encephalopathy has been described in a number of studies related to infants and children infected with HIV (Belman et al, 1996; European Collaborative Study, 1990). Encephalopathy may be the first clinical sign of HIV infection (Falloon et al, 1989), it usually initially presents with developmental delays, loss of milestones and a deterioration in intellectual abilities. The developmental delay usually progresses to include pyramidal tract signs, ataxia, abnormal muscle tone and pseudobulbar palsy (Falloon et al, 1989; Tardieu, 1998). Acquired microcephaly is common in infants (Falloon et al, 1989). Ultimately the encephalopathy may result in spastic quadriparesis with dystonic posturing and regression in motor milestones (Tardieu, 1998). The development of severe encephalopathy in infancy has been correlated with serious symptomatic disease and an increased and early mortality (Belman, 1992).

METHOD

This study was conducted in the unit follow-up clinic of Coronation Hospital, Gauteng, South Africa. Children who have had an admission to one of the medical wards at Coronation Hospital attend this clinic for out-patient follow-up appointments after having been discharged. Patients attending the clinic are drawn from similar sociol-economic backgrounds.

Prior to the commencement of this study, ethical clearance from the Committee for Research on Human Subjects of the University of the Witwatersrand was obtained.

All infants under one year of age attending the unit follow-up clinic at Coronation Hospital were identified by checking their date of birth in the clinic booking book. Informed consent was obtained from the caregivers of the child prior to any assessment being performed.

Inclusion criteria for the experimental sample included; infants between six weeks and 12 months of age who tested HIV positive on Polymerase Chain Reaction (PCR) testing or infants between six weeks and 12 months of age who tested HIV positive on ELISA and manifested clinical signs and symptoms of HIV infection as stipulated by the Centre for Disease control. HIV was to have been perinatally acquired. Only subjects who were deemed fit for developmental assessment by the examining doctor were assessed.

Exclusion criteria for participation in the study included; gestational age of less than 36 weeks, any infant with a history of brain damage due to perinatal factors or acquired post-natally; children who were resident in an institution and therefore did not have a single primary caregiver.

The control group was selected from infants aged between six weeks and 12 months who attended the same follow-up clinic. The infants in the control group had not tested HIV positive nor had clinical signs and symptoms suggestive of HIV infection. This information was obtained from the infants file once the assessment had been performed.

Thirty HIV positive and 30 HIV negative infants were assessed. The children all came from Coronationville, the western outskirts of Soweto, Brixton and Crosby. The families from these areas have similar socio-economic and educational backgrounds. Cultural beliefs about child rearing may vary slightly in the different racial groups represented. The vast majority of the sample were black or coloured infants with only one white and one Indian infant being assessed.

The Neurodevelopmental Assessment Score (NDS) was used to assess developmental delay. The Neurodevelopmental Assessment Score was chosen as a measuring tool as it was developed using a similar population to the study sample. It is a screening tool and is quick and easy to administer and to score. Taking contextual factors into account the NDS was thought to be an adequate assessment tool which would provide internal sample coherence.

The NDS has been validated for assessing children from six weeks to 12 months of age. The scale assesses 12 areas of motor development namely: moro reflex, protective reactions, ATNR, eye contact, head control, hand function, neck and shoulder retraction, prone function, sitting, rolling, standing and horizontal and oblique suspension (Goodman et al, 1985).

All infants under one year of age attending the follow-up clinic at Coronation hospital were assessed by means of the NDS. The infant and the caregiver/guardian were taken from the waiting area to a private room where the study was explained to them and their participation requested. The caregiver was given the information sheet to read. The nursing staff were always available to assist with translating if necessary.

Once written consent had been obtained from the caregiver the infant was assessed by the researcher. The infants performance in each of the 12 areas was evaluated by the researcher and compared to the age specific norms of the assessment sheet. The sheet was marked with a '0' if the infant was functioning at, or above an age appropriate level and was marked with a '1' if the infant was functioning below an age appropriate level. A score out of 12 was then determined and the infant was assigned to NDS category I, II or III depending on its score.

Category:

I - Normal ie NDS 0 - 4

II - Developmentally delayed ie NDS 5 - 9

III - Neurologically impaired in NDS 10 - 12

The following information was obtained from the child's file gestational age, method of delivery, sex of the infant and the infant's weight in kilograms as recorded on that day by the clinic sisters. Many of the caregivers were eager to discuss their child's condition and spoke at length to the researcher. These spontaneous, informal conversations were documented and three case scenarios will be discussed further. The infant's weight was classified as being above or below the 50th percentile using the growth charts routinely used in South African hospitals. Infants identified as being developmentally delayed or neurologically impaired were referred to the physiotherapy department at Coronation hospital for further assessment and management.

All the data collected was analysed by Dr P Becker of the Medical Research Council of South Africa. Data were summarised using means for continuous variables and frequencies and proportions for categorical variables. Descriptive analyses were used to evaluate most of the data. HIV positive and HIV negative infants were compared with respect to their NDS classification using the Two Sample Proportion Test. The software used was STATISTIX for Windows V2:0. A p-value of less than 0,05 was considered to indicate statistical significance in this research report.

RESULTS

The two groups were well matched in terms of age, sex, mode of delivery and weight. There was no statistically significant difference between the two groups for any of these parameters. The demographic data of the two groups are summarised in Table 1.

Forty percent (12/30) of the HIV positive group could be classified as either developmentally delayed or neurologically impaired whereas only 13% (4/30) of the HIV negative group were assigned this category. Using the Two Sample Proportion test a p-value of $p = 0,0195$ was obtained. This is statistically significant. The NDS classification of the study sample is presented in Table 2:

Table 1: Summary of Demographic Data of the Experimental and Control Groups

	HIV Positive	HIV Negative
Mean Age (months)	7,5	5
Female	15	13
Male	15	17
Caesarian Section (%)	16,5 (5/30)	20 (6/30)
Below 50th Percentile (%)	73 (22/30)	50 (15/30)

Table 2: Classification of Subjects According to Their NDS Category

NDS Category	HIV Positive	HIV Negative
I	60% (18/30)	87% (26/30)
II	33% (10/30)	13% (4/30)
III	7% (2/30)	0%

Further analysis of the NDS of the HIV positive infants was done to determine on which areas of the assessment the infants performed worst. It was found that the areas where HIV positive infants consistently failed to performed at an age appropriate level were:

- Pull to sitting (14/30)
- Prone (16/30)
- Sitting (14/30)
- Rolling (11/30)
- Horizontal and oblique suspension (13/30)

Many of the caregivers who consented to have their infants assessed spoke at length about the problems facing them and their families and their need for information and support. The infants assessed in this study were too young to attend a specific HIV clinic as these clinics only cater for children over two years old.

Three case histories have been chosen, they represent a microcosm of the problems caregivers are experiencing and highlight the need for support systems for caregivers of young infants with HIV.

Case 1

Mr A brought his nine month old son to be assessed. His wife passed away when the baby was eight weeks old due to an AIDS related illness. The baby was initially looked after by his maternal grandmother who is 76 years old. By the time the baby was four months old it had been hospitalised three times for gastroenteritis and was severely malnourished. At this point Mr A took a month's leave from his clerical job and brought the baby to live with him. The child has since flourished and scored very well on the NDS. At present he attends a creche during the day and lives alone with his father.

In his own words Mr A says he is 'clueless' about normal development and worries whether he is feeding his baby properly. He asked whether the researcher knew any other fathers raising HIV infected children on their own whom he could meet. He also asked whether he could see the researcher on a regular basis to have his baby's developmental progress monitored.

As he was leaving he turned to the researcher and asked: "If my wife died of AIDS and my boy has AIDS, should I also go and have an AIDS test?"

Mr A had obviously never been counselled about having a HIV test, or if he had he had certainly not come to terms with the fact that, in all likelihood, he was also HIV positive.

Case Two

Ms B brought a three month old girl to be assessed. She looked very young and I thought she may be the baby's sister. When asked what her relationship to the child was, she burst into tears and said that the researcher must not be angry with her.

She is a 15 year old girl who was raped by one of her teachers when she was in grade eight. She left school as

soon as it became apparent that she was pregnant. She tested HIV positive when she went to the ante-natal clinic when she was six months pregnant.

She now sits at home with her baby. She says she is too ashamed to contact her old school friends and can not get a job because she has no skills. Her mother continues to support her and the baby. It is highly unlikely that Ms B will ever be financially independent of her mother. She is conscious of being 'a burden' to mother.

Ms B said that she felt lonely and depressed and showed little insight or interest in her baby's condition. She said it felt good to talk to someone and asked for a phone number where she could contact the researcher.

Case Three

Ms C is married with three children. She brought her youngest child to be assessed - a daughter of eight months.

Mrs C watched with interest as the researcher assessed her baby and commented that she had noticed that the baby was 'lazier' than her previous two children and had wondered whether this was because the baby had HIV. She also asked the researcher to show her what she could do at home to help her baby sit better.

As she was dressing her baby Mrs C turned to the researcher and said there was one thing she did not understand and that was how could her baby be HIV positive if she was HIV negative. She had one HIV test when she attended the ante-natal clinic at the hospital which had been negative, her baby tested positive on Polymerose Chain Reaction. Mrs C had not been advised about being retested and did not know about the 'window' period or the possibility of a false negative result.

DISCUSSION

The prevalence of developmental delay in the study sample was relatively high at 40%. The prevalence of developmental delay or neurological involvement in other studies varies from 9,52% (Emodi and Okafor, 1998) to 90% (Spiegel and Mayers, 1991). It is very difficult to compare the results of previous studies done due to the fact that they often have very different inclusion criteria, use different assessment tools and draw their subjects from very different socio-economic and cultural back-grounds.

The study sample in this case is a biased one. Due to the fact that PCRs are not routinely done and that clinical signs and symptoms had to be present along with a positive ELISA test in order to confirm diagnosis, means that the infants assessed had already all had a hospital admission. These infants who present with clinical signs of HIV infection at an early age generally have a less favourable prognosis that those who remain healthy for longer (Quinn et al, 1994; Falloon et al, 1989). The results of this study can therefore not be taken to be representative of all HIV positive infants under a year of age, but only for those with clinical evidence of HIV infection. A similar bias is present in many of the studies reviewed and is difficult to avoid without incurring significant laboratory expenses (Emodi and Okafor, 1998; Vetter et al, 1996; Msellati et al, 1993).

One may argue that the mere fact that the children have been ill and have been hospitalized could have a negative impact on the normal developmental progress of a child (Spiegel and Mayers, 1991). Spiegel and Mayers (1991) report that a controlled study found that environmental factors such as hospitalization and social isolation did not account for the developmental delays seen in children with HIV infection.

It is interesting to note that the areas in which the infants were most delayed ie pull to sit, sitting, prone, rolling and horizontal suspension, are all activities which require proximal muscle strength as well as co-ordination of movement. It is impossible to say whether the infants found these activities difficult due to muscle weakness and the effects of their chronic illness or whether it is a result of inco-ordination of muscle activity due to a central nervous system deficit. The developmental delay evident in this study can therefor not be attributed to CNS involvement alone. More in-depth longitudinal neurological assessments would be needed to draw conclusive results.

Apart from the Bayley Scales of Infant Development, which is costly and time-consuming to administer, there is no one assessment tool which has been consistently used in previous studies. The NDS was developed from a number of sources and was validated against the Griffith's Mental Development Scale (Goodman et al, 1985). An assessment tool that was quick to administer was needed as the study was conducted in a busy out-patient clinic. Caregivers would be reluctant to spend another hour in the clinic while their infants were assessed. For many caregivers, attending the clinic requires leaving work and losing pay for the hours lost. In retrospect whilst the NDS was easy to administer and to score, it failed to give in-depth information about the child's development. The NDS is also exclusively a gross motor test and therefore does not detect fine motor or speech involvement.

The need for support groups for caregivers of HIV positive infants was expressed by a number of caregivers and many asked for follow-up appointments with the researcher to have their infants reassessed. The better informed caregivers are about their child's illness the more in control they feel, this reduces anxiety (Spiegel and Mayers, 1991). Support groups do not necessarily need to be run by a health care professional. A more cost effective method would be to facilitate the formation of groups organised by the caregivers themselves. Spiegel and Mayers (1991) found that informal support groups were perceived as being less threatening by the caregivers.

Spiegel and Mayers (1991) identified the importance of maintaining a degree of self-esteem for caregivers. They claim that this can be achieved by helping the caregivers to develop a sense of competence when dealing with their child. The have found that the regular use of a physiotherapy programme within the home provides a sense of purpose and competence for the caregivers. In addition to this, when the child does die the caregivers derive comfort from the fact that they were personally involved in the child's health care.

The South African government has identified community and home based

care of HIV infected individuals as a key strategy to be implemented by 2005 (HIV/AIDS/STD Strategic Plan for South Africa: 2000 - 2005, 2000). They propose that the funding for such programmes should come from the departments of Health and Welfare, as well as from Non Governmental Organizations. Home based programmes can reduce costs for hospitals by reducing the number of out patient visits and by reducing the direct contact time with health care professionals. Costs incurred by the patients can also be reduced in terms of transport to the hospital as well as time off work. Models used successfully in other developing countries e.g. Uganda need to be appraised for possible implementation in South Africa. Budgetary constraints are a very real issue and any programme implemented would have to prove cost effective. Ethically we cannot continue to withhold clinical and emotional support from HIV infected infants and their caregivers.

The limitations of this study are that the sample was a biased one and the results can therefore only be said to apply to this particular group of infants who have already manifested signs of HIV infection. The NDS proved to be an insensitive assessment tool and therefore the results of this study lack depth.

Despite the limitations of this study, the results obtained do confirm the fact that children who are HIV positive are predisposed to developmental delay, and that these developmental problems may manifest very early on in the child's life.

As the number of HIV positive children admitted to hospital continues to escalate at an alarming rate, physiotherapists need to be fully aware of the possible clinical complications with which these children may present. A holistic multi-disciplinary approach which could address the emotional and educational needs of the caregivers as well as the therapeutic needs of the children needs to be investigated. Models from other parts of the world, and especially from other African countries, need to be evaluated.

Based on the results of this study the following recommendations can be made:

- Infants diagnosed as being HIV positive should be routinely screened for neurological complications.
- Physiotherapists should play a more active role in the long term management of infants who are HIV positive, in terms of developing appropriate home programmes and monitoring developmental progress.
- A need exists for support groups for the parents of HIV positive children of all ages. These groups should encompass an educational component as well as addressing the emotional needs of the parents.
- Future studies should make use of the a more comprehensive assessment tool e.g. Bayley Scales of Infant Development.
- A prospective longitudinal study would yield useful information on the natural progression of neurological involvement of children who are HIV positive.

CONCLUSION

The findings of this study confirm that developmental delay is a common finding in infants with HIV infection. It may manifest in the first year of the child's life. The severity of developmental delay varies from loss of, or failure to attain milestones, to severe neurological impairment resulting in multiple handicaps.

A need exists for physiotherapists to become involved in the long term management of infants who are HIV positive. This involvement needs to be appropriate and cost effective in keeping with budget and staff constraints. The emotional and educational needs of caregivers of HIV infected infants are not currently being met. Holistic support groups may help to address these issues.

The findings drawn from this study cannot be extrapolated to include infants who are HIV positive but remain asymptomatic, nor those who are older than 12 months. It can however be assumed that all children who are HIV positive will at some stage become vulnerable to CNS involvement and that neurodevelopmental screening should be an integral part of the management of all children who are HIV positive.

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