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Children caught in the long shadow of COVID-19

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Despite the more transmissible delta variant being associated with higher rates of COVID-19 in unvaccinated adolescents, children have remained relatively spared from severe disease. Nevertheless, children are indirectly affected by the COVID-19 pandemic, which threatens to have far-reaching consequences. The effect of disruptions of seasonal patterns of circulation of respiratory pathogens on future immunity against such pathogens, childhood immunisation programmes, and HIV and tuberculosis treatment programmes poses a threat to the future wellbeing of children. Furthermore, the economic devastation caused by the pandemic, including an increase in unemployment, gives rise to numerous challenges, such as food insecurity, which is likely to worsen childhood nutritional status. Also, COVID-19 has ongoing effects on the mental wellbeing of children, driven in part by the interruption of schooling and other opportunities to socialise. An increase in psychological illnesses has manifested in children consequent to the stresses of the pandemic, lockdowns, caregiver deaths. In this article, we highlight the indirect effects of COVID-19 on children, and suggest solutions to mitigate against the long-term sequelae. A focused health, nutrition, education and child protection response is required from government and healthcare practitioners to safeguard the health and wellbeing of South African children.

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The COVID-19 pandemic, caused by the SARS-CoV-2 virus, represents one of the greatest threats experienced by mankind during the past century, with 245 million reported cases and >5 million confirmed deaths by November 2021 worldwide.[1] Notably, the pandemic has been characterised by waves of heightened transmission rates, hospitalisation and death, temporally associated with the easing of movement restrictions, behavioural changes and the emergence of different, more highly transmissible variants.

To date, the major burden of disease has been in the adult population, particularly among individuals >65 years of age and in those with underlying medical conditions. Vaccination against SARS-CoV-2 is the most promising and sustainable public intervention to protect against severe COVID-19 and death, but has only been modestly effective in preventing infection and mild disease.

The aspiration to achieve herd immunity against SARS-CoV-2 is receding, even in countries with high vaccine coverage, consequent to the emergence of more transmissible variants of concern, and waning of antibodies associated with declining protection against infection and mild COVID-19. Breakthrough cases in fully vaccinated individuals are, however, less infectious than infections occurring in unvaccinated SARS-CoV-2-naive individuals.

Despite children being as susceptible to infection by SARS-CoV-2 as adults, they have remarkably been spared from developing severe COVID-19 after infection – in contrast to most other infectious diseases. Several reasons have been postulated. Nevertheless, recent trends in high-income, high vaccine-coverage regions have shown a disproportionate rise in COVID-19 infections in unvaccinated adolescents, possibly due to the reduced disease burden in adults because of COVID-19 vaccines being prioritised for them.[2] Another explanation is the emergence of the delta variant, which is twofold more transmissible than the original Wuhan virus. Surveillance data from the National Institute for Communicable Diseases (NICD) show a 1.57 (95% confidence interval (CI) 1.55 - 1.59) increased odds of disease among children aged 15 - 19 years when comparing the first and third waves.[3] However, the burden of COVID-19 in children is unlikely to ever reach the high rates observed in adults at the peak of the pandemic.

In South Africa (SA), by the end of October 2021, 22 million doses of COVID-19 vaccines had been administered, with 38% coverage in adults >18 years of age.[4] As vaccination rates increase, a return to pre-pandemic behaviour patterns will inevitably result. Despite vaccine coverage rates >80% in adults in many high-income countries, the risk of resurgence of COVID-19 persists owing to waning of vaccine-induced antibodies. The risk of resurgence is exacerbated by vaccine hesitancy and lack of access to vaccines in some settings.

Consequently, children remain at ongoing risk of exposure to SARS-CoV-2. Hospitalisation of children with severe COVID-19 and multisystem inflammatory syndrome (MIS-C) has occurred during the previous waves, and children have also been vulnerable to post-acute sequelae of COVID-19 (PASC). Vaccination for 12 - 17-year-old South Africans commenced in October 2021. While the focus of vaccination should primarily be centred on the optimal protection of children with underlying medical conditions, other indirect benefits may include limiting disruptions to schooling, sport and social activities.[5]

COVID-19 hospitalisation, MIS-C and PASC may continue to occur in children. However, independent of what transpires next, the long shadow of COVID-19, i.e. its devastating effects on the lives of children currently and over the next decade or longer, is worthy of further consideration. We highlight several other ways in which children have been adversely affected by the pandemic:

Disproportionately increased burden of other infectious diseases

There has been a noticeable decline in the seasonal peaks of common respiratory diseases, such as respiratory syncytial virus (RSV) and influenza, and other common infections.[6] In 2020, Chris Hani Baragwanath Academic Hospital (CHBAH), Johannesburg, SA, child viral surveillance data indicated a virtual disappearance of the RSV peak season (~25 cases between February and May 2020 compared with 400 - 500 cases in previous years) and no cases of influenza. Consistent with findings in other countries, an increase in RSV cases has been observed outside of the usual seasonal pattern.[7] Nonetheless, concerns have been raised about the possibility of consequent epidemics in the years to come.[8]

Many studies have also noted significant reductions in primary healthcare services and child healthcare visits during the COVID-19 pandemic.[9] Importantly, in children, the negative impact on the Expanded Programme on Immunisation (EPI (SA)) and the inadvertent increase in vaccine-preventable diseases are of concern.[9] Although catch-up programmes have been instituted in a number of settings, measures need to be put in place to prevent further erosion of EPI vaccine coverage rates in future COVID-19 waves, particularly in less-resourced settings.[10]

Over- and under-nutrition

The COVID-19 pandemic has shifted dietary and lifestyle habits of many families owing to job losses and disrupted livelihood activities. Many families have been forced to ration food and opt for cheaper and unhealthy food choices. Poor and vulnerable children globally have experienced interruptions in school feeding programmes and access to health services and nutrition-assistance programmes, exacerbating food insecurity. In SA, the National Income Dynamics Study – Coronavirus Rapid Mobile (NIDS-CRAM) survey (cramsurvey.org), which followed food insecurity in children through the different waves, concluded in July 2021 that higher household and child hunger rates since the start of the pandemic persisted even after severe lockdown levels were terminated.

In contrast to poorer households, more than a third of members of wealthier families experienced moderate to high weight gains linked to decreased physical activity and fresh food consumption, increased sedentary time, snacking, sweet consumption and eating in response to boredom or anxiety. The poorer diet quality and sedentary behaviours potentially acquired during the prolonged lockdown periods may not be easily reversible in children and their parents.

Modelling studies have predicted dire consequences, particularly acceleration in child wasting, stunting, micronutrient deficiency and overweight rates, with their attendant physical, intellectual, productivity and social impacts. The proposed required responses, not surprisingly, advocate for strengthening of existing strategies and interventions, including identification and management of wasting, support for breastfeeding, maintaining school feeding schemes and social protection measures.[11]

HIV and tuberculosis care

COVID-19 has ominously impacted on the care of HIV-infected South Africans. During the 2020 lockdown, HIV testing and antiretroviral therapy (ART) initiation decreased by almost half.[12] From a paediatric perspective, not only are testing and access to ART in children essential, but also the negative impact on the prevention of mother-to-child transmission programme could be disastrous – missed antenatal visits in HIV-infected pregnant women doubled during COVID-19 lockdown in SA.

Similarly, patients with tuberculosis (TB) have been affected. For the first time in over a decade, the World Health Organization (WHO) reported an increase in TB deaths during the pandemic.[13] Interruptions in diagnostic, therapeutic and follow-up services from the inadvertent redirection of resources to combat the COVID-19 pandemic, as well as reduced healthcare facility visitation by people either afraid of contracting COVID-19 or discouraged by long screening processes and queues, were apparent. The impact of inadequately treated TB increases the possibility of transmission to children in households, creating challenges well beyond the COVID-19 pandemic.

School and education interruption

Being at school and in a structured environment for learning is important for most children. The benefits of being at school extend beyond the classroom – feeding schemes are important in low-resourced settings. Furthermore, schools are often safe spaces for children at risk of abuse, drugs and mental health problems.[14] Therefore, COVID-19 has widened the already existing educational gap resulting from socioeconomic differences. Moreover, children with learning difficulties will possibly suffer more losses, as most therapy occurs within the school setting. The school interruptions have not only denied children these benefits, but have enormously increased the stress on their caregivers, who are ill-equipped to meet these needs.[15] School interruptions should cease, given that transmission of COVID-19 can be prevented in most education settings, and the evidence that school transmission fuels community transmission is negligible.[16]

Loss of caregivers and extended family structures

With the staggered rollout of the vaccine programme in SA, the relative proportion of younger adults who have died from COVID-19 has increased. Therefore, many more individuals who died during the second and third waves were likely to have been a parent or breadwinner of a family. These deaths have spelled economic ruin for families, with the effects most keenly felt by vulnerable children.

Psychological burden

Adverse life experiences at a young age are associated with increased risk of mental health disorders in adulthood. Even very young children are not immune to the psychological strain inherent in living during this pandemic.[17] Lockdowns and enforced home confinement have disrupted normal patterns of education, physical activities and socialisation. This situation has had a profound impact on the emotional and social development of young children and adolescents. Manifestations of psychological distress include increased anxiety, clinginess, irritability, inattention, fear and feelings of helplessness.[17] Younger children have also displayed more rebellious behaviour, while teenagers have presented with more affective symptoms.[17] Studies undertaken during earlier phases of the pandemic among adolescents in China and the USA reported an increased incidence of anxiety, depression and post-traumatic stress disorder.

The death of parents and other family members adds heavily to the psychological trauma suffered by children during and even after a possible end to the pandemic.[17] Children from impoverished homes are less likely to access therapy to mitigate the effect of these psychological injuries.

Resource allocation and intensive care services

Until recently, children suffered a noticeably lower burden of severe COVID-19 than adults. An increase in paediatric COVID-19 and

other infectious disease burdens threatens to overwhelm existing SA healthcare sector resources. This situation is especially true in the context of critical care, given that only 20% of intensive care unit (ICU) beds are dedicated to children despite them comprising more than a third of the population.

What response is required?

The formidable impact of the COVID-19 pandemic on children extends well beyond that of 'usual' viral infections. The indirect effects of COVID-19 on children may have lifelong consequences. An adequate response to the devastation of COVID-19 requires intervention at multiple levels. From a public health perspective, the re-establishment of routine vaccination services for children is a priority. Re-established school nutritional support programmes will partially alleviate hunger in older children, but an accelerated nutrition supplementation support programme for younger children is warranted to manage high hunger and under-nutrition levels.

All schools must remain open, also during future waves, and entire school closure due to local outbreaks must be exceptional and carefully managed. Schools must also play a greater role as sites of psychological support and as areas for the identification and referral of abuse, violence and adolescent pregnancy.

Paediatricians and child health practitioners should be mindful of the psychological burden of disease, reinforce the need for routine childhood immunisations and continue to play a central role in safeguarding the health and wellbeing of children.

The SA government should increase social spending to meet the additional needs of children consequent to the COVID-19 pandemic. These needs include greater investment in health, nutrition, education, child protection and social protection. Although the additional social protection offered through family cash transfers during the lockdown was welcome, ongoing long-term support is required. Appropriate measures could include a substantial increase in the child social support grant and/or the introduction of a basic income grant.

The shadow of COVID-19 on the lives of SA children is indeed long, and getting some sunshine back into the lives of affected children requires a commitment from everyone – be they caregivers or parents, communities, service support staff or government. The future of a generation depends on doing this successfully.

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Utilisation of paediatric surgical theatres at the Chris Hani Baragwanath Academic Hospital, Johannesburg

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Background. Optimal theatre utilisation is essential to reduce long waiting lists for elective surgeries and to increase cost-effective theatre operation. Utilisation rates well below the global benchmark of 80% have been reported for government hospitals in Johannesburg, South Africa (SA).
Objective. To investigate utilisation of three paediatric theatres at the Chris Hani Baragwanath Academic Hospital (CHBAH) in Johannesburg.
Methods. Surgery lists of the three theatres were reviewed for three one-week periods over a four-month study period. Preoperative, intraoperative and postoperative data were collected to create a timeline for each theatre and each surgical case, including reasons for cancellations, delays or expedited times.
Results. A total of 152 surgeries were scheduled during the reviewed study period, of which 44 cases were cancelled. The utilisation rate was 59.8% across the three theatres combined, with individual rates calculated as 62.7%, 58.2% and 57.0% in the burns, general and neonatal theatres, respectively. The primary factor contributing to under-utilisation was early completion of the scheduled list. Surgery delays were mainly due to delays in transferring the patient to the theatre and between anaesthetic induction and the start of surgery.
Conclusion. Utilisation of the paediatric theatres at CHBAH is below the ideal benchmark of 80%; however, utilisation was better than expected when compared with findings from other public-sector hospitals in SA. However, theatre efficiency was found to be very low and perhaps better explains the reasons for backlogs in paediatric surgeries at CHBAH.

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Scheduled elective surgeries are increasing in the public health sector in Gauteng province, South Africa (SA), with the waiting list for these procedures consequently extending. Prior to the COVID-19 pandemic there were ~200 cases on the waiting list in the Paediatric Surgery Pepartment at Chris Hani Baragwanath Academic Hospital (CHBAH). (The backlog in elective surgeries has subsequently increased considerably owing to pressure on healthcare facilities during the ongoing pandemic.) Efficient use and scheduling of operating theatres are essential to reduce waiting lists and improve patient outcomes.

In the SA context, where public healthcare is constrained by both limited funds and staff, it is imperative to optimise theatre utilisation to alleviate the pressure on these resources.[1] Theatres are expensive to run, even when not in use. Better theatre utilisation can, therefore, contribute to improved cost-effectiveness of surgical departments and hospitals.

Theatre utilisation is defined as the ratio between time spent operating and the daily available theatre time. (Theatre time is defined as the period during which a theatre is available for operations, usually from 08:00 to 16:00. The cut-off time for the last patient having to leave the operating theatre is 16:00.) A utilisation ratio of 80% is accepted as ideal across the world, and takes into account unavoidable parameters such as theatre sterilisation and patient preparation.

A study describing theatre utilisation in a private setting in SA has shown that the theatre complex ran at less than half the optimal rate, despite being privately funded;[1] another at a public hospital in North West Province, SA, showed that theatres were similarly under-utilised, with an average utilisation rate of 39%.[2] These studies suggest that theatre utilisation rates are likely comparable in the public and private sector in SA, and well below the ideal benchmark in both settings.

This prospective study investigated theatre utilisation in three units of the Paediatric Surgery Department at CHBAH. Identifying factors that affect the use of paediatric operating theatres can be useful in understanding how theatre utilisation and efficiency can be improved and, in turn, shorten the waiting list for pending elective surgeries.

Methods

This was a prospective study conducted in the paediatric burns theatre, the general paediatric theatre and the neonatal theatre of CHBAH in Johannesburg, SA. These theatres handle neonatal emergencies and general elective paediatric surgeries. All elective procedures were included in the data collection process. The study was performed over a cumulative three-week period between April and July 2019.

Data handling

Three sets of data were collected for each case (preoperatively, intraoperatively and postoperatively) and entered into a database system (REDCap). Preoperative data included: records of any cancellations, the expected duration of a procedure, the time at which the patient was collected from the ward and the time when the patient arrived in theatre.

Intraoperative data included the time stamp of the anaesthetist's and surgeon's arrival, the time of anaesthetic induction, start and end times of the surgery, and the time at which the patient left the theatre.

Postoperative data included: the time at which the patient was admitted to the recovery unit, their length of stay, and the time at which they arrived back at the ward. At each point of the data collection process, it was noted whether documented times were appropriate and if not, a reason was provided.

Data were collected for a total of three weeks over a four-month period. Documented times were used to calculate descriptive statistics (mean, standard deviation, median and mode) and interquartile ranges (IQRs) were calculated for each time interval.

The duration between the start of anaesthetic induction and when the patient left the theatre was totalled for each theatre list. Total values for each list were then divided by the total available time for that list (8 hours; from 08:00 to 16:00) to express theatre utilisation as a percentage. Average durations per theatre and also for all three theatres combined were subsequently calculated.

Efficiency was calculated according to Pandit *et al.*[3] as: (Utilisation – Fraction of scheduled time overrunning) × Fraction of scheduled operations completed.

Ethical considerations

Ethical approval for the study was obtained from the Human Ethics Research Committee of the Faculty of Health Sciences, University of the Witwatersrand (ref. no. M180941).

Results

There were 152 surgeries scheduled in the three weeks of data collection, of which 71 were in the neonatal theatre, 50 in the general theatre and 31 in the burns theatre. Of these surgeries, 147 were elective procedures and 5 were emergencies. Slightly more than a quarter of the scheduled surgeries (*n*/*N*=44/152; 29%) were cancelled (25 from the neonatal theatre; 14 from the general theatre; 5 from the burns theatre). The two most common reasons for cancellation were that the patient did not show up and time constraints (Fig. 1a). Specific reasons for cancellation in the respective theatres are shown in Fig. 1b.

Of the 27 lists run during the data collection period, only seven were completed as booked; the other 20 had at least one cancellation.

Fig. 2 shows the average time for each step in the normal theatre process, both for each theatre individually and for the complex as a whole.

Table 1 shows the most common reasons for the delays between recorded points and the percentage of cases affected by these delays. In general, the neonatal theatre had the latest start time, and the burns theatre the earliest (See Appendix 1 for the specific start times of lists in the respective theatres on each day of data collection.) The median start and end times for the theatre complex were 08:36 (IQR: 38 min) and 15:17 (IQR: 2 h 13 min), respectively. The median end times for lists were 14:09 (IQR: 3 h 14 min), 15:10 (IQR: 2 h 15 min) and 15:36 (IQR: 57 min) for the general, burns and neonatal theatres, respectively. A third of the 27 lists (*n*=9) reviewed during the data collection period ended late (i.e. after 16:00); of these, five were from the neonatal theatre, two from the general theatre and two from the burns theatre.

The general utilisation percentage at the CHBAH paediatric theatre complex was 59.8%. Utilisation rates for the specific

Table 1. Surgery delays reported for theatres of the paediatric theatre complex at Chris Hani Baragwanath Academic Hospital, Johannesburg

Reason for delays	Cases
Patient called late	25
Patient arrived at theatre reception late	37
Patient arrived in theatre late	29
Delay between anaesthetic induction and surgical start	37
Surgeon arrived late	19
Anaesthetist arrived late	7

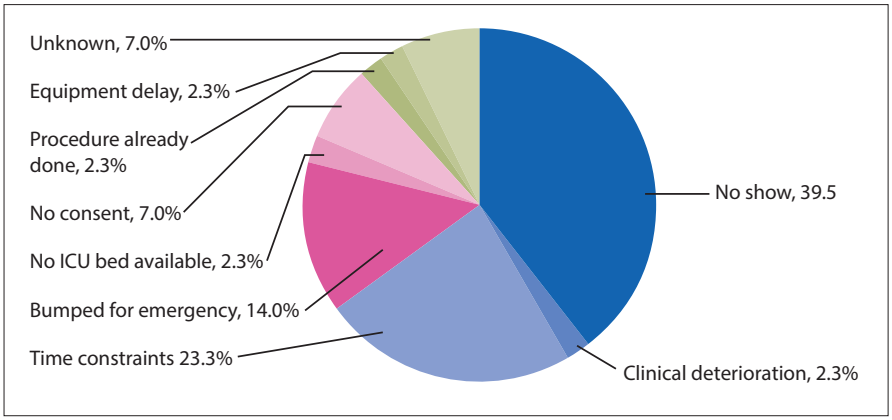

Fig. 1a. Reasons for surgeries being cancelled at the paediatric theatre complex of Chris Hani Baragwanath Academic Hospital, Johannesburg.

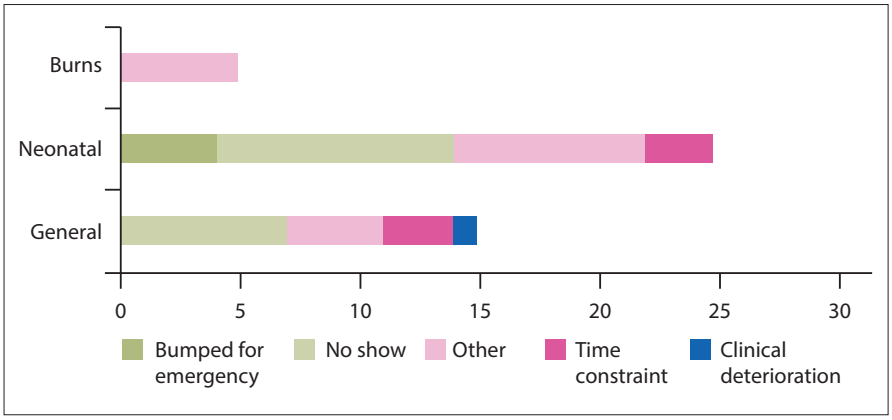

Fig. 1b. Breakdown of reasons for cancellations per theatre.

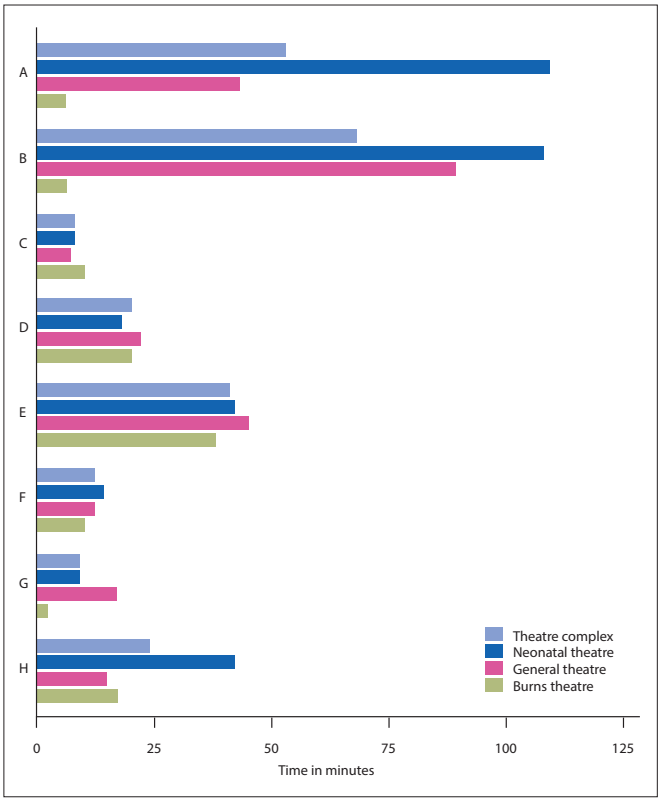

Fig. 2. Average time per task in the respective theatres and the complex combined. A: Time from calling patient to arrival at theatre reception; B: Time from arrival at theatre reception to patient arriving in theatre; C: Time from arrival in theatre to anaesthetic induction; D: Time from anaesthetic induction to start of surgery; E: Time from start of surgery to end; F: Time from end of surgery to patient leaving theatre; G: Time from patient leaving theatre to arriving back in ward; H: Time from previous patient leaving theatre to arrival of next.

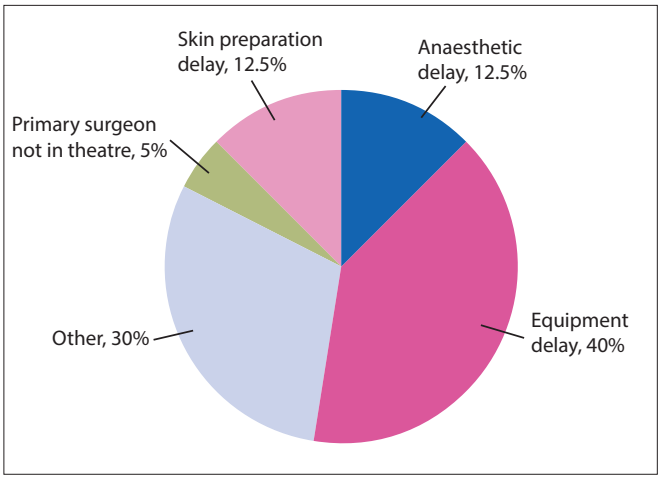

Fig. 3. Reasons for delay between anaesthetic induction and surgical start.

theatres were 62.7% for the neonatal theatre, 58.2% for the general theatre and 57.0% for the burns theatre.

The primary factors contributing to under-utilisation were delays in getting the patient from the ward to theatre reception and delays between anaesthetic induction and the start of surgery (Fig. 3).

Efficiency across the three theatres was calculated as 45.05%, with the lowest efficiency seen at the neonatal theatre (40.29%) and the highest in the burns theatre (50.04%). Efficiency at the general theatre was 47.75%.

Discussion

The data collected in this study yielded some unexpected results. Ideal theatre utilisation is considered to be approximately 80%, and although the utilisation in the current analysis fell below this, it was higher than anticipated. Overall utilisation for the paediatric theatre complex was 59.8%. This was similar to values in the USA (according to Lobelo[2]) but notably higher than values recorded in other SA studies, with utilisation rates from 3.2% in the public setting to 52% in private settings.[2,4]

Despite the utilisation rates of all three theatres being higher than expected, and higher than what has been observed in other SA studies, there is still a considerable backlog for elective surgeries at CHBAH. In addition, cancellations were most often ascribed to time constraints (23%), yet most theatres closed before the official closing time.

We propose that 'theatre utilisation' and 'efficiency' should be considered in parallel to understand the results. Efficiency can be defined as the completion of all scheduled cases without any under- or overrun. In our study, efficiency was below 50% (calculated as 45.05% across all three theatres) and, on days with many cases, this could drop to as low as 6%. Yet utilisation rates were higher than expected. This points to a logistical disconnect, which may be related to several factors.

CHBAH serves a large population, with referrals for elective cases coming from across the Gauteng and North West provinces. This results in a large number of pending cases purely because of the high demand having to be handled by a facility with a finite number of theatre lists per week. In an attempt to accommodate these numbers, theatre lists are often 'overbooked', to take advantage of possible no-shows or other cancellations. So, despite acceptable turnover times, a high number of surgeries had to be cancelled because of 'time constraints' on days when all booked patients arrived for theatre. In addition, cases on the scheduled list would typically be cancelled to accommodate emergency cases that had to be handled in these theatres. As a result, the available time for elective surgeries was reduced, thereby decreasing efficiency but conversely still allowing for high utilisation of the theatres.

Another factor that contributed to high utilisation rates is the time between anaesthetic induction and start of the procedure. This time was longer than expected in 37% of surgeries, and in half of these cases the delays were due to equipment malfunctions. The delays therefore did not affect utilisation in our analysis, yet markedly affected efficiency. When emergency surgeries and the time between anaesthetic induction and surgical start are taken into account, the overall utilisation dropped to 33.76%, a value more in line with what has been reported previously for SA settings.[1]

Cancellations are cited in the literature as negatively affecting theatre utilisation and efficiency.[3] This was also seen in the current study. Lists with more cancellations were associated with poorer utilisation and efficiency values. This suggests that introducing measures to reduce the number of cancellations could improve the efficiency of the operating theatres. Only seven of the 27 lists reviewed over the data collection period were completed; at least one cancellation was recorded in the remaining 20.

As seen in Fig. 1A, the most common reasons for cancellations were patients not showing up (39.5%), time constraints (23.3%) and cases being bumped off the list to accommodate an emergency (14%). In cases of patients not arriving, theatres were left empty, which reduced both utilisation and efficiency. In cases of time constraints and emergency surgeries, theatres were still being utilised, leading to increased utilisation but decreased efficiency. Improved list scheduling and elective cases being admitted the day

before the scheduled surgery could help to limit the number of no-shows and so improve both utilisation and efficiency.

Despite theatre lists generally ending before the official theatre closing time, it should be noted that a third (n=9) of the 27 reviewed lists ended late. This resulted in a paradoxical increase in utilisation. These findings suggest that utilisation by itself is not an adequate proxy for operating theatre efficiency. This finding agrees with that from a UK study, which revealed the shortcomings of using utilisation as a measure of efficiency when emergencies and cancellations were not adequately accounted for.[3]

Other reasons for delays were analysed in order to identify further areas of improvement. The most notable delay occurred when patients were transferred to the theatre. This included patients not being ready, administrative delays and porters being late. Delays were also noted between a patient's arrival at theatre reception and entering the operating room owing to administrative delays, heater malfunction, and patients not being adequately starved as per anaesthetic protocols. There were no notable delays between a patient's arrival in the operating theatre and anaesthetic induction, despite late arrival of anaesthetists or difficulties with preoperative procedures being noted in some cases. All of these aspects contribute to utilisation rates and are noted as areas for improvement in the administrative context.

Lastly, although the data for these three theatres were combined to provide a general view of utilisation and efficiency of the CHBAH paediatric theatre complex as a whole, the respective theatres all faced different challenges, related to factors such as the location of the theatre relative to that of the wards and the specific subset of patients the theatre caters for. The interpretation of data drawn from the three theatres is therefore nuanced.

Despite calculated values showing the general and burns theatres theoretically having 'superior' efficiency, they generally completed their lists before 16:00 (14:09 for the general theatre and 15:10 for the burns theatre); standing empty for the remaining time thus decreases utilisation. In contrast, despite the neonatal theatre having the most cancellations (n=25), it also finished its lists last and had the most lists running over time (n=5, compared with two each in the general and burns theatres). This was likely due to greater delays in the neonatal theatre and compounded by it being the primary theatre for emergencies. The neonatal theatre was also used for cases on the general list once. Therefore, despite cancellations and delays, the utilisation rate of this theatre was the highest of the three and its efficiency the lowest (40.29%). This is an interesting example of how a theatre can be over-utilised in an inefficient manner, which again points to utilisation being a poor proxy for efficiency. The finding is similar to that of Pandit *et al.*,[3] who noted that gaps between start times of surgeries had very little effect on theatre efficiency and suggested that list scheduling was more important for improving efficiency.[3]

The findings of the current study suggest that surgical staff utilise the theatre efficiently, but that administrative issues such as list scheduling and improved systemic access to reduce the number of cancellations could help to increase efficiency.

Conclusion

At 59.8%, the paediatric theatre complex at CHBAH operates below the ideal utilisation rate, although higher than that of surrounding government and private hospitals (and seemingly comparable to utilisation rates in the USA).[2,3] However, low theatre efficiency (<50%) observed in this analysis indicates systemic dysfunction. This points to the need for corrective action to improve list scheduling and putting measures in place to limit the number of no-shows and cancellations. Such actions could markedly improve both utilisation and, more importantly, efficiency at CHBAH.

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Complications associated with central venous lines for paediatric oncology patients at Universitas Academic Hospital, Bloemfontein, from 1992 to 2018

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Background. Central venous access devices are associated with complications such as central-line infections and systemic sepsis.
Objective. To determine the complication rates associated with central venous lines used to administer chemotherapy at the Paediatric Haematology Oncology Unit, Universitas Academic Hospital, Bloemfontein, from January 1992 to March 2018.
Methods. A retrospective descriptive analysis of paediatric oncology patients who received intravenous catheterisation and were treated at the unit. Cases with incomplete data, age >16 years and treatment after 31 March 2018 were excluded.
Results. Records of 293 Hickman lines were analysed. The median patient age was 64.7 months. Sepsis was noted in 13.3% of the cases; no in situ local complications were found in 62.5% of the lines. Of the 39 cases that presented with line sepsis, 23.1% showed no signs of systemic sepsis, whereas 61.5% were neutropenic and septic. In total, 190 patients had symptoms of systemic sepsis and accompanying neutropenia. Of these, 67.4% did not develop in situ line complications. Lines were removed mostly because the end of treatment had been reached (44.7%); line sepsis was noted as the reason for removal in only 16.3% of cases.
Conclusion. Despite the study population having a high risk for infections because of a young age, a large proportion of haematological malignancies and surgical placement of Hickman lines, there was a low incidence of line sepsis complications. The special care taken intraoperatively and meticulous aseptic postoperative handling and maintenance are suggested as contributing to limited infective complications.

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A venous access device is a catheter designed for continuous access to the venous system, which may be required for long-term parenteral feeding, administration of intravenous (IV) fluids and medication, or taking blood samples.[1,2] Several types of central venous access devices (CVADs) are used, such as external tunnelled cuffed catheters (e.g. Hickman and Broviac lines), chemo ports (totally implanted catheter ports) and peripherally inserted central catheters (PICCs).

In oncology patients, CVADs are typically used for administering pro-inflammatory chemotherapy agents, bone marrow transplants, antibiotics and fluids, and for blood sampling. With these patients needing medium- to long-term treatment (2 - 3 years),[3] CVADs are commonly used to avoid multiple needle pricks of peripheral veins, thereby decreasing their anxiety and improving patients' quality of life during the treatment period, especially in patients with difficult peripheral IV access (non-visible or non-palpable veins).[4-6]

Central venous catheters may cause complications in up to 40% of paediatric patients.[7] Common complications seen in paediatric patients with chemo ports are those associated with bloodstream infections, local skin infections, wound dehiscence, mechanical complications, venous thrombosis and skin necrosis.[8] The use of CVADs can also be associated with arterial puncture, haemothorax, stroke, arrhythmias and nerve damage.[9]

Although fewer complications and risks are associated with Hickman lines, just like with any other CVAD, their lumens may become blocked, they may become infected, and the cut-down may result in scarring of the skin.[2] Precaution must be taken not to contaminate the exposed external part of the line. External tunnelled cuffed catheters are more prone to line sepsis than chemo ports (4.7 v. 1.5 episodes per 1 000 catheter days).[10]

PICC lines are often used in oncology patients receiving short-term treatment or in patients outside the oncological setting, but can be associated with complications such as extravasation (81.6%) and infections (78.3%).[11] Multiple attempts to insert a PICC line may introduce infection, which is a risk in an already immunocompromised patient. In addition, the use of PICCs can lead to compromised integrity of the peripheral veins over time, which makes reliable peripheral venous access increasingly difficult in these patients. Other options of CVADs which are more reliable and less prone to complications, are therefore preferred.[11]

Chemo ports are totally implanted and therefore do not have an external part that can become contaminated and infected by direct contact to the environment. The only maintenance required is monthly flushing of the line when not in use. Patients with a chemo port can bath, shower and swim as normal. Because of these benefits, and also a lower rate of removal due to mechanical complications, chemo ports are preferred over Hickman lines for central venous access.[1]

Risk factors for CVAD complications include the type of CVAD, underlying disease (more common in haematological malignancies) and patient age (more common in younger patients).[7] Neutropenia is one of the most important risk factors for the outbreak of infections.[12-15]

The choice of a CVAD depends on the typical complication rate of the approach and the risk of thrombotic or septic complications associated with a specific device, together with the planned therapy course and the clinical experience of the provider.[16,17] Choosing the appropriate device for the oncology patient should be part of proactive vascular access planning.

The Paediatric Haematology Oncology Unit at the Universitas Academic Hospital, Bloemfontein, mainly uses Hickman lines. This is due to availability and most of the staff at the hospital being familiar with and skilled in using this type of CVAD. The preferred site of insertion is the right internal jugular vein, but the left internal jugular vein is also used if thrombosis has occurred on the right side following a previous line.

These lines are inserted under general anaesthesia in theatre by paediatric surgeons. The device is placed in an iodine solution prior to insertion, provided that the patient is not allergic to iodine. Cefazolin is given as a prophylactic antibiotic at induction of anaesthesia. The device can be inserted either through ultrasound-guided percutaneous puncture (Seldinger technique) or a surgical cut-down using anatomical landmarks. To confirm correct positioning of the catheter tip, fluoroscopy is performed intraoperatively.

The open cut-down technique in the neck is commonly used at Universitas Academic Hospital, as the Hickman lines available at the facility do not always support the Seldinger technique because of instrumentation constraints. However, if the equipment supports the use of the Seldinger technique, it is preferred. The line is tunnelled to exit just inferior to the xiphisternum. This exit position supports better postoperative maintenance of the line (e.g. enough space for dressing application to protect the line against environmental contamination). The tip of the line is positioned in the superior vena cava (SVC).

The line is then flushed with heparinised saline and the external part is covered with a sterile dressing on the chest and upper abdomen wall. In patients who had a previous line, Doppler ultrasound is performed before placement of the new device to evaluate the vessel for patency and possible thrombus formation. Routine evaluation for vessel thrombosis is performed only if the patient presents with symptoms and signs of vessel occlusion (SVC syndrome, swollen limbs).

The combined Paediatric Haematology Oncology and Paediatric Surgery Unit at Universitas Academic Hospital is the only referral centre for children with malignancies and index cases of paediatric surgical conditions in central South Africa. This unit serves the Free State, Northern Cape and selected areas of the North West and Eastern Cape provinces. It also serves as a referral unit for Lesotho.

According to the protocol used in our unit, the catheter may only be used 48 hours after placement. The external part of the line is cleaned with chlorhexidine soap and flushed with heparinised saline twice per week, regardless of whether the patient is admitted or at home. Likewise, IV sets are replaced with new ones and the external part of the line is dressed with a clean dressing against the patient's chest and upper abdomen wall twice per week.[18]

Catheter-associated bloodstream infection (CABSI) is diagnosed by a positive blood culture taken from the line when the patient is clinically septic (i.e. presenting with fever) and is treated with antibiotics administered through the line. Initial treatment involves piperacillin/tazobactan and amikacin used empirically, but this can be changed according to sensitivity results of the blood culture. If the same organism is cultured after a week of treatment, the line is regarded septic and consequently removed. Blood samples for culture are never taken from a peripheral site while the Hickman line is functional. Sepsis at the tunnel exit site and pocket is treated conservatively by draining an abscess, wound cleaning and administering antibiotics without removal of the line. If there is no improvement, the line is removed and the tip is sent for culture.[15] Line cultures are performed only per indication when a patient appears septic, not as routine. Blood sampling is performed as a sterile procedure and any growth is regarded as pathogenic.

This study assessed the complications of central venous lines for chemotherapy in paediatric oncology patients treated in the Paediatric Haematology Oncology Unit at the Universitas Academic Hospital in Bloemfontein from January 1992 to 31 March 2018.

Further objectives were to describe subgroups that developed line sepsis complications and had increased risk factors for line sepsis.

Methods

This was a retrospective descriptive study of paediatric oncology patients (16 years or younger) who received CVADs and were treated in the Paediatric Haematology Oncology Unit at Universitas Academic Hospital in Bloemfontein from January 1992 to March 2018.

A pilot study was run using data from three cases.

Data collection

Data were collected from the unit's database and included: the patient's age (months) at line insertion, diagnosis and reason for line insertion; data on specific insertion parameters (site of insertion, days in situ, any complications at insertion); and post-insertion developments (namely purpose served without complications during treatment, in situ line complications, reason for line removal, and presence of sepsis). Data collection and preparation for analysis were shared by the authors. All authors verified the information recorded.

Data analysis

As no changes were made to the methodology after the pilot study, those three cases could be included in the final dataset. Data were entered into a spreadsheet (MS Excel) for statistical analysis. Categorical variables were summarised as frequencies and percentages, whereas means, standard deviations and percentiles are reported for numerical variables.

Ethical considerations

Approval for the study was obtained from the Health Sciences Research Ethics Committee of the University of the Free State (ref. no. UFS-HSD2018/0389/3010) and the Free State Department of Health. To ensure patient confidentiality, no identifying information such as names or admission numbers was captured.

Results

Clinical characteristics (*N*=293)

A total of 300 Hickman lines were inserted over the study period; seven cases were excluded owing to missing information or the patient being older than 16 years. The final sample size was therefore 293 lines. The median patient age was 64.7 months (range: 3.2 - 193.3 months). The median days in situ were 132 (range: 0 - 769 days). The most common patient diagnoses were leukaemia (60.8%), solid tumours (28.3%) and lymphoma (10.9%). Insertion sites were recorded as the internal jugular vein (64.2%) or subclavian vein (1.7%); no insertion site was recorded in 34% of the cases. The main reasons for line insertion included: protocol requirement (56.0%); difficult peripheral IV access (23.2%); and patient requests (16.7%). Diverse other reasons accounted for the remainder of cases.

Complications associated with line placement (procedural complications) were found in only 12% of cases, and were recorded

as: bleeding (3.4%), incorrect position (3.1%), failure to insert (1.0%), pneumothorax (0.7%), and 'other' (3.8%). In situ complications were encountered in 37.5% of the cases, of which the most common complications included line sepsis (13.3%), blockage (6.1%) and the line having pulled out (5.5%) (Table 1).

Complications (procedural and in situ) were recorded in less than half (43.3%) the cases. CABSI was noted as reason for line removal in 14.3% of cases. In the remaining cases, removal was due to the end of treatment (37.9%), relapse (5.1%), line blockage (10.6%) or diverse 'other' reasons (21.2%). In 10.9% of cases, patients died with their lines in situ. Overall, 75.1% of the lines served their purpose.

In situ complications of line sepsis (*n*=39)

Line sepsis was an in situ complication in 13.3% of the total number of cases (Table 1). No systemic sepsis was noted in almost a quarter of these 39 cases (23.1%), whereas 61.5% of this set of cases were both neutropenic and septic, and 15.4% presented with symptoms of sepsis without neutropenia. The diagnoses in these patients were leukaemia (56.4%), solid tumours (35.9%) and lymphoma (7.7%).

Line sepsis as a reason for removal was recorded in 38.5% of these cases (Fig. 1). The total number of line days over the course of the study period was 39 889. The number of sepsis episodes (*n*=39) translated to a total rate of 0.98 episodes per 1 000 catheter days. The median number of line days for cases complicated with sepsis was 143 days (range: 14 - 704 days). The lines still served their purpose in 79.5% of cases.

Symptoms of systemic sepsis and accompanying neutropenia (*n*=190)

Symptoms of systemic sepsis and accompanying neutropenia were noted in 190 cases (64.8%). Of these 190 lines, 12.6% developed CABSIs, with blockage recorded as the second most common in situ line complication (5.8%). Approximately two-thirds (67.4%) of patients did not develop any in situ line complications. The diagnoses in the patients in this subgroup were leukaemia (71.6%), solid tumours (17.3%) and lymphoma (11.0%).

Table 1. In situ local complications (*N*=293)

Complications	*n* (%)
None	183 (62.5)
Sepsis	39 (13.3)
Pulled out	16 (5.5)
Blocked	18 (6.1)
Ruptured	3 (1.0)
Unable to take blood	5 (1.7)
Swelling	10 (3.4)
Other	19 (6.5)

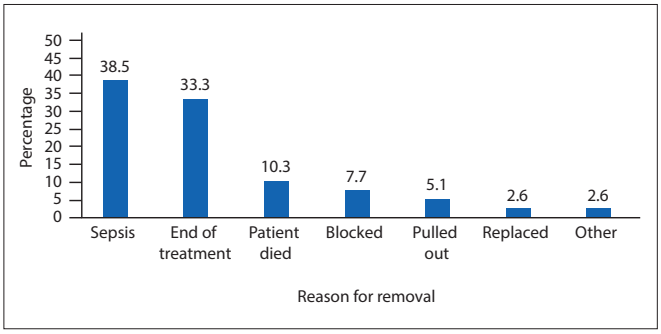

Fig. 1. Reasons for line removal in cases with sepsis (n=*39*)

Only 16.3% of the 190 lines were removed because of sepsis. We found that 14.7% of patients in this group died with their lines in situ and 44.7% had their lines removed because they reached the end of their treatment.

The median number of catheter days for cases with systemic sepsis and accompanying neutropenia was 152 (range: 7 - 769 days). The majority of these lines (*n*=161/190; 84.7%) still served their purpose.

Discussion

The median age of 64.7 months (5.4 years) at line placement is younger than the 7.1 years reported by Adler *et al.*,[10] who noted a young age being a risk factor for complications developing with the use of CVADs.[9] Patients with leukaemia made up 60.8% of our cohort and lymphoma accounted for 10.9%, meaning haematological malignancy featured in almost three-quarters (71.7%) of the patients in our study. This is a higher proportion than reported by Adler *et al.*[10] (57.4%). Haematological malignancies and neutropenia are risk factors for line sepsis.[12-15] Data in the current study showed 0.98 sepsis episodes per 1 000 catheter days, which is lower than the rates reported by Adler *et al.*[10] (4.7 episodes per 1 000 catheter days) and Basford *et al.*[19] (11.4 sepsis episodes per 1 000 catheter days). The median of 132 in situ line days is comparable with the 140.7 days reported by Adler *et al.*[10]

Procedural complications were noted in 12.0% of cases, with in situ complications in 37.5% of cases. Some overlap of complications resulted in a combined complication figure of 43.3%. Almost all the lines were inserted surgically, as per the preferred method during the period reviewed in this study. It is well described that surgically placed lines are associated with more infectious and mechanical complications[19] compared with radiologically assisted (i.e. ultrasound-guided) percutaneous techniques in the paediatric oncological setting. However, the combined complication rate (43.3%) in our study compares well with the rate of 59.6% (infectious or mechanical complications) reported by Basford *et al.*[19] for external tunnelled catheters.

The observed rate of line sepsis (CABSI) in our study (13.3%) compares favourably with that reported for chemo ports in other studies (21.7%[19] 23.5%,[10]) and is better than rates reported for external tunnelled catheters (36.5%,[19] 35.4%,[10] and 47.1%[20]).

In the cases that presented with line sepsis, 61.5% had a combination of neutropenia and systemic sepsis. Of these, almost two-thirds (64.1%) were diagnosed with haematological malignancies. Lines were removed owing to sepsis in only 38.5% of these cases and therefore CVAD use could be successfully salvaged by the administration of antibiotics in a large number of cases.

In the 64.8% of the study population that had neutropenia and symptoms of systemic sepsis, 67.4% had no in situ line complications and only 12.6% developed line sepsis, despite being neutropenic and systemically ill, both risk factors for line sepsis. Lines were removed owing to sepsis in a smaller proportion (16.3%) than expected. Almost half of these patients reached the end of their treatment and the lines would have been removed in any case. Central lines served their purpose in a high proportion of the cohort (84.7%).

Study limitations

The retrospective nature of the study is regarded as a limitation, as vital information was missing from some cases, which resulted in their being excluded from the analysis.

Conclusion

Our analysis shows a low percentage of line sepsis (CABSI) in this cohort (13.3%), despite the study population being young, a large

proportion of haematological malignancies being included and the use of Hickman lines placed surgically. With these characteristics, our study population would have had a high risk for infective complications. The special care taken intraoperatively and the meticulous aseptic handling and maintenance of these lines postoperatively (by teaching staff to manage the lines within strict protocols) may have contributed to the low infective complication rates.

Further studies are recommended to investigate the role of neutropenia and haematological malignancies (leukaemia and lymphoma) in the development of line sepsis.

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Author contributions. LM, PN, KM, KT and RR developed the study protocol, collected the data and prepared the initial draft of the manuscript. EB was the study supervisor, suggested the concept and assisted with protocol development, data collection and interpretation, and manuscript preparation. GJ assisted with study conceptualisation, analysed the data and assisted with interpretation and manuscript development.

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Incidence, types and outcomes of congenital anomalies in babies born at a public, tertiary hospital in South Africa

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Background. Limited information is available on the incidence of major congenital abnormalities (MCAs) in low- and middle-income countries (LMICs).
Objective. To determine the incidence and types of MCA and associated all-cause mortality from a facility with a large delivery service in an LMIC.
Methods. Births and neonatal admission registers of live inborn births between 1 January 2012 and 31 December 2013 at the Chris Hani Baragwanath Academic Hospital, South Africa, were reviewed for diagnosis of MCA.
Results. A total of 201 infants were admitted with a diagnosis of MCA, of which 114 were inborn. This translated to an incidence of 2.60 per 1 000 live births. The cardiovascular (43.9%), gastrointestinal (21%), musculoskeletal (13.2%) and central nervous system (12.3%) were commonly affected systems. Most MCAs were single defects (75.4%), followed by trisomies (19.3%). A significant number of infants with trisomies were born to multigravid women older than 35 years ($p<0.001$). A significant number of infants with single defects were preterm ($p<0.002$) and of low birth weight ($p<0.002$). One third (34%) required surgical intervention before hospital discharge. All-cause mortality at hospital discharge was 20.2%, with more deaths among patients with trisomy 13 (50%) and trisomy 18 (40%) compared with patients with single defects (19.8%) or trisomy 21 (7.8%) ($p<0.05$).
Conclusion. The incidence of MCAs found in this study is much lower than what has been reported from HICs but similar to findings from other LMICs. MCAs in LMIC settings are associated with high mortality rates.

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Congenital anomalies – also commonly referred to as birth defects, congenital disorders, congenital malformations or congenital abnormalities – are conditions of prenatal origin that are diagnosed before, at or after birth.[1] Major congenital anomalies generally have a negative impact on an infant's health, including developmental or survival outcome.[2] They are also most likely to be associated with high social and financial demands on the family and healthcare system. Children with major congenital anomalies often have complex needs within the home setting.[3-5] Globally, approximately 3.2 million children are born with congenital anomalies every year. These conditions are a major contributor to infant and under-5 mortality.[6,7] According to the World Health Organization, 17 - 42% of infant deaths are attributed to congenital anomalies.[8] In South Africa (SA), congenital abnormalities are the fourth highest cause of neonatal mortality, accounting for 17.6% of all neonatal deaths.[5]

The incidence of major congenital anomalies in high-income countries (HICs) has been reported as 26.9 per 1 000 live births for the period 2005 - 2009.[8] However, there is a paucity of data on incidence and types of congenital anomalies and the subsequent outcome of neonates with these anomalies from low- and middle-income countries (LMICs). Although the incidence of congenital abnormalities in LMICs is likely similar to that in HICs, outcomes during the neonatal period may be different because of the difference in resource availability in the settings.

The aim of this study was to determine the incidence and types of congenital abnormalities in SA, as an LMIC, together with the outcomes of affected infants at the time of hospital discharge.

Methods

Study design and setting

This retrospective, descriptive study was conducted at the Chris Hani Baragwanath Academic Hospital (CHBAH), which is a public tertiary hospital in Johannesburg, SA. It is a major referral centre for neonates with congenital anomalies from local clinics and hospitals elsewhere in Gauteng and neighbouring provinces. At the time of the study, it was one of only two centres in southern Gauteng that offered tertiary and surgical services for neonates with congenital anomalies.

This hospital handles ~22 000 in-hospital births per year and offers secondary or tertiary healthcare to approximately 8 000 births from community health centres or midwifery obstetric units in Soweto.

Study population

All live births at CHBAH from the period January 2012 - December 2013, with clinically apparent major congenital abnormalities and those subsequently diagnosed on investigative studies during the neonatal period, were eligible for inclusion in the study. Patients admitted to either medical or surgical neonatal wards were included.

Data collection and analysis

Hospital registers from labour and delivery rooms in medical and surgical neonatal wards were reviewed for documentation of a diagnosis of congenital anomalies. Hospital records of patients diagnosed with a congenital anomaly as documented in the

registers were reviewed. Data were collected on maternal and infant characteristics, types of abnormality, need for surgical management, and outcome to hospital discharge.

Data were entered into a Excel spreadsheet (Microsoft Corp., USA) and then analysed using Statistica (v. 13.3; Dell, USA). Abnormalities were classified as either multiple or single. Cases of multiple abnormalities were subsequently grouped as being either syndromic/association or non-syndromic. For multiple abnormalities, the affected organ system was noted as the system with major abnormalities or for which the patient needed admission.

The analysis focused on inborn infants only. Categorical variables were described according to frequencies and percentages of the total cohort. Continuous variables were described using means and standard deviation (SD) (if normally distributed) or medians and ranges (if not normally distributed). Chi-squared (χ^2) and Fisher's exact tests, with a significance level of $p<0.05$, were used to compare characteristics and outcomes of neonates with trisomies and those who had single defects.

Results

Incidence and types of anomalies

Records of 201 neonates born with major congenital abnormalities were found for the study period, of whom 87 were referred from other facilities and 114 were inborn. With a total of 43 876 in-hospital live births during the study period, the incidence of major congenital anomalies at CHBAH was 2.6 per 1 000 live births. Of the 114 neonates with major congenital anomalies, 86 cases (75%) presented with single defects and 28 cases (25%) with multiple defects (Fig. 1). Among the 28 neonates with multiple defects, 22 had trisomies, three had associations and three had multiple anomalies that could not be allocated to a known syndrome (non-syndromic).

Maternal and infant characteristics

Maternal and infant characteristics are presented in Table 1. Most of the infants (*n*=107; 94.7%) were born to African mothers. The majority of mothers (*n/N*=63/102; 61.7%) were between 20 and 35 years old. Two-thirds (*n*=68; 66%) were multigravida and approximately three-quarters of the women whose HIV status was known were negative (*n*=86; 74%). Just over half (56%) of neonates were born by caesarean section. The mean (SD) birth weight of infants was 2 530 (785) g. Of the 110 records, 58% (*n*=64) showed low birth weight (<2 500 g). The mean (SD) gestational age was 36 (3) weeks. Of the available records, 61% showed preterm births (gestational age <37 weeks). The proportion of male to female infants was even. Most abnormalities (>90%) were diagnosed post-delivery.

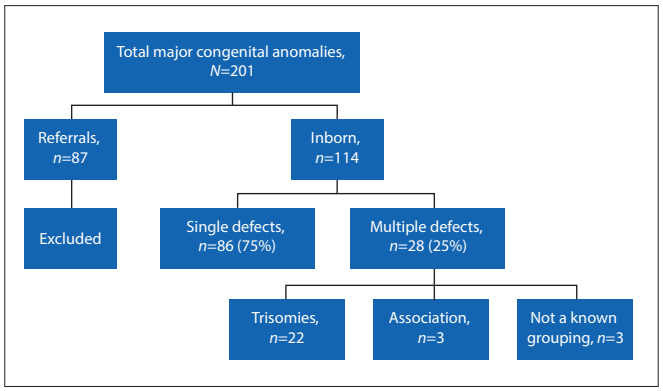

Fig. 1. Study population and major congenital anomalies identified.

Organ systems affected by congenital anomalies

Cardiovascular anomalies accounted for 43.9 % of cases, followed by anomalies of the gastrointestinal (21%), musculoskeletal (13.2%) and central nervous systems (12.3%) (Table 2). Among the cardiovascular anomalies, the majority were acyanotic (79%), with ventricular septal defects and patent ductus arteriosus being the commonest; patent ductus arteriosus diagnosed in preterm infants was excluded. The most common gastrointestinal tract abnormalities were abdominal wall defects (*n*=11/24; 45.8%), with gastroschisis being more common than omphalocele, followed by tracheoesophageal fistula (*n*=4/24; 16.7%). Skeletal dysplasias (*n*=6/15; 40%) and isolated cases of club foot (*n*=3/15;20%) were common musculoskeletal abnormalities. Common central nervous system abnormalities included congenital hydrocephalus (*n*=5/14; 35.7%) and meningomyelocele (*n*=5/14; 35.7%) (Table 3).

Table 1. Characteristics of mothers and their infants with congenital abnormalities

Characteristics	*n* (%)
Maternal characteristics	
Maternal age (years), *N*=102*	
<20	13 (12.7)
20 - 35	63 (61.7)
>35	26 (25.6)
Gravidity (*N*=103)*	
<2	35 (34.0)
2 - 4	59 (57.3)
>4	9 (8.7)
HIV status (*N*=107)*	
Positive	28 (26.2)
Negative	79 (73.8)
Mode of delivery (*N*=105)*	
Vaginal delivery	46 (43.8)
Caesarean section	59 (56.2)
Antenatal care attendance (*N*=114)	
Yes	108 (94.7)
No	6 (5.3)
Infant characteristics	
Birth weight (g), mean (SD) (*N*=110)*	2 530 (785)
Birth weight >2 500 g	46 (41.8)
Birth weight ≤2 500 g	64 (58.2)
Gestational age (weeks), mean (SD) (*N*=108)*	36 (3)
≥37	42 (38.9)
<37	66 (61.1)
Sex (*N*=114)	
Male	55 (48.2)
Female	56 (49.1)
Ambiguous	3 (2.6)
Apgar score, median (range) (*N*=110)*	
At 1 minute	8 (1 - 9)
At 5 minutes	9 (2 - 10)
Period of diagnosis (*N*=93)*	
Antepartum	9 (9.7)
Post partum	84 (90.3)

*Data not available for all 114 patients.
SD = standard deviation

Characteristics of infants with trisomies

The maternal and infant characteristics of neonates with trisomies are noted in Table 4. Of the 28 neonates with multiple congenital abnormalities, 22 (20%) met the criteria for trisomies. Trisomy 21 was most commonly observed (n=13/22; 59%), followed by trisomy 18 (n=5/22; 23%) and trisomy 13 (n=4/22; 18%). Infants who presented with trisomies were all born to multigravid women, most of whom were older than 35 years. Mean (SD) birth weight of infants with trisomy was 2 452 (622) g, and mean (SD) gestational age was 37 (3) weeks. Of the 22 infants who presented with trisomies, 12 (55%) were male. The majority of trisomy 21 patients had congenital cardiac defects (n=10/13; 76.9%). The most common cardiac anomaly was atrioventricular septal defect, followed by atrial septal defect and patent ductus arteriosus.

Outcomes to hospital discharge

Approximately a third of the infants with congenital anomalies (34%) required surgical intervention before hospital discharge (Table 5). Less than half required mechanical ventilator support (40%). Overall survival to hospital discharge was 79.8% (mortality rate = 20.2%). There was no statistically significant difference in mortality rate according to need for surgery (23.1% v. 21.2%, p=0.821) or mechanical ventilation (28.3% v. 15.4%, p=0.110) compared with those who did not need these interventions. Common causes of mortality were healthcare-associated infections, mainly in those who required surgical intervention, and severe or complex congenital anomalies that could not be corrected or were inoperable. Of the 13 cases of trisomy 21, two patients required mechanical ventilation, of whom one died following Gram-negative sepsis. Two deaths occurred in the trisomy 18 group (not related to sepsis); the other three patients survived to hospital discharge. Two of the four patients who presented with trisomy 13 died, both from sepsis.

Table 2. Organ systems affected by congenital anomalies (N=114)

Affected system	n (%)	Incidence (per 10 000 live births)	Incidence (per 1 000 live births)
Cardiovascular	50 (43.9)	11.4	1.14
Gastrointestinal	24 (21.1)	5.5	0.55
Musculoskeletal	15 (13.2)	3.4	0.34
Central nervous system	14 (12.3)	3.2	0.32
Urogenital	13 (11.4)	3.0	0.30
Head and neck	13 (11.4)	3.0	0.30
Respiratory	5 (4.4)	1.1	0.11
Skin	3 (2.6)	0.7	0.07
Total	137*	26	2.6

*In some patients, more than one organ system was affected, hence the total number of anomalies exceeds the total number of patients (114).

Comparison between neonates with trisomies and those with single defects

There were 22 patients with trisomies and 86 with single defects (Table 6), with more infants born to mothers of advanced age (>35 years) in the group with trisomies than the group with single defects (63.6% v. 11.6%; p<0.001). All trisomy infants were born to multigravid women, whereas 59.3% of women whose infants presented with single defects had had previous pregnancies (p<0.001). More infants with single defects were of low birth weight (<2 500 g) or born preterm (<37 weeks' gestational age) compared with those who presented with trisomy (for both categories: 74.4% v 36.4%; p=0.002). There were no statistically significant differences in maternal HIV status, infant sex, need for surgery, or mortality between infants with trisomies and those with single defects.

Discussion

This study was a retrospective record review to investigate the incidence and types of major congenital anomalies and the associated all-cause mortality from a hospital in an LMIC. The study showed an incidence of 2.6 congenital abnormalities per 1 000 live births at a public tertiary hospital in Gauteng, SA. The majority of babies with congenital abnormalities were born preterm and were of low birth weight. The cardiovascular and gastrointestinal systems were the most commonly affected. Single defects accounted for the majority of congenital abnormalities. Most patients who presented with multiple defects had trisomies. About a third of neonates with major congenital abnormalities required corrective interventions before hospital discharge. A fifth demised before

Table 3. Specific diagnosis in systems commonly affected by congenital anomalies

Cardiovascular (N=53), n (%)		Gastrointestinal (N=24), n (%)		Musculoskeletal (N=15), n (%)		Central nervous system (N=14), n (%)	
Acyanotic	42 (79.2)	Gastroschisis	7 (29.2)	Skeletal dysplasia	6 (40)	Congenital hydrocephalus	5 (35.7)
Ventricular septal defect	14 (33)	Omphalocele	4 (16.7)	Club foot	3 (20)	Meningomyelocele	5 (35.7)
Patent ductus arteriosus	15 (35.7)	Tracheoesophageal fistula	4 (16.7)	Myopathy	2 (13.3)	Encephalocele	2 (14.3)
Atrial septal defect	9 (21.4)	Anorectal malformation	3 (12.5)	Abnormal vertebrae	2 (13.3)	Microcephaly	1 (7.1)
Atrioventricular septal defect	(7.1)	Duodenal atresia	3 (12.5)	Hip dysplasia	1 (6.7)	Anencephaly	1 (7.1)
Coarctation of aorta	1 (2.4)	Jejunal atresia	2 (8.3)	Knee dislocation	1 (6.7)		
Cyanotic	11 (20.8)	Others	1 (4.2)				
Double outlet right ventricle	3 (27)						
Tetralogy of Fallot	2 (18.2)						
Pulmonary atresia	2 (18.2)						
Others	4 (36.4)						

Table 4. Characteristics of mothers of infants with trisomies

Characteristics	All (*N*=22), *n* (%)	Trisomy 21 (*N*=13), *n* (%)	Trisomy 18 (*N*=5), *n* (%)	Trisomy 13 (*N*=4), *n* (%)
Maternal age (years)				
<20	0	0	0	0
20 - 35	8 (36.4)	5 (38.5)	2 (40.0)	1 (25.0)
>35	14 (63.6)	8 (61.5)	3 (60.0)	3 (75.0)
Gravidity				
Primigravida	0	0	0	0
Multigravida	22 (100)	13 (100)	5 (100)	4 (100)
Mode of delivery				
Caesarean section	6 (27.3)	5 (38.5)	0	1 (25.0)
Vaginal delivery	16 (72.7)	8 (61.5)	5 (100)	3 (75.0)
HIV status				
Negative	16 (72.7)	10 (76.9)	3 (60.0)	3 (75.0)
Positive	6 (27.3)	3 (23.1)	2 (40.0)	1 (25.0)
Antenatal care				
Yes	22 (100)	13 (100)	5 (100)	4 (100)
No	0	0	0	0

Table 5. Survival to hospital discharge according to type of abnormality and intervention

Patient group	Deaths, *n* (%)
All patients (*N*=114)	23 (20.2)
Survival according to abnormalities	
Trisomy 21 (*N*=13)	1 (7.7)
Trisomy18 (*N*=5)	2 (40.0)
Trisomy13 (*N*=4)	2 (50.0)
Non-syndromic (*N*=3)	1 (33.3)
Association (*N*=3)	0 (0)
Single-defects (*N*=86)	17 (19.8)
Survival according to need for neonatal surgical intervention	
Surgery required (*N*=39)	9 (23.1)
Surgery not required (*N*=66)	14 (21.2)
Survival according to need for mechanical ventilation	
Ventilated (*N*=46)	13 (28.3)
Not ventilated (*N*=65)	10 (15.4)

Table 6. Characteristics (maternal and infant) and outcomes of infants with trisomies compared with those with single defects

Characteristic	Trisomies (*N*=22), *n* (%)	Single defect (*N*=86), *n* (%)	*p*-value
Maternal age (years)			
<20	0	13 (15.1)	
20 - 35	8 (36.4)	63 (73.3)	<0.001
>35	14 (63.6)	10 (11.6)	
Gravidity			
Primigravida	0	35 (40.7)	<0.001
Multigravida	22 (100)	51 (59.3)	
HIV status			
Positive	6 (27.3)	28 (32.6)	0.798
Negative	16 (72.7)	58 (67.4)	
Sex*			
Female	10 (45.5)	42 (50.6)	0.811
Male	12 (54.5)	41 (49.4)	
Birth weight (g)			
<2 500	8 (36.4)	64 (74.4)	0.002
≥2 500	14 (63.6)	22 (25.6)	
Gestational age (weeks)			
<37	8 (36.4)	64 (74.4)	0.002
≥37	14 (63.6)	22 (25.6)	
Need for surgical intervention			
Yes	4 (18.2)	35 (40.7)	0.080
No	18 (81.8)	51 (59.3)	
Survival to hospital discharge			
Yes	17 (77.3)	69 (80.2)	0.771
No	5 (22.7)	17 (19.7)	

*Three infants among those with single defects had ambiguous genitalia.

hospital discharge, with the major cause of death being healthcare-associated infections.

The incidence of congenital abnormalities found in this study is similar to that reported from Nigeria (2.8 per 1 000 live births), also an LMIC.[4] It is ten times lower than the incidence of 26.9 per 1 000 live births reported from an HIC,[9] likely owing to better surveillance systems and data registries typically being in place in developed countries than in LMICs.[10] Given the retrospective design of the current study, it is possible that some infants with major congenital anomalies but who were not recorded in the registries could have been missed. In contrast, surveillance for congenital abnormalities in HICs includes antenatal ultrasound examinations, which would allow for early detection of abnormalities and consequently better documentation.

The review suggests that the opportunity to detect congenital anomalies in utero was missed in this cohort, as although most women in the study (90%) attended antenatal care, only 10% had a diagnosis made in the antenatal period. In addition, stillbirths were not included in this study. It is possible that the small number of anomalies detected in utero is due to antenatal sonar examinations not having been offered routinely to all pregnant women during the study period. Excluding stillbirths and data on termination of pregnancy for fetal anomalies leads to the burden of disease due to congenital anomalies being underestimated, obscuring the lack of progress with regard to primary, secondary and tertiary prevention measures and programmes.

The incidence of central nervous system anomalies in this study was 3.2 per 10 000 live births, which is much lower than what has been reported from three other studies in SA.[5,11,12]. The most recent of these, conducted in 2004 - 2005, reported an incidence of 9.8 per 10 000 live births.[5] The difference in the incidence rates may be due to regional variation in this type of abnormality. Globally, the incidence of neural tube defects varies greatly, with estimates ranging from 1.2 to 124.1 per 10 000 live births.[13]

In SA, staple foods such as maize and wheat products are fortified with folic acid.[6,14,15] Fortification has had a major effect in reducing central nervous system abnormalities in other countries.[9,16] However, as the current study reviewed a small set of data from a single centre, it is difficult to know whether fortification contributed to the low incidence of neural tube defects.

Surgical intervention is an important but unheralded component of the services required to treat birth defects. Many of these are cost-effective, life-saving interventions that can improve long-

term prognosis. In LMICs, where resources are typically limited, the availability of surgical services and access to intensive care beds might result in delays in offering children with congenital abnormalities the necessary interventions. Sepsis was a major contributor to mortality, highlighting the importance of reducing hospital stay of these patients and observing infection control measures in managing these patients while awaiting surgery.

The mortality rate found in the current study (20%) is higher than that reported in a study from Nigeria (10%),[17] and much higher than a rate of 1.13% in Italy (an HIC).[18] The higher mortality rate seen in the current study may be ascribed to only major congenital anomalies having been included, whereas the two other studies[17,18] included all congenital anomalies, including minor cases such as inguinal hernias, hypospadias and genu recurvatum.

Congenital anomalies are a considerable health problem throughout the world. Knowledge of their incidence, intervention requirements and outcomes can assist in planning and expectant management of infants with major anomalies as well as management of affected pregnancies. As the aetiology of some conditions may be elusive and multifactorial, continued surveillance is important in identifying causal or preventive factors associated with the development of major congenital anomalies.[19,20]

Study limitations

Incomplete data introduce a limitation in a retrospective study design and complicate identifying factors that might have been associated with the incidence and outcomes of congenital anomalies. Possible risk factors, such as outcomes of previous pregnancies (previous abortions or presence of congenital anomalies), maternal illness and drugs used before or during pregnancy were often not recorded, and as such prospective data collection would be a more effective approach in a study of this kind.

Conclusion

The incidence of congenital anomalies found in this study is lower than what has been reported from HICs, but is likely an underestimation of the true incidence in our population. The findings suggest that more efforts should be directed at early identification and registration of congenital abnormalities to allow for better understanding of the burden of congenital anomalies and improve healthcare planning and management of patients, possibly reducing mortality. Collaboration between major centres that offer tertiary and surgical services to children with congenital abnormalities might assist in establishing a sentinel site surveillance system. The development of efficient provincial or national registries and population-based studies in public health settings in LMICs is important to determine the incidence and types of congenital abnormality accurately. Accurate data can contribute to identifying possible aetiological factors in the development of congenital abnormalities, which, in turn, may help to prevent them.

Declaration. XX.

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Correlation between pulse oximetry and the clinical profile of children with acute lower respiratory tract infection

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Background. Hypoxaemia is a common predictor of mortality and a potent marker of severe illness in children with acute lower respiratory tract infection (ALRTI).
Objective. To determine the mean oxygen saturation (SpO2) in children with ALRTI and its correlation with selected clinical and anthropometric variables.
Methods. A cross-sectional study of 178 children, aged between 2 months and 5 years, treated in two teaching hospitals in southeast Nigeria. All patients were assessed for ALRTI, focusing on their clinical profile and sociodemographic risk factors. Student's *t*-test was used to compare means of discrete variables. Pearson correlation was used to express association between discrete variables and multiple regression was used to predict dependent variables.
Results. Patients with severe ALRTI had significantly lower oxygen saturation (SpO2=89%) than those with mild disease (SpO2=95%) (p=0.001). A negative correlation was found between oxygen saturation and respiratory rate. Multiple regression analysis showed respiratory rate to be the only variable predicting oxygen saturation in children with ALRTI, with a negative association between the two variables.
Conclusion. Low oxygen saturation is associated with decreased respiratory rate in children with ALRTI. Oxygen supplementation should always be considered in children with ALRTI, especially those with severe disease.
Key words: *acute lower respiratory infection, pulse oximetry, oxygen saturation*

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Acute lower respiratory tract infection (ALRTI) is defined as an infection that affects the airways just below the epiglottis and the aryepiglottic fold and which lasts for 28 days, with the commonest forms being pneumonia and acute bronchiolitis.[1] ALRTIs are a major cause of morbidity and mortality in children under the age of 5 years worldwide[1] and as such are important indicators of health indices in developing countries.[2]

Hypoxaemia is a common predictor of mortality and a potent marker of severe illness in children with pneumonia and bronchiolitis.[3-5] Pulse oximetry is typically used to measure a patient's peripheral arterial oxygen saturation, which Modi *et al.*[6] noted as the best clinical predictor of pneumonia.

The use of pulse oximetry to predict the severity of symptoms in children with ALRTIs seems uncommon, with previous studies correlating oximetry readings with respiratory rate but without considering pulse rate and other clinical correlates. This current study therefore focused on determining mean oxygen saturation (SpO2) in children with ALRTIs and correlating findings with weight, height, respiratory rate, pulse rate and body temperature. An additional objective was to determine whether pulse oximetry readings have predictive value for respiratory rate.

Method

Study design and setting

This was a prospective, cross-sectional study to assess pulse oximetry readings and the clinical profile of children younger than 5 years with an ALRTI (pneumonia or bronchiolitis). The study was conducted at the Enugu State University Teaching hospital, Enugu, and Ebonyi State University Teaching Hospital, Abakaliki, in southeast Nigeria. Enugu, the capital city of Enugu State, has an altitude of 180 metres above sea level and an average humidity of 94%.

The study population comprised children between 2 months and 5 years old who had been admitted to the paediatric emergency room or ward with an ALRTI. Children with a history of catarrh, wheezing, fever, cough and dyspnoea that lasted for up to 2 weeks were included in the study. Clinical features considered were tachypnoea, chest retractions (with or without crepitation or rhonchi) and chest X-rays showing bilateral patchy opacities, lobar opacification or hyperinflation of the lungs.

Children with personal or family history of asthma or other chronic lung or cardiac disease were excluded from the study, as were patients who were HIV positive or whose caregivers declined consent.

Measurements

Pulse oximetry

The pulse oximeter consists of a probe containing a photodetector and light-emitting diode (LED). The diode emits light at a specific wavelength while the photodetector measures the amount of light transmitted through a selected vascular bed such as in the earlobe, toes or fingertips.[7] According to the Beer–Lambert law of light absorption, light is absorbed when it passes through plasma that contains a solute (such as haemoglobin), which absorbs light at a specific wavelength. Arterial blood subsequently appears bright

red, whereas venous blood has a blue hue. The absorption readings are fed into an algorithm in a microprocessor to calculate the oxyhaemoglobin saturation, which is displayed to the user.[7]

To measure saturation, a patient's finger was wiped with alcohol and any nail polish was removed to allow for maximum light absorption. The fingers were also examined for features that could have influenced readings, such as excessive skin pigmentation.

The device was placed to fit the digit without restricting circulation, which could have resulted in a false reading. A pulse rate compatible with age and normal oxygen saturation was evidence of a correct reading.[8-10] We used normative values for heart rate and age to verify readings. The displayed pulse rate was cross-checked against radial pulsation, measured by palpation on the other hand.[8-10] The best of two SpO2 readings was recorded.

Anthropometry

Weight and height were measured using a stadiometer (Detecto, USA).[10] Recordings were made to the nearest 0.5 kg and 0.5 cm, respectively.[10] Body mass index (BMI) was calculated according to the standard formula $\text{BMI (m}^2\text{)} = \frac{\text{weight (kg)}}{[\text{height (m)}]^2}$,[11,12] while body surface area (BSA) was calculated according to the Mosteller formula:[13]

$$\text{BSA (m}^2\text{)} = \sqrt{\frac{\text{height (m)} \times \text{weight (kg)}}{3600}}$$

Data analysis

Data were analysed using IBM Statistics for Windows, version 20 (IBM Statistics, Chicago). Categorical variables were expressed as proportions and percentages, whereas discrete variables were expressed as means and standard deviations (SDs) and compared for statistical difference using Student's *t*-test. Pearson's correlation coefficient was used to express the association between discrete variables, with a significance level of $p<0.05$, and multiple regression analysis was used to predict the dependent variable (SpO2) when other independent variables were kept constant.

Ethical considerations

Approval for the study was obtained from the University of Nigeria Teaching Hospital's Health Research and Ethics Committee (ref. no.: IRB00002323).

Results

A total of 178 patients were assessed for ALRTI, of whom 97 (54.5%) were male and 81 (45.5%) were female. The mean (SD) age across the sample was 13.1 (11.7) months. Other anthropometric indices are summarised in Table 1, with clinical parameters indicated in Table 2.

Table 3 shows the correlation between oxygen saturation and clinical parameters and anthropometric indices. Oxygen saturation was negatively correlated with respiratory rate($p=0.001$). Patients with severe ALRTI had significantly lower mean (SD) oxygen saturation (89% (8.0%)) than those with mild disease (95% (4.0)) ($p<0.001$). Mean (SD) oxygen saturation was not significantly different between male (91% (7.0)) and female (91% (8.0)) patients ($p=0.9$).

Multiple regression analysis revealed a significant negative association between oxygen saturation and respiratory rate ($p=0.002$) (Table 4). This indicates that as respiratory rate decreases, the oxygen saturation also decreases when other variables are kept constant. A one-unit decrease in respiratory rate resulted in a 0.28% decrease in oxygen saturation.

Discussion

The mean oxygen saturation recorded across the sample was 90.6%. Respiratory rate and pulse rate were 61 breaths per minute and 140 beats per minute, respectively. These values suggest the action of cytokines and substances of acute respiratory phase reactants, which cause inflammatory changes in ALRTI.

Hypoxaemia determined by means of pulse oximetry has been used as clinical indicator in children with ALRTI who require hospitalisation.[3,14] The increased respiratory and pulse rate at a saturation level of 90% seen in this study agrees with findings from another study, which showed children with a saturation level <90% to have 5.4 times higher risk of mortality.[15]

Our results show a significant negative correlation between oxygen saturation and respiratory rate in the sample, with children with severe ALRTI having significantly lower saturation levels (SpO2=89%) than those with mild disease (SpO2=95%). According to a multiple regression analysis, respiratory rate was the only vital sign that predicted oxygen saturation. The findings suggest that using clinical signs to determine whether a patient needs oxygen is unreliable.[16] This is in line with findings from a systematic review, which showed that neither single nor combined symptoms are effective predictors of hypoxaemia in young children with ALRTI.[16,17]

In this study, a decrease of one breath per minute resulted in a

Table 1. Anthropometric parameters (*N*=178)

Variable	Mean (SD)
Age (months)	13.1 (11.7)
Weight (kg)	8.8 (4.5)
Height (cm)	72.1 (17.3)
Mid upper-arm circumference (cm)	14.4 (4.6)
Head circumference (cm)	44.5 (5.5)

SD = standard deviation.

Table 2. Clinical variables of patients presenting with an acute lower respiratory tract infection (*N*=178)

Variable	Mean (SD)
SpO2 (%)	90.6 (7.6)
Respiratory rate (breaths/min)	61 (17)
Pulse rate (beats/min)	140 (19)
Body temperature (°C)	38.2 (1.1)

SD = standard deviation; SpO2 = oxygen saturation.

Table 3. Correlation between oxygen saturation and clinical variables

Variable	Pearson correlation coefficient	*p*-value
Age (*N*=162)	0.09	0.2
Temperature (*N*=161)	0.1	0.1
Pulse rate (*N*=153)	–0.007	0.9
Respiratory rate (*N*=161)	–0.4	0.001
Weight (*N*=160)	0.01	0.8
Height (*N*=162)	0.09	0.2
Mid upper-arm circumference (*N*=140)	0.04	0.6
Head circumference (*N*=152)	0.1	0.2

Table 4. Multiple regression analysis showing association between the dependent variable (oxygen saturation) and various clinical and anthropometric variables

	Unstandardised coefficients		Standardised coefficients		
Variables	β	SE	β	*t*-statistic	*p*-value
Constant	91.376	10.485		8.715	0.000
Respiratory rate	−0.131	0.042	−0.280	−3.135	0.002
Pulse rate	0.004	0.034	0.010	0.116	0.908
Weight	−0.177	0.398	−0.071	−0.445	0.657
Height	0.065	0.063	0.142	1.018	0.311
Mid-arm circumference	0.011	0.161	0.006	0.071	0.944
Head circumference	0.078	0.237	0.045	0.330	0.742

SE = standard error.

0.28% decrease in oxygen saturation. This finding can be useful in calculating the exact amount of oxygen to be given to a paediatric patient with severe respiratory distress due to ALRTI.

Conclusion

Respiratory rate was found to be the only vital sign to accurately predict oxygen saturation in the sample of children with ALRTI. A decrease of one breath per minute was associated with a decrease of 0.28% in oxygen saturation.

Declaration. None.

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Conflicts of interest. None.

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Physical activity and sedentary behaviours during pregnancy are associated with neonatal size at birth

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Background. Pregnancy is a crucial time to examine modifiable maternal behaviours associated with neonatal outcomes so that preventative measures can be taken against childhood obesity.
Objectives. This study aimed to examine the pathways through which maternal physical activity impacted neonatal size and body composition.
Methods. A subsample of participants who had objectively measured physical activity data were included from a pregnancy cohort study. Sociodemographic data were collected at the first visit during pregnancy. Gestational weight gain (GWG) was calculated at each visit, and the presence of gestational diabetes, hypertension and HIV were assessed. Physical activity was measured using a hip-worn triaxial accelerometer, at 14 - 18 weeks' and 29 - 33 weeks' gestation. At delivery, gestational age, birthweight and length were measured and neonatal body composition was analysed. A structural equation model (SEM) was run with either weight-to-length ratio (WLR) or fat mass index (FMI) as the outcome.
Results. A total of 84 participants were included in this study, and a subsample of neonates (n=45) also had FMI data. Most (66%) mothers presented as overweight or obese at their first visit, and gained on average 0.35 (19) kg per week. The SEM showed that only gestational age at delivery and sedentary time were positively associated with WLR. Step count was directly associated with GWG (ß=-0.02, p=0.01), and with gestational age (ß=0.16, p=0.04), and was therefore indirectly associated with decreased fetal abdominal circumference.
Conclusion. This study showed that increasing daily step count and decreasing sedentary behaviour could have beneficial effects on maternal health as well as delivery outcomes and neonatal size.

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Pregnancy is a complex physiological state including a number of interrelated physiological processes; health behaviours prior to, and during, this time can have effects on both maternal and neonatal health. Some risk factors may even continue to impact on the offspring's health into adulthood.[1] Therefore this is a crucial period to examine modifiable maternal behaviours, and to determine which of these behaviours are associated with neonatal body size and composition outcomes so that preventative measures can be taken against childhood and later life obesity.

Previous research from a South African (SA) pregnancy cohort has shown that factors occurring pre conception and during pregnancy were associated with fetal growth, and in some cases with neonatal body composition (fat mass index (FMI)) or size (specifically weight-to-length ratio (WLR)). Specifically, preconception factors such as socioeconomic status (SES), whether or not the pregnancy was planned, and parity; and maternal lifestyle factors such as body mass index (BMI) at the start of pregnancy and diet have been associated with fetal and/or neonatal size.[2-4] Furthermore, pregnancy factors such as gestational diabetes mellitus (GDM), HIV status and treatment, and gestational weight gain (GWG), have also been associated with fetal growth and/or FMI or WLR.[2-4] Additionally, objectively measured physical activity during pregnancy was shown to be associated with GWG in a sub-sample of this population, but not with any delivery outcomes.[5] Various other potential predictors have been examined in relation to fetal growth and FMI or WLR in this population,[2-6] and we have therefore been able to develop a conceptual model showing the potential pathways through which maternal factors before and during pregnancy are related to FMI and/or WLR (Fig. 1).

However, differential effects have been shown when considering either WLR (size) or FMI (body composition) as the outcomes. While neonatal size is used as a predictor of childhood obesity and disease risk, newborn adiposity has been shown to be more indicative of metabolic programming and thus short- and long-term risk of obesity and disease risk.[7] Additionally, we have not yet studied the combined effects of all of these pathways in the same model, in order to determine which pathways are directly or indirectly associated with FMI or WLR. Furthermore, while maternal physical activity has been examined in relation to delivery outcomes, we have not yet examined how physical activity and sedentary behaviours are related to fetal growth or neonatal FMI or WLR; previous research on this topic shows varied results.[8-15] As maternal physical activity has been associated with GWG,[5] we suspect that physical activity patterns may play a role in the relationship between maternal health during pregnancy and neonatal body composition and size outcomes.

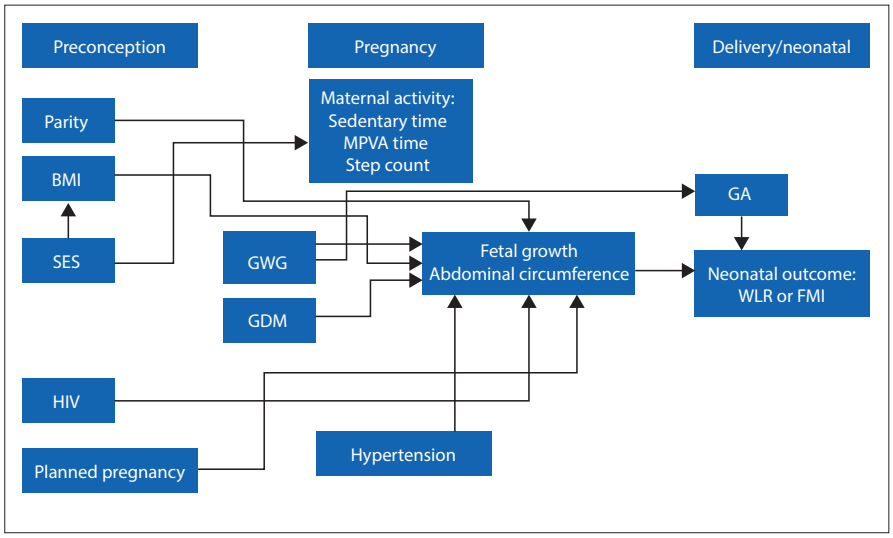

Fig. 1. Conceptual model based on previous literature in this population. (BMI = body mass index; GWG = gestational weight gain; GDM = gestational diabetes mellitus; SES = socioeconomic status; HIV = human immunodeficiency virus; MVPA = moderate to vigorous physical activity; GA = gestational age; WLR = weight to length ratio; FMI = fat mass index.)

The present study therefore aims to examine the interrelationships between maternal biological and lifestyle factors, and fetal growth (Fig. 1) using a structural equation model (SEM) in order to specifically determine the pathways through which maternal physical activity behaviours influence (*i*) neonatal size (WLR), and (*ii*) body composition in a subsample who had FMI measures.

Methods

Study setting and participants

Participants were recruited from a prospective longitudinal pregnancy cohort study (the Soweto First 1000-Days Study (S1000)) which was conducted at the South African Medical Research Council (SAMRC)/ Wits Developmental Pathways for Health Research Unit (DPHRU), at the Chris Hani Baragwanath Academic Hospital (CHBAH) in Soweto, Johannesburg, South Africa. The S1000 study has been explained in detail elsewhere,[2] but in brief, 1 017 naturally conceived pregnant women were enrolled from Soweto at <14 weeks' pregnant. Data were collected at six time-points during pregnancy (<14 weeks; 14 - 18 weeks; 19 - 23 weeks; 24 - 28 weeks; 29 - 33 weeks and 34 - 38 weeks), as well as at delivery. For the purpose of this analysis, a subsample of participants who had objectively measured physical activity data as well as complete WLR data (n=84) were assessed;[5] and a subsample of these also had FMI data (n=45). Ethical clearance for the study was obtained from the University of the Witwatersrand's Human Research Ethics Committee (ref nos. M120524 and M130309). All study participants provided informed written consent prior to their inclusion in the study.

Maternal data

Sociodemographic data were collected at the first visit during pregnancy (<14 weeks' gestational age) in an interview using questionnaires administered by trained research assistants. Household socioeconomic status (SES) was estimated by scoring each participant according to the number of physical assets possessed out of a possible 11, based on standard items used in the Demographic and Health Surveys household questionnaire.[16,17] Women self-reported their date of birth at enrolment, from which their age was calculated. Women reported whether their current pregnancy was planned or unplanned. Parity was defined as the number of previous births at a gestational age of 24 weeks or more – regardless of whether the infant was born alive or was stillborn. Self-reported HIV-status was collected at baseline as well as at each subsequent pregnancy visit, and confirmed using the results from the participant's antenatal clinic card. All HIV-positive participants were receiving antiretroviral treatment (ART) during the study.

Maternal anthropometry was collected at the first pregnancy visit by trained research assistants. Maternal height was measured to the nearest 1 mm at baseline using a wall-mounted stadiometer (Holtain, UK). A digital scale was used to measure maternal weight to the nearest 0.1 kg at each pregnancy visit. Weight at recruitment (<14 weeks) was used as a proxy for pre-pregnancy weight and, together with height, was used to calculate maternal BMI (weight (kg)/height (m^2)).[18] GWG (kg/week) was calculated as (weight at final pregnancy visit – weight at recruitment)/weeks of follow-up). A two-hour 75 g oral glucose tolerance test (OGTT) was conducted at 24 - 28 weeks' gestation in order to determine whether gestational diabetes mellitus (GDM) was present according to the World Health Organizations' (WHO) 2013 criteria.[19] Maternal blood pressure (mmHg) was measured at the fourth pregnancy visit (24 - 28 weeks) using an Omron 6 automated machine (Kyoto, Japan). A 5-minute seated rest was observed before blood pressure measurements were taken. Seated blood pressure was measured three times on the right side, with a 2-minute interval between each measurement. Hypertension was defined as a systolic measure ≥140 and/or a diastolic measure ≥90 using the mean of the second and third readings according to the NICE guidelines (NG133, 2019).

Physical activity was measured using a hip-worn triaxial accelerometer (ActiGraph GT3X+, ActiGraph, Pensacola), at 14 - 18 weeks' and 29 - 33 weeks' gestation as described previously.[5] Non-wear time was defined as periods lasting three hours or longer where the standard deviation of acceleration in each axis remained below 5 mg.[20] All data from midnight to 06h00 were excluded as sleep time. A day was considered valid if it contained at least seven hours of wear time, and a minimum of three valid days of wear time was required for a record to be included in this analysis. Acceleration was calibrated to local gravity,[20] following which a measure of overall PA volume was derived. Moderate to vigorous physical activity (MVPA) was set at a cut point ≥1 952 counts per minute, and presented as minutes/ valid day in trimesters one and three. The percentage of participants meeting WHO guidelines for physical activity (≥150 MVPA/ week) was calculated and reported. Sedentary behaviour was set at a cut point of 100 counts per minute and presented as minutes/valid day in trimesters one and three. Steps per day were recorded in trimesters one and three by the accelerometer and reported as steps per day when counts per minute were higher than 100 (i.e. not sedentary behaviour).

Fetal ultrasonography

All participants had a pregnancy dating scan at the first visit (median (interquartile range (IQR)) 12 (11 - 13) weeks) using a Philips HD-9 (Philips Ultrasound, Bothell, Washington) ultrasound machine.[21] Participants were invited for follow-up scans every five weeks

at the following visits: 14 - 18 weeks', 19 - 23 weeks', 24 - 28 weeks', 29 - 33 weeks' and 34 - 38 weeks' gestation, and abdominal circumference, biparietal diameter, head circumference and femur length were recorded each time.[22] All five serial measurements of abdominal circumference from first to the third trimester of pregnancy were included in the analyses. These data were modelled using the Superimposition by Translation and Rotation (SITAR) as described previously,[2] and are represented as individual variation along the y-axis, giving an absolute deviation of each individual from the sample mean in the units of the measurement. While SITAR produces three parameters [23] – corresponding to the size, tempo and velocity of growth for each measurement, this study focuses only on the abdominal circumference size variable, as abdominal circumference has been shown to be the most reliable predictor of birthweight.[24,25] Males and females were modelled together and the sex variable was included as an interaction term in the model to assess sex differences owing to previous analyses on this cohort demonstrating sex differences in fetal growth.[3]

Neonatal data

Gestational age at delivery (weeks) was calculated as: (duration of pregnancy follow-up (date of delivery – date of baseline ultrasound dating scan) + gestational age at baseline (days)). Birthweight and length were measured by trained research nurses within 24 hours of delivery. Where assessment within this window was not possible– for example, owing to the infant being admitted to hospital for observation – measurements were taken within 48 hours (18% of total sample). WLR ratio (kg/m) was calculated to represent the best anthropometric predictor of neonatal body composition at delivery.[26]

Neonatal body composition was analysed via either air displacement plethysmography (ADP) using the Peapod (Cosmed, USA) or dual-energy X-ray absorptiometry (DXA; Hologic DiscoveryA S/N 86254, APEX software version 4.0.2, Hologic Inc., USA) within the first month of life. Both of these measures have been described previously.[4] ADP was utilised when possible (n=32), but in cases where a neonate had only DXA measurements (n=13), fat mass and fat-free mass were converted to their ADP equivalent estimates as described previously.[4] FMI (kg/m^3) was calculated from these estimates to describe adiposity in neonates.

Statistical methods

Data were analysed in STATA V13.0 (StataCorp., USA). All data are presented as mean (SD), median (IQR) or n (%). A p-value <0.05 was considered statistically significant. However, confidence intervals and beta coefficients are presented to determine the strength of the associations between variables. Maternal and fetal/neonatal descriptive data were summarised and reported. Maternal predictors of physical activity, step count, and sedentary behaviour in trimesters one and three were determined using linear regression models. Thereafter, a SEM was developed based on the conceptual framework presented in Fig. 1 and the regression results. SEM is used to test and estimate the relationships between multiple variables when more than one pathway is suspected, and mediation or moderation may exist, and provides a complete picture of how all the variables interact with one another. The structural model defines the relationship between any composite latent variables and other observed variables. Two SEM models were run with either WLR or FMI (in a smaller subsample who had these data (n=45) as the outcome variables. Direct and indirect (whereby one variable is acting through another) effects were calculated, and total effects (overall model results when direct and indirect effects are combined) were presented with the pathways detailed.

Results

A total of 84 participants were included in this study. A *post hoc* power calculation showed that with the given sample size, we had >80% power in the regression models with 95% confidence. Table 1 shows the descriptive data for this sample. Mothers were on average 30 years old. Most (66%) mothers presented as overweight or obese at their first visit, and gained on average 0.35 (1.9) kg per week. Just under half (47%) of pregnancies were planned. In trimester one, 50% of mothers met the physical activity guidelines and 50% were accumulating 10 000 or more steps per day while, in trimester three, only 29% met the guidelines and only 41% were accumulating 10 000 or more steps per day. Average minutes per day of MVPA and sedentary time in trimester one v. trimester three are presented in Fig. 2. Neonates weighed on average 3 kg at birth, were born at a mean (SD) of 38 (SD=2) weeks' gestational age, and 51% were male.

The results from the linear regression models showed that in trimester one, parity trended towards a positive associated with sedentary time (ß=16.75, p=0.05), and a negative association with step count (ß=-764.39, p=0.07). In trimester three, only maternal age was positively associated with sedentary time (ß=4.25, p=0.02), and negatively associated with MVPA (ß=-0.59, p=0.02). BMI, GWG, GDM, HIV and SES were not associated with MVPA or sedentary time. However, GWG was negatively associated with step count in trimester three (ß=-5865, p=0.02), whereby each kg increase in average weight gain per week was associated with nearly 6 000 fewer steps per day. None of the maternal factors was associated with the change in physical activity from trimester one to trimester three, yet maternal age was associated with less change in sedentary time (ß= -1.24, p=0.02).

Finally, the SEM (model pathways shown in supplementary Fig. 1) showed that only GA (directly and positively) and sedentary time (negatively acting through GA), were associated with WLR (Table 1). While not directly related to WLR, step count (values

Table 1. Descriptive characteristics of the study sample

Characteristics	Mean (SD)*
Maternal variables	
Age (years)	30 (6)
BMI (kg/m^2)	27.14 (4.86)
GWG (kg/wk)	0.35 (0.19)
Parity	2 (1)
GDM (yes), %	12
SES (score/11)	6 (1)
Planned pregnancy, %	47
Hypertension, %	5
HIV+, %	30
Fetal/neonatal variables	
Abdominal circumference (cm)†	-0.02 (0.90)
GA at delivery (weeks)	38.13 (2.05)
Infant sex (male), %	51
Birthweight (g)	3 033 (542)
WLR at delivery (kg/m)	6.26 (0.82)
FMI within first month (kg/m^3)	3.69 (1.45)

STD = standard deviation; BMI = body mass index; GWG = gestational weight gain; GDM = gestational diabetes mellitus; SES = socioeconomic status; HIV = human immunodeficiency virus; GA = gestational age; WLR = weight-to-length ratio; FMI = fat mass index.
*Unless otherwise specified.
†SITAR-modelled abdominal circumference size.
‡Age at examination of FMI = 6.7 (3.6) days, n=45.

Table 2. SEM results for the WLR outcome (*n*=84)

Characteristics	Significant pathways	Coef.	Overall *p*-value	95% CI	
GWG (kg/wk)	None	0.712	0.176	-0.320	1.745
BMI (kg/m^2)	Indirectly through abdominal circumference	-0.003	0.835	-0.0327	0.0264
Parity	None	-0.064	0.302	-0.186	0.058
GDM	Indirectly through abdominal circumference	-0.102	0.612	-0.494	0.291
SES (score/11)	Indirectly through BMI	-0.004	0.836	-0.040	0.032
Planned pregnancy	Indirectly through abdominal circumference and GA	-0.075	0.255	-0.204	0.054
Hypertension	None	-0.267	0.398	-0.888	0.353
HIV $^+$	None	-0.002	0.939	-0.049	0.046
Steps per day	Indirectly through GA and GWG	0.000	0.136	-0.000	0.000
MVPA (min/wk)	None	-0.005	0.413	-0.018	0.008
Sedentary (min/day)	Indirectly through GA	-0.005	0.006	-0.009	-0.001
Abdominal circumference (cm)	Direct	0.160	0.205	-0.088	0.409
GA (weeks)	Direct	0.278	0.000	0.21	0.346

SEM = structural equation model; WLR = weight-to-length ratio; CI = confidence interval; BMI = body mass index; GWG = gestational weight gain; GDM = gestational diabetes mellitus; SES = socioeconomic status; HIV = human immunodeficiency virus; MVPA = moderate to vigorous physical activity; GA = gestational age.

were divided by 1 000 to provide ß-coefficients >0) was directly associated with GWG (ß=-0.02, p=0.01), and with GA (ß= 0.16, p=0.04). Therefore, step count was indirectly (but not significantly) associated with decreased fetal abdominal circumference. Fetal abdominal circumference was also directly associated with GA (ß= -0.82, p=0.02) and WLR (ß=0.39, p<0.01), yet was not associated with WLR in the overall SEM results. BMI and GDM were also directly associated with increased abdominal circumference, and whether or not the pregnancy was planned was directly associated with decreased abdominal circumference. All significant pathways are shown in Fig. 3. When considering FMI as the outcome in a subsample of participants (n=45), only BMI was associated with FMI, indirectly through GA and abdominal circumference (ß=0.02, p=0.04); shown in supplementary Table 1. Although there were no significant correlates of trimester one physical activity and sedentary behaviours, sensitivity analyses were run including trimester one physical activity and sedentary behaviours in the SEM models, yet these did not result in any changes to the pathways and so results are not presented.

Discussion

This study aimed to determine the interrelationship between maternal biological factors, maternal lifestyle behaviours and fetal growth, with neonatal size and body composition. We found that maternal sedentary behaviour during pregnancy was negatively associated with neonatal size (WLR), and that their step count was associated with decreased GWG and a higher gestational age. However, none of these factors was associated with neonatal FMI, indicating that activity behaviours may not affect adiposity deposition. Therefore, it seems that increased activity and decreased sedentary time are associated with later delivery of bigger neonates but not necessarily with higher adiposity in these neonates.

This study confirmed some of the pathways that have been previously examined in this population, while also elucidating some of the pathways through which these associations act. Specifically, we were able to clarify the detrimental effects of an increased BMI at the start of pregnancy for poor delivery outcomes and increased fetal and neonatal adiposity and size. Furthermore, the development of GDM predisposes neonates to the same detrimental delivery outcomes, and could thus compound the effects of entering pregnancy overweight. This study adds to the multitude of data describing the risks of entering pregnancy overweight or obese,[2,27-30] and further elucidates these relationships by showing that maternal BMI increases both fetal and neonatal adiposity – both of which have been linked to later life obesity.[2,10,15,31] In this study, 60% of mothers entered pregnancy overweight or obese – which is indicative of a population of young women at risk, who are transferring this risk on to the next generation.

While half of women entering pregnancy were sufficiently physically active, this had decreased to only 30% by the third trimester of pregnancy. This significant decrease in physical activity levels during pregnancy has been shown in other studies.[5,32,33] The maternal benefits of acquiring sufficient physical activity and decreasing sedentary time during pregnancy include lower GWG, decreased risk of GDM and hypertension, increased sense of wellbeing, and improvements in peripartum depression scores.[13,34,35] Yet there is less research describing the effects of physical activity during pregnancy on the offspring in utero or after delivery. Most studies have reported no adverse effects to the neonate and have therefore deemed exercise during pregnancy as safe – with the exception of maximal exertion training and potentially resistance training in a supine position.[9,10] A few studies have shown that exercise is related to neonatal birth size[14] or to increased gestational age,[32] and that decreased sedentary time is related to decreased neonatal adiposity.[8] Associations with placental perfusion have also been observed.[10] Previous reviews of the literature have encouraged studies to include factors such as pre pregnancy BMI, GWG and GDM status.[10] The present study, when considering the interrelationship between those maternal factors, found that increased physical activity (step count) and decreased sedentary behaviour had beneficial effects on both maternal health and on neonatal size at delivery, while not increasing fat mass. Interestingly, all of these neonatal associations acted through fetal abdominal circumference – which is suggestive of metabolic programming of in utero abdominal adiposity. This aspect has not previously been studied in association with maternal physical activity.

In the present study, women who were accumulating more steps per day during the last trimester of pregnancy were likely to have gained less weight during their pregnancy, and their offspring were likely to be delivered later into gestation. However, MVPA did not

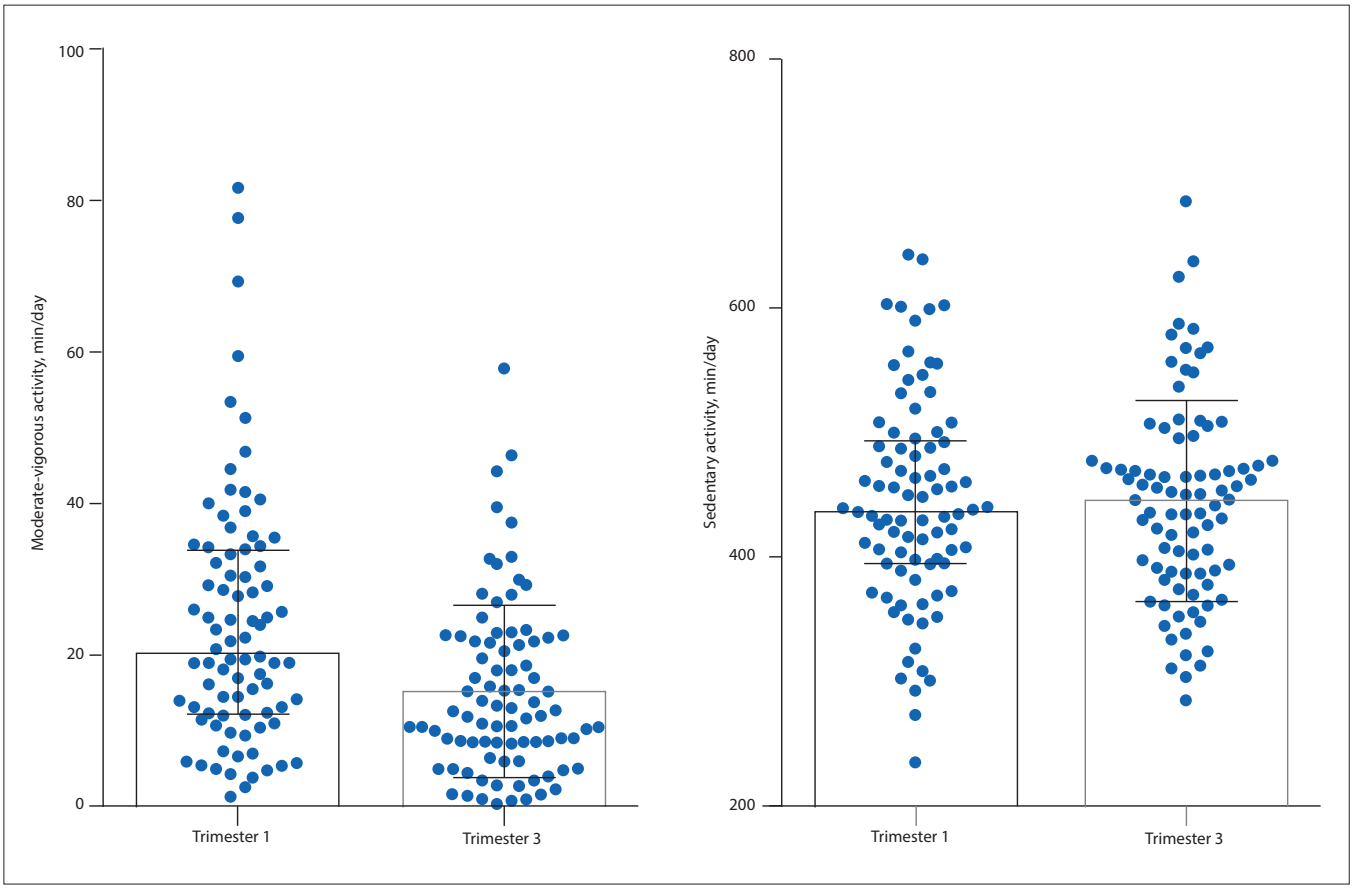

Fig. 2. Average minutes per day of moderate to vigorous physical activity (panel 1) and sedentary time (panel 2) for each participant in trimester one (left column) v. trimester three (right column). Box represents the median for the sample, while the thinner lines represent interquartile range.

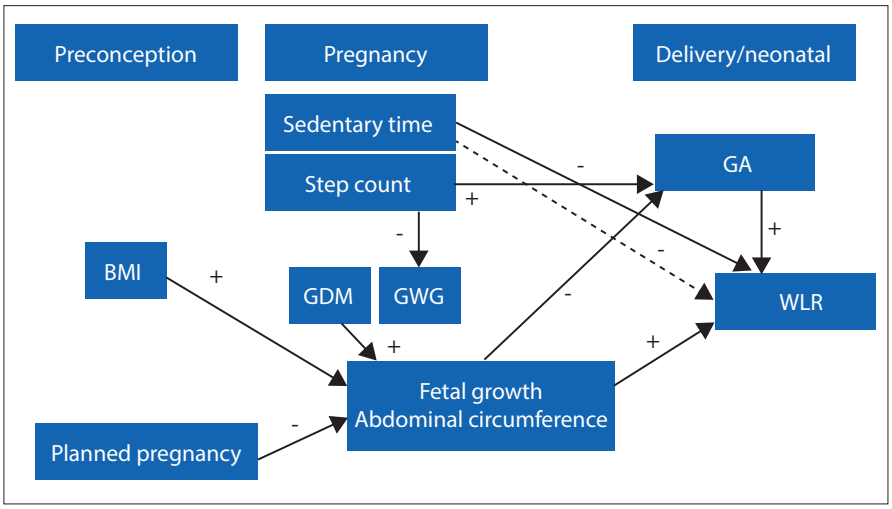

Fig. 3. Overall significant results for the SEM model with WLR as the outcome. (BMI = body mass index; GWG = gestational weight gain; GDM = gestational diabetes mellitus; GA =gestational age; WLR = weight-to-length ratio.)

show the same relationship. Other studies have shown that light physical activity has beneficial effects on placental perfusion, as well as fetal cardiac adaptability,[10] while higher intensity exercise can lead to transient fetal distress (while not causing any long-term detrimental effects).[9,10] As walking to accumulate steps is generally considered light to moderate intensity activity, it could present a safe, translatable and easy-to-achieve goal to improve pregnancy and fetal health.[36] This would be a particularly important public health message, given that South Africa does not currently have any routine physical activity recommendations for pregnant women, or for women who are entering pregnancy overweight or obese. Conversely, sedentary behaviour was associated with a lower gestational age, and thus with decreased neonatal size. In trimester one, half of women were achieving the recommended 10 000 steps or more, while by trimester 3 this had decreased to 41%. As the SEM results showed that each extra 1 000 steps per day were associated with just over a day's extra gestation time and 200 g less GWG per week, it would be advisable to encourage women to accumulate as many steps as possible per day during their pregnancy. Furthermore, encouraging women to replace sedentary time with walking would potentially provide additional benefits to gestational age and to neonatal size at delivery. Additionally, increasing physical activity and decreasing sedentary time could decrease risk of GDM, and work towards decreasing obesity prevalence in this population of women and for any future offspring.[12,13,37] The combined effects of these behaviours are therefore highly relevant.

The present study is limited by the small sample size and by being constrained to one setting. However, a *post hoc* power calculation showed that with the given

sample size, we had >80% power in the regression models with 95% confidence. Additionally, the longitudinal and precise objective measurement of physical activity and sedentary behaviour adds value and power to the analyses. The inclusion of repeated fetal growth measurements throughout pregnancy is unique to this study, and again adds power. Furthermore, by including maternal biological and behavioural correlates into the SEM model, we were able to unravel direct and indirect pathways through which these associations act.

In conclusion, this study has shown that a high maternal BMI at the start of pregnancy has deleterious effects on both fetal and neonatal body composition outcomes. Additionally, increasing daily step count and decreasing sedentary behaviour could have beneficial effects on both maternal health as well as on delivery outcomes and neonatal size. Walking is therefore recommended as a safe and accessible means to improve pregnancy health, while also potentially decreasing risk of GDM and obesity.

Declaration. The authors assert that all procedures contributing to this work comply with the ethical standards of the Human Research Ethics Committee of the University of the Witwatersrand and with the Helsinki Declaration of 1975, as revised in 2008; and have been approved by the Human Research Ethics Committee of the University of the Witwatersrand.

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Conflicts of interest. None.

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Early language development in children with autism (ages 3 - 5 years) in Bloemfontein, South Africa: A comparative study

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Background. Autism is a developmental disorder, which presents during the childhood years, with social communication difficulties and signs of delay in early language development.

Objectives. The aim of the study was to compare the early language development of children aged 3 - 5 years with a Diagnostic and Statistical Manual of Mental Disorders (DSM) V diagnosis of autism with that of children of the same age with typical early language development. The secondary aim was to determine if certain children with autism have better language development in the language to which they are exposed on television (English) than in their home language (Afrikaans).

Methods. The Language Development Survey was translated into Afrikaans, modified and used as a questionnaire. For the control group, questionnaires were distributed at preschools and completed by the parents. For the sample group, questionnaires were distributed at the practice of a developmental paediatrician.

Results. The median percentages of Afrikaans words used in all the categories were lower in the sample group than in the control group. More children in the sample group tended to speak English the best, use words not spoken at home, and imitate words and sounds in the incorrect context. Most of the parents of children in the sample group considered their child's language development poor. Children in both groups watched television for long periods of time.

Conclusions. Afrikaans-speaking children with autism have a poorer vocabulary in Afrikaans and used more English words than in the control group. The television exposure of children under the age of two years is high.

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Autism is a lifelong developmental disorder that influences social interaction. It is not a scarce condition and epidemiological studies indicate a minimum prevalence of 1 in 59 children.[1] The core problem in autism is that of social communication which normally manifests with slow and atypical language development.[2,3]

There is a subgroup of children with autism who do not acquire language from interaction with their parents but from television, which can manifest as palilalia (involuntary repetition of phrases heard on television), among other signs.[2] In a multilingual country such as South Africa (SA), this can create the impression that the language these children are exposed to on television is better than their home language.

Measuring instruments are available that may act as screening tools to evaluate the early language development of toddlers (age 18 - 35 months).[4] An example is the Language Development Survey, which has been adapted for multicultural conditions, translated into Sesotho and Afrikaans, and specifically adapted for SA.[5]

At present, no study has been published in SA that describes the early language development of a group of children on the autistic spectrum. It would be useful to investigate a specific language development variant (that of children whose vocabulary in the language that they are exposed to on electronic media is better than in their home language) to evaluate if this specifically applies to autism.

Objective

The main aim of the study was to compare the early language development of children aged 3 - 5 years with a Diagnostic and Statistical Manual of Mental Disorders (DSM) V diagnosis[6] of autism with that of children of the same age with typical early language development in Bloemfontein.

The secondary aim was to determine if certain children with autism have better language development in the language to which they are exposed on television (English) than in their home language (Afrikaans).

Methodology

Study design and setting

This was a comparative study.

Study population and sampling strategy

A sample group of 12 children, aged 3 - 5 years, diagnosed with autism according to the DSM V by a developmental paediatrician in Bloemfontein, was compared with a group of 24 children with typical early language development, also aged 3 - 5 years. Typical language development is the development between variances (two standard deviations) according to standard development tables, e.g. the Ages and Stages questionnaire.[7]

To be included in the study, all children had to be 3 - 5 years of age with only Afrikaans as home language and with access to a television at home.

Children who were never exposed to any other language on television except for their home language were excluded from the study. Children with deafness, who had a delay in language development for reasons other than autism, or who had a developmental delay but did not show the diagnostic characteristics of autism, were also excluded.

For the control group, two preschools were initially selected using random sampling from a list of five Afrikaans medium preschools in Bloemfontein. Owing to low response, other preschools and organisations were approached to recruit children for participation.

Data collection and measurement

The measuring instrument, the Language Development Survey,[4] is a standardised and validated checklist.[5] The survey has been adapted for South African (SA) use, and was included as part of the questionnaire. The survey comprised words in 14 categories and parents had to indicate which words the child said, and in which language (Afrikaans or English).

The questionnaire also determined demographic information as well as the time exposed to electronic media and the language of the children's audiovisual media exposure.

Pilot study

A pilot study was conducted on three children in the control group. Questions were simplified and reordered and the layout of the questionnaire improved based on pilot feedback. These three control children were excluded from the main study.

Data analysis

Data were captured on an Excel spreadsheet and analysed by the Department of Biostatistics, Faculty of Health Sciences, University of the Free State. Medians and percentiles were calculated to summarise numerical data. Frequencies and percentages were calculated for categorical data. Fisher's exact tests (categorical variables) and Mann-Whitney or median tests (numerical variables) were performed to compare groups. Statistical significance was set at 0.05.

Ethical considerations

The study was approved by the Ethics Committee of the Faculty of Health Sciences, University of the Free State (ref. no. HSREC-S 08/2016). Permission to conduct the study was obtained from the clinic where the sample group was obtained, Head of the Department of Paediatrics and Child Health, Free State Department of Health, Free State Department of Education, and school principals of the preschools. Parents of the participating children gave written informed consent. Data were handled confidentially and no identifiable information was recorded on the questionnaire itself.

Results

The median age of the children included in the sample group (n=12) was 4.3 years while the median for the children in the control group (n=24) was 5.0 years. The median weight at birth for the sample group was 3.24 kg and for the control group 3.09 kg. Only 16.7% of the sample group children and 20.8% of the control group were born before 37 weeks. Before the age of two years, 90.9% (n=10/11) of the sample group and 87.5% (n=21/24) of the control group had five or less ear infections. A family history of a delay in language development was reported by 16.7% (n=2) children in the sample group and 8.3% (n=2) children in the control group. There were no statistically significant differences between the sample group and the control group regarding any of these variables.

Table 1 shows that significantly more parents of children in the sample group felt that their child's language development was poorer than his or her peer group (p<0.01). Significantly more parents of children in the sample group were concerned about this delay in language development (p<0.01). More children in the sample group tended to speak English the best, use words not spoken at home, and imitate words and sounds in the incorrect context. Some feedback from parents of children in the sample group were '*Hy herhaal frases of sinsnedes uit kinderstories, bv. "Thomas the Tank Engine.*" [Translation: He repeats phrases or clauses from children's stories, for example Thomas the Tank Engine.] and '*Hy sal Engels goed naboots.*' [Translation: He will mimic English well.]

Most children in both the sample group (n=7/12; 58.3%) and in the control group (n=14/23; 60.9%) were first exposed to television before the age of one year (p=1.00).

According to Table 2, 83.4% of the sample group watched television between 1 and 4 hours per weekday and 75.0% on weekends. The majority of children (87.0%) in the control group watched television between 1 and 4 hours per weekday and 95.6% on weekends. There was no statistically significant difference between the two groups (p=0.69 and 0.61, respectively).

Most of the children in both groups (66.7% sample group; 82.6% control group) watched television in both English and Afrikaans (p=0.40). In the sample group, 91.7% of children watched television mainly in English v. 77.0% in the control group (p=0.08).

Most of the children in both groups (91.7% sample group; 87.0% (n=20/23) control group) watched DVDs, which included Afrikaans and English DVDs.

In the sample group, 41.7% of the children watched DVDs between 1 and 4 hours per weekday and 83.4% on weekends (Table 3). In the control group, 60.0% watched DVDs between 1 and 4 hours per weekday and 90.0% on weekends. There was no statistically significant difference between the two groups (p-values 0.48 and 0.46, respectively).

A higher percentage of children in the sample group (n=5/11; 45.5%) watched only English DVDs v. 10.0% (n=2/20) in the control group (p=0.07). Almost all children in the sample group (n=10/11; 90.9%) watched DVDs mainly in English v. 40.0% (n=8/20) in the control group (p=0.01).

According to Table 4, the median percentages of Afrikaans words used in all the categories were lower in the sample group than in the control group.

The median percentage of English words used per category was 0 in both groups, but owing to differences in the 75th percentile, the sample group had significantly higher percentages for the categories 'animals', 'body parts', 'vehicles', 'actions', 'places', 'modifiers' and 'other'.

Discussion

The slow early language development of the children with autism v. that of children with typical early language development was apparent. More parents of children in the sample group were concerned about their child's language development. It would be of interest to see how old the child was when the parents became concerned and whether they sought professional help. This finding shows the importance of delving deeper to determine the underlying reasons. We should, therefore, be careful about only reassuring these parents. This finding is also important as early intervention in autism makes a difference.[8,9] Children with this condition are still

Table 1. Parental responses regarding early language development

Early language development	Sample group (n=12), n (%)	Control group (n=24), n (%)	p-value
Other languages (English, Sesotho), apart from Afrikaans, also spoken at home	3 (25.0)	4 (16.7)	0.66
Child speaks English the most/best	2 (16.7)	0 (0)	0.10
Child's language development is poorer than his/her peer group	11 (91.7)	1 (4.2)	<0.01
Parents are concerned about child's language development	7 (58.3)	1 (4.2)	<0.01
Child uses words not spoken at home	5/11 (45.5)	6/23 (26.1)	0.43
Child imitates words and sounds in the correct context	8 (66.7)	22 (91.7)	0.15

Table 2. Comparison between the two groups regarding the number of hours of television exposure per day

	Sample group (n=12), %		Control group (n=24), %	
Hours	Weekdays	Weekends	Weekdays	Weekends
0	8.3	8.3	8.7	4.4
1 - 2	41.7	25.0	60.9	47.8
2 - 4	41.7	50.0	26.1	47.8
>5	8.3	16.7	4.4	0

Table 3. Percentage comparison between the two groups regarding the number of hours watching DVDs per day

	Sample group (n=11), %		Control group (n=20), %	
Hours	Weekdays	Weekends	Weekdays	Weekends
0	45.5	0	40.0	10.0
1 - 2	27.3	72.7	50.0	80.0
2 - 4	18.2	18.2	10.0	10.0
>5	9.1	9.1	0	0

Table 4. Summarised data of the percentage of Afrikaans words used per category by children in the sample group and the control group

Category	Sample group, Median (IQR)	Control group, Median (IQR)	p-value
Food	54.8 (41.5 - 87.1)	88.7 (80.7 - 98.4)	0.01
Toys	59.1 (36.4 - 90.9)	100 (100 - 100)	<0.01
Outdoors	75.0 (50.0 - 75.0)	100 (75.0 - 100)	<0.01
Animals	83.3 (50.0 - 97.6)	100 (95.2 - 100)	0.01
Body parts	88.1 (66.7 - 97.6)	100 (100.0 - 100)	<0.01
Vehicles	100 (50.0 – 100)	100 (100.0 - 100)	0.01
Actions	76.5 (59.8 - 91.2)	100 (96.0 - 100)	<0.01
Household	69.4 (35.5 - 91.9)	96.8 (91.9 - 100)	0.01
Personal	75.0 (21.4 - 92.9)	100 (92.9 - 100)	<0.01
Places	50.3 (37.5 - 87.5)	87.5 (75.0 - 100)	0.02
Modifiers	71.7 (45.0 - 88.3)	100 (95.0 - 100)	<0.01
Clothes	56.3 (37.5 - 93.8)	100 (93.8 - 100)	<0.01
People	84.6 (61.5 - 92.3)	100 (92.3 - 100)	0.01
Other	59.4 (45.3 - 81.3)	85.9 (81.3 - 98.4)	<0.01

IQR = interquartile range.

identified often too late after the age of three years, and awareness of the importance of a delay in language development may help early identification.[10]

Nearly half of parents of children in the sample group (n=5/12) were not concerned about their child's early language development. This may indicate that the parents are not aware of important language developmental milestones.

As language should be acquired during social interactions,[11] it was concerning that many children before the age of two years spent hours watching television. The parents of one child in the sample group indicated that their child spent more than five hours in front of the television daily. There is concern about the effect of screen activities on a child's brain development, and the American Academy of Pediatrics recommends no screen activity before the age of 18 months.[12]

It is unclear why more children in the sample group watched television and DVDs in English. This may explain why the sample group used more English words, but it can also mean that the parents allowed the child to watch English programmes and DVDs, as they perceive this to be the child's best language. This statement is supported by the parents of children in the sample group who indicated that English was their child's best or most complete language. This aspect should be addressed in a larger prospective study.

Though different factors play a role in a child's language development, the children in this study came from a relatively homogeneous, socio-economic group. This included families with Afrikaans as their home language, with children in a preschool, and who could afford private medical services.

A study by Griessel and Van Jaarsveld[13] comparing two groups of children with attention deficit, of which one group was initially incorrectly diagnosed with autism, showed an 80% sensitivity and a 100% specificity for this occurrence. It was found that learning a language seen on television rather than the home language was an early indication of autism. This atypical language development is thus a specific finding in children with autism, something that has not been previously described in the literature.

This is the first study in SA that quantified the early language development of young children with autism, and can serve as a basis for a more comprehensive study.

Children with autism have a specific cognitive profile in that they are more visually inclined and focus more on objects than on people. They also tend to have difficulty with make-believe games.[14] It is of interest that the children with autism had the weakest results in the body parts, clothing (people) and toys categories. The group performed best in the vehicle category.

Study limitations

The two study groups were smaller than planned, which may have influenced the

accuracy of the findings. Factors such as socio-economic background and quality of stimulation were not controlled. The different media platforms, e.g., YouTube and streaming, that the children were exposed to, were not specified and were only listed as 'other'.

Recommendations

A larger study should be done to determine whether the findings of the present study can be replicated. It would also be of value to hold a similar investigation in other languages, such as Sesotho, in the case of the Free State.

Parents should be made aware, through the media, magazines, etc., of the importance of the influence of early language stimulation on later school performance and the importance of quality language stimulation through social interaction.

Parents should be made aware of the typical development of language milestones and where to go for assistance, should they be concerned.

The public should be part of the debate around the dangers of early exposure to electronic media.

Conclusion

This study is the first in SA to use a valid measuring instrument to determine the language ability of children with autism and compare it with a control group with typical early language development. Most parents of the children with autism were aware of their child's delay in language development; however, not all these parents were concerned about this. Children with autism have a vocabulary that is poorer than a group of children with typical early language development. We found a trend in that children with autism use more English words than the control group, which is possibly due to audiovisual media exposure. An unacceptably high exposure to audiovisual media was found in children under the age of two years.

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Prevalence of coeliac disease in children and adolescents with type 1 diabetes mellitus in a tertiary hospital in South Africa

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Background. International literature has shown the prevalence of coeliac disease (CD) in children and adolescents with diabetes to range from 1 - 10%. Prevalence rates in African countries are limited or unknown.
Objective. The objective was to describe the prevalence of CD in all children and adolescents with type 1 diabetes mellitus presenting to the paediatric and adult diabetic clinic at Steve Biko Academic Hospital, Pretoria, South Africa.
Method. A retrospective review of the files of all children and adolescents in the paediatric and adult diabetic clinic with type 1 diabetes mellitus between August 2016 and June 2019 was conducted. Children requiring screening and/or intestinal biopsies were also prospectively included during this period. The setting of this study was Steve Biko Academic Hospital, a tertiary referral centre, in Pretoria, South Africa. Coeliac screening included anti-deaminated gliadin antibodies and anti-tissue transglutaminase antibodies (both IgA and IgG). All biopsies were obtained by a paediatric gastroenterologist or an experienced paediatric surgeon.
Results. A total of 184 files were screened; 132 met inclusion criteria but only 108 patients in total had coeliac screening. Positive antibody screening for CD was found in 11 out of 108 patients (10.2%). Nine of the 11 serology-positive patients had biopsies performed. Out of the nine biopsies, two (22.2%) were positive for CD based on the Marsh-Oberhuber classification.
Conclusion. This study found a prevalence of serology-positive CD in our local population of South African children with type 1 diabetes mellitus of 10.2%, while the prevalence of biopsy-confirmed CD was found to be 1.9%.

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Coeliac disease (CD) is a chronic inflammatory autoimmune intestinal disease. It develops as a result of an interplay among immunological, genetic and environmental factors.[1] Genetically predisposed individuals who ingest gluten develop an inflammatory enteropathy, characterised by intra-epithelial lymphocyte proliferation, crypt hyperplasia as well as complete or partial small intestinal villous atrophy with subsequent malabsorption.[2,3]

International literature has shown the prevalence of CD in children and adolescents with diabetes to range from 1 - 10%, with an incidence of about 8 per 1 000 patients per year.[4,5] Studies conducted in developed countries show a prevalence rate of CD in children with type 1 diabetes mellitus of 5% in Turkey and 10% in Danish children. In a paediatric diabetes clinic in London, serology-confirmed CD prevalence was 6.2%, while 4.4% was biopsy confirmed.[6-8] The largest study performed, which included 52 721 youth with diabetes mellitus across Europe (Germany, Austria, England and Wales), the USA and Australia showed an overall prevalence rate of biopsy-confirmed CD of 3.5%, with prevalence rates ranging from 1.9% in the USA to 7.7% in Australia.[5,9]

In developing countries, far fewer data are available on the prevalence of CD, particularly in African countries. A study conducted in a paediatric endocrinology clinic in Western India showed a prevalence (based on serology) of 15.49%, while biopsy-confirmed CD prevalence was 7.04%.[10] The prevalence rate in Brazil was reported to be 3.1%; a prevalence of 5.5% was reported in Omani children, and 10.4% non-biopsied confirmed CD was found in Saudi Arabian children.[11-13] Four studies were conducted on the prevalence of CD in Iranian children with type 1 diabetes mellitus; the first, conducted in 2004, showed a prevalence of 3.4% while the second report was a review based on three studies conducted and was published in 2014, showing a combined study prevalence of 5.66%. In African countries, research in Egypt showed a prevalence of 6.4%, 16.4% in Algeria and 2.3% biopsy-proven CD in Tunisia.[14-16] In South Africa, a study conducted in KwaZulu-Natal reported a prevalence of positive coeliac serology in type 1 diabetic children of 44.5%. However, only 16% of these patients underwent biopsy, of whom three (0.06%) had biopsy-confirmed CD. The small number of biopsies performed was attributed to lack of a qualified paediatric gastroenterologist; this challenge resulted in a significant limitation to the study.[17] A later study of adult type 1 diabetic patients in the same region, which included patients who were diagnosed in childhood (with earliest onset of diagnosis of 10.3 years) showed a prevalence of 32.2% for serology-positive CD, while the prevalence of biopsy-confirmed CD was 2.5% (similar to Western countries).[18]

The diagnosis of CD is based on a combination of serology testing, small-intestinal biopsy and response to a gluten-free diet.[3] Confirmation of the diagnosis of CD can be made by demonstrating subtotal villus atrophy (as outlined in the Marsh Classification) on small-bowel biopsy.[4,5,19] Despite the high prevalence of CD in

children with type 1 diabetes mellitus, there has been much debate regarding routine screening in this population.[7]

Studies on the prevalence of CD in children with type 1 diabetes mellitus are limited, especially in developing countries. Current guidelines for screening children with CD are based on international guidelines, as there is a lack of regional and national data on the prevalence of CD in South African (SA) children with type 1 diabetes mellitus. Knowledge regarding the prevalence of CD in our setting will assist in the application of international guidelines in our resource-limited environment based on local prevalence rates.

Method

The objective of the present study was to investigate the prevalence of CD in all children and adolescents with type 1 diabetes mellitus presenting to the paediatric diabetic clinic at Steve Biko Academic Hospital, a tertiary referral centre, in Pretoria, SA.

The study design was a retrospective review of the files of all children and adolescents in the paediatric diabetic clinic with type 1 diabetes mellitus between August 2016 and January 2019. Children requiring screening and/or intestinal biopsies were also prospectively included during this period. Exclusion criteria for this study were all children with type 2 diabetes mellitus, neonatal diabetes mellitus, maturity-onset diabetes of the young, secondary diabetes mellitus, and adults (over the age of 18 years).

Clinical information and signs or symptoms of CD were reviewed from the charts retrospectively. The following serology was recorded, namely tissue transglutaminase antibodies (tTG-A) IgA and IgG antibodies, antibodies against deaminated forms of gliadin peptides (anti-DPG) IgA and IgG antibodies and total IgA, which was routinely done to exclude IgA deficiency. For testing, a Thermo Fischer Scientific (South Africa) kit was used; both tTG-A and anti-DPG IgA and IgG were tested via fluorimetric enzyme immunoassays. All above-mentioned serological tests were deemed positive on the kit if ≥10 U/mL or equivocal if ≥7 U/mL but <10 U/mL. Endomysial antibodies (EMA) are unfortunately not performed by our laboratory. HbA1C and diabetes autoantibodies were also recorded. Patients who had positive coeliac serology had intestinal biopsies taken via gastroscopy. Laboratory and histology results relied on the experience of laboratory technicians and pathologists for accuracy of results. All biopsies in our setting were obtained by a paediatric gastroenterologist (in seven patients) or a paediatric surgeon with experience in gastroscopies (in two patients) according to coeliac screening protocols with at least 4 - 6 biopsies from the distal duodenum and 2 - 4 biopsies from the duodenal bulb. All serological tests and biopsies were obtained while children were on gluten-containing diets. Duodenal biopsies were examined under light microscopy using the modified Marsh classification.[19] The diagnosis of CD was based on the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines.[5,20] ESPGHAN and ISPAD guidelines state that a small-bowel biopsy demonstrating subtotal villus atrophy (as outlined in the Marsh classification), while the patient is on a gluten-containing diet, is required to confirm the diagnosis of CD once elevated antibodies are detected.[5,19,20] However, for clearly symptomatic children with tTG-A titres ≥10 times upper limit of normal (x ULN), CD may be diagnosed without a duodenal biopsy if the patient has a positive HLA DQ2 or DQ8 haplotype and the EMA IgA is also positive.[5,20] In the latter, ESPGHAN requires only additional EMA IgA positivity; HLA determination and symptoms are not obligatory criteria for the diagnosis of CD.[20]

Data were collected on an Exel spreadsheet (Microsoft Corp., USA) and analysed using STATA (v15.1; STATACorp., USA). Categorical variables were assessed using the Fisher's exact test and Pearson's χ^2 test, and continuous variables were assessed using the Wilcoxon's rank sum test. A p-value <0.05 was considered statistically significant.

The information gathered was treated confidentially and no patients' names were recorded. Informed consent was obtained from the parents/guardians and informed assent from all children between 8 and 17.9 years of age for all children added prospectively. The study obtained permission and approval from Steve Biko Academic Hospital. Ethical approval was obtained from the Research Ethics Department of the University of Pretoria (695/2018) and the National Health Research Database.

The potential benefits of this study included knowledge regarding the prevalence of CD in children and adolescents with type 1 diabetes mellitus in our setting, which will aid us in drawing up guidelines for CD screening in our population. There were no potential harms or known conflicts of interest associated with this study.

Results

The results of this study are depicted in the flow diagram in Fig. 1, showing 10.2% of the patients to have serology-positive CD, while only 22.2% of these patients had biopsy-confirmed CD.

Patient demographics

Of the 132 patients who met inclusion criteria for the study, the majority were

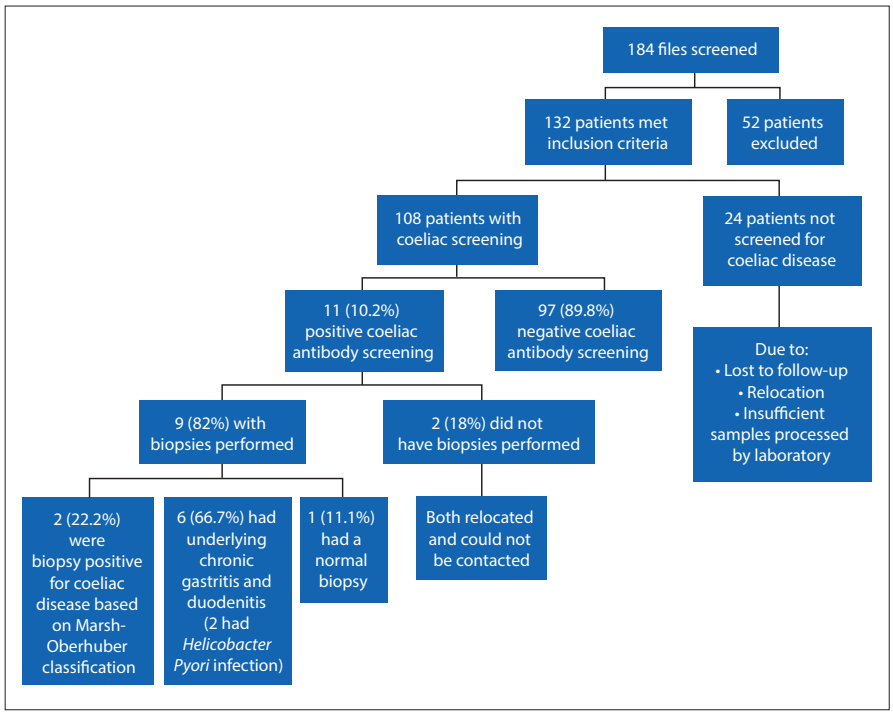

Fig. 1. Flow diagram of patient screening, coeliac serology and histology results.

female (54%), of whom most (65%) were black, while 24% were white, 6% coloured, 4% Indian and 1% Asian. Ethnicity of the patient compared with biopsy-confirmed CD was not significant (*p*-value 0.0629). Biopsy positivity specifically in the female gender v. male was statistically significant (*p*-value 0.007) (Table 1).

The mean age of patients was 11.7 years (range 1.2 - 18 years), with a median of 12.3 years. The mean duration of diabetes was 4.4 years (range 0.1 - 17 years), with a median of 3.5 years. The mean HbA1C was 11.1% (range 5.1 - 20.2), with a median HbA1C of also 11%. The age of the patient compared with biopsy-confirmed CD was not significant (*p*-value 0.0874). The duration of diabetes compared with biopsy-confirmed CD or serology positivity was also not significant (*p*-value 0.9333 and 0.6116, respectively) (Table 1).

Coeliac serology

Coeliac serology was deemed positive if tTG-A and/or anti-DPG were positive or equivocal. All 11 (100%) patients had positive anti-DPG (IgA and/or IgG) and five (45%) also had positive tTG-A (IgA and/or IgG). None (0%) of patients screened had an IgA deficiency. The greater the positivity of the coeliac serology antibodies (≥10 x ULN) and the combination of positive anti-DPG plus tTG-A significantly increased the chances of a positive biopsy (*p*-value 0.003 and 0.001, respectively) (Table 2). Eight (72.7%) of the 11 serology-positive patients were black, two (18.2%) were coloured (mixed race) and one (9%) was white. The mean age of the serology-positive patients was 8.5 years (range 3.3 - 13.9 years). There was a predominance of serology positivity in females of 82% (nine patients). Thirty-three (25%) of the 132 patients screened had signs or symptoms of CD; however, only three (9%) of the symptomatic patients had positive coeliac antibodies and none (0%) had biopsy-confirmed CD. Of the patients who had positive coeliac screens, 73% (8 patients) were asymptomatic.

Table 1. Summary of *p*-value results

Outcome	*p*-value
Ethnicity compared to biopsy-confirmed CD	0.0629
CD biopsy positivity compared to gender	0.0070
Age compared to biopsy-confirmed CD	0.0874
Duration of diabetes compared to biopsy-confirmed CD	0.9333
Duration of diabetes compared to serology positivity	0.6116

CD = coeliac disease.

Interestingly, as seen in Fig. 1, only one (11.1%) out of the nine gastrointestinal biopsies taken was found to be completely normal; this patient was a 5-year-old black girl. Two were confirmed to have CD: a 4-year-old white girl and a 7-year-old black girl, both with CD grade 3a Modified Marsh-Oberhuber classification. The mean age of biopsy-confirmed CD was six years, with a female predominance of 100%. Both patients with confirmed CD had coeliac serology testing with both antibodies (tTG-A and anti-DPG) ≥10 x ULN and both were asymptomatic. The other six (66.7%) biopsies were abnormal, showing a picture of chronic gastritis and chronic duodenitis. Two of these six abnormal biopsies also cultured *Helicobacter pylori* infection for which the patients received eradication; one patient also had a co-existing *Giardia* infection. The demographics of these six patients were quite varied and included two boys and four girls, with an age range of 3 - 12 years, and were of black and coloured descent. All patients with abnormal biopsies not confirming CD had antibodies <10 × ULN.

Statistically, the diabetes-associated antibody positivity rate compared to biopsy-confirmed CD was not significant (*p*-value 0.276); out of a total 86 patients who had confirmed positive diabetes-associated antibodies, only one (1.2%) had biopsy-confirmed CD. The presence of signs and symptoms of CD compared with biopsy-confirmed CD was also not significant (*p*-value 0.514); 103 patients had documented signs and symptoms, 74 (71.8%) were asymptomatic for CD and only two (1.9%) patients had biopsy-confirmed CD and both were asymptomatic.

Discussion

As seen in the results of this study, the prevalence rate in our population of diabetic children and adolescents in Pretoria, South Africa, of serology-positive CD was 10.2%. This is much lower than the reported prevalence of 44.5% and 32.2% in paediatric and adult patients, respectively in Durban, South Africa.[17,18] This may occur as a result of different antibody testing. Serology was positive based on either tTG-A or EMA, while in the adult study patients' serology was deemed positive if any of the three antibodies were positive (tTG-A, EMA, anti-gliadin antibodies [AGA]).[17,18] EMA and tTG-A both have a specificity and sensitivity >90% in symptomatic individuals (Table 3).[3-5,21] When used as screening tests, however, their positive predictive value is lower, in the range of 70 - 83%.[21] The population studied was investigated with a panel of tests, rather than screened with a single antibody test as recommended in the ESPGHAN and ISPAD guidelines. Our laboratory, unfortunately, does not test for

Table 2. Breakdown of positive/equivocal coeliac serology results and correlation with biopsy positivity

Patient	1	2	3	4	5	6	7	8	9	10	11
tTG-A (U/ml)											
IgA	**P**	**P**	**E**	N	N	N	N	**E**	N	N	N
	200.0	288.0	8.2	2.3	0.5	0.8	0.4	8.8	6.7	0.3	1.4
IgG	**P**	**P**	N	**P**	N	N	N	**E**	N	N	N
	12.0	46	2.2	60	0.5	0.0	0.4	7.2	1.0	0.0	1.2
Anti-DPG (U/ml)											
IgA	**P**	**P**	**P**	N	**P**	**E**	**E**	N	N	**P**	**P**
	96	302	10.1	0.1	12.0	9.1	7.8	2.4	3.7	29.0	13.0
IgG	**P**	**P**	**E**	**P**	N	N	N	**P**	**P**	N	N
	164	815	7.1	18	1.4	0.1	1.3	16.0	11.0	1.1	0.5
Coeliac disease on biopsy	**P**	**P**	N	N	N	N	N	N	N	ND	ND

P = positive; E = equivocal; N = negative; ND = not done.
Positive and equivocal results are in bold font to make them stand out.

Table 3. Sensitivity and specificity of different serological tests used in the diagnosis of CD (adapted from Pelkowski and Viera[3])

Serological test	Sensitivity (%)	Specificity (%)	Positive likelihood ratio	Negative likelihood ratio
IgG DPG	80	98	40	0.20
IgA DPG	88	95	17.6	0.13
IgG tTG-A	40	95	8	0.63
IgA tTG-A	95 - 98	94 - 95	17.5	0.04
IgG EMA	40	95	8	0.63
IgA EMA	>90	>95	>18	<0.11
IgG AGA	80	80	4	0.25
IgA AGA	80 - 90	85 - 95	8.5	0.17

CD = coeliac disease.

EMA; however, we included anti-DPG (which is more specific than AGA) as part of our serological testing. It is important to note that children younger than two years old in particular lack EMA and tTG antibodies and therefore serology testing in children younger than even five years old is thought to be less reliable and requires additional investigation.[1,3] The specificity of coeliac serology testing in black SA patients is also unknown; this may have an influence on the results obtained.

The prevalence of definite biopsy-confirmed CD was found to be 1.9% in the present study. This is in keeping with the international literature that has shown the prevalence of CD in children and adolescents with diabetes to range from 1 - 10%.[4,5] It is also in keeping with the study done in adult type 1 diabetic patients in Durban, SA, which showed a prevalence of biopsy-confirmed CD of 2.5%.[18] Our prevalence seems to be lower than those reported in children in some other African countries, with a prevalence of 16.4% and 6.4% in Algeria and Egypt, respectively, while similar to the prevalence of 2.3% reported in Tunisia.[14-16] More research in paediatric local prevalence rates of biopsy-confirmed CD would be valuable.

The present study found a higher predominance of coeliac serology positivity (82%) as well as confirmed CD (100%) in females compared with males; this is in keeping with international literature as well as local studies.[17] In patients who had positive coeliac screens, 73% were asymptomatic, which is in keeping with a systematic review in paediatric patients in which 85% of patients were asymptomatic at diagnosis.[22] This further emphasises the need for routine screening of all type 1 diabetic children as per international guidelines in order to minimise long-term morbidity and possibly mortality.[4,5] Interestingly, none of the patients tested in this study was found to have an IgA deficiency. Irrespectively, all patients underwent both IgA and IgG serological testing, thus eliminating false negative coeliac antibodies.

Sixty-five percent of the patients screened were black; however, this reflects our local population. It is also important to note that higher-level socioeconomic children from the private sector were not included. The effect of ethnicity on the prevalence rate of CD remains unclear; however, weak evidence has suggested that it is rare in black patients.[18] Our study shows an equal prevalence of biopsy-confirmed CD in white and black patients. This is statistically not significant and cannot be interpreted effectively owing to the small sample size and the predominance of black patients in this study; however, it does suggest that CD may very well not be rare in black patients.

Recent ISPAD guidelines recommend that symptomatic children with high tTG-A titres (≥10 x ULN) may be diagnosed with CD without a small-bowel biopsy, but only if the EMA is also positive or if the patient carries HLA-DQ2 or HLA-DQ8.[4,5] This recommendation is inconsistent with some other guidelines, but is consistent with recent guidelines from ESPGHAN.[3,4,20] ESPGHAN guidelines also state that HLA testing is not an obligatory criterion for a serology-based diagnosis of CD without biopsy (Fig. 2).[20] If we had used this approach in our study, both patients confirmed to have biopsy-proven CD could have been diagnosed with definite CD without a biopsy, purely based on serology testing ≥10 x ULN, using anti-DPG as the second sample. The use of anti-DPG as the second sample in place of EMA is, however, not documented in international guidelines and further research in this regard would be valuable for centres in which EMA is not available for testing. Conclusions in this regard cannot be made owing to the small sample size.

It is not surprising that almost all the serology-positive patients who did not have biopsy-confirmed CD were shown to still have abnormal intestinal biopsies (two (18%) patients were, however, not biopsied). Several studies of intestinal integrity in patients with type 1 diabetes have shown evidence of increased intestinal permeability.[23,24] The intestinal microbiome contributes a great deal to the maintenance of intestinal integrity. Type 1 diabetics tend to have bacteria in their gut microbiomes that have increased expression of genes related to adhesion and motility compared with controls, with some studies showing an increase in *Bacteriodetes* (associated with beta cell autoimmunity in children).[23-25] Microstructural changes, including changes to tight junctions and microvilli, are frequently seen in the intestines of patients with type 1 diabetes. Intestinal biopsies in these patients have revealed higher densities of interleukin 1α and interleukin 4 cells, which suggest a heightened intestinal inflammatory state in type 1 diabetics.[23] Small-bowel biopsies of type 1 diabetics exposed to gliadin reveal an exaggerated inflammatory response and thus, gliadin exposure has been shown to further affect intestinal integrity in these patients.[23]

Our study further supports the concept of gut dysbiosis with a heightened inflammatory state, as the remaining abnormal intestinal biopsies showed a picture of chronic gastritis and chronic duodenitis. Two biopsies also cultured *H. pylori* infection, with one patient also having a co-existing *Giardia* infection. A further study in a mixed paediatric and adult cohort of 240 patients with biopsy-proven CD found peptic lesions in the stomach or duodenum in 12% on endoscopy; however, no control group was reported and, in another retrospective study, abnormal findings were reported in 11 out of 115 paediatric patients.[20] Premature conclusions regarding gut dysbiosis cannot be deduced from this study owing to the minimal number of patients requiring intestinal biopsy. It would be difficult to ethically justify intestinal biopsies for all the type 1 paediatric patients to evaluate gut dysbiosis and inflammatory states in asymptomatic children without proven benefit or intervention in this regard.

Our study had some limitations. It was predominantly a retrospective study and, as a result, some patients had insufficient serological testing. The capturing of signs and symptoms also

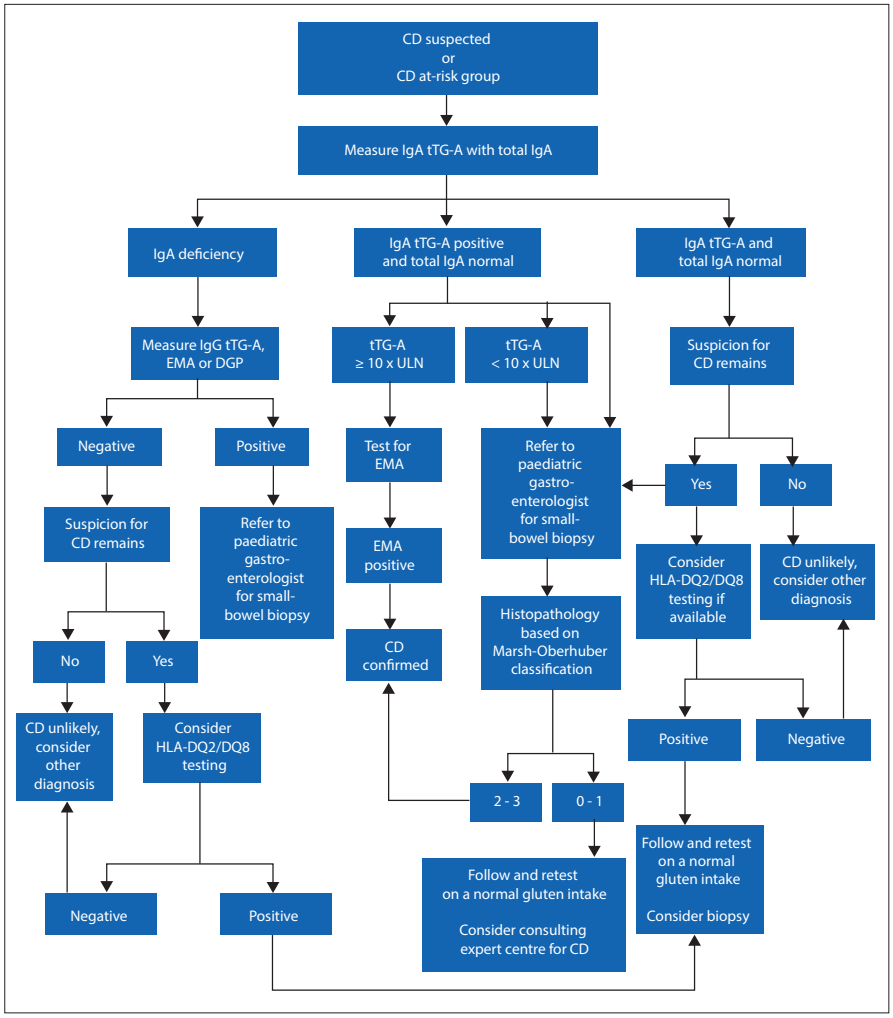

Fig. 2. Approach to coeliac disease (CD) diagnosis (adapted from Admou et al. and Pelkowski and Viera).[1,3]

relied on retrospective chart reviews. Two patients requiring gastrointestinal biopsies also relocated, were lost to follow-up and we were unable to contact them. This study is also limited by a lack of control subjects, the lack of inclusion of children from the private sector (with different dietary exposure) and the inability of our laboratory to test for EMA. HLA analysis was unfortunately also not performed owing to resource limitations. Only a small number of patients required biopsy, as it was not ethically justifiable to expose patients to unnecessary procedures; however, all our biopsies were standardised in the way in which they were taken by one of two specialists.

This study was not specifically designed to establish whether screening of asymptomatic children (even if they are at risk) is valuable, in general and in the South African context. Some literature has questioned the risk-benefit ratio of screening asymptomatic children for CD.[26,27] This evidence is, however, for all children and not specifically for at-risk groups, namely diabetic children who are mostly asymptomatic.[26,27] The prevalence of CD in our South African population of type 1 diabetic children correlates with international prevalences and therefore it would be worthwhile following the ISPAD and ESPAGN guidelines, as this would not only aid in the earlier diagnosis and treatment of CD in these children but would also aid in the management of their concurrent diabetes mellitus.

Conclusion

This study found a prevalence of serology-positive CD in our local population of South African children with type 1 diabetes mellitus of 10.2%, while the prevalence of biopsy-confirmed CD was found to be 1.9%. This finding is in keeping with international literature, which has shown the prevalence of CD in children and adolescents with diabetes to range from 1 - 10%. Therefore, international guidelines for screening of these patients are applicable to our patients and should be followed as far as possible, taking into account local resources. More research from other sub-Saharan countries, especially in paediatric patients, is required to verify the findings of this study and assist in the formation of local South African guidelines.

Declaration. Ethical approval for this study was obtained from the Research Ethics Department of the University of Pretoria (ref. no. 695/2018) and the National Health Research Database. All research was conducted according to the principles outlined in the Declaration of Helsinki.

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Author contributions. The authors confirm contributions to this paper as follows: study conception and design by MK, AJT, TK, JCvD; data collection, analysis and interpretation of results by MK; draft manuscript preparation by MK, AJT, TK, JCvD. All authors reviewed the results and approved the final version of the manuscript.

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A scoping review to identify the type and effect of hand hygiene interventions on the reduction of infectious diseases (including COVID-19) in preschool children

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Background. Proper handwashing can reduce the burden of diseases related to hand hygiene (HH) and so contribute reducing under-5 mortality. Preschoolers can benefit from HH interventions by the burden of disease and absenteeism being reduced.
Objective. To perform a scoping review of literature to assess the types and effectiveness of HH interventions at preschools, with a view to providing a guideline for appropriate interventions for South African facilities.
Methods. A literature search was conducted through the PubMed database to identify relevant studies. An iterative screening process to focus the review allowed for information on the type and effectiveness of interventions to be collated. An updated PubMed search was conducted to determine whether any interventions related to COVID-19 at preschools could be included.
Results. No additional studies relating to COVID-19 were found. Of the 305 studies identified during the initial search, only 12 fitted the specific search criteria. Of these, 10 studies showed improvements in HH-related indicators following the interventions. Only two studies used health education as an intervention, whereas the others included the supply of HH products (to varying extents) as part of the intervention.
Conclusion. HH interventions appear successful in reducing diseases spread by poor HH, improving general HH practices and reducing absenteeism among preschoolers. Studies using innovative, entertaining methods of educating children have shown to be successful in improving handwashing techniques and decreasing microbial growth on children's hands. HH interventions are suggested as an effective measure to improve HH during the COVID-19 pandemic.

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Diseases associated with insufficient hand hygiene (HH), such as diarrhoea and respiratory diseases (including COVID-19), remain a leading cause of death worldwide in children under the age of 5 years. The United Nations reports that 12% of deaths related to pneumonia and 8% of diarrhoeal deaths occur in this age group.[1] Diarrhoea is estimated to cause between 7.7% and 20% of deaths among under-5s in South Africa (SA).[2-5]

COVID-19 was declared a pandemic by the World Health Organization (WHO) on 11 March 2020. Although most paediatric cases of COVID-19 acquire their infection from adults, children may also transmit SARS-CoV-2 to adults.[6] As handwashing has been shown to reduce the risk of infection with SARS-CoV-2 and MERS dramatically,[7] the directive to adhere to strict HH practices in the context of COVID-19 has been emphasised as a measure to help curb the spread of the disease.

The value of proper HH in health has been recognised for more than 150 years. In 1854, Dr John Snow identified the incorrect placement of a water pump as the cause of a cholera outbreak.[8] Similarly, Dr Ignaz Semmelweis was able to reduce mortality rates in hospitals through a handwashing intervention in the mid nineteenth century.[9] Today, water, sanitation and hygiene (WASH) interventions are accepted measures to considerably reduce HH-related diseases.[10]

WASH interventions are implemented either as single interventions, such as through the provision of water, sanitary facilities or hygiene programmes, or as a combination of these elements.[11] These interventions can range from the supply of infrastructure (e.g. in the form of entire water purification and reticulation systems[12]) to teaching target groups to wash their hands correctly.[13,14] Education efforts can be aimed at entire communities or focus on smaller groups such as households, caregivers, parents or children.[15-18]

Hand washing with soap and water at key times is considered the most effective method to ensure proper HH; however, only 19% of people adhere to correct HH practice.[19] A study from Wuhan, China, showed that only 42% of children exhibited good HH practices.[20] When it is considered that over 2 million children attend day care in SA, practical, cost-effective interventions to improve HH can help to reduce related diseases among preschoolers, particularly in the time of the COVID-19 pandemic.

This study presents a scoping literature review to identify HH intervention methods and tools that would be suited for implementation in SA preschools, as well as to assess their effectiveness in preventing HH-related diseases.

Methods

The scoping review was guided by the Arksey and O'Malley framework stages as recommended by Calqohoun *et al.*[21] The framework consists of six stages, namely: identifying the research

question; identifying the relevant studies; study selection; charting the data; collating, summarising and reporting results; and, ideally, a final stage of consultation. The PRISMA statement[22] was used to guide article selection (Fig. 1).

A PubMed search of literature published between 2010 and 2020 was conducted using the key words 'hand hygiene, 'preschool' and 'intervention'. This search was updated on 24 June 2020 to include any literature specific to HH in preschools during the COVID-19 pandemic; however, no literature was found to meet the search criteria in the updated search. The original search yielded 305 results. Of the initial set, 98 articles that were clearly based in a healthcare setting (e.g. a hospital) or dealt with medical procedures were discarded. Of the remaining 207 titles, 95 were discarded as they did not include terms such as 'intervention', 'practice', 'hand hygiene promotion', 'hand hygiene improvement' or other terms that suggested a type of intervention activity. A further 56 titles were removed as they did not include any reference to schools or preschools.

This resulted in a set of 56 studies of which the abstracts were read to determine whether the intervention was implemented at preschools and included a hygiene component. If a hygiene component was not included, the study was disregarded, as the aim of the scoping review was specifically to identify hygiene interventions implemented in preschool settings.

This yielded a set of 25 studies to be read in full. Of these, 10 studies did not specifically address hygiene interventions, one was a protocol, which was discarded, and three were reviews that did not meet the specific focus criteria or were too old. One of the reviews[23] included a study from 2012 that complied with the scoping criteria[24] and was therefore included in the scoping set. The described screening process yielded a final set of 12 studies for analysis.[11,16,18,24-32]. Extracted information was collated in table format (see Table 1).

Seven of the articles in the scoping set were randomised controlled trials. The quality of these studies was scrutinised using the 5-point JADAD scoring system.[33] The average score was 2.4, with all studies having randomised sample groups and five including a description of the randomisation process. In five of the studies, drop-outs or withdrawals could be accounted for. However, none of these seven randomised controlled trials were conducted blind, which is seen as a general weakness in HH intervention studies.[12,34]

Of the 12 studies eligible for analysis, all were examined for publication bias based on the following criteria: positive results in line with accepted norms; funding for the study; and reporting of statistically significant results.[35] Eight of the articles reported positive results in line with the expected results for a particular indicator, two were sponsored by pharmaceutical companies, which could have resulted in bias had the results not shown positive improvement, and nine showed statistically significant results. These three factors can influence publication bias. It should also be noted that it is possible that unpublished studies may exist that contradict the outcomes of the studies included in this review.

Regression models were used in seven of the final set of 12 studies reviewed, providing evidence of homogeneity. The use of *t*-tests was mentioned in three articles to determine significant differences. Two studies did not describe the data analysis process comprehensively.

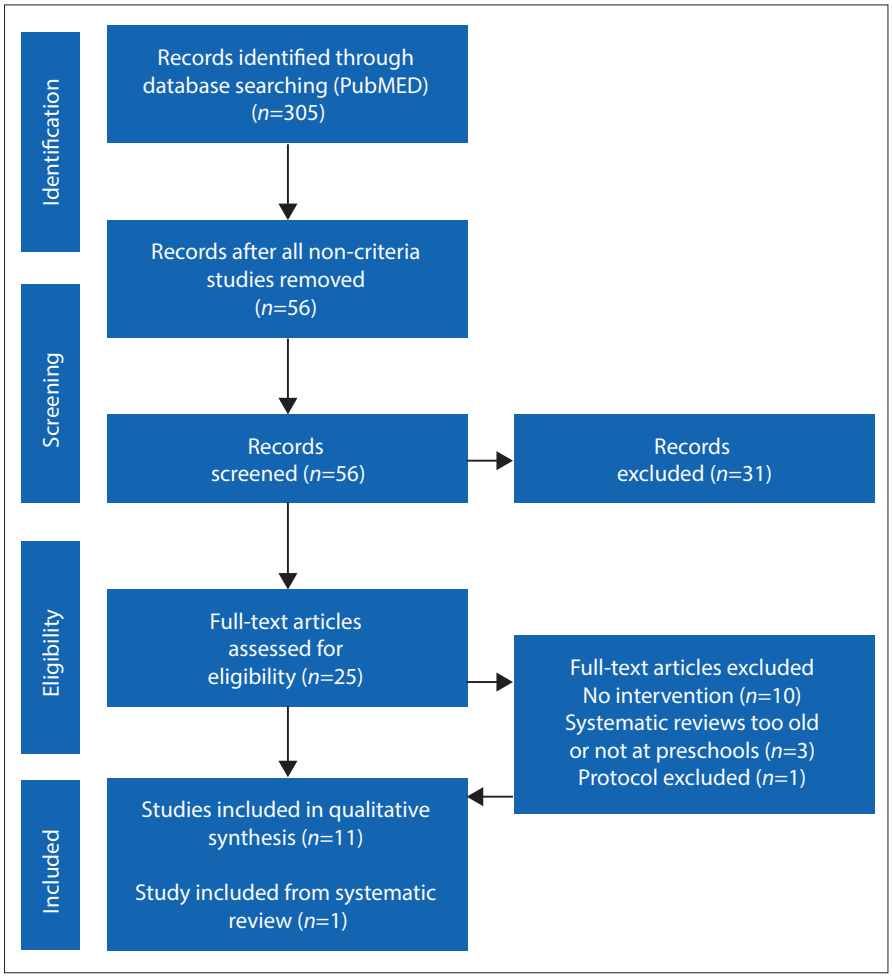

Fig. 1. Study selection process.

Results

A total of 12 studies were included in the scoping review. Only one of the studies was conducted in Africa,[11] five were set in European countries,[16,25,30-32] three in Asia,[26,28,29] two in the Middle East[18,27] and one in South America.[24]

To determine the success of an intervention a measurable variable needs to be defined. Four of the studies used the decrease in diarrhoea or respiratory infections[11,16,24,31] as primary outcome. This was measured through varying degrees of record-keeping based on a type of incident register, where parents, caregivers or medical personnel noted the incidence of disease cases prior to and after the intervention. Definitions of a positive disease case were provided (most commonly for diarrhoea, defined by the WHO as passing three loose stools within a 24-hour period). Absenteeism was also recorded, either by the parent or the caregiver at the preschool, although in one study it also included the use of the temporary parental benefit provided by that country's government and claimed by parents when taking time off to care for sick children.[32]

Table 1. Collation of information analysed as part of the scoping review

Authors	Date	Country	HH-related indicator	Intervention	Result
Dreibelbis *et al.*[11]	2014	Kenya	Diarrhoea	Three arms: HP and WT; HP, WT and additional latrines; control (water available) – two arms: water supply + sanitation + HP and WT; control (water scarce): HP given to school children – test to see if it affected the children under 5 years at home	Reduced clinic visits related to diarrhoea gastrointestinal disease in children under 5 years; biggest reduction seen in clusters where intervention involved water + sanitation + HP + WT
Gudnason *et al.*[16]	2013	Iceland	Fever, colds, acute otitis media, pneumonia, bronchial asthma and diarrhoea	Education of staff and children; liquid soap, paper towels, hand sanitiser, gloves for nappy changing and child toileting, disposable nose wipes, toys washed once a month. All products supplied by study.	Increased use of disinfectant materials in intervention group; insignificant effect of intervention; possible that hygiene standard already high at start of study.
Rosen *et al.*[18]	2011	Israel	HH environment	Provision of handwash products where necessary; puppet show for children; education for caregivers	Provision of soap, paper towels, individual cups; HH environment improved significantly in intervention group
Correa *et al.*[24]	2012	Colombia	Diarrhoeal disease and respiratory infections	Provision of alcohol-based hand rub; workshop on HH; visual reminders; monthly refresher course	Significant reduction in ADD and ARI in second and third trimester of study in intervention group
Azor-Martinez *et al.*[25]	2018	Spain	RI, antibiotic use and absenteeism	Education of staff, parents and children; provision of liquid soap and hand sanitiser to intervention groups	–12% absenteeism in HSG; –23% in RI episodes in HSG compared with control group; –30% in antibiotic prescription in HSG compared with control group
Or *et al.*[26]	2019	Hong Kong	Absenteeism with influenza symptoms	4 training sessions on hand hygiene and WHO 7-step hand washing	–25% in absenteeism; improved handwashing performance
Arikan *et al.*[27]	2018	Turkey	Bacterial growth on hands	Clown demonstrating handwashing and cartoon video over 4 weeks	No difference in handwashing frequency; –31% in microbial growth in experimental group
Mohd Rani *et al.*[28]	2020	Malaysia	Handwashing	Tablet device showing handwashing demonstration video fitted at each washbasin; provision of Betadine hand soap	52.1% improvement of handwashing technique in experimental group
Mohamed *et al.*[29]	2019	Malaysia	Absenteeism	Tablet device showing handwashing demonstration video fitted at each washbasin; provision of Betadine hand soap	Absenteeism was higher post intervention in both groups; however, absenteeism in intervention group was lower compared with control group
Zomer *et al.*[30]	2015	The Netherlands	Gastrointestinal illness and respiratory infections monitored by parents	6-month supply of HH products; booklet for teachers; team education for teachers; posters and stickers for teachers and children	Intervention had no effect on incidence of disease
Zomer *et al.*[31]	2016	The Netherlands	HH compliance among caregivers	6-month supply of HH products; booklet for teachers; team education for teachers; posters and stickers for teachers and children	Significant increase in HH compliance among caregivers
Hall & Lindahl[32]	2016	Sweden	Child absenteeism	Hygiene inspection and 2-hour lecture to caregivers on HH and reducing contagious diseases	Not able to measure whether hygiene was improved; intervention had no effect on children's absence due to illness; significantly less absenteeism in groups <15 children

HH = hand hygiene; HP = health promotion; WT = water treatment; HSG = hand sanitiser group; RI = respiratory infections; ADD = acute diarrhoeal disease; ARI = acute respiratory disease.

One study measured the success of an intervention according to the improvement in children's handwashing skills. Wall-mounted tablet devices (running an Android operating system) at hand wash basins automatically recorded children's handwashing motions, rating their adherence with stars after they had completed the process.[28] Handwashing compliance was also assessed through observation of caregivers' compliance with HH practices,[31] and another study assessed the improvement of the HH environment through hygiene inspections at baseline and end line.[18] Determining bacterial colony density on children's hands was used as the main indicator of HH compliance between intervention and control groups in one study.[27]

The sample population of these studies included parents, caregivers and preschool children aged 5 years or younger, either singly or in combination. Sample sizes ranged from 40 preschool facilities[18] to 3 523 children,[11] depending on the study design. The methodology of the studies was mostly based on a pretest–post test design, as data were collected at baseline and at the end of the intervention (sometimes also during the course of the intervention).

Questionnaires were used as the data collection tool in five of the studies.[11,16,25-27] Of these, two articles mentioned administering a simple questionnaire to the children participating in the study,[26,27] two administered questionnaires to parents[11,25] and in one the questionnaire was administered to both parents and caregivers.[16] The registers used to track whether children were ill or absent were kept variously by parents, the school or both. In one study, government records were accessed to determine whether parents had used their temporary parental benefits to care for children at home[32] and in some cases medical professionals were used to scrutinise registers to determine whether recorded disease incidents complied with the defined descriptions of the disease.

Interventions in nine of the studies included education to caregivers. This was in the form of lectures, workshops, pamphlets or training sessions. One study provided health education to siblings of children under the age of five at school, to determine whether the intervention provided at school would transfer to younger children at home. The type of health promotion given to the school-going children was not described.

The provision of hygiene products such as soap, paper towels, alcohol-based rub and, in one study, separate drinking cups,[18] for the duration of the intervention, the study or a period of 6 months was identified in nine of the studies.

Two of the studies provided only HH training as an intervention, with one being directed at children (a clown character demonstrating handwashing)[27] and the other being directed at caregivers (a 2-hour lecture).[32] Three of the studies used incidents of diarrhoea or respiratory infections to assess the effectiveness of the intervention and in two others absenteeism was used as the indicator. The results of the interventions were tabulated according to the indicator used for each study.

HH interventions resulted in no improvement in only two studies, both of which used a combination of diarrhoeal and respiratory infections as indicator of effectiveness. The authors of one of the studies propose that the most likely explanation for this outcome is that the standard of hygiene at baseline was too high to support any significant effect of the intervention.[16] They were able to show compliance with hygiene protocols by caregivers, as measured by the use of the hygiene products during the study. In the other study showing no effect,[31] the authors explained that the HH compliance of the caregivers possibly did not increase enough to result in fewer infections. In addition, children attended school on average only 2.7 days per week and so may have been ill elsewhere.

In one of the studies using a decrease in absenteeism as indicator of the intervention's effectiveness, no decrease in absenteeism was observed. This may have been a result of strict guidelines regarding absenteeism being implemented to prevent the spread of communicable diseases prior to the start of the study.[32] However, as a secondary result, there was a significant decrease in absenteeism in preschool groups smaller than 15 children. The authors speculated that this may have been because caregivers were able to direct more time and attention to hygiene protocols in smaller groups.

The 10 other studies all showed positive effects of the interventions, although authors also listed possible reasons for this in addition to the actual intervention. In the study by Dreibelbis *et al.*,[11] which assessed the effect of an intervention delivered at school on diarrhoea incidents among under-5 siblings at home, it was noted that the most effective intervention was a combination of water provision, sanitation, health promotion and water treatment.[11] In a study that showed a significant reduction in diarrhoeal and respiratory infections after intervention, the authors attributed the outcome to intensive follow-up and the guaranteed supply of alcohol-based hand sanitisers.[24] Interestingly, of the 12 studies reviewed, nine included the provision of various HH-related products as part of the intervention. However, there is little evidence that availability of these products can be sustained in the relevant study populations after completion of the study.

A study assessing absenteeism as a result of respiratory infections also showed a decrease in both absenteeism and infections in the test group, who were provided with hand sanitiser.[25] Another study using this indicator showed a 25% reduction in absenteeism due to respiratory infections, following four training sessions in which a fluorescent staining gel and ultraviolet light were used to improve children's handwashing technique.[26] Another study focused on handwashing showed a 52.1% improvement in children's technique, which the authors attributed to the use of tablet devices fitted at wash basins, showing the proper handwashing technique and recording their actions.[28] However, the authors note that human observations are preferable, as they would be able to identify strengths and weaknesses in the technique.

Caregivers' compliance with HH practices was found to increase in a study where information was disseminated to this target group, although the authors noted the possibility of the Hawthorne effect due to direct observation and also possible bias by observers as potential concerns.[31] The environment where HH is practised has been shown to influence the effectiveness of hygiene interventions, as seen in increased use of HH products supplied as part of a study where the environment was positively enabled. This study also showed that there was no difference between secular and religious environments, but that HH practices could generally be improved at all preschools, with the researchers commenting that 'it is not possible to wash one's hands with soap if soap is not available.'[18]

Finally, in a study using microbial growth as an indicator of the effectiveness of the intervention, a 31% reduction in microbial growth was seen on the hands of children in the intervention group, despite no marked increase in handwashing frequency in either group. The intervention included a character (clown) to teach children about pathogens ('germs') and proper handwashing, and the authors concluded that health messages to children could be more effective if entertaining methods are used.[27]

Discussion

The aim of this scoping review was to synthesise information on the effectiveness of HH interventions in preschools or among children of preschool age. The analysis shows that interventions led to decreases in diarrhoeal diseases, respiratory infections, absenteeism and microbial growth on hands, although there was no definitive

'one-size-fits-all' intervention. This review did not assess the quality of the studies included, but rather used the analysis to determine a way forward when looking at formulating a proposed intervention for preschools in SA to improve the health of under-5s and decrease the burden of HH-related diseases in this population.

Many of the studies showed improvements in child health, absenteeism or HH, but in a number of studies the outcome relied on the provision of HH products as part of the intervention. As the studies do not comment on the long-term sustainability of these interventions, it was not clear whether preschools continued to procure these products themselves after the conclusion of the study. In a country such as SA, where there are large socioeconomic divides, an intervention would need to be sustainable in a way that does not place additional financial burdens on the school or parents.

Two of the 12 studies included in this scoping review did not include the provision of HH supplies as part of the study, but relied on health promotion and education activities as an intervention. Using a fluorescent gel and ultraviolet light in teaching children to wash their hands resulted in a decrease in absenteeism due to influenza and the authors regarded the intervention as successful; the education campaign continued for four weeks to improve the children's attention to the handwashing process. This is consistent with findings showing that automaticity of an action increases steadily over time when the action is repeated in a constant setting.[36]

Another study that used health promotion as an intervention, not only offered HH education to the caregivers but also used a character (clown) to teach children about HH in an entertaining manner. Although there was no change in handwashing frequency or increase in the use of HH materials, bacterial colonisation was reduced by 31% in the experiment group and the growth rate of bacterial coliforms was reduced as a result of using the correct handwashing technique, as was demonstrated during the intervention.[27] The authors subsequently recommended that children should be taught in an entertaining way to achieve positive results. This is reiterated in a recent letter to the editor of the *Journal of Hospital Infection*,[37] which suggested a song to be used to teach children the correct handwashing procedures, which in the COVID-19 pandemic have become an important preventive measure. Experimentally, music has been shown to facilitate verbal and motor learning, which facilitates correction of a missed step or action through repetition and rehearsal.[37]

Using hygiene inspections and a two-hour lecture to caregivers on HH had no effect on children's absenteeism. This may have been as a result of stricter contagious disease control guidelines that had been implemented at baseline; however, other studies have shown interventions to be effective if they are directed at children and caregivers and, where practical, parents. Electronic communication with parents or sending health messages via email, short message services or other digital platforms can be effective, as has been shown with other health interventions for disease prevention.[38]

Study limitations

The scoping of literature in this review is limited to studies found through the PubMed database, which could have introduced bias. However, many of the articles are also available on other platforms. PubMed was chosen as search platform as it provides data in both text and comma-separated value (csv) format, which allowed for easy sorting.

The search was limited to studies published between 2010 and 2020 and therefore may have excluded articles on other interventions published earlier. Studies published after the COVID-19 pandemic may provide additional insights into effective and sustainable HH interventions in future.

Conclusion

The analysis presented here suggests that the interventions described by the reviewed studies can successfully improve HH, and possibly reduce disease incidents or absenteeism related to HH. Interventions where the necessary HH products were supplied would be expected to result in better outcomes, although the sustainability of this approach is unknown and warrants further study. However, using an innovative, entertaining approach to teach children about HH, repeating these lessons and including caregivers and, if possible, parents, could be a cost-effective, sustainable intervention to successfully improve HH practices among preschool children in SA. Given that HH is considered a crucial element of infection control and its effectiveness in reducing viral transmission,[20] the analysis presented here may help to implement effective interventions to combat the spread of HH-related diseases, such as COVID-19, in preschools and communities at large.

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Author contributions. SL was the main author and data collector. TGB provided additional information and contributed to manuscript development. NN was involved in checking the dataset and manuscript development. All authors read and approved the final manuscript. The datasets used in this analysis are available from the corresponding author on reasonable request.

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Sirenomelia with major cardiac anomalies

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Sirenomelia is a rare and serious congenital anomaly characterised by fusion of the lower limbs, usually a single umbilical artery and malformations of the genitourinary and gastrointestinal tracts. In this report, we present clinical and radiological features, as well as autopsy findings, in a patient with sirenomelia diagnosed at the time of delivery. Major cardiac defects were observed, namely transposition of the great vessels and a hypoplastic left ventricle.

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Sirenomelia is a congenital anomaly characterised by lower limb fusion associated with varying degrees of abnormalities of the genitourinary, cardiovascular, gastrointestinal and musculoskeletal systems.[1] Although the cause of this defect is not known, the vascular steal hypothesis[2] appears to be the most likely mechanism for its development.

The incidence of sirenomelia is reported to be about 1 per 100 000 births, with a male-to-female ratio of 3:1.[1,2] Its outcome is nearly always fatal, with death occurring in the perinatal period owing to renal tract abnormalities and associated complications.[3] We present a patient with sirenomelia with cardiac abnormalities, which are not commonly reported in patients with this condition.

Case presentation

A 22-year-old primigravida mother, at 36 weeks' gestation, was referred from a local clinic for poor progress in labour. She attended antenatal care at the local clinic and her pregnancy was assessed to be normal and she had no history of diabetes mellitus. An antenatal ultrasound scan was not performed. She delivered via caesarean section for failed augmentation of labour.

The infant weighed 2 700 g at birth, with Apgar scores of 3 at 1 minute and 1 at 5 minutes. On examination, there was a midline lower-limb tapering to a single digit-like structure with a single nail (Figs 1a and b). No cloacal, anal, genital or urethral opening was present and there was only a single umbilical artery. A fleshy skin-covered appendage was seen over the sacrum, but the spine felt normal on palpation.

Case management

Owing to the severe abnormalities seen, it was decided not to resuscitate the infant but offer supportive care instead; the infant subsequently demised. The parents were counselled about their infant's diagnosis and outcome. Death was attributed to severe congenital abnormalities.

Investigations

The X-rays of the bones showed sacral agenesis, a hypoplastic pelvis and a single distal limb resembling a femur (Fig. 2). A markedly hypoplastic common tibia was also observed. The bones of the upper limbs appeared normal.

On autopsy, the presence of a single umbilical artery was confirmed. The great vessels were transposed, with hyperplasia of the right ventricle and hypoplasia of the left ventricle. The lungs were hypoplastic, with the right lung showing three lobes and the left lung only a single lobe. The rectum ended blind and was distended by meconium. A large cystic mass was observed in the pelvis, containing urine and lined by large papillae, which proved to be a kidney on histological examination. Two small masses were found within the wall of the kidney and these were confirmed to be adrenal glands on histology. No genital organs were found within the abdomen. Chromosomal analysis of blood showed a 46XY karyotype.

Discussion

Sirenomelia, or mermaid syndrome, is a rare structural congenital abnormality characterised by fusion of the lower limbs, together with

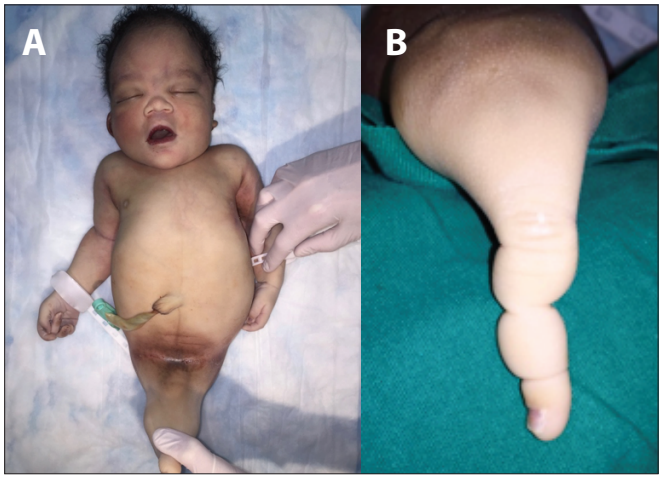

Fig. 1a. General appearance: bell-shaped chest, widely spaced nipples, single lower extremity, absence of external genitalia.
Fig. 1b. Finger-like appendage at distal end of single lower extremity.

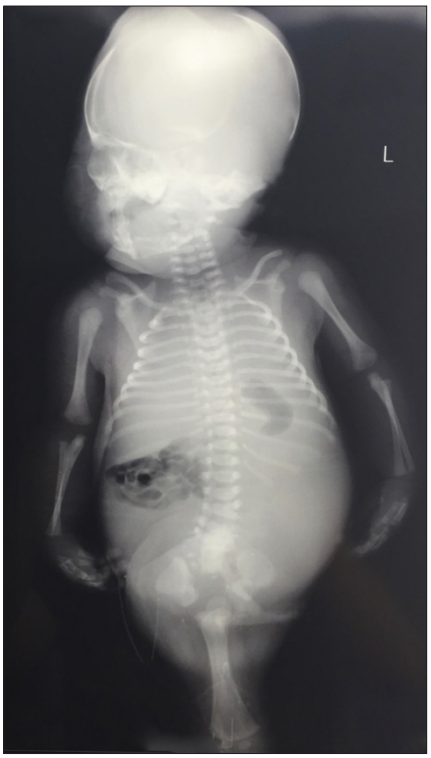

Fig. 2. Babygram (AP view): bell-shaped ribcage, rib-crowding, hypoplastic lungs, abnormal abdominal gas pattern, abnormal pelvis, normal upper limbs, single femur, absent tibia.

urogenital and anorectal malformations of varying degrees. Fatality usually results from complications of fetal renal tract abnormalities. Sirenomelia was first described in 1542 by Rocheas, and later also by Palfya in 1553. The syndrome derived its name from this deformity resembling the single lower appendage of the mermaids, or 'sirens', of Greek mythology.[2]

Debate exists as to whether sirenomelia is a separate entity or if it represents a severe form of caudal regression syndrome. Evidence in favour of the former is that sirenomelia seems to be associated with a single umbilical artery, whereas this is not a finding characteristic of caudal regression syndrome. Furthermore, only 2% of sirenomelia cases have a history of maternal diabetes mellitus compared with 22% of cases described as representing caudal regression syndrome.[2]

The occurrence of a single umbilical artery has led to the pathogenesis of this syndrome being ascribed to the vascular steal hypothesis. The basic premise of this theory is that aberrant formation of the umbilical artery leads to persistence of the vitelline artery (type II single umbilical artery), which then assumes the role of both umbilical arteries. This single, large artery, or 'steal vessel', arises as a continuation of the abdominal aorta just distal to the diaphragm and diverts blood away from the caudal extremity of the embryo, towards the placenta. This results in deficient blood flow and nutrient supply to the caudal mesoderm, which, in turn, causes abnormal development or agenesis of caudal structures and the characteristic features of sirenomelia.[2]

Although the infant had a male genotype, no internal or external genital organs were noticed. The observation supports the vascular steal theory, as it points to disrupted blood supply to the gonads from the abdominal aorta below the origin of the steal vessel.[2]

The 'defective blastogenesis hypothesis' is an alternative theory for the pathogenesis of sirenomelia, proposing that abnormal development of the caudal mesodermal structures results from an embryological insult occurring at 28 - 32 days of gestation. Proposed examples of such an insult include maternal diabetes, pressure on the caudal extremity or maternal exposure to teratogens.[1,3] In this case, no identifiable insults were noticed that could have resulted in abnormal development. Furthermore, the presence of a normal karyotype highlights that the pathogenesis of this case is unlikely to be related to a chromosomal abnormality but rather to a developmental or otherwise undetermined genetic abnormality.

The external morphological appearance of the lower limb fusion in sirenomelia encompasses a wide spectrum. Given the large number of possible morphologies, various classification systems have been proposed. The most widely accepted is that by Stocker and Heifetz.[4] According to this classification system, this infant presented with type VII sirenomelia.

Although antenatal diagnosis of this condition is possible, resource constraints in public-sector healthcare settings in developing countries (such as South Africa) mean that appropriate antenatal ultrasound scans are performed only in high-risk pregnancies. As a result, there were no antenatal scans indicated for this pregnancy and the diagnosis was therefore made postnatally. Post-mortem examination was performed to confirm the diagnosis and assist with counselling of the parents.

In the literature, sirenomelia cases has rarely progressed to autopsy examination and consequently there are limited cases reporting cardiac abnormalities.[1,5,6] None of these cases have reported transposed great vessels or a hypoplastic left ventricle. Neither of the mentioned theories on pathogenesis explains the cardiac anomalies, suggesting that these either are coincidental findings or due to a variant form of sirenomelia.

Conclusion

This paper presents a case of (type VII) sirenomelia[4] with additional congenital abnormalities that have not been reported in the literature previously. This case report therefore adds to the body of literature, in that another variation in the abnormalities seen in this condition is described.

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Author contributions. RTS and RC conceptualised the report, reviewed the literature and wrote the manuscript. PN and SCV supervised the study. All authors contributed to reviewing and revising earlier drafts of the report and approving the final manuscript.

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Orchiepididymitis in a 14-year-old boy with concurrent SARS-CoV-2 infection

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The symptoms of SARS-CoV-2 infection and COVID-19 provoked by this virus are poorly described in children. Here we analyse a case of orchiepididymitis associated with COVID-19 in a 14-year-old boy. We discuss the possibility of SARS-CoV-2-associated testicular inflammation. This report strengthens the necessity for more in-depth study of the clinical presentation of paediatric COVID-19 and the potential association with non-respiratory symptoms.

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) provoking coronavirus disease 2019 (COVID-19) was first described in Wuhan, China, in December 2019. Within months, COVID-19 spread rapidly worldwide, becoming the first pandemic of the 21st century. COVID-19 produces mainly mild symptoms in most infected children. However, it can cause a plethora of inflammatory complications including multisystem inflammatory syndrome in children (MIS-C). Since COVID-19 is an emerging infectious disease, there are limited data about the effects of this infection on patients, especially in the paediatric population. We describe here a case of the co-occurrence of orchiepididymitis and SARS-CoV-2 infection in a 14-year-old adolescent. As a similar case has already been reported by Gagliardi *et al.*,[1] our description is a potential next argument for the possible link between orchiepididymitis and COVID-19.

Case report

On 27 March 2020, a 14-year-old boy had a fever (39.4 °C), complained of dysuria, vesical tenesmus and frequent urination. Owing to the COVID-19 pandemic, the patient telephoned his general practitioner, who diagnosed cystitis and prescribed cefuroxime axetil. Resolution of dysuria was observed one day after treatment. However, the patient developed a mild dry cough when moving.

Because of anorectal pain, on 29 March the patient presented at Jan Bogdanowicz Children's Hospital in Warsaw, where swelling of the scrotum was observed; the testicles were enlarged and painful on palpation, predominantly on the right side. The child was admitted to this hospital's paediatric emergency department, where an ultrasonogram (USG) revealed testicular torsion. Laboratory tests showed neutrophilic leukocytosis (white blood cells 20 700 K/μL, neutrophils 17 400 K/μL) with elevated C-reactive protein (85.2 mg/L). Urinalysis showed leukocyturia and leukocyte aggregates. On admission to the hospital, a nasopharyngeal swab for SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test was taken.

A surgical revision of the scrotum was performed, showing no testicular torsion but inflammation of the epididymis. The day after surgery, a positive result for the SARS-CoV-2 PCR test was received. The social history revealed that the patient's father had been in contact with international lorry drivers. It was of interest because, by the end of March 2020, the COVID-19 epidemic was not yet widespread in Poland, and foreign contacts could be the source of SARS-CoV-2 infection. The father of the patient had not been tested for SARS-CoV-2. The patient and his father were referred to the Medical University of Warsaw Pediatric Teaching Hospital COVID-19 ward on 30 March because of the positive PCR test for SARS-CoV-2 and mild respiratory symptoms.

Here, we performed a USG follow-up because of persistent inguinal pain. The imaging detected thickening of the tunica albuginea, vasitis, and epididymitis features. We switched antibiotic therapy to one-dose ceftriaxone and oral levofloxacin. This treatment resolved scrotal oedema and testicular pain within three days of hospitalisation. We took a urine sample for the SARS CoV-2 RT-PCR test on 2 April, which was negative.

A second swab was taken nine days after the first swab according to the criteria for releasing COVID-19 patients from isolation published by the World Health Organization in January 2020. This PCR test was negative. The patient was discharged home with the recommendation of 14-day family quarantine under the county sanitary agency's surveillance.

Discussion

The clinical presentations of SARS-CoV-2 infection in children are highly diverse. Respiratory symptoms are among the most common, with a cough occurring in 40% of children. Our patient presented with only mild respiratory symptoms. However, other systems may be affected, among them the urogenital being one of the rarest.

High levels of the receptor for angiotensin-converting enzyme 2 (ACE2) were found in the testicular spermatogonia and Leydig and Sertoli cells. ACE2 receptors allow the virus to infect the cells and, possibly, cause damage, even in asymptomatic cases. In individuals with respiratory symptoms, SARS-CoV-2 RNA can be detected in semen during the acute phase of COVID-19 and later.[2]

Epididymal cells may also be the target for the virus. Infected individuals have a higher concentration of human epididymal protein 4 (HE4) than healthy individuals.[3]

Despite the ongoing COVID-19 pandemic, only a few cases of symptomatic testicular involvement in adults and children have been described. Testicular pain and fever were the dominant symptoms.[4,5] For this reason, there is a debate whether COVID-19 may be involved in the aetiology of testicular complications.[1] Our case report brings new light to the possibility.

The history of our patient resembles the case reported by Gagliardi *et al*.[1] The boy was treated with an antibiotic first, and when scrotal swelling progressed, and high fever and pain persisted, he was suspected of having an acute scrotum. In addition, our patient underwent an unnecessary surgical revision of the scrotum. It must be noted that our patient is only the second case of concomitant orchiepididymitis and SARS CoV-2 infection reported at the time of writing this report, after one year of the COVID-19 pandemic. The previous case also concerned a child; no case involving an adult has been described so far. It seems, therefore, that the orchiepididymitis related to SARS-CoV-2 infection may be child-specific. Moreover, COVID-19 produces mild or no symptoms in children and only the severest orchiepididymitis cases present to hospitals, where routine PCR tests for SARS-CoV-2 are done, as in the case described here. This may explain why the relationship between orchiepididymitis and SARS-CoV-2 infection is still ignored.

Conclusions

In the COVID-19 era, SARS-CoV-2 infection should be included in the differential diagnosis of orchiepididymitis, and the use of personal protective equipment considered for the medical staff. Moreover, in the co-occurrence of orchiepididymitis and SARS-CoV-2 infection, the use of antibiotics for treatment may not be justified.

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Choreoathetosis and dystonia in a child with COVID-19 and multisystem inflammatory syndrome

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Neurological complications of COVID-19 or multisystem inflammatory syndrome in children (MIS-C) are well described. We report an unusual presentation in a 9-year-old girl presenting with status epilepticus, who thereafter developed choreoathetosis and dystonia. She was initially managed with intravenous immunoglobulins and methylprednisolone for presumed autoimmune encephalitis. However, she tested positive for SARS-CoV-2 and met the clinical and laboratory criteria for MIS-C. She remained encephalopathic with abnormal movements and dystonia for 8 days from presentation but was discharged home with complete clinical recovery after 2 weeks.

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The novel coronavirus (SARS-CoV-2) was first reported in December 2019 in Wuhan, China, and has become a global pandemic.[1] The first reported case in South Africa (SA) was on 5 March 2020.[2] In late April 2020, an alert about the multisystem inflammatory syndrome in children (MIS-C) and adolescents between the ages of 0 and 19 years was issued. [3] This syndrome is characterised by fever, inflammation and evidence of multi-organ involvement.[3] Case definitions have been proposed by the World Health Organization (WHO), the Royal College of Paediatrics and Child Health and the Centers for Disease Control and Prevention – most of the clinical and laboratory criteria are similar.[3-6] The WHO classification system has been adopted in SA.

Coronavirus disease 2019 (COVID-19) can present with a range of neurological manifestations including headache, decreased level of consciousness, seizures, encephalopathy and disturbance of smell and taste, as reported in adult patients.[1] An adult study identified five categories of neurological presentations:(*i*) encephalopathies with delirium/psychosis and no distinct magnetic resonance imaging (MRI) or cerebrospinal fluid (CSF) abnormalities; (*ii*) inflammatory central nervous system syndromes including encephalitis, myelitis and acute disseminated encephalomyelitis; (*iii*) ischaemic strokes associated with a prothrombotic state; (*iv*) peripheral neurological disorders; and (*v*) miscellaneous central disorders. In addition, neurological organ involvement has been described in some case definitions of MIS-C and encompasses seizures, coma and encephalitis, among others.[7] This case report describes an unusual neurological presentation in a child with COVID-19 who met the criteria for MIS-C.

Case presentation

A 9-year-old HIV-negative girl presented to the Chris Hani Baragwanath Academic Hospital during the first wave of COVID-19. She had a fever and was in status epilepticus. She reported a preceding 3-day history of headache, multiple episodes of vomiting, rhinorrhoea, cough and fever. Her temperature on arrival was 38.3°C, she had a normal blood glucose level and she displayed no features of hypoperfusion. On clinical examination, she was encephalopathic but with normal tone and reflexes. She needed two doses of intravenous midazolam and two phenytoin loading doses (20 + 10 mg/kg intravenously) to abort the seizures. A lumbar puncture was initially deferred, as she had a reduced level of consciousness (Glascow Coma Scale (GCS) 10: E4M4V2), and intravenous ceftriaxone was commenced empirically to cover for possible bacterial meningitis. The blood work on admission showed leukocytosis with neutrophilia and lymphopenia, and normal C-reactive protein (CRP) (Table 1). The computed tomography scan of the brain (CTB) was unremarkable.

Her temperature remained above 38.5°C for the first 24 hours of admission. On the second day of admission, she developed dystonia, choreoathetosis and facial grimacing with hypotonia and normal reflexes. The working diagnosis was autoimmune or viral encephalitis. Phenytoin-induced dyskinesia was also considered, given that two loading doses of phenytoin were needed to abort her seizures. She was treated with intravenous immunoglobulin (2 g/kg/day, administered over 2 days), methylprednisolone (30 mg/kg/day, for 5 days) followed by oral prednisolone (1 mg/kg/day), and acyclovir was commenced on day 2 of her hospitalisation. The CSF was acellular with normal biochemistry and without organism growth on culture. The CSF and blood were sent for testing for oligoclonal bands and N-methyl-D-aspartate receptor (NMDAR) antibodies. There was insufficient CSF for viral PCR studies. Common toxins were screened for and excluded.

Within 48 hours of admission, the SARS-CoV-2 nasopharyngeal swab taken on admission was confirmed as positive, and she was transferred to the paediatric COVID-19 isolation ward. The hospital did not have access to SARS-CoV-2 antibody testing at the time of her presentation. On day 4, her CRP increased to 257 mg/L and her extrapyramidal signs persisted. Her clinical presentation and

laboratory results were compatible with a diagnosis of MIS-C; she had fever, evidence of SARS-CoV-2, organ involvement, non-purulent conjunctivitis, coagulopathy and raised inflammatory markers (Table 1). Low-molecular-weight heparin was added to the treatment because of raised serum d-dimers, and azathioprine was initiated because of the persistence of encephalopathy and abnormal movements.

On the 10th day of admission, she began to show signs of improvement. The abnormal movements became less apparent and GCS normalised. By the 14th day, she was ambulating independently, and able to feed herself and communicate. The repeat SARS-CoV-2 swab was negative on the 15th day, and she was discharged home the following day.

Ethical considerations

Consent for the writing of this report was obtained from the parents. Ethics approval was obtained from the University of the Witwatersrand Human Research Ethics Committee (HREC ref. no. M2009101).

Discussion

To our knowledge, this is the first reported clinical presentation of choreoathetosis and dystonia in a child with COVID-19. It remains unclear whether the unusual clinical presentation in this case was a manifestation of COVID-19 itself or part of MIS-C. There have been other reported cases of neurological involvement associated with COVID-19 and MIS-C in children, but none has described choreoathetosis and dystonia.[7-9] The proposed pathogenesis of neurological involvement includes infection of neurological tissue, maladaptive inflammatory and/or immune-mediated host responses, vascular endothelial injury or cerebrovascular disease caused by coagulopathy.[10,11] Another possibility was phenytoin-induced dyskinesia, which may occur in cases with toxic serum levels, polypharmacy or underlying neurological diseases; however, it does not generally last longer than the serum half-life.[12,13] This diagnosis was considered less likely because the choreoathetosis and dystonia manifested 17 hours after phenytoin was administered, and persisted for a further 8 days.

Case reports of two children with severe neurological complications associated with MIS-C described middle cerebral artery infarction in both patients. One of the children had cerebral oedema and diffuse subarachnoid haemorrhage, and the other had a posterior cerebral artery infarct.[14] In another case series of 27 children with MIS-C, 4 had neurological findings such as encephalopathy, headaches, brainstem and cerebellar signs, muscle weakness and reduced reflexes.[8]

While CTB remains an excellent diagnostic tool for patients with infarction and/or haemorrhage,[14] it appears less sensitive in patients with other neurological complications associated with COVID-19, particularly encephalitis.[8, 9,15,16] Our patient's CTB was reported to be normal. In contrast, MRI has proved much more useful both in children and adults with COVID-19.[17] All four of the abovementioned children with MIS-C and neurological involvement demonstrated possibly reversible lesions in the splenium of the corpus callosum from inflammation-induced focal intramyelin oedema.[8]

Electroencephalography (EEG) is another useful investigation in encephalopathic patients with COVID-19, showing an excess of slow activity even when MRI has failed to detect abnormalities.[8,15] Given these initial data, both MRI and EEG are essential diagnostic investigations in children with neurological signs associated with COVID-19 or MIS-C. Our patient, however, did not undergo these investigations for fear of contamination of the single MRI suite and limited portable EEG machines in our setting. Similarly, in other low-resourced settings, children with COVID-19 have been denied access to important and necessary investigations.[18]

The management of COVID-19-associated neurological disorders remains the subject of debate and scientific enquiry. Some have opted to manage these patients with no specific therapy and have reported full recovery,[9] while others have used agents such as mannitol to decrease intracerebral pressure and provide symptomatic relief.[16,19] In our setting, the South African Paediatric Critical Care Working Group recommends a combination of intravenous immunoglobulins and systemic glucocorticoids together with aspirin in patients with MIS-C.[20] Similarly, three of the four children mentioned above

Table 1. Laboratory investigation undertaken in this child

Investigation	Case	Reference values
WCC (× 10^9/L)	35.04	3.90 - 10.20
Hb (g/dL)	13.4	3.80 - 5.40
MCV (fL)	91.8	77 - 81
Plt (×109/L)	596	180 - 440
Neutrophils (× 109/L)	29.84	1.40 - 5.20
Lymphocytes (× 109 /L)	3.82	1.50 - 4.20
CRP (mg/L)	257	<10
Oligoclonal bands	Normal	
SNMDAR-Ab	Insufficient sample	
Sodium (mmol/L)	139	136 - 145
Potassium (mmol/L)	5.9	3.4 - 4.7
Chloride (mmol/L)	99	98 - 107
Urea (mmol/L)	4.8	1.4 - 5.7
Creatinine (µmol/L)	57	28 - 57
ALT (U/L)	39	5 - 25
AST (U/L)	110	0 - 41
ALP (U/L)	352	69 - 325
GGT (U/L)	20	4 - 22
LDH (U/L)	707	110 - 295
Troponin-T (ng/L)	18	
COVID-19 PCR (nasopharyngeal)	Positive	
Ferritin (µg/L)	216	7 - 84
D-dimers quantitative (mg/L)	4.45	0.00 - 0.25
INR (sec)	0.69	
PTT Pt (sec)	26.2	23.4 - 31.8
Fibrinogen (g/L)	3.7	1.7 - 4.2
Ammonia (µmol/L)	51	11 - 35
Toxins	Negative	

WCC = white cell count, Hb = haemoglobin, MCV = mean cell volume, Plt = platelets, CRP = C-reactive protein, SNMDAR-Ab = synaptic-N-methyl-D-aspartate receptor antibodies, ALT = alanine aminotransferase, AST = aspartate aminotransferase, ALP = alkaline phosphatase, GGT = gamma-glutamyltransferase, LDH = lactate dehydrogenase, INR = international normalised ratio, PTT Pt = partial thromboplastin time of the patient.

were treated with immunomodulatory agents (methylprednisolone, dexamethasone, intravenous immunoglobulin, anakinra and rituximab).[8]

Conclusion

This unique case presentation of choreoathetosis and dystonia highlights additional neurological signs in children with COVID-19 and/or MIS-C. Furthermore, the road to recovery in this child was favourable despite the initial poor response to therapy – this warrants further investigation.

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Conflicts of interest. None.

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SAPA NEWSLETTER: DECEMBER 2021

PICC PLACEMENT IN NEONATES

The recent *New England Journal of Medicine* (NEJM) video tutorials on the placement of peripherally inserted central catheters (PICC) in neonatal patients is comprehensive and provides both video and written instruction related to the procedure. Furthermore, indications, contraindications, site selection, required equipment and considerations for parental consent prior to the procedure have been detailed. This tutorial is a valuable refresher for registrars and general paediatricians who consult on neonates in intensive care or high care units. Visit the ***NEJM* website** for subscribers (it can be accessed by logging in through your academic institution).

UPDATE ON MEASLES ELIMINATION

The World Health Organization **Progress toward Measles Elimination report** shows a resurgence of measles cases throughout the world, with the African region most affected. The COVID-19 pandemic has negatively affected the goal to eliminate measles globally. There has been a dramatic decline in the number of children who receive Expanded Programme on Immunisation (EPI) vaccinations, and country/regional surveillance programmes have been interrupted. Immunity gaps lead to outbreaks in settings where large pockets of children were not vaccinated. South Africans experienced a measles outbreak in 2009; given what is known about vaccination rates presently it is possible that we will see a similar outbreak in the near future. For insights into the effect of measles infection on the immune system, take the time to **review this article** on the topic. And remember to check that every patient you see has had all their routine vaccinations! The National Department of Health's **Field Guide for the Catch Up of Child Health Interventions in South Africa** provides clear guidance to ensure that every child receives the medical care he or she needs when the usual schedule has been missed.

SAPA COVID-19 WEBINAR: 26 JANUARY 2022

COVID-19 has given us the opportunity to review how we teach, how we learn, what our priorities are and the path forward personally and professionally. This disease entity will continue to evolve, and it seems will remain with us for the foreseeable future. A report in this edition of *SAJCH* on the indirect effects of COVID-19 on children guides our thoughts beyond the clinical aspects of this disease and provides a starting point for various role players to assist our children to move beyond these challenges and thrive (see *'Children caught in the long shadow of COVID-19*).

SAPA is committed to providing evidence-based guidance to both paediatricians and parents as various aspects of this pandemic brings new challenges to our daily lives. In January 2022 we will provide an update for clinicians on long-COVID and revisit the topic of COVID-19 vaccination in children. For reminders and a calendar link, **register here**.

SAPA webinars are recorded and are freely available on the **SAPA YouTube channel**, via live streaming and after the event has aired. SAPA members who attend the live session are eligible for CPD points. You can become a SAPA member with **just a click**.

GET INVOLVED WITH SAPA!

Do you want to get involved in *Striving for Thriving Kids* with SAPA? We have many committees working on a variety of topics such as paediatric education, COVID-19 and social media among others. To become a part of the team, contact us at **info@paediatrics.org.za**. Let us know your area of interest or if you would prefer to be placed in a team – we would be glad to have you! This is an exciting way to engage with colleagues from across the country and contribute to child health outside of the usual day-to-day work in the wards. We look forward to welcoming you to the team.

CPD December 2021

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CPD questionnaires must be completed online at www.mpconsulting.co.za

Regarding the scoping review to identify the type and effect of hand hygiene (HH) interventions on the reduction of HH-related diseases (including COVID-19) in preschool children

1. A literature search was done using which of the following?
a. Google Scholar
b. PubMed
c. Science Direct
d. Scopus.

2. By how much percent did a tablet device showing handwashing demonstration videos improve children's handwashing technique?
a. 42
b. 31
c. 52.1
d. 12.

3. Positive results were indicated by authors in how many studies?
a. 12
b. 25
c. 10
d. 2.

Regarding the incidence, types and outcomes of congenital anomalies in babies born at a public, tertiary hospital in South Africa (SA)

4. What was the incidence (per 1 000 live births) of major congenital anomalies (MCA) at Chris Hani Baragwanath Academic Hospital (CHBAH)?
a. 20.6
b. 10
c. 3
d. 2.6.

5. What was the most common abnormality in the cardiovascular system?
a. Tetralogy of Fallot
b. atrial septal defect
c. ventricular septal defect
d. aortic stenosis.

6. What was the mortality rate in neonates with congenital abnormalities at CHBAH?
a. 35%
b. 1.12%
c. 20.2%
d. 18%.

Regarding the correlation between pulse oximetry and clinical profile of children with acute lower respiratory tract infection (ALRTI)

7. The mean oxygen saturation rate among children with acute lower respiratory tract infection was
a. 100%
b. 92.6%
c. 90.6%
d. 91.4%.

8. Which of the following has the strongest association with oxygen saturation in children with ALRTI?
a. pulse rate
b. respiratory rate
c. blood pressure
d. temperature.

Regarding early language development in children with autism

9. Which of the following statements about the exposure of young children to electronic media, such as television, is true?
a. It is recommended because it exposes a toddler to different languages and cultures.
b. It improves a young child's conversation skills as well as social interaction.
c. It is only recommended after the age of 12 months by the American Academy of Pediatrics.
d. There are concerns about the negative effects of exposure to electronic media on the developing brain.

10. Which statement about autism is correct?
a. Autism spectrum disorder is a neurodevelopmental disorder that is currently diagnosed by using biomarkers.
b. Although children with autism talk later than their peers, they do not have social interaction difficulties.
c. Atypical language development is an important way autism manifests in children.
d. DSM V criteria for the diagnosis of autism is only applicable after the age of 5 years.

Regarding the prevalence of coeliac disease in children and adolescents with type 1 diabetes mellitus in a tertiary hospital in SA

11. The international prevalence of coeliac disease in children and adolescents with diabetes mellitus type 1 has been shown in literature to range between
a. 5 and 10%
b. 1 and 10%

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c. 1 and 5%
d. 10 and 15%.

12. Endomysial antibody (EMA) and tissue transglutaminase (tTG) antibodies are generally lacking in children in which age group?
a. any age
b. <12 years of age
c. <5 years of age
d. <2 years of age.

13. The prevalence of biopsy-confirmed coeliac disease in this study was similar to which other African country?
a. Tunisia
b. Egypt
c. Algeria
d. Nigeria.

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