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Protecting Children in Need: A Salute to Our Medical Professionals!
Ip

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Cheung

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The April 2020 issue of the Hong Kong Journal of Paediatrics is an exceptionally memorable issue, particularly for our fellow colleagues working in high-risk clinical settings taking care of sick patients infected with SARS-CoV-19. The novel coronavirus infection has already killed thousands of people worldwide and has had a significant impact on children and parents and their families not only in Hong Kong, but also in other parts of the world. Since the first confirmed paediatric case admitted to Queen Mary Hospital in late February, the situation has dramatically worsened, with infected children as young as 16-month-old currently being cared for by paediatricians in hospitals scattered around the city.

As a result of the ongoing Novel Coronavirus disease 2019 (COVID-19) pandemic, all school have closed and children have been confined to their homes, which potentially has severe consequences in those with disabilities and special educational needs (SEN), as they are vulnerable to neglect and under-stimulation. The school closures have disrupted all students’ education, and special educational needs (SEN), as they are vulnerable to neglect and under-stimulation. Parents with children with SEN already face more severe effects from social disparity and the digital divide, particularly as the home learning environment is a critical consideration in the provision of sensible developmental support to children and their families, especially at this current time. Four original articles related to supporting the needs of disabled children and their parents, and the influence of their environment on early child development have been selected to highlight this very important issue. Hopefully, reading these articles will allow us to gain a better understanding of the needs of children with SEN and the potential environmental influences on child development.

In Hong Kong, there are over 57,000 children with SEN, 7,950 students with SEN are enrolled in the city’s 60 aided special schools and 49,080 students with SEN are enrolled in mainstream public sector schools. These children have a wide range of developmental problems including Attention-deficit/Hyperactivity Disorder (ADHD), Autistic Spectrum Disorders (ASD), speech and language pathology, visual or hearing impairment, intellectual disability, and mental illnesses. Given the general lack of support and comprehensive interventions in the community, many parents and caregivers of disabled children experience huge amounts of stress, anxiety, insomnia, and other mental health symptoms.

Children with SEN are the most vulnerable in our society and they require parents’ full attention and a great deal of resources including time and money. Simsek et al studied a representative sample of families in Turkey and identified the critical factors leading to lower health-related quality of life and higher depressive levels among mothers of disabled children. Strengthening parents’ social network and providing assistance to mothers, such helping them to develop coping strategies or relieving them of the daily caring tasks, were
potentially effective ways to improve their quality of life and mental well-being.  

Autistic Spectrum Disorder is a major neurodevelopmental disorder associated with severe language impairment, poor social skills, difficulty in communicating with others, and obsessive and stereotypic behaviours. Children with ASD also usually suffer from global developmental delays, learning difficulties, and emotional dysregulation. Özyurt et al conducted a randomised controlled trial on a group of families of children with ASD from similar socioeconomic background to evaluate the effectiveness of augmentative and alternative communication systems for improving autistic symptoms, language abilities, and emotional regulation. Autistic children using a computer-based voice output communication aid device (VOCA) showed improvements in receptive and expressive language skills, better emotional regulation, and reduced autistic symptoms. This study sheds light on future interventions designed to be integrated into the educational curriculum of children with ASD.

Children with profound intellectual disability with severe learning difficulties, and behavioural and caring problems, such as sleeping disorders, put their parents and caregivers in a difficult position as they often experience exhaustion and frustration. Chow et al and colleagues in the United Christian Hospital, Hong Kong conducted an interesting study on sleep-related problems among special school students with profound intellectual disabilities. Sleep disorders are very common among intellectually disabled children, and epilepsy is a common comorbidity associated with sleep-related problems. Adequate attention should be paid to potential sleep disturbances during the management of children with profound intellectual disabilities. Emerging evidence from overseas and local studies showed that a socioeconomic gradient exists in child development and school readiness. Children in families from a lower socioeconomic status (SES) are more vulnerable to lower school readiness and are at risk of delays in different developmental domains. An under-stimulated environment has been associated with insufficient school readiness, and such an unfavourable learning environment is particularly detrimental in children with lower SES who face the double jeopardy of more severe learning and behavioural outcomes. Leung et al echoed this observation in their study that examined a large representative sample of preschoolers with different socioeconomic backgrounds. They utilised the Hong Kong Comprehensive Assessment Scales for Preschool Children (HKCAS-P), a locally developed and validated measurement for holistic development of Chinese preschool children. The findings raised concerns on the worsening social disparity in Hong Kong, which has harmful effects on children and could lead to potential intergenerational transmission of poverty. With the establishment of the Hong Kong Commission on Children (CoC) in June 2018, comprehensive support for children with SEN has become a major focus for the government. Resources are being provided in the form of services such as the Onsite Preschool Rehabilitation Services (OPRS) and the School Social Worker Scheme that support the educational and developmental needs of children with disabilities. The implementation of such services for children with SEN and developmental needs represents a remarkable milestone in the recognition of the importance of early childhood development, and we hope there is continued investment in evidence-based early interventions.

I would like to take this exceptional opportunity to express my whole-hearted appreciation and salute our nurses, clinicians, and medical professionals who go above and beyond to provide the best care for all our patients and children in need. Let us pray for Hong Kong and support each other during this challenging time, and take comfort in the knowledge that tomorrow is only a day away.

P Ip
Associate Editor

References

Message from the Chief Editor

Amid the coronavirus outbreak, we are socially distanced in a way unlike anything in our lifetime. Yet, in various ways and using different means, we shall remain socially connected. For us, in this challenging historic moment, the baton of the Editorial Board is now passed from members of one generation to those of the next.

Over the last three years, our past Editorial Board members have made immense efforts to ensure the continued improvement of the quality and standard of the Journal. Their constructive suggestions and insights have ensured the publication of Journal articles that appeal to the readers and researchers in Hong Kong and abroad. Please allow me to express my heartfelt gratitude for their invaluable contribution.

It is with great pleasure that I announce the formation of the new Editorial Board for the next three years. I have no doubt that the new Board members would continue to work hard, as did their predecessors, for the betterment of our Journal. I am also honoured to have the opportunity to serve the Editorial Board as the Chief Editor for another three years.

Let us join our hands in our heart to strive through adversities and remind ourselves that light always follows darkness!

YF Cheung
Chief Editor
Original Article

Factors Affecting Health Related Quality of Life and Depression Levels of Mothers in Families Having Children with Chronic Disabilities

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Abstract

**Purpose:** This study aimed to investigate the contributing factors to health related quality of life (HRQoL) and depression levels of mothers in families having children with chronic disabilities. **Methods:** The study was designed as a cross-sectional survey including 580 families recruited from 45 cities across Turkey. HRQoL, depression levels and impact of chronic disabilities of a child on the mothers were gathered by using Nottingham Health Profile, Beck Depression Inventory and Impact on Family Scale (IPFAM), respectively. Other data were acquired using a face-to-face interview method. **Findings:** Regression analysis showed that the time spent for daily caring activities, disruption of social relations and coping subscale-scores of IPFAM were significant contributors to poor HRQoL and higher depression levels (p<0.05). **Conclusion:** The results suggest that providing a release time from daily caring tasks, increasing level of social interaction and provision of sustained assistance to help to develop coping strategies, would likely increase HRQoL and decrease level of depression of the mothers.

Key words

Children with chronic disabilities; Health related quality of life; Impact on family; Quality of life

Introduction

The concept, advocated by World Health Organization under the framework of International Classification of Functioning, Disability and Health indicates an important relationship between the health of children with chronic disabilities and the health of caregiver(s).

Current body of evidence suggests that parenting children with chronic disabilities has consequences on the health of parents/caregivers and as a result on family functioning.

The impact of children with chronic disabilities on family functioning may be defined as the varying implications of care that are propagated over the family members throughout the life of children with disabilities. These implications are further described as effectively coping with cultural, environmental, psychosocial, and socioeconomic stresses throughout the family life cycle, which are underestimated over the years due to the complexities of care. The focus usually resides on the primary disabling condition of the child; hence, even the closest environmental factors such as family are often underestimated and even neglected. However, as Reichman et al stated, care giving process for children with chronic disabilities is completely different from raising a healthy child, which presents unique challenges for all members of the family, especially the parents.
Some of the many challenges for families raising children with chronic disabilities may include economical, physical, psychological and social issues that may contribute to health related quality of life (HRQoL) which is "an all-inclusive concept incorporating all factors that impact upon an individual's life". After the birth of a child with chronic disabilities, financial restraints may alter the occupational course of the family. Several financial needs may give rise to unexpected crisis. Besides, integrating into the community life with a new and different daily routine causes an extra social pressure on the family. Eventually, economical and physical burden, combined with psychological distress and a set of negative emotions may develop detrimental effects on the HRQoL of parents/caregivers. These negative emotions include anxiety, depression, and worrisome thoughts. In addition, low levels of energy, physical activity and impaired social relationships are common findings in families having children with chronic disabilities.

Parents/caregivers of children with chronic disabilities also experience higher rates of depression compared to parents of children without disabilities. This rate increases proportionally with the impact exposed on the family/caregiver(s). The process of adaptation to daily stressing conditions and changes in community and family life seems to trigger a negative mood over the family, which concludes with varying levels of depression.

These major differences, differentiating a normal family life from the altered functioning of families having children with chronic disabilities, also necessitate measuring the burden on the families and its relation to the parents'/caregivers' HRQoL. In a recent Canadian survey by Brehaut et al, it is concluded that the number of studies on the issue with large sample groups is limited. Thus, the aim of the current study was to project the status of HRQoL and the level of depression of mothers having children with chronic disabilities and quantify the contributing factors. It was hypothesized that as the impact of children with chronic disabilities on the mothers increases, the level of depression would increase and the HRQoL would decrease.

Methods

Participants

The study was designed as a cross-sectional survey study. The participating mothers were recruited from 45 cities in Turkey, representing all seven regions of the country. The participants were recruited from special education and rehabilitation centres and physiotherapy and rehabilitation departments of the universities located in Turkey. A total of 580 families were included in the study between May 2008-March 2012. The data related to informative socio-demographic characteristics were gathered in a face-to-face interview session by the primary physiotherapist from only the mothers who lived in the same household with the child and spent most of her time for the provision of caregiving activities to the child with chronic disability. The self-report instruments were completed only by the mothers. The families of the children with non-progressive chronic disorders were also included in the study. Mothers with insufficient Turkish language and those who declined to participate in the study were excluded (a total of 10 caregivers). Informed consent was obtained for all subjects and ethical approval was obtained from the university's ethics board and commissions (non-interventional clinical research ethics board) (FON07/17).

Instruments

Socio-demographic data of the children and mothers were collected via a structured form including presence of mental retardation, presence of medical insurance, duration of the disorder, duration of daily care-time and total income. The impact of children with chronic disabilities on their families, HRQoL, and depression levels were evaluated using Impact on Family Scale (IPFAM), Nottingham Health Profile (NHP) and Beck Depression Inventory (BDI), respectively.

IPFAM, is a 33 item inventory that takes approximately 10-15 minutes to complete and can be used either as a questionnaire, when reading levels are adequate, or an interviewer-administered form. It measures a parent’s perception of the effects of the child’s ongoing health condition on family life. The instructions on the instrument asks parents to rate each item on a scale from 4 (strongly agree) to 1 (strongly disagree). The first 27 items are reflective of impact on the family in general, while in the last six items of the scale, the respondent is asked to rate the impact of the child with disability on his/her siblings. The subscales of IPFAM are: total score, general impact, disruption of social relations, coping and financial impact. Lower scores indicates lower impact. Internal consistency (Cronbach’s Alpha) for the total impact ranges from 0.83 to 0.89 according to important normative samples. For the Turkish version test-retest reliability (ICC) was found to range between 0.787 and 0.953 and the internal consistency (Cronbach’s Alpha) was reported to be 0.902.
for total impact. Construct validity was tested against WeeFIM (Functional Independence Measure for Children) and physiotherapists’ evaluation of disability using visual analogue scale (VAS). Inter-correlations among IPFAM items and the benchmark criterion were \( r = -0.532 \) (\( p < 0.001 \)) for WeeFIM and \( r = -0.519 \) (\( p < 0.001 \)) for VAS. In this study, the Turkish version of IPFAM was used.\(^9\)\(^,\)\(^11\)

In order to evaluate the HRQoL, the Turkish version of NHP was used. All subjects completed NHP once. The NHP is a self-administered questionnaire composed of two sections containing 45 items. The first section contains 38 items assessing physical mobility (8 items), pain (8 items), sleep (5 items) emotional reactions (9 items), social isolation (5 items) and energy level (3 items). All items have a yes/no answer format. Scores for each section can range from 0 (no problems) to 100 (all problems listed are present).\(^{12}\) Reported test-retest reliability and internal consistency of the English version range between 0.77-0.85 and 0.61-0.88, respectively.\(^{13,14}\) The analysis for the Turkish version indicated that internal consistency (Cronbach’s Alpha) ranges between 0.56-0.83 and test-retest reliability between 0.70-0.92. Construct validity of the Turkish version was assessed using correlations between the sections of NHP and Health Assessment Questionnaire \( r = 0.15-0.73 \).\(^15\)

BDI was used to evaluate the symptoms of depression of the mothers. BDI is a 21-item scale that gathers information on different symptoms of depression. Summary scores quantify depression as follows: minimal depression (0-13), mild depression (14-19), moderate depression (20-28), and severe depression (29-63). Convergent validity of the English version ranges from 0.58 to 0.79.\(^{16}\) Internal consistency for the English version is 0.81 for non-psychiatric subjects.\(^{17}\) The Turkish version of BDI was used in the present study.\(^{18}\) The validation of BDI was studied against Minnesota Multiphasic Personality Inventory-Depression scale and the correlation was found to be \( r = 0.63 \) (\( p < 0.001 \)).\(^{19}\) The internal consistency (Cronbach’s Alpha) was reported to be 0.89.

**Statistical Analysis**

For statistical analyses statistical Package for Social Sciences™ (SPSS) 20.0 program was used. Means and standard deviations \( (X \pm \text{SD}) \) were calculated and percentages were provided for all variables. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/ Shapiro-Wilk’s test) to determine whether or not they are normally distributed. If the data were normally distributed Pearson correlation analysis (and if not spearman correlation analysis) was used to analyse the effects of socio-demographic characteristics, the duration of the disorders and the duration of care time on families. A multi-linear regression model was used to identify independent predictors of NHP and BDI. The model fit was assessed using appropriate residual and goodness-of-fit statistics. The correlation coefficient was accepted as 0.05.

**Results**

All data were normally distributed. The socio-demographic data related to the children and their families are presented in Table 1.

The correlation indicated that the total impact was negatively correlated with the educational level of the mothers and the presence of medical insurance \( (p < 0.05) \). The same relation was also detected between the level of depression and the level of education of the mothers, the level of income, presence of medical insurance. The duration of daily care time was the only exception that showed a positive correlation with depression levels \( (p < 0.05) \). Meanwhile, HRQoL was negatively correlated with the level of education of the mothers, the level of income and presence of medical insurance \( (p < 0.05) \) (Table 2). HRQoL, total impact and the level of depression were not related to the age of the mothers and the duration of the disorder \( (p > 0.05) \). The duration of care was also not correlated to total impact and HRQoL \( (p > 0.05) \) (Table 2). Total impact and all subscales of IPFAM were correlated to NHP and BDI \( (p < 0.05) \) (Table 3).

The regression analysis indicated that the daily care time spent for the child, coping and disruption of social relations subscale scores were significant contributing factors to HRQoL in families having children with chronic disabilities \( (p < 0.05) \). Marital status, diagnosis, mothers’ age, level of education, the duration of the disorder, total income and the remaining subscales of IPFAM (financial support and general impact) were not found to be significant contributors to the depression levels \( (p > 0.05) \) (Table 4).

The time spent for daily care activities, disruption of social relations and coping subscales of IPFAM all contributed to depression level \( (p < 0.05) \). Marital status, diagnosis, mothers’ age, level of education, the duration of the disorder, total income, financial support and general impact subscale scores were not found to be significant contributors to the depression levels \( (p > 0.05) \) (Table 4).
Discussion

This study showed that in mothers having children with chronic disabilities the main contributors to depression levels and HRQoL were the daily care time spent for the child, disrupted social relations and the coping ability.

In families having children with chronic disabilities, stress may not always be the result of the ongoing disability, but also of multi-factorial reasons (i.e. environmental factors). This had most assuredly been stated in Folkman and Lazaruss’s study that defined stress as a resultant of the interaction of an individual (or family) with the environment. Stress levels directly increase as the family cannot cope with problematic situations. In other words, parents are usually stressed when a stressor is introduced through daily life and the general family coping strategies fail, resulting in depression, fatigue and restlessness. Thus, it is not surprising that in this study one of the main contributors to depression level is found to be the coping ability along with disrupted social interactions, which are both routine stressors throughout the daily life of a family (especially the mothers) having a child with chronic disability. Whiteneck et al also indicated that the factors encompassing a child’s (with chronic disabilities) social, physical and political environment may hamper inclusion in leisure activities initiated by the parents/caregivers. This may affect familial sense of fit to their environment as termed by Park et al, which may also be considered as among the parameters of family quality of life. One of the most important factors related to the environment is the access to health care services as advocated by several researchers that may change quality of life outcomes. Furthermore, simple access seems to be not necessarily enough, also meeting the families’ needs by the disability related services that may have a great influence on familial quality of life as Jones et al reported. In parallel with these notions, we have found that presence of medical insurance is negatively correlated to depression levels.

In some studies, comparing families having children with various chronic disability conditions (down syndrome, cerebral palsy, autistic spectrum disorders, fragile X syndrome, cystic fibrosis) and families having children with typical normal development, it has been suggested that in those families having children with chronic disabilities stress factors were higher than the latter. In parallel, it is also known that in those families, depression levels were higher and well-being was negatively affected. Another study indicated that in fathers having children with chronic disabilities life satisfaction was lower and that they needed support for developing coping strategies with stress.

In the present study, it was shown that the impact was, in part, related to educational status and the presence of medical insurance. Also the increased impact level was related to decreased levels of HRQoL and higher depression levels. The family income was positively related to HRQoL and negatively with depression levels.

Table 1  Demographic data related to families and children

<table>
<thead>
<tr>
<th>N=580</th>
<th>X±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>6.74±3.71</td>
</tr>
<tr>
<td>Duration of the disorder (months)</td>
<td>67.80±37.68</td>
</tr>
<tr>
<td>Daily care time spent (hours)</td>
<td>9.77±4.89</td>
</tr>
<tr>
<td>Presence of mental retardation n %</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>369</td>
</tr>
<tr>
<td>No</td>
<td>211</td>
</tr>
<tr>
<td>Diagnosis n %</td>
<td></td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>312</td>
</tr>
<tr>
<td>Muscle disease</td>
<td>159</td>
</tr>
<tr>
<td>Meningitis</td>
<td>6</td>
</tr>
<tr>
<td>Mental motor retardation</td>
<td>74</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>5</td>
</tr>
<tr>
<td>Myelomeningocele</td>
<td>17</td>
</tr>
<tr>
<td>Obstetric brachial plexus palsy</td>
<td>2</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Rare disorders</td>
<td>2</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>1</td>
</tr>
<tr>
<td>Amputation</td>
<td>1</td>
</tr>
<tr>
<td>Educational level (mothers) n %</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>23</td>
</tr>
<tr>
<td>Primary school</td>
<td>317</td>
</tr>
<tr>
<td>Secondary school</td>
<td>67</td>
</tr>
<tr>
<td>High school</td>
<td>127</td>
</tr>
<tr>
<td>University</td>
<td>44</td>
</tr>
<tr>
<td>Postgraduate</td>
<td>2</td>
</tr>
<tr>
<td>Presence of medical insurance n %</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28</td>
</tr>
<tr>
<td>No</td>
<td>552</td>
</tr>
<tr>
<td>Marital status n %</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>559</td>
</tr>
<tr>
<td>Divorced</td>
<td>17</td>
</tr>
<tr>
<td>Living separately</td>
<td>4</td>
</tr>
<tr>
<td>Total income n %</td>
<td></td>
</tr>
<tr>
<td>Very low</td>
<td>108</td>
</tr>
<tr>
<td>Moderate</td>
<td>275</td>
</tr>
<tr>
<td>Moderate-high</td>
<td>197</td>
</tr>
</tbody>
</table>
Meanwhile, the daily time spent for caring activities, disrupted social relations and decreased coping abilities detected by IPFAM seem to enhance depression. Caring demands of children with chronic disabilities that increase day by day and various unpredicted or obscure needs (education of the child, additional and regular health problems, variability in medical services, financial issues) may hamper coping strategies with the ongoing disability. All of these reasons may eventually cause increased stress levels and result in depression and/or anxiety problems.

The impaired psychological status (depression) may lead to decreased HRQoL. Likewise, in this study it was shown that increased time consumption for daily care giving activities, increased total impact and disruptions in social relations all negatively affect the HRQoL of the mothers having children with chronic disabilities. Although there was a relation between mothers’ educational level, total income and HRQoL, HRQoL was not affected by the duration of the disability, mothers’ age, educational status and family income according to the regression analysis. Besides, the general impact (burden) is affected by several other factors in those families. The severity of these influences may change when in combination. Socio-demographic factors and economic status are among the indicators of HRQoL, however, when considered with the diagnosis, mental status and severity of the disability, their resultant effect may be lesser than predicted.

In the literature, it is indicated that the families are affected by the duration of the disability. 35-38 In our report, the average duration of the disability was approximately 5.6 years. Thus HRQoL and the impact may differently be affected as the years go by due to the stress influence of a child with chronic disability on the mothers and indirectly on the family which increase as the child grows older. 39,40 It has been previously reported that the families with older children with disabilities feel more isolated with increased demands for services compared to when their children were younger. 41 It is obvious that the aging child with increased caring demands will result in increased time consumption for the primary caregiver (usually the mother). This may cause social isolation for the mothers with no spare time left for social and personal self-caring activities. In this respect, there are insufficient number of studies in the literature that have long follow-up durations. Observing the ever changing economic, social and personal

<table>
<thead>
<tr>
<th>N=580</th>
<th>Total impact</th>
<th>BDI</th>
<th>NHP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mother)</td>
<td>-0.016</td>
<td>0.708</td>
<td>-0.027</td>
</tr>
<tr>
<td>Educational level (mother)</td>
<td>-0.092</td>
<td>0.028*</td>
<td>-0.160</td>
</tr>
<tr>
<td>Duration of the disorder</td>
<td>0.029</td>
<td>0.481</td>
<td>0.072</td>
</tr>
<tr>
<td>Total income</td>
<td>-0.050</td>
<td>0.231</td>
<td>-0.142</td>
</tr>
<tr>
<td>Presence of medical insurance</td>
<td>-0.103</td>
<td>0.014*</td>
<td>-0.148</td>
</tr>
<tr>
<td>Daily care time spent for the child</td>
<td>0.057</td>
<td>0.175</td>
<td>0.129</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed). Pearson correlation coefficient.

<table>
<thead>
<tr>
<th>N=580</th>
<th>BDI</th>
<th>NHP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Financial support</td>
<td>0.299</td>
<td>0.000*</td>
</tr>
<tr>
<td>General impact</td>
<td>0.231</td>
<td>0.000*</td>
</tr>
<tr>
<td>Disruption of social relations</td>
<td>0.301</td>
<td>0.000*</td>
</tr>
<tr>
<td>Coping</td>
<td>0.294</td>
<td>0.000*</td>
</tr>
<tr>
<td>Total impact</td>
<td>0.151</td>
<td>0.000*</td>
</tr>
<tr>
<td>BDI</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.01 level (2-tailed).
necessities of these families in the long term may help to acquire important data to fully understand the ongoing situation which require further studies on the topic.

In studies related to the impact of children with chronic disabilities on their families, it has been suggested that these families need a different kind of medical service and social support. One of the policies that has been widely advocated and implied is providing financial support, which at least is hoped to alleviate the economic burden. Another one is preventing social isolation by supporting the establishment of associations and leagues to provide a basic structure for families to integrate into community life. Also specialised psychologists may provide family rehabilitation in order to decrease depression related reduction in HRQoL. Still, in practice it is not recognised well enough that the overall burden of families having children with chronic disabilities is multi-dimensional; demanding professionals like rehabilitation nurses and physical therapists who may offer some practical information as well as helping families to achieve their social or economic rights.42

Limitations of the Study

This study was designed to present an overall perspective related to the impact of children with chronic disabilities on their mothers. Keeping this mind, the readers should note that although there are referrals to "family", these are indirect conclusions and presented just to provide some insight. In addition, due to heterogeneity of the disabilities included in the study, one should carefully make

| Table 4 | Regression analysis related to HRQoL (NHP) and Depression Level (BDI) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                | B               | Standard Error  | Beta            | t               | P               |
| **Dependent variable: NHP, R²: 0.211** |                 |                 |                 |                 |                 |
| Diagnosis       | 0.246           | 0.789           | 0.012           | 0.312           | 0.755           |
| Marital status  | -6.248          | 6.368           | -0.037          | -0.981          | 0.327           |
| Age (mother)    | -0.071          | 0.216           | -0.012          | -0.329          | 0.742           |
| Education level (mother) | -2.959 | 1.25           | -0.103          | -0.952          | 0.342           |
| Daily care time spent for the child | -0.238 | 0.25           | -0.037          | -2.368          | **0.018**       |
| Total income    | 1.079           | 1.912           | 0.025           | 0.564           | 0.573           |
| Duration of the disorder | -0.031 | 0.032           | -0.038          | -0.974          | 0.330           |
| Financial support | -0.771          | 0.552           | -0.262          | -1.396          | 0.163           |
| General impact  | -0.134          | 0.878           | -0.009          | -0.153          | 0.879           |
| Disruption of social relations | 2.331 | 0.642           | 0.422           | 3.631           | **0.000**       |
| Coping          | 1.811           | 0.577           | 0.304           | 3.141           | **0.002**       |

| **Dependent variable: BDI, R²: 0.128** |                 |                 |                 |                 |                 |
| Diagnosis | -0.34            | 0.723           | -0.019          | -0.471          | 0.638           |
| Marital status | 3.22            | 5.858           | 0.023           | 0.576           | 0.565           |
| Age (mother) | -0.096          | 0.196           | -0.02           | -0.492          | 0.623           |
| Education level (mother) | -1.801          | 1.135           | -0.075          | -1.586          | 0.113           |
| Daily care time spent for the child | 0.646           | 0.234           | 0.115           | 2.765           | **0.006**       |
| Total income | -1.778           | 1.712           | -0.049          | -1.039          | 0.299           |
| Duration of the disorder | 0.042            | 0.029           | 0.061           | 1.454           | 0.147           |
| Financial support | -0.811          | 0.504           | -0.333          | -1.61           | 0.108           |
| General impact | 0.339            | 0.804           | 0.028           | 0.422           | 0.673           |
| Disruption of social relations | 1.664            | 0.577           | 0.365           | 2.885           | **0.004**       |
| Coping | 1.261            | 0.521           | 0.255           | 2.420           | **0.016**       |

NHP: Nottingham Health Profile; BDI: Beck Depression Inventory
assumptions related to a single chronic disorder as the construct behind different disabilities may well change.

Furthermore, our convenience sample of participants does not cover mothers having typically developing children. It is recommended that, in future studies, a group of mothers having typically developing children as a control group would also be included in order to present data from a comparative perspective. In addition, all the contributing factors and correlations presented may also work the other way around (for example caregiver burden may cause depression and meanwhile depression may cause an extra burden).

Another limitation is the allocation of participants from various regions of the country with different access to health care services, leisure and other activity participation opportunities. This point should be addressed in future studies as advocated in other studies.

Conclusion

In conclusion, in mothers having children with chronic disabilities, depression and HRQoL seem to be correlated to several parameters like level of education, financial status, presence of medical insurance, and daily care time spent for the child. In addition, multivariate regression analyses indicated that the main contributors to depression levels and HRQoL were daily care time spent for the child, level of coping and disrupted social relations. Still, one should note that among the variables investigated in this study, the above mentioned factors explained relatively a small percent of the multi-factorial nature of these two constructs. Thus, it is obvious that more research is needed to determine the most significant factors so that they could be handled properly. In addition, in order to allocate resources and/or make policies, more focused research is needed for specific types of disabilities.

This study was designed to generally describe the influence of having a child with chronic disability and its relation to HRQoL and depression levels in mothers. We believe the results of this study present a perspective of the mothers having children with chronic disabilities.

Conflict of Interest

The authors reported no conflict of interest.

References

Augmentative and Alternative Communication for Children with Autism Spectrum Disorder: A Randomised Study of Awareness and Developmental Language Interventions

G ÖZYURT, Ç DINSEVER ELİKÜÇÜK

Abstract

Using a computer-based voice output communication aid (VOCA) device, the present study aimed to evaluate the effectiveness of augmentative and alternative communication systems for autistic symptoms, language features and emotion regulation of children diagnosed with autism spectrum disorders (ASD's). The child and adolescent psychiatrist (an experienced clinician) diagnosed the children as ASD according to Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM 5) and clinical observation and follow up. Forty-two children (36-72 months old) diagnosed with ASD participated in the study. Subjects were randomised into two groups (Twenty-one children were in the intervention group and 21 children were in the control group) and the first group received the augmentative and alternative communication systems treatment while the second received routine treatment. The socio-demographic features of groups were similar and children who were part of the experimental group showed improvements in receptive and expressive language skills, had better emotion regulation skills and their autistic symptoms decreased. Furthermore, the experimental group's mean length of utterance and language sample size increased. This study provided preliminary evidence that augmentative and alternative communication systems using computer-based voice output communication aids, which are portable and simple, may help children diagnosed with ASD develop communication and language skills.

Key words

Augmentative and alternative communication; Autism spectrum disorder; Emotion regulation; Voice output communication aid

Introduction

One of the core features of autism spectrum disorder (ASD) is the impairment in social-communication skills. Such impairments may manifest themselves in a limited range of communication functions such as; reduced use of communication acts to share interests and emotions, and problems with appropriately initiating and responding to communication with others.¹ Children with ASD have impaired communication – both verbal and non-verbal communication – and the impairment in communication affects the children's ability to request for objects and actions as well and the use of such acts have been limited in terms of social interaction (e.g. requests for social routines and permission, showing off, greetings, calling, and acknowledgements) or acknowledging a joint effort (e.g. comments, requests for information, and clarifications).²,³ These findings have been replicated in succeeding studies.⁴ Comparison of this pattern indicates a contrast between children with ASD and children who follow typical development since a range of communication functions develop at the same time for the
latter even before they start speaking.\textsuperscript{2} Findings of research studies in which researchers utilised augmentative and alternative communication (AAC) interventions to target communicative acts for behavioural regulation support the idea that children with ASD who are taught how to use AAC increase their attempts to regulate behaviour of another person through, for example, requesting needs and wants.\textsuperscript{5-7} In fact, systematic reviews conducted by Ganz et al (2010) and Meer and Ripsoli (2010) presented strong empirical evidence that such interventions can be successful when conducted for children with ASD.\textsuperscript{8,9}

In ASD, one of the important reasons for maladaptive emotional and behavioural responses is considered to be emotion dysregulation.\textsuperscript{10,11} Maladaptive emotional and behavioural responses may result in temper tantrums, difficulties in anger control, self-injurious behaviour, aggressive behaviours, and mood dysregulation.\textsuperscript{12-14} In addition, children with ASD have been found to make frequent uses of non-appropriate or idiosyncratic strategies like breath holding, crying and avoidance.\textsuperscript{14,15} On the other hand, Jahromi and colleagues showed that impaired functioning may become worse with maladaptive emotional responses and difficulties in emotion regulation.\textsuperscript{16} In a different study, Jahromi and colleagues also found that children with ASD use less frequent and less effective adaptive emotion regulation in comparison to children who follow typical development.\textsuperscript{15} Samson and colleagues found an association between emotion dysregulation and the core symptoms of ASD.\textsuperscript{17} Current studies report high rates of emotion dysregulation in individuals with ASD,\textsuperscript{18,19} but the associations between AAC, language profiles and emotion dysregulation have not been investigated before. Considering the fact the positive effects of AAC treatments with voice output communication aids (VOCA) on children with ASD (i.e. teaching single-step requesting), it can be interpreted that AAC treatments that utilise VOCAs might help children’ development of receptive and expressive language development.\textsuperscript{8,9}

Recent research suggests that there has been a notable increase in the use of computer-based AAC systems, with advanced input systems such as touch screens or eye tracking sensors.\textsuperscript{20} It is argued that such systems, regardless of the technology level, are positive for children who have social and communication needs and this is because such systems promote linguistic, cognitive, and social development.\textsuperscript{21,22}

AAC with aided interaction may help simplify the communication with peers. For example, in their studies, Clarke and Wilkinson reported on the process in which children operate and orient towards a VOCA while interacting with peers.\textsuperscript{23-25} Their results revealed the positive effects of the sound output (bleep sounds during word construction) in negotiating meaning in relation to peers’ immediate sequential context. On a different note, parents, unlike teachers and/or therapists who spend a limited amount of time with children, have the unique capacity to be able to impact on their children's lives. The recognition of this role resulted in the development of parent-mediated intervention and training programmes.\textsuperscript{26} Training parents is a crucial component of intervention programmes since such training helps children with ASD receive consistent and daily support.\textsuperscript{27} In Patterson and colleagues’ review, it is reported that parents of children with ASD can become effective language facilitators after attending appropriate training.\textsuperscript{28} In addition, parental well-being and behaviours may be positively affected as a result of parents being included in the treatment process (e.g. a decrease in depression levels, better communication skills, and knowledge of ASD); furthermore, this can positively impact on children's language and behavioural development.\textsuperscript{28,29} Programmes, in which parents take active roles with therapists, have more positive effects on children's early social communication skills,\textsuperscript{30} language development,\textsuperscript{31} and augmented communication.\textsuperscript{32} AAC may promote linguistic, cognitive, and social development in ASD and parents’ active roles with therapists, might provide positive effects on ASD symptoms and emotional dysregulation.

The aim of the present study was to evaluate the effectiveness of AAC using a computer-based VOCA device with a touch-sensitive screen-input system for autistic symptoms, language features, and emotion regulation of children diagnosed with ASD.

\section*{Method}

\subsection*{Setting and Protocols}

Firstly the children were screened for hearing problems and only children whose audiological evaluations were normal with normal bilateral hearing thresholds were included in the study. Families of children with ASD worked for 55 minutes a day for 5 days a week over the course of eight weeks (i.e., a total of 40 days). Each session focused on a 40-minute AAC condition. During the treatment, the VOCA was either placed within reach or outside the reach of children with ASD. The parents participated in the therapy process by playing an active role in the regulation
of the home environment and providing the verbal cues that signalled the start of a requesting opportunity. In addition, opportunities emerged for parents to teach children communication skills during their daily routines in the therapy (e.g. rounding and reinforcing social and physical environment). The parents were shown different sizes and types of graphic representations (e.g. line drawings, photographs) and were asked to provide their opinions about the visual features as well as number and content of messages that would be most useful for teaching each child how to use a VOCA during their daily routine. We also included an element of book reading, in which a speech and language therapist (SLT) read from a storybook, into the process of using VOCAs. This activity primarily focused on receptive vocabulary gains for children. The parents became part of the therapy process by playing an active role in the regulation of home environment for the children involved. In the VOCA therapy, the role of the family was using remarkable expressions or the selected vocabulary for simple talk (small talk). This is because the core word category increases the interest of the children and stimulates them to give more natural answers, talk more about the story or topic, interact, initiate a joke, or complete a sentence. If a child stops at one point, then, the parents provide hints for interpretation and encourage the child in a natural way to tell the rest of the story. The children are in constant dialogue with their parents during their use of the VOCA devices without interruptions.

Parents' use of remarkable expressions or the selected vocabulary for simple talk is intended to increase the interest of the children and stimulate the children to give more natural answers by encouraging them to talk more about the story or topic, interact, and initiate a joke or complete a sentence. The VOCA devices used included picture or word representations of one to eight pieces of the food and/or drink that a child preferred to eat and/or drink. When a child pressed one of the symbols, the VOCA device produced a verbal request which was then fulfilled. A VOCA device with an active panel was provided and given to parents of children with ASD. This VOCA device had a micro switch with a picture. The picture represented “WANT” and was connected to a verbal recording of “I want more” which was used to request (and obtain) any of several preferred food/drink and activity items. The parent provides hints for interpretation and encourages the child in a natural way to tell the rest of the story. Through the use the VOCA, the children with ASD in children are enabled to turn the interaction into a conversation without stops. During this process, verbal and physical prompts were provided by the SLT to complete work-related tasks such as sorting items when necessary. Clinical evaluation was conducted twice a week by investigating and controlling the child and family relationships. The computer-assisted methods of transcript analyses were utilised for analysing spontaneous language, the production of non-targeted actions on either a target or non-target focus, and phonological awareness on the recordings of treatment sessions. Systematic Analysis of Language Transcripts (SALT) software was used as a language reference point and this software was used to calculate mean length of utterances (MLU) and language sample size (LSS) in utterances. These procedures were performed by an audiology and language speech therapist.

**Data Collection Tools**

Autism Behaviour Checklist (ABC): The ABC contains 57 items in five areas: Sensory, Relating, Body and Object Use, Language, and Social and Self-help Skills. Each item is scored from 1 to 4 and the total score is obtained by adding the weight of the different areas. The minimum score that can be achieved is 0 while the maximum is 159. The validity and reliability study of the scale for the Turkish version was conducted by Irmak and colleagues. The procedures in relation to the administration of the ABC checklist were performed by a child psychiatrist.

Denver II Developmental Screening Test (DDST): The test was developed by Frankenburg and colleagues and was adapted and standardised by many countries for their own communities. This is the first and only available developmental test standardised for Turkish children. It was revised and adapted into the Turkish context in 1990s. The Turkish validity and reliability study was conducted by Anlar and Yalaz. Being an easily applicable test for children between the ages of 0 and 6 years, DDST is important for following children’s development and early identification of developmental deviations within this time period. DDST evaluates four areas: a) personal-social (the ability to get along with people and meet one’s personal needs), b) fine motor (the ability of having hand-eye coordination, using small objects and solving problems), c) language (the skills of hearing, comprehending, and using both receptive and expressive language), and d) gross motor (the ability of using large muscles to complete actions such as sitting, walking, and jumping). These procedures were performed by the SLT.

Test of Early Language Development-Third Edition (TELD-3): This is a norm-based assessment instrument developed by Hresko, Reid and Hammill for measuring the skills of receptive and expressive language in children aged
between 24 months (2 years) and 95 months (just under 8 years). It is commonly used for purposes such as diagnosing children with early-period language disorders, showing the weak and strong aspects of their language development, and understanding their language development process. The test was adapted in Turkey with the title of Turkish Test of Early Language Development (TELD). Including three of the five basic components of language; TELD assesses the semantics, syntax and morphemes through the test items. TELD contains two subtests as receptive language and expressive language. There are 24 items assessing the semantics in Form A (the Subtest of Receptive language); 25 items assessing the semantics in Form B (the Subtest of Receptive language); 13 items assessing the syntax in Form A (the Subtest of Receptive language), and 12 items assessing the syntax in Form B (the Subtest of Receptive language). There are 22 items assessing the semantics in Form A (the Subtest of Expressive language); 24 items assessing the semantics in Form B (the Subtest of Expressive language); 17 items assessing the syntax in Form A (the Subtest of Expressive language); and 15 items assessing the syntax in Form B (the Subtest of Expressive language). In case of meeting the pass criteria specified besides the enumerated items in the form, one point is obtained for a correct answer and in case of failing to meet the pass criteria, zero points is obtained for a wrong answer (or 'did not pass'). Raw scores are converted into standard scores from the tables at the end of the Handbook for Users. Both Form A and Form B of TELD was used in the study and the forms were administered by the SLT. Emotion Regulation Checklist (ERC): ERC is used for assessing the emotion regulation in children. The scale consists of 24 items which assesses the regulation and expression of emotional reactivity and emotions of preschool and school-age children according to the conditions of environment under two subscales; a) "Emotion Regulation" and b) "Emotional Lability – Negativity". The former subscale consists of 15 items and the latter of nine items. Items are responded on a Likert scale with four anchors (1= never, 2= rarely, 3= frequently, 4= always). If a child scores high in the first factor that means that s/he cannot regulate his/her emotions. On the other hand, if a child scores high in the second factor then this suggests that the child can regulate his emotions very well. Not only parents and teachers, but also an adult who knows the child well enough can fill the questionnaire. The studies show that the Turkish adaptation of the scale has high reliability and distinctive validity. The validity and reliability study of the scale was also conducted by Kapci and colleagues. In the present study, the ERC scales were filled by the mothers with the guidance of a child psychiatrist.

**Participants**

The participants in the present study were 42 children (36-72 months old) who were diagnosed with ASD and who had limited expressive vocabulary at the onset of the study. Those children met the following criteria for minimal expressive vocabulary: less than 14 spoken words produced spontaneously according to; a) a teacher report, b) a parent report, and c) a language sample collected during our assessment process. Children who had chronic organic diseases, epilepsy or genetic diseases were excluded from study. Also children who had language problems due otolaryngologic problems (cleft palate or lip) were excluded. The intervention took place in Nevşehir State Hospital within the department that specialises in AAC assessment and intervention for children with complex communication needs. Subjects were randomised into two groups according to the order of applying to outpatient clinic; odd numbers were included to the intervention group. (Twenty one children were in intervention group and 21 children were in control group). The first group attended the experimental AAC treatment and speech sound practice using a computer-based voice output communication aid (VOCA) device with a touch-sensitive screen-input system was used to teach children individualised words that were selected on the basis of initial speech sound repertoires and principles of phonotactic probability and neighbourhood density. The second group was the control group and received only routine treatment. Routine treatment consisted of monthly psychiatric session and weekly special education lessons (two lessons in a week). Both intervention and control group received routine treatment during current study. We have examined the impact of using VOCAs on children's organisation of communicative activities. Visual schedules utilising VOCAs were used with children with ASD during the speech therapy sessions. The assessor was blind to whether the child had participated in the VOCA programme. Test of Early Language Development (TELD) was used to evaluate language profiles, autistic symptoms were evaluated with Autism Behaviour Checklist (ABC) and children's emotion regulation skills were evaluated with Emotion Regulation Checklist (ERC). TELD was administered in the child's native tongue. A communication profile was obtained through informal analysis of a 20-
minute video-recorded session in both play and snack-time contexts prior to baseline. This profile was then combined with parents' reports of their children's expressive communication skills. The MLU was calculated for each instance of spontaneous speech that occurred at a spontaneous speech opportunity using SALT. The evaluation was conducted by applying the DDST. Lastly, the ABC was used to investigate autistic symptoms just before and after sessions. Those children receiving only routine treatment were assessed again in the time that children finished VOCA sessions.

Ethical Considerations
Since the participants in the present study were children who had limited language skills, parents were asked if they would allow their children to participate in this research. As such, parents of the 42 children described above signed the informed consent form prior to the collection of any data. The consent form that was filled by parents was in accordance with the Declaration of Helsinki as amended by the World Medical Association Declaration of Helsinki (World Medical Association, 2013) and received ethical clearance from the Non-Invasive Clinical Trials Ethics Committee at Nevşehir Hacı Bektaş Veli University.

Statistical Analysis
Some socio-demographic and clinical categorical variables of the case group and the control group were assessed through descriptive statistics. Chi-square test was used for comparing the classified categorical variables (e.g. gender). Distribution of the data was primarily assessed by using the Kolmogorov-Smirnov test and since the data did not meet the requirements of a normal distribution, the binary groups were assessed using Mann-Whitney U test. In addition, the Wilcoxon analysis was used to evaluate changes in the same group. The p value was accepted to be statistically significant at <0.05.

Results
The average age was determined as 52.19 (±6.91) months for children diagnosed with ASD in the intervention group while it was 53.76 (±6.59) months for children in the control group. The difference between the groups was not statistically significant (p=0.307). The comparison of the children in terms of their mental age using the data acquired from the DDST suggested that children in the intervention group had a mental age of 38.81 (±8.92) months and children in the control group had a mental age of 38.40 (±7.69; p=0.907). The assessment of children’s speech levels showed that the experimental group’s average speech level was 36.66 (±10.55) and the control group’s was 36.57 (±9.22; p=0.798). The groups were similar in terms of sex distribution, maternal age, education and working condition. The socio-demographic characteristics of the groups are displayed in Table 1.

Prior to the intervention, Mann Whitney U test was used to compare the experimental and control group members’ skills by analysing their ABC scores in terms of receptive

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Comparison of groups' age, mental age, language levels, and sociodemographic data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention</td>
</tr>
<tr>
<td>Age (months)</td>
<td>37.48±7.38</td>
</tr>
<tr>
<td>Mental age (months)</td>
<td>38.81±8.92</td>
</tr>
<tr>
<td>Speech level (months)</td>
<td>36.66±10.55</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
</tr>
<tr>
<td>Mothers' age (year)</td>
<td>32.80±3.59</td>
</tr>
<tr>
<td>Mothers' education (year)</td>
<td></td>
</tr>
<tr>
<td>Over 8</td>
<td>9</td>
</tr>
<tr>
<td>Under 8</td>
<td>12</td>
</tr>
<tr>
<td>Mother’s social status</td>
<td></td>
</tr>
<tr>
<td>House wife</td>
<td>14</td>
</tr>
<tr>
<td>Works</td>
<td>7</td>
</tr>
</tbody>
</table>
and expressive language use. No significant difference was found between the groups. Table 2 shows the values obtained from language skills and all subscales of ABC before the intervention. As can be seen from the table none of the test results were significant which supports the idea that both the control and the intervention groups were similar.

Post-intervention comparison of the intervention and control group's scores, however, showed that children who were in the intervention group scored significantly better than those in the control group in terms of receptive and expressive language and all subscales of ABC (see Table 3). Test results indicated that there was a significant increase in the intervention group's emotion regulation but also they experienced a decrease in emotional lability. The results of the remaining tests were also significant in favour of the intervention group (see Table 3).

The calculation of MLU requires sufficient numbers of intelligible utterances per sample. Table 4 reports on the MLU and LSS results of both groups for pre and post-treatment. It can be seen that, with AAC, children increased the number of utterances and there was a significant difference between pre and post treatment in MLU and LSS. The correlations remained significant in both groups under both partner conditions. Overall, LSS was a close parallel to MLU within the same language samples after controlling for language sample size in post treatment groups. This indicates that there is a statistically significant relationship between using AAC treatment with VOCA and the children with ASD's language development.

### Discussion

Our findings showed that AAC can be effective in improving language development, autistic symptoms and emotion regulation in individuals with ASD. There were 3 main findings.

First of all, to the best of our knowledge, this is the first study to provide preliminary evidence supporting effectiveness of AAC in emotion dysregulation of autistic children. As explained at the beginning of this paper, recent

<table>
<thead>
<tr>
<th>Table 2</th>
<th>The scores of Denver Developmental Screening Test II, Test of Early Language Development, Emotion Regulation Checklist, and Autism Behaviour Checklist prior to the intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>N</td>
</tr>
<tr>
<td>---------</td>
<td>----</td>
</tr>
<tr>
<td>Denver total</td>
<td>Int.</td>
</tr>
<tr>
<td>Denver total</td>
<td>Cont.</td>
</tr>
<tr>
<td>Denver language</td>
<td>Int.</td>
</tr>
<tr>
<td>Denver language</td>
<td>Cont.</td>
</tr>
<tr>
<td>Receptive language</td>
<td>Int.</td>
</tr>
<tr>
<td>Receptive language</td>
<td>Cont.</td>
</tr>
<tr>
<td>Expressive language</td>
<td>Int.</td>
</tr>
<tr>
<td>Expressive language</td>
<td>Cont.</td>
</tr>
<tr>
<td>Emotional lability</td>
<td>Int.</td>
</tr>
<tr>
<td>Emotional lability</td>
<td>Cont.</td>
</tr>
<tr>
<td>Emotional regulation</td>
<td>Int.</td>
</tr>
<tr>
<td>Emotional regulation</td>
<td>Cont.</td>
</tr>
<tr>
<td>ABC sensory</td>
<td>Int.</td>
</tr>
<tr>
<td>ABC sensory</td>
<td>Cont.</td>
</tr>
<tr>
<td>ABC relating</td>
<td>Int.</td>
</tr>
<tr>
<td>ABC relating</td>
<td>Cont.</td>
</tr>
<tr>
<td>ABC body and object use</td>
<td>Int.</td>
</tr>
<tr>
<td>ABC body and object use</td>
<td>Cont.</td>
</tr>
<tr>
<td>ABC language</td>
<td>Int.</td>
</tr>
<tr>
<td>ABC language</td>
<td>Cont.</td>
</tr>
<tr>
<td>ABC social and self-help skills</td>
<td>Int.</td>
</tr>
<tr>
<td>ABC social and self-help skills</td>
<td>Cont.</td>
</tr>
</tbody>
</table>

ABC=Autism Behaviour Checklist; Int.=Intervention; Cont.=Control
studies have reported high rates of emotion dysregulation in children with ASD.\textsuperscript{18,19} Emotion dysregulation may be explained as failing in regulating emotions appropriately and effectively. Parents and clinicians have long emphasized the important role that maladaptive emotional responses in ASD\textsuperscript{11} which might be a result of dysregulated emotions. In Samson and colleagues' study, all core features (including deficits in social and communication functioning, repetitive behaviours, and sensory abnormalities) of autism were found to be related to emotion dysregulation.\textsuperscript{17} These findings, especially the association between emotion dysregulation and social and communication deficits, were in accordance with previous reports of an association between poor social abilities (i.e., theory of mind, perspective taking abilities) and emotion dysregulation.\textsuperscript{16,17} Considering these, our results are significant in the development of efficient treatment for emotion dysregulation which could be used to improve the social communication and interaction of children with ASD. These effects may be reciprocal, thus it is possible that development in linguistic and social areas might provide positive effects on emotional dysregulation. It is a known fact that disruptive behaviours related to emotion dysregulation, such as irritability, temper tantrums, aggression, or self-injurious behaviour are the basic reasons for pharmacological treatment.\textsuperscript{45} In light of the evidence presented so far, it could be, tentatively, interpreted that the availability of training programmes such

Table 3  The scores of test of Early Language Development, Emotion Regulation Checklist, and Autism Behaviour Checklist post intervention

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean rank</th>
<th>Sum of ranks</th>
<th>p</th>
<th>z</th>
<th>U</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptive language</td>
<td>Int.</td>
<td>21</td>
<td>30.76</td>
<td>646.00</td>
<td>0.001*</td>
<td>-4.928</td>
</tr>
<tr>
<td></td>
<td>Cont.</td>
<td>21</td>
<td>23.00</td>
<td>483.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expressive language</td>
<td>Int.</td>
<td>21</td>
<td>28.40</td>
<td>596.50</td>
<td>0.001*</td>
<td>-3.666</td>
</tr>
<tr>
<td></td>
<td>Cont.</td>
<td>21</td>
<td>23.14</td>
<td>486.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional lability</td>
<td>Int.</td>
<td>21</td>
<td>16.48</td>
<td>346.00</td>
<td>0.008*</td>
<td>-2.662</td>
</tr>
<tr>
<td></td>
<td>Cont.</td>
<td>21</td>
<td>26.52</td>
<td>557.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional regulation</td>
<td>Int.</td>
<td>21</td>
<td>29.67</td>
<td>623.00</td>
<td>0.001*</td>
<td>-4.349</td>
</tr>
<tr>
<td></td>
<td>Cont.</td>
<td>21</td>
<td>13.33</td>
<td>280.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC sensory</td>
<td>Int.</td>
<td>21</td>
<td>17.79</td>
<td>373.50</td>
<td>0.046*</td>
<td>-1.992</td>
</tr>
<tr>
<td></td>
<td>Cont.</td>
<td>21</td>
<td>25.21</td>
<td>529.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC relating</td>
<td>Int.</td>
<td>21</td>
<td>16.71</td>
<td>351.00</td>
<td>0.010*</td>
<td>-2.593</td>
</tr>
<tr>
<td></td>
<td>Cont.</td>
<td>21</td>
<td>26.29</td>
<td>552.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC body and object use</td>
<td>Int.</td>
<td>21</td>
<td>16.81</td>
<td>353.00</td>
<td>0.012*</td>
<td>-2.516</td>
</tr>
<tr>
<td></td>
<td>Cont.</td>
<td>21</td>
<td>26.19</td>
<td>550.00</td>
<td></td>
<td></td>
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<tr>
<td>ABC language</td>
<td>Int.</td>
<td>21</td>
<td>14.74</td>
<td>309.50</td>
<td>0.001*</td>
<td>-3.599</td>
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<tr>
<td></td>
<td>Cont.</td>
<td>21</td>
<td>28.26</td>
<td>593.50</td>
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<tr>
<td>ABC social and self-help skills</td>
<td>Int.</td>
<td>21</td>
<td>15.81</td>
<td>332.00</td>
<td>0.002*</td>
<td>-3.038</td>
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<tr>
<td></td>
<td>Cont.</td>
<td>21</td>
<td>27.19</td>
<td>571.00</td>
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</table>

*p is significant at <0.050

ABC=Autism Behaviour Checklist; Int.=Intervention; Cont.=Control

Table 4  Mean length of utterance (MLU) and language sample size (LSS) before and after intervention

<table>
<thead>
<tr>
<th></th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MLU</td>
<td>LSS</td>
</tr>
<tr>
<td>Intervention</td>
<td>3.01±0.33</td>
<td>117.46±31.82</td>
</tr>
<tr>
<td>Control</td>
<td>3.11±0.64</td>
<td>107.32±24.33</td>
</tr>
</tbody>
</table>

*p is significant at <0.001, the number of utterances used to calculate MLU was used for LSS.
as the one employed in this study might decrease the use of pharmacological agents associated with severe side effects (e.g., antipsychotic medications). Thus, AAC can be considered as an option to supplement or augment an individual's speech and facilitate emotional regulation.\(^{46}\) AAC, with increasing verbalisation, may provide expressing feelings and that cause better emotion regulation skills.

Secondly, this is one of the first studies to show increases in minimally verbal children's spontaneous communication including parental intervention. Involvement of parents may positively influence the development of language skills and emotional regulation. Treating the social exchanges between the child and caregiver as a crucial component of learning is a milestone for development.\(^{47}\) In their research, Adamson and colleagues found that the amount of time young children with ASD spend with caregivers is 20 to 30 per cent lower than the typically developing children.\(^{48}\) Having a child with developmental difficulties, indisputably, means that a parent needs to spend more effort; however, having a child with ASD makes this situation even more difficult. Thus, teaching parents how to facilitate joint interactions with their children with ASD becomes an important and necessary consideration.

In a study by Shire and colleagues', 61 children with ASD, who were between five- and eight-years old and who had minimal spontaneous communication, received a six-month social communication intervention including parent training which resulted in positive outcomes for the children.\(^{27}\) Adamson and colleagues recorded parent–child play interactions and coded them for parents' strategy implementation and the time they spend together with their children.\(^{49}\) They found that parents mastered an average of 70% of the strategies and children's joint engagement was associated with parents' implementation success of the strategies across time, which demonstrated that parents' implementation of those strategies was relevant to children's social engagement.\(^{48}\) Thus, it can be interpreted that emotion regulation skills may be gained with reciprocal parent-child relations and availability.

Thirdly, autistic symptoms decreased after the AAC intervention. Due to previous studies' effectiveness of treatment packages involving speech output, the vast majority included a dedicated speech generated device (SGD). It is, however, reported in a recent study that, given the revolution in mobile technologies, AAC-specific apps that can be installed on mobile devices can also be used during the treatment process. A review of 23 studies which used an SGD included a total of 51 children with ASD whose ages ranged between three and 16.\(^{9}\) All studies were single-subject designs, and most focused on teaching, requesting, or responding to questions using the SGD. Few studies assessed maintenance and generalisation. While it appears that using an SGD increases children's communicative abilities, particularly in terms of requests,\(^{6,9}\) there has not been any rigorous group designs which have replicated those findings, and few studies have demonstrated different communicative functions than requests (e.g., commenting) or an increase in spoken language.

Our study was one of the first studies to use the TELD-3-T as a tool for assessing language development in children with ASD in AAC. Additionally, there were statistically significant relationships between AAC with VOCA and the children with ASD's language development and linguistic skills. The speed of learning for children with ASD might be enhanced through the use of SGD and applications in VOCA which delivers a graphic illustration for communication and integrates visual discriminations as part of the interaction. Many communication training programmes initially teach labelling, a process which involves teaching the child to identify an object with a symbol, a hand gesture, or a vocal response.\(^{49,50}\) Such programmes may contribute to the initiation of verbal behaviours. Thus, it is considered using AAC with VOCA can be an advantage for children' receptive and expressive language development. In particular, children start to acquire expressive vocabulary. In our study, the correlations between language sample size and MLU reached statistical significance after the AAC intervention. The language sample size is not necessarily a confounding variable in our results; it is, nevertheless, a useful component that should be included in an attempt to predict language development. Additionally, there were statistically significant relationships between AAC with VOCA and the children with ASD's language development with MLU-TELD scores. MLU is not a language malfunction indicator but supports language disorder recognition.

To conclude, children showed significant improvements in emotion regulation and social communication in a low intensity, parent attributed, behaviourally based intervention in a short time. Potential advantages and the pragmatic features of AAC have been adopted in the autism treatment community. Unfortunately verbal comprehension of children were not evaluated in current study and long term effects of AAC in children were not
evaluated in current study as important limitations. Our sample size and duration of the intervention are not sufficient to generalise results but our study provides preliminary evidence to support the use of AAC for promoting emotional regulation, social communication & interaction for children with ASD. Thus, further research in this area is encouraged.

**Declaration of Interest**

None

**References**

46. Hustad KC, Miles LK. Alignment between augmentative and alternative communication needs and school-based speech-language services provided to young children with cerebral palsy. Early Child Serv (San Diego) 2010;4:129-40.
The Risk Factors Associated with Sleep-related Problems in Children with Profound Intellectual Disability

CK CHOW, SN WONG, LCK MA, GPG FUNG, WL YAM, HB CHAN

Abstract

Objective: To estimate the prevalence and identify the risk factors of different sleep disorders, in a local sample of children with profound intellectual disability. Methods: The study was conducted in students with profound intellectual disabilities in a special school. Each student was evaluated by the Chinese version of Children’s Sleep Habits Questionnaire by their parents. Other medical information was collected and analysed with the score of the questionnaire. Results: Data from 67 participants were included in the analysis. 84% of the subjects were considered as having sleep disorders. Children with epilepsy had a significantly higher total sleep score compared to children without epilepsy (49.66±7.53 vs 45.27±6.87, p=0.02). Non-boarding students and those with medical problems also had significantly higher scores. Logistic regression analysis showed that epilepsy was significantly associated with sleep disorder (adjusted odd ratio 7.99, p=0.02). Epilepsy was associated with higher sub-scores for bedtime resistance, sleep onset delay and sleep-disordered breathing. Obesity was associated with higher sub-score for sleep-disordered breathing. Conclusions: Sleep disorders were common among children with profound intellectual disabilities, and epilepsy was significantly associated with sleep disorder in this group of children. Correct identification of the sleep disorders, followed by provision of different sleep interventions are recommended.

Key words Cerebral palsy; Epilepsy; Intellectual disability; Sleep-related problem

Introduction

Intellectual disability (ID) is a lifelong neurodevelopmental disorder, characterised by both intellectual and adaptive functioning deficits in conceptual, social and practical domains. In addition to cognitive impairment, students with ID also face many health-related problems, including motor deficits, epilepsy, sleep disturbance, mental illness, vision and hearing impairment.

The classification of ID into different grades of severity, which was previously defined by the intelligence quotient (IQ), is now emphasized on the adaptive functioning of the subject. A "three-tier system" is still normally used in Hong Kong for operational classification. Children are classified into "mild", "moderate" and "severe" grades for the purpose of special education and training services. For example, the "severe" grade in Hong Kong corresponds to "profound" grade in the previous World Health Organisation (WHO) classification system. Therefore, a "school for children with severe ID" in Hong Kong is receiving students with IQ less than 20 (results in severe limitation in self-care, continence, communication and mobility). In Hong Kong, the prevalence rate of ID is...
estimated to be 1.0% to 1.4% and in this population, about 85% are within mild grade, 10% are within moderate grade, and the rest are within the severe grade range. In 2015, 679 students were enrolled in a school for children with severe ID, in contrast with over 300,000 enrolments in ordinary primary schools.

Sleep disorders can be classified according to different classification systems, but in general, they can be divided into two major categories: dyssomnias and parasomnias. Dyssomnias refer to those involving initiation or maintenance of sleep, or excessive sleepiness. Parasomnias refer to abnormal events that disrupt sleep after its initiation. The International Classification of Sleep Disorders (third edition, ICSD-3), developed by American Sleep Disorders Association, is one of the most comprehensive classifications available currently. The ICSD-3 identified seven major categories that include insomnia disorders, sleep-related breathing disorders, central disorders of hypersomnolence, circadian rhythm sleep-wake disorders, sleep-related movement disorders, parasomnias, and other sleep disorders. In this classification system, for example, paediatric obstructive sleep apnoea belongs to the category of sleep-related breathing disorders, which its clinical findings (such as snoring, laboured or obstructed breathing, daytime consequences) and polysomnographic criterion have been described. On the other hand, the parasomnias are divided into three groups, namely non-rapid eye movement (such as confusional arousal, sleep walking, sleep terrors), rapid eye movement (such as nightmares) and others.

Sleep disorders in children with ID are common yet under-recognised problems. They gain relatively little attention from parents, clinicians and researchers as compared with other clinical agendas. Parents rarely voice out the problem until it becomes long term and affects the whole family. Clinicians, however, have tended to regard the use of medication as the only key to this problem. Nonetheless, this problem is often a significant source of parental stress. The estimated prevalence of children with ID having sleep disorders vary from 13% to 86%, depending on case definitions. For example, a questionnaire-based study assessed the prevalence of sleep problems in children with ID and found that 8.6%, 14.8%, 27.9% and 35.3% of children with mild, moderate, severe, and profound ID had severe sleep problems respectively. It was also noticed that there were higher proportions of dyssomnias, including obstructive sleep apnoea, and parasomnias in children studying in special schools.

As mentioned, children with ID have different co-morbidities, and the associations between these and sleep disorders have been explored in previous studies. There is often a bi-directional association, in which these co-morbidities have a negative impact on their sleep, and in turn the sleep disorders can potentiate the co-morbidities. For the aforementioned questionnaire-based study, it assessed children with ID from mild to profound range and concluded that children with severe sleep problems had more severe levels of ID, had greater frequencies of epilepsy and cerebral palsy than those without severe sleep problems. Besides, children with severe sleep problems showed more daytime behavioural problems, such as aggression and hyperactivity. These findings corroborate the results of other epidemiological studies. A study using a standardised observation protocol studied subjects with ID living in a rehabilitation centre, and it concluded that severe locomotor disability and active epilepsy were independent predictors of increased daytime sleep and wake-sleep transitions. A study recruited children with ID and epilepsy and found that about one-third of them had obstructive sleep apnoeas and periodic limb movements. A study also demonstrated the association between sleep problems and anxiety, in which higher levels of sleep problems are associated with higher levels of anxiety in children with ID. Therefore, it is important to identify these co-morbidities as potential risk factors for sleep disorders in this group of children, as interventions targeted at the co-morbidities could potentially improve the sleep disorders and vice versa.

Local data on the prevalence of sleep disorders in children with ID is lacking, but an understanding of this important issue may help improve planning and management of this group of children. Few studies have examined the risk factors of sleep disorders in children with profound ID, especially in a special school setting. They are the ones who have more complex medical background but receive relatively little attention from society and researchers. The aim of this study was to estimate the prevalence and identify the risk factors of different sleep disorders in a local sample of children with profound ID studying in a special school.

**Methods**

**Recruitment of Subjects**

We recruited all the families with children studying in Haven of Hope Sunnyside School in the academic year...
2015/16 as the study population (82 families in total). This special school is one of the 10 “schools for children with severe ID” in Hong Kong, for children from six to 18 years old. As discussed above, its students were all classified as profound ID (IQ less than 20, according to previous WHO classification system) in the pre-school assessment before they entered this school. This school also provides boarding services for the students at the discretion of their families, but all of them will return home in weekends and long holidays. All the students in this school are under the Integrated Care and Community Support (ICCS) programme, which medical staff in a regional hospital are providing medical assessment, visits and opinion to the students and the school staff.

Data Collection

As part of the ICCS programme, all the families of the students in this school received an invitation letter to fill in a sleep questionnaire (see "materials" below). This questionnaire was distributed by the school staff and the process was co-ordinated by the ICCS nurse in the school. Besides the results of the questionnaire, other information of the students, including demographic information and co-morbidities was collected from the students’ medical profile, and all data was entered in a standardised data collection form without any personal identification.

In particular, demographic information including age, sex, boarding status, latest body weight and height was provided by the school in the students’ school record. The co-morbidities collected were epilepsy, cerebral palsy, visual impairment and psychiatric disease. The use of medication and mobility status (walk unaided, walk with assistance, wheelchair-bound or bed-bound) were also included. The medical diagnoses of the co-morbidities were all reviewed by the medical team, so as to ensure they were appropriate and most updated.

Subjects would be excluded if the family could not provide any information about the children’s sleeping habit, or the family did not consent to use children’s data for research purpose. Written approval from the school and local ethics committee was obtained for this study.

Materials

Each participant’s sleep habit was evaluated with the Chinese version of the Children’s Sleep Habits Questionnaire (CSHQ). This questionnaire is a screening instrument designed for surveying sleep habits and sleep disturbances, and identifying both behaviourally-based and medically-based sleep problems in school-aged children. It was seen as acceptable for use with older children and those with developmental delay. It is a parent-reported questionnaire consisting of 50 questions, in which 33 of them are scored, and it takes around 15-20 minutes for the family to complete the whole questionnaire. Each question enquires about an item of the child’s usual sleeping habit, and is scored as 3 if this item occurs usually (5-7 times per week), 2 if it occurs sometimes (2-4 times per week) or 1 if it occurs rarely (0-1 times per week). The 33 scored items can be divided into eight subscales, namely bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep-disordered breathing and daytime sleepiness. Each completed questionnaire will yield eight sub-scores and a total score. Therefore, this questionnaire is a comprehensive tool for assessing different types of sleep disorders, including dyssomnias and parasomnias. Other non-scored items allow the assessors to gather more information about the children’s sleeping habits. Families were instructed to consider the child’s usual sleeping habit (preferably in past 1 week and free of recent deviation from the norm such as illness or change of environment).

CSHQ has been validated and showed adequate internal consistency for both the community and clinical sample. A cut off total score of 41 yielded a sensitivity of 0.80 and specificity of 0.72. The Chinese version of CSHQ has been developed, and shows good reliability, content validity and construct validity.

A high CSHQ score warrants further medical attention, which the correct diagnosis of sleep disorders may require further information. For example, detailed history especially complaints from the care-taker, developmental and family history, sleep diary and physical examination may be required to establish a diagnosis.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences software (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Categorical data were compared using the Chi-square test or Fisher Exact test (for cells less than 5), and odds ratio (OR) with 95% confidence interval (CI) was calculated. Continuous variables were compared using the independent t test or Mann-Whitney U test. Multivariate logistic regression was used to determine the effect of individual risk factors on outcome. A two-sided p-value of ≤0.05 was considered significant.
Results

Eighty-two families were invited to fill in the sleep questionnaire. Sixty-seven completed questionnaires were received which constituted a response rate of 82%. None of the subjects fulfilled the exclusion criteria as stated above. The mean CSHQ total score of all the subjects was 48.3±7.6. The demographics and characteristics of the subjects are summarised in Table 1.

In this study, we investigated possible risk factors that may affect sleep in these children. Comparison of total sleep score between children with or without risk factors is shown in Table 2. Children with epilepsy had a significantly higher total sleep score compared to children without epilepsy (49.66±7.53 vs 45.27±6.87, p=0.02). Non-boarding students also had a significantly higher score, as well as presence of medical problem. Other factors including adolescent age group ≥13 years old (49.00±7.94 vs 47.68±6.91) and obesity (51.71±7.89 vs 47.88±7.49) showed a trend towards higher score, but did not reach statistical significance. Presence of cerebral palsy, psychiatric disorder or mobility status was not significantly associated with higher scores.

If a total score of 41 is used as cut-off value for sleep disorder, 56 children in this study were defined as having sleep disorder and were included into the "Study Group". Eleven children had total score less than 41 and were included in the "Comparison Group". Comparison of risk factors for sleep disorder (Table 3) showed that epilepsy (OR 4.78, 95% CI 1.22-18.7, p=0.02), as well as presence of medical problem (OR 5.83, 95% CI 1.26-27.02, p=0.02) were associated with significantly higher risk of sleep disorder.

Logistic regression analysis comparing the two groups (Table 4) showed that, after elimination of confounding

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographics and characteristics of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of subjects</td>
<td>67 (100)</td>
</tr>
<tr>
<td>Male</td>
<td>37 (55)</td>
</tr>
<tr>
<td>Female</td>
<td>30 (45)</td>
</tr>
<tr>
<td>Age (year)</td>
<td>14±4.7</td>
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<tr>
<td>Boarding student</td>
<td>38 (57)</td>
</tr>
<tr>
<td>Obesity (Body mass index &gt;25)</td>
<td>7 (10)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>22 (33)</td>
</tr>
<tr>
<td>No</td>
<td>4 (6)</td>
</tr>
<tr>
<td>Yes. Not on AED</td>
<td>21 (31)</td>
</tr>
<tr>
<td>Yes. On one AED</td>
<td>20 (30)</td>
</tr>
<tr>
<td>Yes. On two or more AEDs</td>
<td>28 (42)</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>32 (48)</td>
</tr>
<tr>
<td>Mobility status</td>
<td>35 (52)</td>
</tr>
<tr>
<td>Walk unaided or with assistance</td>
<td>11 (16)</td>
</tr>
<tr>
<td>Wheelchair-bound or bed-bound</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Psychiatric disease</td>
<td>5 (7)</td>
</tr>
</tbody>
</table>

| AED = Anti-epileptic drug |

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Comparison of total sleep scores between different groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sleep score</td>
<td>Condition present</td>
</tr>
<tr>
<td>Male gender</td>
<td>48.05±8.11</td>
</tr>
<tr>
<td>Adolescent age group</td>
<td>49.00±7.94</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>49.66±7.53</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>47.46±7.49</td>
</tr>
<tr>
<td>Bed or wheelchair bound</td>
<td>49.23±7.97</td>
</tr>
<tr>
<td>Psychiatric problem</td>
<td>45.80±8.23</td>
</tr>
<tr>
<td>Live in hostel</td>
<td>46.29±7.51</td>
</tr>
<tr>
<td>Obesity</td>
<td>51.71±7.89</td>
</tr>
<tr>
<td>Presence of medical problem</td>
<td>49.10±7.41</td>
</tr>
</tbody>
</table>

* p-value ≤0.05
factors, epilepsy was significantly associated with sleep disorder (adjusted OR 7.99, 95% CI 1.48 - 43.25, p=0.02).

Further analysis of sub-scores for risk factors for sleep problems (Table 5) showed that different risk factors were associated with higher sub-scores for different categories. Epilepsy was associated with higher scores for subscales 1, 2 and 7 (bedtime resistance, sleep onset delay and sleep-disordered breathing respectively). Obesity was associated with higher scores for subscale 7 (sleep-disordered breathing).

### Discussion

#### Sleep Disorders and ID

The result of our study corroborates those of other epidemiological studies, showing a high prevalence of sleep disorders in children with ID. Using the cut-off point of 41, which was also used in other similar studies, 84% of the subjects were considered as having sleep disorders. Prevalence rate of up to 77% and 86% have been reported. We believe the wide range of prevalence rates could be attributed to different methodology, clinical definition and sample group. We focused on children with profound ID while some were studying a heterogeneous group of children with different levels of ID. A higher rate of sleep disorders would be expected in students studying in special school with more severe ID.

The biological basis of sleep disorders in children with ID had been described in the literature. These children may have altered perception of different environment clues (such as light-dark cycle, food schedule) and also show endogenous dysfunction in hormonal release. These factors are important in establishing a synchronised circadian rhythm, so it will potentially affect the development of a normal sleep-wake cycle. They may present with abnormal sleep architecture as seen in polysomnographic study, such as abnormal duration of the sleep cycle.

Despite the high prevalence rate of sleep disorder in this group of children, we notice that this problem receives relatively little attention in society and amongst medical practitioners. It was described as “a neglected topic”, which medical students, nurses, clinical psychologists and even paediatric postgraduates receive very little teaching and training. Medical practitioners seldom enquire about this, partly because they may be overwhelmed by other topics considered to be more important. Some parents themselves may also hesitate to seek help as they may consider this problem a chronic one and thus become part of the “normal life” of these children. Even when this problem is brought to the medical practitioners, they are often offered sedatives which do not help, and sometimes even worsen the clinical situation. Therefore, with the result of our study, we hope to alert clinicians and other related disciplines of this under-recognised yet highly prevalent problem in children with ID, especially those in profound grade and studying in special school.

### Table 3

<table>
<thead>
<tr>
<th>Factor</th>
<th>Study group (n= 56)</th>
<th>Comparison group (n=11)</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>31/56 (55.4%)</td>
<td>6/11 (54.5%)</td>
<td>1.03 (0.28-3.77)</td>
<td>0.96</td>
</tr>
<tr>
<td>Adolescent age group</td>
<td>34/56 (60.7%)</td>
<td>4/11 (36.4%)</td>
<td>2.70 (0.71-10.33)</td>
<td>0.19</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>41/56 (73.2%)</td>
<td>4/11 (36.4%)</td>
<td>4.78 (1.22-18.7 )</td>
<td>0.02*</td>
</tr>
<tr>
<td>On anti-epileptic drugs</td>
<td>37/56 (66.1%)</td>
<td>4/11 (36.4%)</td>
<td>3.41 (0.88-13.11)</td>
<td>0.06</td>
</tr>
<tr>
<td>On ≥2 anti-epileptic drugs</td>
<td>19/56 (33.9%)</td>
<td>1/11 (9.1%)</td>
<td>5.14 (0.61-43.16)</td>
<td>0.15</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>22/56 (39.3%)</td>
<td>6/11 (54.5%)</td>
<td>0.54 (0.15-1.98 )</td>
<td>0.35</td>
</tr>
<tr>
<td>Bed or wheelchair bound</td>
<td>29/56 (51.8%)</td>
<td>6/11 (54.5%)</td>
<td>0.90 (0.24-3.28 )</td>
<td>0.87</td>
</tr>
<tr>
<td>Psychiatric problem</td>
<td>4/56 (7.1%)</td>
<td>1/11 (9.1%)</td>
<td>0.77 (0.07-7.62 )</td>
<td>0.80</td>
</tr>
<tr>
<td>Lives in hostel</td>
<td>29/56 (51.8%)</td>
<td>9/11 (81.8%)</td>
<td>0.24 (0.05-1.21 )</td>
<td>0.09</td>
</tr>
<tr>
<td>Obesity</td>
<td>7/56 (12.5%)</td>
<td>0/11 (0%)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Presence of medical problem</td>
<td>51/56 (91.1%)</td>
<td>7/11 (63.6%)</td>
<td>5.83 (1.26-27.02)</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

CI = Confidence interval; NS = Not significant; OR = Odd ratio
* p-value ≤0.05
### Sleep Disorders and Co-morbidities

A number of co-morbidities and factors are associated with more severe sleep disorders. Those which were previously studied or hypothesised to affect sleep include: age, body weight or obesity, epilepsy, cerebral palsy or mobility problem, psychiatric diseases (such as autism spectrum disorder), visual impairment, active insults (such as acute stroke, head trauma, encephalitis, brain tumour), neurodegenerative disorders (such as Parkinson disease, Huntington disease, spinocerebellar atrophy) and neuromuscular disorders (such as muscular dystrophy, congenital myopathy, myotonic dystrophy, myasthenia gravis, hereditary motor sensory neuropathy). For our study, we included the possible factors that affect sleep as listed above in the statistical analysis. There were no subjects suffering from active insults, neuromuscular or neurodegenerative disorders, so these were not included. In such a way, we hoped to identify the risk factors associated with sleep disorders in this group of children.

Our study found that in this group of children with profound ID, there was an association between epilepsy and sleep disorders, and we concluded from the logistic regression model that epilepsy is an independent risk factor for sleep disorders in these children. This association was shown to be unrelated to the use of anti-epileptic drugs. This corroborates results from other studies in children with ID as discussed in the introduction. The biological basis of the association between epilepsy and sleep disorders had been extensively investigated in the literature. Epileptic seizure can affect the sleep state, which includes post-ictal hypersomnolence, decreased sleep efficiency, increased wakefulness, sleep stage shifts, arousals and sleep fragmentation. Children with poorly controlled seizure may also have higher percentages of rapid eye movement sleep which is a relatively anti-epileptic state. Clinically, this group of children may be more prone to different types of sleep disorders, including dysnomial and parasomnias. This will be reflected in different CSHQ sub-scores, which will be elaborated further below (see "sub-score analysis"). In turn, poor sleep quality will also have negative impact in seizure control, as sleep deprivation is well-recognised to lower seizure threshold.

#### Table 4 Logistic regression analysis of risk factors with presence of sleep disorder

<table>
<thead>
<tr>
<th>Condition</th>
<th>aOR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>7.99 (1.48-43.25)</td>
<td>0.02*</td>
</tr>
<tr>
<td>On anti-epileptic drugs</td>
<td>3.11 (0.19-52.35)</td>
<td>0.43</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>2.61 (0.43-15.79)</td>
<td>0.29</td>
</tr>
<tr>
<td>Wheelchair or bedbound</td>
<td>1.95 (0.28-13.62)</td>
<td>0.50</td>
</tr>
<tr>
<td>Psychiatric problem</td>
<td>3.48 (0.24-50.36)</td>
<td>0.36</td>
</tr>
<tr>
<td>Lives in hostel</td>
<td>4.64 (0.80-26.86)</td>
<td>0.08</td>
</tr>
<tr>
<td>Obesity</td>
<td>0.06 (0.01-3.38)</td>
<td>0.17</td>
</tr>
<tr>
<td>Presence of medical problem</td>
<td>2.02 (0.15-26.58)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

CI = Confidence interval; aOR = Adjusted odd ratio

* p-value ≤ 0.05

#### Table 5 Comparison of different risk factors on sub-scores

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Epilepsy</th>
<th>Cerebral palsy</th>
<th>Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
<td>p-value</td>
</tr>
<tr>
<td>1</td>
<td>9.20±2.11</td>
<td>8.00±2.33</td>
<td>0.04*</td>
</tr>
<tr>
<td>2</td>
<td>2.00±0.64</td>
<td>1.64±0.71</td>
<td>0.04*</td>
</tr>
<tr>
<td>3</td>
<td>5.31±1.62</td>
<td>4.59±1.68</td>
<td>0.10</td>
</tr>
<tr>
<td>4</td>
<td>5.71±1.47</td>
<td>5.45±1.79</td>
<td>0.54</td>
</tr>
<tr>
<td>5</td>
<td>4.67±1.54</td>
<td>4.09±1.41</td>
<td>0.14</td>
</tr>
<tr>
<td>6</td>
<td>9.56±2.15</td>
<td>9.50±2.11</td>
<td>0.92</td>
</tr>
<tr>
<td>7</td>
<td>4.07±1.42</td>
<td>3.41±0.59</td>
<td>0.04*</td>
</tr>
<tr>
<td>8</td>
<td>12.36±2.81</td>
<td>11.55±2.26</td>
<td>0.24</td>
</tr>
</tbody>
</table>

* p-value ≤ 0.05

Subscale: 1 = Bedtime resistance, 2 = Sleep onset delay, 3 = Sleep duration, 4 = Sleep anxiety, 5 = Night wakings, 6 = Parasomnias, 7 = Sleep-disordered breathing, 8 = Daytime sleepiness
sleep was also evident in some specific epileptic syndromes, such as benign childhood epilepsy with centrotemporal spikes or autosomal-dominant nocturnal frontal lobe epilepsy. Although our study did not demonstrate any cause-effect association between epilepsy and sleep disorders, we believe their relationship is bidirectional. Therefore, it is important to take note that children with ID and epilepsy have a higher chance to develop sleep disorders than those without epilepsy, these children should deserve more attention concerning their sleep. Management should be targeted on both the sleep disorders and epilepsy per se.

Our study failed to identify cerebral palsy as an independent risk factor for sleep disorder in children with ID, in contrast to some previous studies. This difference may be attributed to the following: Firstly, our sample consisted of a heterogeneous group of cerebral palsy, from those who could walk without assistance, to those who were bedbound. Those studies which demonstrated the association mainly focused on children with severe locomotor disability. Secondly, it may be due to different case definitions. Some studies included children with neurodegenerative disorder or those with progressive clinical course, which might not be classified as cerebral palsy in strict definition. Thirdly, incontinence care during night-time is also a cause for sleep fragmentation. This practice may be different among institutions or the boarding status of the subject.

We also failed to identify the association between visual impairment and psychiatric disease with sleep disorders. This may be due to low prevalence rates of these disorders in our sample population. In particular for visual impairment, some studies use “blindness”, defined as no behavioural responses to visual stimuli, instead. In our sample however, there was no subject fulfilling the criteria of "blindness". It was known that circadian rhythm is heavily influenced by environmental light to the eyes, so this may explain the difference in outcome between different case definitions.

**Sub-score Analysis**

CSHQ has eight sub-scores, each represents a different type of sleep disorder, including dyssomnias and parasomnias. The analysis of these sub-scores can help us delineate the contributing factors to the underlying whole picture of sleep disorder.

1. **Epilepsy and sleep-disordered breathing.** Our result corroborates other studies, showing higher prevalence of sleep-disordered breathing in those with epilepsy than their counterparts. Children with profound ID and epilepsy have been shown to have a higher risk of having sleep-disordered breathing associated with hypoxaemia at night. The underlying sleep architecture has been described. The presence of sleep fragmentation, higher percentage of slow-wave sleep and higher total cyclic alternating pattern rate have been reported. It was hypothesised that increased slow-wave activity could be caused by the influence from epileptic discharges, with relation to the thalamo-cortical activity. The use of antiepileptic drugs can also potentially worsen sleep-disordered breathing, as many of these drugs act on the central nervous system and can suppress breathing during sleep. In turn, sleep-disordered breathing can also worsen the seizure control, as it causes frequent arousal and nocturnal hypoxia, which can potentially trigger a seizure attack. Frequent desaturations causing hypoxaemia is likely to lower the seizure threshold in children with epilepsy. It was shown that treatment of sleep-disordered breathing (such as by adenotonsillectomy) could reduce the seizure frequency in some of the children with profound ID, and it was hypothesised that an improvement in the oxygen saturation could account for the seizure reduction.

2. **Epilepsy and bedtime resistance/sleep onset delay.** Our result showed that those with co-morbid epilepsy had more problem of bedtime resistance and sleep onset delay, which corroborates with a study showing children with epilepsy had these two CSHQ sub-scores higher than the control group. The disturbance of the circadian rhythm by the underlying epileptic disorder is seen to affect the sleep architecture. This may form a basis for the management strategy of this group of children, by using both medication and non-pharmacological means.

3. **Obesity and sleep-disordered breathing.** The association between body weight and sleep-disordered breathing has long been described in the literature. The proposed mechanisms include: narrowed airway (including fat deposits around the upper airway structure and increased pharyngeal collapsibility); altered respiratory mechanics (including decreased chest wall compliance and diaphragm movement); possible blunted hypercapnic ventilatory response causing abnormal ventilatory drive. These mechanisms are more pronounced in children with ID. There is also growing evidence that sleep-disordered breathing can worsen obesity, partly because of excessive daytime sleepiness causing inactivity. It also increases the risk of cardiovascular disease, hypertension, and metabolic abnormalities. Children with profound ID are more prone...
to these complications, which should be actively looked for in this population. Sleep behaviour was shown to be associated with obesity, physical activity and sedentary lifestyle in a group of adolescents with ID.99 These have to be taken into account when managing sleep disorders in this group of children.

**Limitation of This Study and Future Direction**

The relatively small sample size of this study renders the analysis of subgroup difficult. We also did not include a control group with normal population as comparison. We propose that in future studies this can be included, and the study population can be expanded, such as to include children with different levels of ID.

**Conclusion**

Sleep disorders are common among children with profound ID, and epilepsy was significantly associated with sleep disorder in this group of children. Correct identification of the sleep disorders and provision of different sleep interventions should be fundamental in the care of these children.

**Acknowledgement**

We thank MOE - Shanghai Key Laboratory of Children’s Environmental Health, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, P. R. China for providing the Chinese version of CSHQ and the scoring system.

We would also like to show our gratitude to the staff and parents of Haven of Hope Sunnyside School for their help and support.

**Conflict of Interest**

All authors declare no conflict of interest.

**References**

6. Student Enrolment Statistics. Education Bureau, Hong Kong Special Administrative Region, 2015/16.


Original Article

Socioeconomic Difference in Development Among Preschool Children

C Leung, S Leung, F Lee, SK Lo

Abstract

Introduction: This study examined socioeconomic difference in development among Hong Kong preschool children. Methods: This was a cross-sectional survey of 911 children recruited using multi-stage sampling. Child developmental outcome was measured using the Hong Kong Comprehensive Assessment Scale for Preschool Children. Socioeconomic data was collected through parent report of family income and parental education. Results: Using principal component analysis, a socioeconomic status composite was formed out of family income and parental education. Logistic regression and analysis of variance/covariance results indicated significant associations between socioeconomic status and developmental outcome. The relationship between socioeconomic status and child development was similar to a dose-response model, at population level. Conclusions: Our study, using a large sample drawn territory-wide, found an association between socioeconomic status and early childhood development, consistent with international and local studies. Scaling up evidence-based early intervention programmes at a population level could help address social inequality.

Key words Children; Development; Socioeconomic status

Introduction

Overseas studies indicate that socioeconomic difference in developmental outcomes is evident as early as the age of three. For example, welfare status was associated with less desirable parenting behaviour and poorer child outcome at the age of three while low parent education level and poverty were associated with weaker mathematical reasoning and reading at kindergarten entry and at follow-up four years later. Another study found that the association between socioeconomic status and reading at kindergarten entry was mediated by family characteristics such as home literacy environment. In a longitudinal study, socioeconomic difference in developmental outcome was found at 22 months and there was no evidence that school entry could reverse the disadvantage for the less advantaged group.

In Hong Kong, using the Chinese Early Development Instrument, a population level measure of child development, where teachers were requested to rate their students' development in various domains, it was found that among families with monthly income less than HK$8,000, around 45% of children were vulnerable in at least one domain of development. Among children from families with monthly income higher than HK$80,000, the corresponding figure was only 10%, though the association between family monthly income and vulnerability became
insignificant after controlling for child sex. Furthermore, the lowest mean scores were found among children whose mothers had lower secondary education or below, and the highest mean scores were found among children whose mothers had completed tertiary education. In another study using the Hong Kong Early Child Development Scale as an individual measure of child development, there was a significant difference in performance by family background, with children coming from middle class families performing better than those from working class families in all areas tested. In both studies, the higher proportion of girls from families with higher income and maternal education and the significant gender effect in developmental outcomes favouring girls might have confounded the association between family income and child developmental outcomes.

Furthermore, it was found that the socioeconomic gap in pre-academic learning and cognitive development was narrower for children in higher preschool grades and the authors suggested that preschools could be considered “the great equaliser”. However, as this was only a cross-sectional study, with the sample drawn from two socioeconomically discrepant districts in Hong Kong, it was not possible to draw conclusions on preschool education as a compensatory factor.

In terms of possible mechanisms mediating socioeconomic status and child outcomes, overseas studies indicated that parental involvement mediated between family income and maternal education and child academic achievement. Locally, three cross-sectional studies involving children from the same two socioeconomically discrepant districts attempted to elucidate the possible mechanisms. One study found parental involvement mediated the effect of socioeconomic status on child school readiness. Another found that children from lower socioeconomic status families had shorter sleep duration and sleep deprivation was associated with lower school readiness scores. Placement of electronic device in bedroom was associated with lower school readiness scores and this effect was more prominent among low socioeconomic status families. These studies demonstrated the effect of family socioeconomic status on child development but the studies were cross-sectional studies involving only children from two districts in Hong Kong, and the generalisability of the findings to children in less affluent or deprived areas is unknown.

The present study aimed to examine the association between family socioeconomic status and child developmental outcome. We made use of a large sample recruited for the norming study of the Hong Kong Comprehensive Assessment Scale for Preschool Children (HKCAS-P), which was randomly selected from all districts of Hong Kong, covering a range of socioeconomic status.

Methods

Participants and Sampling

The inclusion criteria were (i) the children and at least one of their parents were residents of Hong Kong and normally residing in Hong Kong; (ii) the children and their parents were Cantonese-speaking (Cantonese being the usual dialect for 89.5% of the population in Hong Kong); and (iii) the children were currently attending preschools. Children with severe physical impairment, severe hearing or visual impairment or Autism Spectrum Disorder were excluded.

A multi-stage sampling method was used. The Education Bureau (EDB) district preschool list was used as the sampling frame. In each of the 18 administrative districts, preschools were selected randomly, using a random number generator. The number of preschools chosen was proportional to the number of enrolled preschool children in the district (based on EDB statistics) which ranged from three to 12. In each selected preschool, the number of children randomly selected depended on the school size, using the class list as the sampling frame. In addition, among the 34 special childcare centres (SCCCs) in Hong Kong, one from each of the four geographical areas (Hong Kong, Kowloon, New Territories East and New Territories West) was selected by convenience sampling through contacts of the researchers. All children in SCCC have been diagnosed as having developmental delay of at least two standard deviations below the mean by paediatricians or psychologists.

In the norming study, sample size calculation was based on the confidence interval (CI) approach for norming. In local intelligence tests such as Wechsler Intelligence Scale for Children - fourth edition (Hong Kong), the length of the shorter side of the asymmetrical 95% CI of the Full Scale IQ scores vary from 4 to 7 units. To allow for a CI as narrow as 3 units on the shorter side, the number of participants needed for each of the six age groups was approximately 96. The six age groups were 3 years 4 months - 3 years 9 months, 3 years 10 months - 4 years 3 months, 4 years 4 months - 4 years 9 months, 4 years 10
months - 5 years 3 months, 5 years 4 months - 5 years 9 months, and 5 years 10 months - 6 years 3 months. The final sample required was 576.

**Measures**

The Hong Kong Comprehensive Assessment Scales for Preschool Children (HKCAS-P) is a locally developed assessment tool for individual administration to Hong Kong preschool children aged 3 years 4 months to 6 years 3 months. It consists of six Scales, namely, Cognition, Language, Social Cognition, Visual Perception, Gross Motor and Fine Motor. For each of the six age groups, age standardised scores could be obtained for each Scale with a mean of 10, and standard deviation of 3. The age standardised scores of the four former Scales could be summed to form a Mental Composite, while those of the latter two summed to form a Motor Composite. A Full Scale Composite could be obtained by summing up the age standardised scores of the six Scales. For the Composite scores, the mean is 100 and standard deviation is 15.

The Cognition Scale measures acquisition of basic concepts, from concrete and immediate, to abstract and conceptual. There are 40 items on basic preschool concepts such as colours, shapes, body parts, quantity, similarity, differences, categorisation, reasoning, and comprehension. Children are presented picture stimuli and they are required to point to the correct answer, or to provide verbal responses.

The Language Scale evaluates core language domains in Cantonese in both expressive and receptive modalities. It consists of 68 items on receptive and expressive vocabulary, receptive and expressive grammar, narrative comprehension and production. Children are presented picture stimuli and they are required to point to the correct answer, or to provide verbal responses.

The Social Cognition Scale provides direct assessment of children’s empathy, social relationships, perspective-taking ability, and understanding of social norms and rules. It consists of 29 items on social relationship with adults and peers, understanding of social norms and rules, as well as empathy and perspective taking. Children are presented picture stimuli and are required to point to the correct answer, or to provide verbal responses.

The Visual Perception Scale consists of 41 items. There are 23 items measuring abilities in form discrimination (from concrete shapes to abstract figures) and figure-ground discrimination (from daily objects to geometric forms) where children are presented with visual stimuli and required to point to the correct answer. Ten items measure spatial relationship and spatial orientation by having children copy designs with cubes and make patterns with magnetic strips. The remaining eight items measure visual motor integration by having children copy figures that consist of a combination of vertical, horizontal and oblique lines.

The Fine Motor Scale consists of 11 items on a variety of basic and complex hand skills. Children are required to perform tasks including threading beads, pasting stickers, tracing straight lines and curve lines, rotating pegs, cutting curve lines and straight lines, folding paper to form triangle, isolating fingers to form a gun, isolating three fingers, and opposing fingers sequentially.

The Gross Motor Scale consists of 15 items measuring children's competence in locomotion, balance and coordination/ball handling. Children have to demonstrate their competence in single-leg standing, walking along a straight line, tandem walk, jumping, hopping, skipping, hitting target with a ball, and bouncing and catching a ball.

Demographic information - parents of the participating children were requested to provide information such as family status, family income, and education attainment. Family income was reported in four levels: monthly income of less than HK$10,000; HK$10,000 - 19,999; HK$20,000 - 29,999; and HK$30,000 or above. The median household income in the 2011 census was HK$20,500. Parental education was reported in six levels: no formal education, primary, lower secondary, upper secondary, diploma, university or above.

**Procedures**

Research assistants (psychology graduates) contacted the selected preschools and SCCCs. Upon securing their consent to participate, students were chosen using a random number generator. Consent letters and questionnaire on demographic information were then sent to parents of the selected children. With parents’ written consent, research assistants administered the HKCAS-P individually to the selected children in preschools or SCCCs.

This study was approved by the ethics committee of the Department of Health, Hong Kong SAR Government.

**Data Analysis**

Analyses were conducted with age standardised Scale scores/Composite scores as well as developmental status as dependent variables. Children were classified into two
categories of developmental status according to their Full Scale, Mental and Motor Composite scores. Those with standard scores \( \leq 85 \) were classified as having developmental delay, and those with scores \( >85 \) were without delay. A composite score on socioeconomic status (SES) was formed by using principal component analysis with family income, maternal education and paternal education.\(^{12}\)

**Results**

**The Sample**

A total of 104 out of the 352 schools contacted consented to participate (response rate: 29.5%). The number of preschools recruited in each district was according to plan. There were 897 children (478 boys and 419 girls) recruited from the 104 consenting preschools, with a response rate of 80.8%. Another 14 children (9 boys and 5 girls) were recruited from the SCCCs; constituting 1.5% of the total sample. The final sample consisted of 911 children (487 boys and 424 girls).

The social demographic details of the sample are shown in Table 1. There was no significant difference in social demographic characteristics across the class levels (K1 to K3).

**Sex Difference in Developmental Outcome**

Independent t tests were used to examine the difference in HKCAS-P scores by sex. Results indicated a significant sex difference in Full Scale Composite score, Mental Composite score, Motor Composite score, and all age standardised Scale scores except Gross Motor Scale scores. In all cases, girls achieved higher scores than boys. The results are shown in Table 2.

Logistic regression was used to investigate the association between sex and developmental status (Composite score \( \leq 85 \) versus \( >85 \)). Results indicated a significant sex difference for the Full Scale Composite. The odds of having a child with developmental delay for the low SES group was 5.00 (95%CI: 2.22, 11.27) times more than the high SES group. The odds of having a child with developmental delay for the middle SES group was 2.60 (95%CI: 1.26, 5.36) times more than the high SES group. The results also indicated a significant SES difference for the Mental Composite. The odds of having a child with developmental delay for the low SES group was 5.79 (95%CI: 2.37, 14.12) times more than the high SES group. The odds of having a child with developmental delay for the middle SES group was 3.10 (95%CI: 1.38, 6.94) times more than the high SES group. The results were not significant for the Motor Composite.

**Difference in Developmental Outcome by Socioeconomic Status Controlling for Child Sex**

As there was a significant association between child sex and HKCAS-P scores and developmental status, analysis of covariance (ANCOVA) and logistic regression were conducted to examine the impact of SES controlling for child sex.

**HKCAS-P Scores**

After controlling for child sex, SES was significantly associated with the Mental Composite score, \( F (2, 730) = \)
Table 1  Social demographic characteristics of participantsa

<table>
<thead>
<tr>
<th></th>
<th>K1(n = 286)</th>
<th>K2(n = 307)</th>
<th>K3(n = 287)</th>
<th>Total (N = 880)</th>
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</thead>
<tbody>
<tr>
<td><strong>Number (percentage)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>146 (51.0%)</td>
<td>171 (55.7%)</td>
<td>154 (53.7%)</td>
<td>471 (53.5%)</td>
</tr>
<tr>
<td>Normal birth condition</td>
<td>265 (93.6%)</td>
<td>283 (94.6%)</td>
<td>266 (94.3%)</td>
<td>814 (94.2%)</td>
</tr>
<tr>
<td>Cantonese spoken at home</td>
<td>279 (97.9%)</td>
<td>292 (95.7%)</td>
<td>282 (98.6%)</td>
<td>853 (97.4%)</td>
</tr>
<tr>
<td><strong>Family status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuclear</td>
<td>174 (62.8%)</td>
<td>208 (68.2%)</td>
<td>190 (67.4%)</td>
<td>572 (66.2%)</td>
</tr>
<tr>
<td>Extended</td>
<td>89 (32.1%)</td>
<td>91 (29.8%)</td>
<td>86 (30.5%)</td>
<td>266 (30.8%)</td>
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<tr>
<td>Reconstituted</td>
<td>3 (1.1%)</td>
<td>4 (1.3%)</td>
<td>0 (0%)</td>
<td>7 (0.8%)</td>
</tr>
<tr>
<td>Others</td>
<td>11 (4.0%)</td>
<td>2 (0.7%)</td>
<td>6 (2.1%)</td>
<td>19 (2.2%)</td>
</tr>
<tr>
<td><strong>Marital status - married</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>259 (91.5%)</td>
<td>280 (93.6%)</td>
<td>260 (92.2%)</td>
<td>799 (92.5%)</td>
</tr>
<tr>
<td><strong>Mother education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower secondary or below</td>
<td>93 (33.6%)</td>
<td>81 (27.5%)</td>
<td>96 (33.6%)</td>
<td>270 (31.5%)</td>
</tr>
<tr>
<td>Upper secondary</td>
<td>113 (40.8%)</td>
<td>123 (41.7%)</td>
<td>112 (39.2%)</td>
<td>348 (40.6%)</td>
</tr>
<tr>
<td>Post-secondary or above</td>
<td>71 (25.6%)</td>
<td>91 (30.8%)</td>
<td>78 (27.3%)</td>
<td>240 (28.0%)</td>
</tr>
<tr>
<td><strong>Father education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower secondary or below</td>
<td>102 (37.5%)</td>
<td>83 (28.6%)</td>
<td>92 (32.9%)</td>
<td>277 (32.9%)</td>
</tr>
<tr>
<td>Upper secondary</td>
<td>91 (33.5%)</td>
<td>109 (37.6%)</td>
<td>92 (32.9%)</td>
<td>292 (34.7%)</td>
</tr>
<tr>
<td>Post-secondary or above</td>
<td>79 (29.0%)</td>
<td>98 (33.8%)</td>
<td>96 (34.3%)</td>
<td>273 (32.4%)</td>
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<tr>
<td><strong>Family income</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; HK$10,000</td>
<td>52 (20.0%)</td>
<td>39 (13.6%)</td>
<td>48 (17.8%)</td>
<td>139 (17.0%)</td>
</tr>
<tr>
<td>HK$10,000 - 19,999</td>
<td>85 (32.7%)</td>
<td>91 (31.8%)</td>
<td>81 (30.0%)</td>
<td>257 (31.5%)</td>
</tr>
<tr>
<td>HK$20,000 - 29,999</td>
<td>29 (11.2%)</td>
<td>42 (14.7%)</td>
<td>42 (15.6%)</td>
<td>113 (13.8%)</td>
</tr>
<tr>
<td>HK$30,000 or above</td>
<td>94 (36.2%)</td>
<td>114 (39.9%)</td>
<td>99 (36.7%)</td>
<td>307 (37.6%)</td>
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<tr>
<td><strong>Mother from Mainland having lived in Hong Kong for less than 7 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>75 (28.5%)</td>
<td>64 (22.6%)</td>
<td>66 (26.0%)</td>
<td>205 (25.6%)</td>
</tr>
<tr>
<td><strong>Father from Mainland having lived in Hong Kong for less than 7 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29 (11.8%)</td>
<td>18 (6.6%)</td>
<td>24 (10.0%)</td>
<td>71 (9.4%)</td>
</tr>
<tr>
<td><strong>Socioeconomic status compositeb</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>34 (15.5%)</td>
<td>26 (10.1%)</td>
<td>39 (16.5%)</td>
<td>99 (13.9%)</td>
</tr>
<tr>
<td>Middle</td>
<td>146 (66.7%)</td>
<td>166 (64.6%)</td>
<td>144 (61.0%)</td>
<td>456 (64.0%)</td>
</tr>
<tr>
<td>High</td>
<td>39 (17.8%)</td>
<td>65 (25.3%)</td>
<td>53 (22.5%)</td>
<td>157 (22.1%)</td>
</tr>
</tbody>
</table>

### Mean (95% CI)

- **Child age (in months)**: 49.53 (48.84, 50.22), 57.36 (56.86, 57.86), 68.60 (68.07, 69.13), 58.48 (57.87, 59.09)
- **Child's length of residence in Hong Kong (in years)**: 3.54 (3.42, 3.67), 4.21 (4.10, 4.32), 5.18 (5.05, 5.31), 4.31 (4.23, 4.39)
- **Mother's length of residence in Hong Kong (in years)**: 20.71 (18.92, 22.51), 22.96 (21.27, 24.64), 20.90 (19.04, 22.76), 21.57 (20.54, 22.59)
- **Father's length of residence in Hong Kong (in years)**: 30.58 (28.82, 32.35), 32.57 (31.14, 34.00), 32.65 (30.78, 34.52), 31.95 (30.98, 32.92)

---

*a31 participants did not provide information on kindergarten grade level

*bBased on 712 children with complete data on family income and parental education and kindergarten grade level
times more than the high SES group. The odds of having a child with developmental delay for the middle SES group was 2.63 (95%CI: 1.27, 5.46) times more than the high SES group. SES was also associated with developmental status as defined by the Mental Composite. The odds of having a child with developmental delay for the low SES group was 5.31 (95%CI: 2.16, 13.01) times more than the high SES group. The odds of having a child with developmental delay for the middle SES group was 3.11 (95%CI: 1.39, 6.99) times more than the high SES group. SES was not significantly associated with developmental status as defined by the Motor Composite.

### Analysis Stratified by Child Class Level

In Hong Kong, there are usually three levels in kindergartens: K1 (3- to 4-year-olds); K2 (4- to 5-year-old); and K3 (5- to 6-year-old). A series of ANCOVAs

---

### Table 2 HKCAS-P scale and composite scores (mean and standard deviation) by sex

<table>
<thead>
<tr>
<th>Scale</th>
<th>Boys (n = 487)</th>
<th>Girls (n = 424)</th>
<th>t test results and significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognition</td>
<td>9.73 (3.05)</td>
<td>10.31 (2.90)</td>
<td><em>t</em> (909) = 2.97, <em>p</em> = 0.003</td>
</tr>
<tr>
<td>Language</td>
<td>9.66 (3.03)</td>
<td>10.93 (2.90)</td>
<td><em>t</em> (909) = 3.70, <em>p</em> &lt; 0.001</td>
</tr>
<tr>
<td>Social cognition</td>
<td>9.64 (3.02)</td>
<td>10.41 (2.90)</td>
<td><em>t</em> (909) = 3.90, <em>p</em> &lt; 0.001</td>
</tr>
<tr>
<td>Visual perception</td>
<td>9.70 (3.11)</td>
<td>10.34 (2.81)</td>
<td><em>t</em> (909) = 3.24, <em>p</em> &lt; 0.001</td>
</tr>
<tr>
<td>Fine motor</td>
<td>9.36 (2.98)</td>
<td>10.74 (2.83)</td>
<td><em>t</em> (909) = 7.15, <em>p</em> &lt; 0.001</td>
</tr>
<tr>
<td>Gross motor</td>
<td>9.99 (3.12)</td>
<td>10.02 (2.84)</td>
<td><em>t</em> (909) = 0.16, <em>p</em> = 0.873</td>
</tr>
<tr>
<td>Mental composite</td>
<td>98.05 (15.41)</td>
<td>102.24 (14.20)</td>
<td><em>t</em> (909) = 4.24, <em>p</em> &lt; 0.001</td>
</tr>
<tr>
<td>Motor composite</td>
<td>97.95 (15.52)</td>
<td>102.35 (14.04)</td>
<td><em>t</em> (909) = 4.46, <em>p</em> &lt; 0.001</td>
</tr>
<tr>
<td>Full scale</td>
<td>97.74 (15.44)</td>
<td>102.60 (14.06)</td>
<td><em>t</em> (909) = 4.94, <em>p</em> &lt; 0.001</td>
</tr>
</tbody>
</table>

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### Table 3 HKCAS-P scale and composite scores (mean and standard deviation) by SES composite

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Low SES Group</td>
<td>8.67</td>
<td>8.85</td>
<td>9.06</td>
<td>9.66</td>
<td>9.64</td>
<td>10.55</td>
<td>94.22</td>
<td>100.60</td>
<td>95.81</td>
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<td>(n = 105)</td>
<td>(3.01)</td>
<td>(3.08)</td>
<td>(3.18)</td>
<td>(3.51)</td>
<td>(3.06)</td>
<td>(3.01)</td>
<td>(16.83)</td>
<td>(15.27)</td>
<td>(16.96)</td>
</tr>
<tr>
<td>(n = 468)</td>
<td>(2.95)</td>
<td>(2.93)</td>
<td>(2.97)</td>
<td>(3.07)</td>
<td>(3.02)</td>
<td>(2.92)</td>
<td>(14.88)</td>
<td>(15.04)</td>
<td>(14.94)</td>
</tr>
<tr>
<td>High SES Group</td>
<td>11.19</td>
<td>10.93</td>
<td>10.66</td>
<td>10.73</td>
<td>10.41</td>
<td>10.05</td>
<td>105.38</td>
<td>101.45</td>
<td>104.66</td>
</tr>
<tr>
<td>(n = 161)</td>
<td>(2.53)</td>
<td>(2.58)</td>
<td>(2.95)</td>
<td>(2.59)</td>
<td>(2.70)</td>
<td>(3.17)</td>
<td>(12.19)</td>
<td>(14.77)</td>
<td>(12.70)</td>
</tr>
<tr>
<td></td>
<td>=24.99, <em>p</em> &lt; 0.001</td>
<td>=16.85, <em>p</em> &lt; 0.001</td>
<td>=9.16, <em>p</em> = 0.002</td>
<td>=6.51, <em>p</em> = 0.002</td>
<td>=2.41, <em>p</em> = 0.102</td>
<td>=2.29, <em>p</em> = 0.091</td>
<td>=19.48, <em>p</em> &lt; 0.001</td>
<td>=1.19, <em>p</em> = 0.305</td>
<td>=12.71, <em>p</em> &lt; 0.001</td>
</tr>
<tr>
<td>Post hoc differences*</td>
<td>L ≠ H, M</td>
<td>L ≠ H, M</td>
<td>L ≠ H, M</td>
<td>H ≠ L, M</td>
<td>ns</td>
<td>ns</td>
<td>L ≠ H, M</td>
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<td>H ≠ L, M</td>
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<td>H ≠ L, M</td>
<td>H ≠ L, M</td>
<td>H ≠ L, M</td>
<td>H ≠ L, M</td>
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<td>ns</td>
<td>L ≠ H, M</td>
<td>ns</td>
<td>H ≠ L, M</td>
</tr>
</tbody>
</table>

*L = Low SES Group, M = Middle SES Group, H = High SES Group*
were conducted with the SES composite (3 levels) as independent variable and child sex as covariate, and aged standardised Scale scores and Composite scores as dependent variables. At K1 and K2 levels, there were significant SES differences for Cognition and Language Scales as well as Mental and Full Scale Composite scores. For K2, there was also a significant SES difference for Social Cognition Scale scores. For K1, there was a significant SES difference for Visual Perception Scale scores. The results are in Table 4.

Logistic regressions were conducted separately for each class level to examine the effect of SES on child developmental status. After controlling for child sex, SES was a significant predictor for developmental status as defined by the Full Scale Composite at K2 level. The odds

---

**Table 4** HKCAS-P scale and composite scores (mean and standard deviation) by SES composite by class level*

<table>
<thead>
<tr>
<th>SES composite</th>
<th>Scale</th>
<th>Cognition</th>
<th>Language</th>
<th>Social cognition</th>
<th>Visual perception</th>
<th>Fine motor</th>
<th>Gross motor</th>
<th>Mental composite</th>
<th>Motor composite</th>
<th>Full scale composite</th>
</tr>
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<tbody>
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<td><strong>K1</strong></td>
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</tr>
<tr>
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<td>8.58</td>
<td>8.52</td>
<td>9.02</td>
<td>9.33</td>
<td>9.50</td>
<td>10.22</td>
<td>93.01</td>
<td>99.13</td>
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</tr>
<tr>
<td>(n = 34)</td>
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<td>(2.93)</td>
<td>(3.27)</td>
<td>(3.75)</td>
<td>(3.01)</td>
<td>(2.76)</td>
<td>(16.18)</td>
<td>(14.92)</td>
<td>(16.51)</td>
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</tr>
<tr>
<td>Middle SES Group</td>
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<td>9.99</td>
<td>9.48</td>
<td>9.78</td>
<td>10.48</td>
<td>104.55</td>
<td>102.06</td>
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<td>(2.93)</td>
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<tr>
<td><em>F and p values</em></td>
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<td></td>
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<tr>
<td>K2</td>
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</tr>
<tr>
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<td>(n = 26)</td>
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<tr>
<td>Middle SES Group</td>
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<tr>
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<td>10.65</td>
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<td>(12.38)</td>
<td>(15.70)</td>
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<td><em>F and p values</em></td>
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<tr>
<td>K3</td>
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<tr>
<td>Low SES Group</td>
<td>9.64</td>
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<td>9.76</td>
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<td>10.27</td>
<td>11.19</td>
<td>99.43</td>
<td>104.53</td>
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<td>(3.01)</td>
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<td>100.03</td>
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<td>(15.34)</td>
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<tr>
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<td>(n = 53)</td>
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<td>(2.44)</td>
<td>(2.62)</td>
<td>(2.12)</td>
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<td>(10.73)</td>
<td>(14.53)</td>
<td>(11.55)</td>
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<td><em>F and p values</em></td>
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</table>

*Post hoc differences* | ns | ns | ns | ns | ns | ns | ns | ns | ns | ns |

*There were 22 children with no information on class level. They were excluded from the analyses above.*
of having a child with developmental delay for the low SES group was 6.90 (95%CI: 1.60, 29.79) times more than the high SES group. After controlling for child sex, SES was not significantly associated with developmental status as defined by the Mental and Motor Composite.

Discussion

Results of this study indicated that socioeconomic difference in developmental outcome was evident during the preschool stage, as early as the age of three. The association between socioeconomic status and developmental outcome in terms of the odds of having a child with developmental delay was similar to a dose–response relationship, at the population level. Our results are largely consistent with the overseas and local literature on socioeconomic difference in early child development.1–6 However, the two local studies were based on a small sample selected from two districts at both extremes of socioeconomic status, and there was a much smaller proportion of boys (15%) in the high socioeconomic group. The present study was based on a large sample drawn from all districts of Hong Kong by stratified random sampling, yielding even proportions of boys and girls, and covered a range of socioeconomic status. The assessment scale has been validated against appropriate instruments in the relevant domains.13,14 These allow us to generalise our results to a wide range of socioeconomic status, instead of only groups at two extreme ends.

Our study found a greater magnitude of socioeconomic difference in developmental outcome in children of K1 and K2, compared with those of K3. These results are similar to the earlier study,6 which indicated that the association between family background and child development outcome was not statistically significant in the older age groups. However, both are cross-sectional studies where age group patterns could be explained by sampling variations. Though the "equaliser" effect of preschool education is an attractive hypothesis, no conclusion could be drawn from these studies. A longitudinal study will throw more light on the equaliser effect.

Limitations

Though the sample was recruited using stratified random sampling from all districts in Hong Kong, the very modest response rate of participating preschools (29.5%) may limit its representativeness. Second, this is a cross-sectional study which does not enable conclusions to be drawn about the "equaliser" effect of preschool education. Third, as the main purpose of the original study was for the standardisation of the HKCAS-P, we did not collect data on variables related to child development such as parental employment, number of family members, parental involvement, parenting skills, home learning environment and parent-child interaction measures. Furthermore, income and education ranges instead of exact numbers were collected, as parents might consider such information too sensitive. Fourth, as the HKCAS-P was developed for Cantonese-speaking children, we only included Cantonese speakers in the study. Our results may not be generalisable to non-Cantonese-speaking groups.

Implication for Practice and Future Research

Studies indicate a robust relation between early stimulation/parental involvement and child developmental outcome2,3,8 while supportive home environment and positive parent-child interactions are important for children's development.15 However, socially disadvantaged families are less able to provide favourable parenting and home learning environment,1,3 and these parents are less involved in their children's learning at home.7,8 Early intervention programmes such as the Abercederian project and Perry Street programme have demonstrated effectiveness in improving the school readiness and long-term outcomes of children from disadvantaged backgrounds.16–18 Locally, programmes such as the Healthy Start Home Visit Programme19 and Parent and Child Enhancement Programme20 target preschool children from disadvantaged families such as low income families, new immigrant families and lone parent families, with the former catering for those in kindergartens and the latter 2-year-old. Both programmes incorporate parenting and child learning, and parents are taught strategies to support their children's learning at home. Both programmes have produced positive learning and behaviour outcomes, albeit for the short-term. Scaling up these programmes at a population level could be a step towards addressing social inequality.

In terms of research, a longitudinal study of the impact of socioeconomic status and associated family environmental factors on child developmental outcomes involving a representative sample would enable conclusions to be drawn about the developmental trajectories of children from different socioeconomic backgrounds. It could also provide stronger evidence on the mediating effects of family environment and the "equaliser" effect of preschool education.
Conclusion

Based on a large sample drawn territory wide representing a range of socioeconomic status, we found that differences in developmental outcome across the socioeconomic range was evident during the preschool stage, as early as the age of three. Our findings are consistent with international and local studies. To tackle social inequality in developmental outcomes, early intervention programmes developed and validated locally\(^{19,20}\) should be made accessible to families with a range of disadvantages.

Conflict of Interest

We declare that we have no conflict of interest.

References

Case Report

A Young Child with Locally Acquired Refractory Brucellosis

ASY Leung, WL Yu, ACH Ho, TF Leung

Abstract

Brucellosis, although not prevalent in Hong Kong, is a challenging zoonotic disease in terms of management and diagnosis. It is often overlooked and misdiagnosed in areas of low prevalence, and treatment strategy is different in paediatric population due to the limitation in drug choices and potential medication side effects. We report a 30-month-old boy with refractory brucellosis who presented with pyrexia of unknown origin.

Key words  
Brucella melitensis; Brucellosis; Pyrexia of unknown origin

Case Report

A 30-month-old locally-born Chinese boy was first referred to our university-affiliated teaching hospital with an 8-day history of high fever without any obvious focus in April 2017. His family admitted that this child fed goat and contacted goat's face in Sai Kung earlier that month. However, he had not been bitten by goats or consumed any unpasteurised milk or undercooked meat. He did not travel outside of Hong Kong in the past 6 months, and his close contacts had been well. His younger brother also fed goat on the same occasion but remained well. Child enjoyed good past health with no history of recurrent infections. His parents were non-consanguineous, and family history was unremarkable.

Patient already had fever for 4 days upon admission to a private hospital, and was empirically covered with IV Cefotaxime and oral Zithromax during his stay. Child was then referred to our unit for further care. Fever was gradually settling, but blood culture taken at private, yielded gram-negative bacilli after incubation for 8 days, and only came back positive for Brucella species on the 10th day of culture. After identification of Brucella species, child was immediately put back on a combination of intravenous gentamicin 60 mg Q24H (BW 12.3 kg, 5 mg/kg/dose) and oral co-trimoxazole 360 mg BD (Trimethoprim 10 mg/kg/day and sulfamethoxazole 50 mg/kg/day) for 10 days followed by oral co-trimoxazole 360 mg BD and rifampicin 100 mg BD (~16 mg/kg/day) for 5 more weeks. Report on the antibiotic sensitivity was delayed till the 15th day of culture, showing susceptibility to trimethoprim/sulfamethoxazole (MIC: 0.25/4.75 mcg/ml) and gentamicin (MIC: 0.5 mg/ml). Gentamicin level was sufficient (pre-dose <0.3; post-dose 10.03), and drug compliance was reported to be satisfactory. Blood culture repeated five days after commencement of antibiotics came back negative. Skeletal survey found no bony lesions. Clinically, his fever subsided and clinical condition improved.

Child presented again with fever for three days, vomiting and 'tired' feeling of his neck on the first week of September 2017. This was around 15 weeks after discontinuation of all antibiotics. Upon admission to a private hospital, he was found to have skin mottling on examination. His complete blood count, C-reactive protein and erythrocyte sedimentation rate were normal, but his liver transaminases...
were raised (ALT 185 IU/L, AST 148 IU/L). Virological workup was negative. Child was empirically covered with intravenous cefotaxime for 4 days, then changed to intravenous meropenem and amikacin in view of persistent fever. Blood culture revealed gram negative bacilli five days after admission, and later identified *Brucella melitensis*.

Child was then transferred to our hospital for further management on day 8 of illness. He had high swinging fever and tachycardia with pulse rate of 140/min despite almost 3 days of intravenous meropenem and amikacin. He was started back on **oral co-trimoxazole 360 mg BD and rifampicin 140 mg BD (BW 14 kg, 20 mg/kg/day)**, but later changed to **intravenous gentamicin 100 mg Q24H (7 mg/kg/dose)** in addition to **oral co-trimoxazole 360 mg BD** in view of deranged liver enzymes (ALT 396 IU/L) and thrombocytopenia (Figure 1). Hepatitis workup excluded hepatitis B, hepatitis C, cytomegalovirus and Epstein-Barr virus infections. Ultrasound abdomen was unremarkable and cerebrospinal fluid examination was also normal.

Blood culture on admission to our ward was also positive for *Brucella melitensis* after 5 days of incubation (Figure 2), and showed in-vitro sensitivity to co-trimoxazole (Minimal inhibitory concentration [MIC] 0.06 mg/mL), gentamicin (MIC 2.0 mg/mL), tetracycline (0.25 mg/mL) and ciprofloxacin (MIC 1.0 mg/mL). Bone marrow aspirate also isolated *Brucella melitensis*, so did repeated blood cultures taken 7 and 11 days later. Gentamicin peak levels were aimed at higher values this time (16-24 ug/ml) but remained suboptimal (pre-dose <0.3-0.68; post-dose 5.3-8.44) despite repeated increment in dosage. Antibiotics were stepped up in view of persistently positive blood cultures. Following the recovery of platelet count and deranged liver enzymes, **oral rifampicin 110 mg BD (15 mg/kg/day)** and **intravenous ciprofloxacin 140 mg Q8H (10 mg/kg/dose)** were added on days 12 and 19 respectively, while gentamicin was discontinued after 14 days. Bone scan did not show any suspicious osseous activities or occult infection, but PET scan showed a non-specific hypermetabolic focus (SUVmax 2.1) over the right sided mid-abdomen likely in the small bowel, which has higher uptake than physiological bowel activity. Patient, however, did not exhibit symptoms of gastrointestinal disturbances. Blood culture taken on day 19 was finally negative, which remained sterile after extended incubation for 21 days.

During the antibiotic course, patient's neutrophil count dropped to a nadir of 0.5x10⁹/L, which was likely to be attributed to the side effects of septrin. Neutrophil count was closely monitored, and it returned to the normal range after a week. In addition, patient developed maculopapular
rash around four days after the addition of rifampicin and before ciprofloxacin. Serum creatinine concentration also increased on week 4 of treatment to 133 mmol/L (GFR 26 ml/min/1.73m²). These features suggested possible delayed hypersensitivity reaction to rifampicin. However, taken into account the mild severity of drug rash and spontaneous resolution of his renal impairment after a week, child was continued on triple therapy with oral co-trimoxazole, rifampicin and ciprofloxacin. Follow-up whole-body CT scan after 2 months showed resolution of previous increased SUV activity at small bowel, and specifically there were no evidence of sacroiliitis and spondylodiskitis. Ciprofloxacin was off after a 4-week course, with continuation of oral rifampicin and co-trimoxazole for a total duration of 4 months after the last positive blood culture. Further follow-up 6 weeks after cessation of antibiotics has been arranged.

Discussion

*B. melitensis* is the most virulent among all *Brucella* species, which causes a severely debilitating and disabling illness. Brucellosis is transmitted from animals to humans by consumption of unpasteurised dairy products, consumption of undercooked meat, or skin penetration after contact with infected animals.¹ Our patient was likely to acquire brucellosis after direct contact with goat’s mucosa. Interestingly, his family members who have goat contact on the same occasion remained asymptomatic.

Symptoms of brucellosis may occur anytime from five days to five months after initial exposure to *Brucella species*, and should be considered as a differential diagnosis for fever of unknown origin. In situations where complications are not promptly recognised and treated, death occurs in 2% of cases of which endocarditis is the commonest cause. In addition, a high index of suspicion is required to maximise the recovery of the organism by prolonged incubation. Physicians should also be cautious about the lower blood culture yield with prior antibiotic treatment.²

Due to high relapse rate of 10-20% in patients receiving monotherapy, brucellosis should be treated with an aminoglycoside in addition to tetracyclines for 6 weeks in adults.³ ⁴ Tetracyclines are avoided in children under eight years old because of the potential for permanent staining of deciduous teeth and inhibition of bone growth. Hence, these young children could receive co-trimoxazole, rifampicin and ciprofloxacin alternatively. The use of ciprofloxacin has been limited by the potential arthropathy in young children. Cartilage and tendon damage was noticed in weight bearing joints of juvenile animals, and arthralgia is not uncommonly reported as an adverse effect after use of ciprofloxacin in children.⁹ Previous systematic reviews have shown that co-trimoxazole and rifampicin-based therapies were associated with higher rate of brucellosis relapse. This combination of co-trimoxazole and rifampicin gave undesirable result (p=0.646 for relapse,

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**Figure 2** Photomicrograph of *Brucella melitensis* showing small, gram-negative, non-motile, non-spore-forming and rod-shaped (coccobacilli) bacteria.
p=0.02 for treatment failure, and p=0.028 for the combined variable of relapse and treatment failure). This might be overcome by extended treatment duration to at least 8 weeks, or if co-trimoxazole was combined with doxycycline.6,7 This is supported by another recently published Iranian study in which clinical isolates of Brucella melitensis have decreased sensitivity to rifampicin in 35.1% of isolates, and less in co-trimoxazole (3.5%) as compared to 5 other antibiotics.10

**Conflict of Interest**

We declare that we have no conflict of interest.

**References**

Case Report
Two Cases of Paediatric Essential Thrombocythaemia with Calreticulin Gene Mutation

MMH Cheng, KFS Leung, ASC Ling

Abstract

Essential thrombocythaemia is a rare entity among the various paediatric haematological disorders. We report two symptomatic cases admitted into a regional hospital in Hong Kong. Both patients were found to have mutated Calreticulin gene at different sites. One patient has a positive family history. The patients were given anti-platelet and cytoreductive agents, as well as interferon-alpha with good clinical outcome. Our report highlights the clinical features and treatment strategies of this myeloproliferative disorder, emphasizing on the contribution of molecular investigations in the diagnostic pathway.

Key words
Calreticulin; Essential thrombocythaemia; Interferon-alpha; Myeloproliferative disorders

Introduction

Essential thrombocythaemia (ET) is a chronic myeloproliferative disorder characterised by persistent thrombocytosis. It is very rare in the paediatric population, with an estimated incidence of one per 10,000,000 children (less than 14 years old) per year. Age of presentation ranged between 0.2 to 19 years. Most patients remain asymptomatic and thrombocytosis is often detected on routine blood check. Here, we report two patients with newly diagnosed ET with different degree of severity at presentation.

Case Report

A 13-year-old Chinese boy presented to Princess Margaret Hospital, Hong Kong for sudden onset of headache, vomiting and left-sided weakness. He also had photophobia and visual aura in the form of flashes. He remained conscious and alert but was unable to walk. He enjoyed good past health. The patient’s mother reported that she was followed up for myelofibrosis by haematologists. There was no history of myeloproliferative disease in the grandparents. On physical examination the patient had left hemiplegia. Power over left upper limbs (4/5) was better than lower limbs (3/5). There was no hepatosplenomegaly. Examination of other systems was unremarkable. Ophthalmological assessment did not reveal any significant abnormality. Complete blood count showed marked thrombocytosis (2326x10^9/L) and leukocytosis (41x10^9/L). Haemoglobin was 12.4 g/dL. Peripheral blood smear showed giant platelets, occasional myelocytes and blast cells. Coagulation profile, liver and renal functions were normal. Plain computed tomography (CT) of the brain was normal. However, magnetic resonance imaging (MRI) of the brain showed multiple bilateral cerebral infarcts, most prominent over the left occipital and right frontal regions. Bone marrow examination showed hypercellular marrow with granulocytic and
megakaryocytic hyperplasia (Figure 1). Cytogenetic study was normal and the patient was negative for BCR/ABL or JAK2 V617F mutation. A diagnosis of ET complicated by cerebral infarcts was made. Further genetic study by polymerase chain reaction and direct sequencing method revealed a 4 bp deletion at exon 9 of Calreticulin (CALR) gene (Figure 2). The same mutation was detected in patient's mother in 2016. In 2010, the patient's mother was found to have thrombocytosis at the age of 31, when she presented to her general practitioner for malaise. She was subsequently diagnosed with myelofibrosis and was put on aspirin and hydroxyurea. She never developed any thrombotic or haemorrhagic complications. Germline mutation analysis using buccal mucosa and hair follicles demonstrated that the CALR mutations of the patient and his mother were somatically acquired.

The patient was started on Aspirin 100 mg on the second day of admission for acute cerebral infarcts. He was initially put on hyperhydration to lower his platelet count. As there was persistent thrombocytosis with platelet count higher than $2000 \times 10^9/L$, he was started on hydroxyurea on the second week of admission. Platelet count gradually

![Figure 1](image1.png)

Figure 1  Bone marrow aspirate (A) shows hypercellular marrow with granulocytic hyperplasia and marked megakaryocytic hyperplasia in clusters, with many large and hyperlobulated ones seen. Megakaryocytes are markedly increased in trephine biopsy (B). Many appear in tight clustering, with some hyperlobulated and hyperchromatic ones present. Para-trabecular clusters of megakaryocytes are also seen.

![Figure 2](image2.png)

Figure 2  CALR exon 9 mutation was analysed by PCR and direct sequencing method using peripheral blood sample. A 4bp deletion at c.1122_1125delGAAA is detected at exon 9 of CALR (p.K374fs*55) gene (RefSeq: NM_004343.3). The patient has the same 4bp deletion as seen in his mother, and this frameshift mutation in exon 9 of the CALR gene has been previously reported in the literature.
dropped below 1000x10^9/L one month later. Von Willebrand factor studies revealed absent ristocetin cofactor activity (VWF:RCo), markedly reduced VWF:RCo/VWF:Ag ratio at zero and preserved FVIII:C/VWF:Ag ratio (0.68). Platelet aggregation study showed diminished aggregation with high dose ristocetin and absent response to low dose ristocetin. The results were suggestive of von Willebrand disease Type 2 due to extreme thrombocytosis. After consideration, aspirin was continued as there was established thrombosis and no evidence of clinical bleeding. The patient made a full neurological recovery on discharge. Three months after diagnosis, the patient was started on pegylated interferon-alpha to replace hydroxyurea in view of the potential risks of subfertility and development of second malignancies in long-term use. The platelet count and laboratory abnormality of Type 2 von Willebrand disease normalised and the patient remained asymptomatic.

The second patient was a 17-year-old teenage girl with good past health presenting with headache, dizziness and vomiting for one week. There was transient visual disturbance involving the left temporal field of vision. Physical examination including neurological examination was normal. Plain CT scan of the brain was normal. Complete blood count showed thrombocytosis (1550x10^9/L) and mild leukocytosis (9.9x10^9/L). Giant platelets were seen in the blood smear. Bone marrow examination showed normocellular marrow with markedly increased megakaryocytes, some in cluster and hyperlobulated. Genetic study detected Type I CALR mutation, a 52-bp deletion at exon 9 (p.L367fs*46). The patient was started on aspirin and pegylated interferon-alpha. Von Willebrand factor assays also showed results consistent with Type 2 von Willebrand disease. The patient remained asymptomatic afterwards and the platelet count was in decreasing trend. Screening of the complete blood count of the parents and sibling revealed no abnormalities.

**Discussion**

Approximately one-third of paediatric patients with ET presented with headache or paraesthesia. Other clinical manifestations are mostly caused by microcirculatory disturbances. These include dizziness, syncope, visual disturbance, digital ischaemia, vomiting and abdominal pain. Splenomegaly is present in one-third of patients. Hepatomegaly is uncommon. Thrombotic complications such as cerebrovascular accidents, myocardial infarction and lower extremity venous thrombosis are rare in children but contribute significantly to the morbidity and mortality in adults with ET. Extreme thrombocytosis (platelet >1000x10^9/L) may be associated with bleeding tendency due to acquired von Willebrand syndrome (AVWS). This is characterised by the loss of large von Willebrand factor multimers and resembles a functional defect, as evident by abnormal ristocetin cofactor activity (VWF:RCo). Von Willebrand factor antigen (VWF:Ag) and Factor VIII levels may still be within normal ranges. The underlying mechanism of AVWS is unknown. Major haemorrhages are reported in up to 10% of adult patients but are rarely reported in children.

The 2008 World Health Organization (WHO) diagnostic criteria for ET required the presence of persistent thrombocytosis, bone marrow abnormalities, exclusion of other malignant or reactive causes of thrombocytosis, and the detection of clonal marker such as JAK2V617F (optional). After the discovery of the CALR mutation in 2013, it was subsequently found to be present in 67% of JAK2- and MPL-negative adults with ET. In the revised version of WHO diagnostic criteria for myeloproliferative neoplasms published in 2016, the presence of CALR mutation was included as a major diagnostic criterion for the diagnosis of ET. The CALR gene is located in the short arm of chromosome 19. Mutations are in the form of insertions or deletions within exon 9 of the CALR gene. The pathogenetic mechanism of thrombocytocytopenia involves activation of the thrombopoietin receptor (TpoR/MPL) by CALR mutants. Giona, et al. detected various types of CALR mutation in 23% of a cohort of 34 paediatric ET patients. The inheritance patterns of familial myeloproliferative diseases were largely heterogeneous. To date, no specific mode of inheritance has been described for CALR-mutated ET. It was observed in a previous study that although familial cases exist, CALR mutations were somatically acquired events in patients with ET. Given the uncertain inheritance pattern, the chance of future offspring having the same disease is uncertain. When compared to JAK2V617F-positive ET, adult patients with CALR-mutated ET tend to present at a younger age, have higher platelet counts, lower leukocyte counts and haemoglobin, and lower thrombotic risk.

The main goals in the management of ET are to prevent thrombotic or haemorrhagic complications and to improve vasomotor symptoms. Treatment of ET in adults is individualised and adopts a risk-based strategy. Patients with history of thrombosis or over 60 years with JAK2 mutation are considered to have high-risk disease.
general, anti-platelet agent such as aspirin is recommended for low-risk patients for alleviating microvascular disturbances and preventing thrombosis. Hydroxyurea has been shown to prevent thrombosis in high-risk patients and is the first-line treatment in combination with aspirin. Controversies remained regarding the potential leukaemogenicity of this cyto-reductive agent. Pegylated interferon-alpha has been shown to induce haematologic remissions and reduce mutant CALR allele burden in patients with ET. Haematological response could be maintained for more than 60 months after discontinuation of interferon. In a study on 31 patients with CALR-mutated ET, two patients achieved complete molecular remission. Their mutant clones dropped to an undetectable level after 8 and 20 months of treatment with pegylated-interferon respectively. The mutant allele was reduced, yet still detectable in 17 patients. There is currently no recommendation on monitoring of mutation burden or the duration of interferon treatment. Side effects of interferon-alpha including neutropenia, deranged liver enzymes, fatigue and diarrhea are reported but are generally well tolerated at a dosage of 90 microgram weekly. Generally, paediatric ET patients will remain stable as long as their platelet count are controlled with no thrombosis or bleeding complications. However, they should be monitored for disease evolution into myelofibrosis or leukaemia requiring consideration of haematopoietic stem cell transplant.

In summary, we described two adolescent patients with CALR-mutated ET, one of them being a familial case. Both patients had extreme thrombocytosis and acquired von Willebrand syndrome. They achieved good clinical outcome after treatment with hydroxyurea and the subsequent use of pegylated interferon-alpha. These two cases featured the relatively new CALR mutation and its diagnostic value in ET. They also provided an insight into the wide spectrum of presentation and complications associated with the condition.

Conflict of Interest

We declare that we have no conflict of interest.

References

Case Report

Papillary Thyroid Carcinoma Mimicking Miliary Tuberculosis in a 14-year-old Boy

ES Song, YY Lee, HJ Baek, E Lee

Abstract
A 14-year-old boy was referred to our hospital because of the incidental finding of numerous nodular lesions in both lungs. He had been hospitalised at a local orthopaedic department for pin removal after fixation for ankle fracture. On chest radiography for regular check-up prior to the operation, multiple nodular lesions were observed. Physical examination revealed normal results. Chest computed tomography (CT) confirmed numerous tiny nodular lesions in both lungs. Mycobacterium tuberculosis was not detected in either the sputum or bronchoalveolar lavage samples. Neck CT showed a 1.1 cm ill-defined nodular lesion with calcification in the right thyroid gland. Fine needle aspiration of the thyroid gland and multiple metastatic neck lymph nodes was performed and the histopathologic finding yielded a diagnosis of metastatic papillary thyroid cancer. He was scheduled to undergo total thyroidectomy in combination with radioactive iodine treatment. If miliary infiltrates are found on chest radiography, metastatic tumours including papillary thyroid cancer as a differential disease mimicking miliary tuberculosis should be considered to avoid misdiagnosis and delayed diagnosis.

Key words
Children; Miliary tuberculosis; Papillary thyroid carcinoma

Introduction

Miliary tuberculosis is a potentially lethal disease with high mortality. Miliary infiltrates on chest radiography indicate the possibility of miliary tuberculosis. However, other diseases mimicking miliary tuberculosis should also be considered. We report a case of metastatic papillary thyroid cancer mimicking miliary tuberculosis in a 14-year-old boy, whose lymph nodes were not palpable because of his obesity.

Case Report

In January 2018, a 14-year-old boy was referred to our clinic because of the incidental finding of numerous nodular lesions in both lungs. He had been hospitalised at
a local orthopedic clinic for pin removal after fixation for ankle fracture. On chest radiography performed during a regular check-up prior to the operation, multiple nodular lesions were observed (Figure 1A). He complained of intermittent cough without any cold sweating, weight loss, or fatigue. He was afebrile. He was obese with a height of 176.0 cm, a weight of 109.0 kg and a body mass index of 35.2 kg/m². Chest auscultation revealed no abnormal sounds. No palpable lymph nodes were present in the neck, axillary, or inguinal areas. Chest radiography and chest computed tomography (CT) revealed multiple nodular lesions in both lungs (Figure 1B and 1C). Arterial blood gas analysis revealed no hypoxemia or hypercapnia. His total white blood cell count was 8,700/µL with 66.8% neutrophils and 24.6% lymphocytes. His lactate dehydrogenase level was 840 U/L and C-reactive protein level was 0.67 mg/dL. Aspartate transaminase and alanine transaminase levels were both 21 U/L. The level of thyroid stimulating hormone was 2.12 µIU/mL (reference range, 0.4-4.8 µIU/mL) and that of free T4 was 1.07 ng/dL (reference range, 0.8-1.7 ng/dL). No respiratory virus was detected in the multiplex real-time polymerase chain reaction of nasopharyngeal aspirates. QuantiFERON and tuberculin skin tests both yielded negative results. Acid-fast bacilli smear and culture for Mycobacterium tuberculosis from the sputum yield negative results. To rule out miliary tuberculosis, bronchoscopy was planned for bronchoalveolar lavage with trans-bronchial biopsy. However, bronchoalveolar lavage was impossible because of the irritability of the patient. Acid-fast bacilli smear, culture, and real-time polymerase chain reaction for tuberculosis bacilli in the transbronchial biopsy specimen also yielded negative results. A transbronchial lung biopsy revealed chronic inflammation without evidence of tuberculosis. Because of the lack of evidence of tuberculosis, the chest CT scan obtained at the local clinic was re-evaluated and tiny calcifications were observed on the thyroid (Figure 1D). Neck ultrasonography was performed to evaluate the thyroid gland, revealing an approximately 1.4 cm ill-defined mixed echoic mass with microcalcifications in the right thyroid gland, with a 0.4 cm hypoechoic lesion. Subsequently, neck CT was performed, revealing a 1.1 cm ill-defined nodular lesion with calcification in the right thyroid gland with several enlarged contrast-enhanced lymph nodes on the right at levels II-IV and VI.

Figure 1  On the chest radiography, multiple tiny nodules were observed (A). His chest tomography showed small-sized calcifications in the right thyroid gland (B). Numerous tiny nodular lesions on both lungs were observed in both lungs (C and D).
The patient was referred to a haemato-oncology specialist. Fine needle aspiration of both the thyroid gland and lymph nodes in the neck was performed and the histopathologic findings yielded a diagnosis of papillary thyroid cancer with multiple metastatic neck lymph nodes (Figure 2). He was scheduled to undergo total thyroidectomy in combination with radioactive iodine treatment.

**Discussion**

Papillary thyroid cancer is a comparatively rare disease in children, particularly in boys and miliary tuberculosis is also rare in these days in South Korea. In the present report, we introduced a case of papillary thyroid cancer mimicking miliary tuberculosis in a boy whose lymph nodes were not palpable because of obesity.

The incidence of differentiated thyroid cancer, including papillary thyroid and follicular histologies, in children is 0.54/100,000 with an increasing trend with age, particularly in young females. The prognosis of papillary thyroid cancer is favorable; however, papillary thyroid cancer in children tends to be diagnosed at more advanced stage and is associated with high rates of recurrence with lymph node or disseminated lung metastasis. The prognosis in boys with papillary thyroid cancer is worse because of a more aggressive biological behaviour, such as larger tumour size and combined lymph node metastasis at diagnosis. Therefore, early diagnosis of papillary thyroid cancer, particularly in boys, is necessary to improve the overall survival. Although there have been few reports of papillary thyroid cancer mimicking miliary tuberculosis in men, a girl, and a boy with cervical lymphadenopathy, no previous study has reported papillary thyroid cancer mimicking miliary tuberculosis in a boy with only incidental findings of pulmonary infiltration.

Most children with papillary thyroid cancer usually present with persistently palpable lymph nodes in the neck or a growing thyroid nodule. However, no palpable lymph nodes were observed in his neck region of the patient in the present report because of obesity, and therefore the diagnosis of papillary thyroid cancer was delayed until regular work-up chest radiography was performed in preparation for surgery.

In a large-scale adult study, approximately 6.7% of patients with thyroid cancer exhibited metastatic lung cancer. However, information on the incidence of thyroid cancer with lung metastases is lacking. Lung metastasis of papillary thyroid cancer can appear as miliary patterns or multiple nodules within the lung parenchyma on chest radiography or chest CT, rarely in combination with bronchiolar involvement. In other cases, lung metastasis of papillary thyroid cancer can manifest as localised pulmonary infiltrations with lymphadenopathy and pleural effusion. As demonstrated by the present case of abnormal miliary infiltration without evidence of infection, metastatic cancer should be evaluated even in patients with age and sex distribution that are rare for this disease.

Tuberculosis is a critical infectious disease with a high global burden and high mortality. The incidence of miliary tuberculosis is 7.1-21% in developed countries. Among

![Figure 2](image)

**Figure 2** Papillary thyroid cancer cells were observed in the thyroid tissue (A) and metastatic cervical lymph nodes (B) obtained by fine needle aspiration.
South Korean children, the incidence of tuberculosis, including miliary tuberculosis, is decreasing.\(^7\) The most common symptoms of miliary tuberculosis are fever and fatigue, followed by weight loss,\(^8\) although children with miliary tuberculosis also less commonly complain of chills, night sweat, and productive cough. The patient in the present case denied fever in the preceding days and complained of intermittent cough with and without sputum. Patients with miliary tuberculosis frequently complain of fever,\(^8\) but can also, uncommonly, be apyretic.\(^9\) Instead, children with miliary tuberculosis present with peripheral lymphadenopathy and hepatosplenomegaly, although organomegaly could not be perceived in this case because of obesity.

Although some authors have denied the need for bronchoalveolar lavage in patients with lung metastasis of papillary thyroid cancer,\(^10\) atypical epithelial cells considered as metastasis can be observed in bronchoalveolar lavage specimens of children diagnosed with papillary thyroid carcinoma with miliary pulmonary metastases. In the present report, we could not detect abnormal cells in the transbronchial biopsy specimen.

In conclusion, if miliary infiltrates are found on chest radiography, metastatic tumours including papillary thyroid cancer should be considered as a differential disease mimicking miliary tuberculosis to avoid misdiagnosis and delayed diagnosis.

**Declaration of Conflicts of Interest**

The authors have no potential conflicts of interest to declare.

**References**

Case Report

Huge Iliopsoas Abscess with Delayed Sigmoid Colonic Perforation in a Child

WY CHEN, HY HO, YT CHANG

Abstract

Iliopsoas abscess is rare in childhood and reported complications include septic shock, ileus and hydronephrosis. The authors encountered such a case in a 2-year-old girl with a huge left iliopsoas abscess adjacent to the sigmoid colon, descending downward into the groin area. Delayed sigmoid colonic perforation occurred after surgical drainage of the abscess. Local inflammation of the bowel wall due to irritation by the abscess may be the pathogenesis of intestinal perforation.

Key words

Child; Colonic perforation; Iliopsoas abscess

Introduction

Iliopsoas abscess, a collection of pus in the iliopsoas muscle compartment, is rare, especially in children. It is difficult to diagnose because of its nonspecific symptoms and signs. Iliopsoas abscesses can be classified as primary or secondary. Primary iliopsoas abscess tends to occur in children and as a result of haematogenous or lymphatic seeding from distant site. Secondary iliopsoas abscess may arise via contiguous spread from adjacent structures. The treatment includes percutaneous or surgical abscess drainage and appropriate antibiotic therapy. Septic shock, paralytic bowel ileus, deep venous thrombosis, hydronephrosis, and death are reported complications. This article discusses a unique case of a 2-year-old girl with a huge iliopsoas abscess who had a rare complication as delayed sigmoid colonic perforation.

Case Report

A 2-year-old girl had had intermittent abdominal pain, fever and diarrhoea for the past three weeks. She was admitted with the above symptoms increasing in intensity and difficulty in walking over the recent week. The physical examination was unremarkable except for the abdominal examination. The lower abdomen was slightly protuberant; there was marked tenderness localised to the left lower abdomen, overlying a firm, fixed mass (10×7 cm). The haemoglobin level was 90 g/L, and total white blood cell count was 35.11×10⁹/L. The platelet count was 534×10⁹/L, and C-reactive protein (CRP) was 1326.5 nmol/L. Abdominal sonography showed left huge intra-abdominal mass. A computed tomographic (CT) scan of the abdomen showed a 90×60×180 mm irregular cystic lesion replaced left iliopsoas muscle adjacent to the left side of the sigmoid...
colon, descending downward into the groin area (Figure 1). A huge iliopsoas abscess was favoured. Empiric antibiotic therapy of cefotaxime, oxacillin and metronidazole was kept initially.

Because of the abnormal image findings, it was decided that a surgical intervention for drainage of the abscess should be performed. During the operation, sigmoid colon was found to adhere to the peritoneum (Figure 2). Two drainage tubes were inserted to the abscess-occupied cavity. Abscess culture was collected and *Staphylococcus aureus* was yielded. Vancomycin was initiated after the culture report. After operation, the drainage amount reduced gradually, and CRP also decreased to 223.14 nmol/L. Repeat surgical drainage for the abscess was performed one week later because of unremitting high fever and sonographic finding showed recurrent abscess accumulation. The intra-operative finding of second operation was oedematous change of sigmoid colon without evidence of perforation. Repeated abscess drainage and debridement was done carefully. However, some faecal-like fluid was drained out three days later after the second operation. Exploratory laparotomy was arranged and a perforation over the sigmoid colon was found. A temporary loop colostomy was made. Postoperative course was uneventful, and fever improved immediately after the operation.

Histology confirmed the diagnosis of a perforated sigmoid colon with abscess formation. On microscopic examination, it showed ulcerative intestinal mucosa with diffusely necrotising inflammation, with acute and chronic inflammatory cells infiltrating transmurally and fibrinoid substance coating on the serosa. The patient was discharged 2 weeks after surgery and her total admission period was 30 days. The operation to restore intestinal continuity was performed 2 months later. The patient continued to remain free of abdominal pain on three-year follow-up at our outpatient clinic.

**Discussion**

Iliopsoas abscess is rare and it is classified as primary or secondary, according to the pathophysiology. In children or young adults with this condition, primary iliopsoas abscess is more common, and the most common bacterial cause is *Staphylococcus aureus*.3 There is a classic triad of back pain, limp and fever, but this may only be present in 30% of cases.6 Many patients start with nonspecific features including malaise or low-grade fever, and this might progress into more specific symptoms such as flank pain or pain on movement. Most cases of primary abscess are due to haematogenous or lymphatic mechanism spread to the iliopsoas muscle. The exact pathogenesis is unknown. Some studies have suggested that transient bacteraemia may cause primary iliopsoas abscess, but primary muscle infection is still a rare condition even in children with septicaemia.7 The pathogenesis of secondary iliopsoas abscess is known as the cause of local inflammation or infection, such as septic arthritis, Crohn’s disease, appendicitis, osteomyelitis and so on. *Escherichia coli* is

**Figure 1** Note an irregular cystic lesion (arrow) took the place of left iliopsoas muscle. The intraperitoneal organs were displaced by the lesion.

**Figure 2** Note the sigmoid colon adhered to the abscess cavity.
the most common organism when its origin is from gastrointestinal or genitourinary systems.3

In the present case, the patient initially presented with fever, abdominal pain and diarrhoea, which were not specific for iliopsoas muscle abscess. The variety of symptoms made it hard for early diagnosis. The initial imaging modality for paediatric iliopsoas muscle is ultrasound, which is more convenient and a device with rapid diagnosis, and ultrasound-guided percutaneous drainage is an effective option. Abdominal sonography is also a useful tool to monitor for any recurrent abscess. CT or magnetic resonance imaging (MRI) appears more sensitive. CT could help us to clearly identify the adjacent structures and perform CT-guided drainage as well. MRI has better delineation of the area of inflammatory tissue,8 but it takes time and sedation is needed for infants or children.

Well-known complications of iliopsoas abscess include paralytic bowel ileus, deep venous thrombosis, or hydronephrosis. Reported incidence of septic shock was about 20%, and the pathogenesis may be caused by leukocyte migration and exposure of subendothelial elements associated with sepsis.9 The pathogenesis of deep vein thrombosis, including venous stasis and endothelium damage, could occur due to extrinsic compression of iliac vein and then cause venous stasis in turn.10 However, delayed sigmoid colonic perforation as a complication of iliopsoas muscle abscess has never been reported. Direct irritation due to infection that affects adjacent organs such as the sigmoid colon causing ileus then further leading to delayed perforation could be the possible mechanism.

**Conclusion**

The case report presented a relatively uncommon clinical problem in a child with iliopsoas abscess complicated by delayed sigmoid colonic perforation. The content and amount of drainage provided us with important information for possible rare complication such as intestinal perforation. Local inflammation of the bowel wall caused by irritation by the huge iliopsoas abscess might be the pathogenesis of perforation. Even though bowel perforation is rarely associated with iliopsoas abscess, it should take into consideration as a possible complication.

**Conflict of Interest**

We declare that we have no conflict of interest.

**References**

Clinical Quiz

What is the Diagnosis?

JLF Fung, VCC Hui, BHY Chung

Case History

This boy was first referred to genetics at 13 months old due to suspected vascular malformation of the left lower limb. He is twin 1 of a twin pregnancy with birth weight 3.23kg. At birth, he was noted to have non-elevated erythematous lesion over the lateral thigh and knee with no limb asymmetry. Subsequently, there was swelling of the left lower limb since 2-3 months old. Ultrasound finding is compatible with lymphangioma.

He was born from a non-consanguineous Chinese family with negative family history.

Figure 1  Clinical photo of patient at 13 months old (with consents for publication by parents).
Abstracts of Articles in Chinese

殘疾兒童母親的健康相關生活質量和抑鬱水平的影響因素

İE Şimşek, TT Şimşek, S Erel, SA Uysal. Factors Affecting Health Related Quality of Life and Depression Levels of Mothers in Families Having Children with Chronic Disabilities. HK J Paediatr (new series) 2020;25:71-78

目的：本研究旨在調查殘疾兒童母親的健康相關生活質量（health related quality of life, HRQoL）和抑鬱水平的影響因素。方法：本研究為橫斷面調查，研究對象包括來自土耳其 45 個城市的 580 個家庭。殘疾兒童母親的 HRQoL、抑鬱水平及兒童殘疾對母親的影響，採用諾丁漢健康量表（Nottingham Health Profile, NHP）、貝克抑鬱量表（Beck Depression Inventory, BDI）、家庭影響量表（Impact on Family Scale, IPFAM）分別收集有關資料。其他資料通過面對面訪談收集。結果：回歸分析顯示，日常生活照顧的時間、社會關係的中斷和應對 IPFAM 亞量表分數是 HRQoL 差和抑鬱水平高的重要因素（p<0.05）。結論：結果顯示，在日常護理外提供休閒時間，增加社會活動和提供持續的幫助以制定應對策略，可能會增加母親的 HRQoL 和降低其抑鬱水平。

關鍵詞：殘疾兒童，健康相關生活質量，家庭影響，生活質量

自閉症譜系障礙中的輔助及另類溝通：意識和語言發展干預的隨機研究


摘要：本研究使用電腦的語音輸出溝通輔助裝置（voice output communication aid device，VOCA），評估輔助及另類溝通系統對自閉症譜系障礙（Autism Spectrum Disorders，ASD）症狀、語言特徵和情緒調節的效能。一位有經驗的兒童及青少年精神科醫生根據第五版《精神疾病診斷與統計手冊》（Diagnostic and Statistical Manual of Mental Disorders fifth edition，DSM 5）、臨床觀察及隨訪，作為診斷這些兒童的指標。42 名被診斷為 ASD 的兒童（36-72 月齡）參與了這項研究。研究對象被隨機分為兩組（干預組 21 例，對照組 21 例），第一組接受輔助及另類溝通系統治療，第二組則接受常規治療。兩組的社會人口特徵相似，實驗組的部份兒童在語言接受和表達技能方面有所提高，有更好的情緒調節技能，他們的自閉症症狀有所減輕。而且，實驗組的平均話語長度和語言樣本容量均有所增加。本研究初步證明，使用電腦的語音輸出溝通輔助裝置的輔助及另類溝通系統，可以幫助 ASD 兒童發展溝通和語言技能。

關鍵詞：輔助及另類溝通、自閉症譜系障礙、情緒調節、語音輸出溝通輔助裝置
嚴重智力障礙兒童睡眠問題的危險因素


目的：通過對當地嚴重智力障礙兒童的抽樣調查，評估不同睡眠障礙的患病率並確定其危險因素。方法：這項研究調查了一所特殊學校裏有嚴重智力障礙的學生。每位學生都由其父母通過中文版的兒童睡眠習慣問卷進行評估。通過問卷評分，收集其他醫療資訊並進行分析。結果：對67名參與者的數據進行了分析。研究顯示84％兒童有睡眠障礙。癲癇患兒的總睡眠分數明顯高於非癲癇患兒（49.66±7.53 vs 45.27±6.87, p=0.02）。非寄宿學生和存在醫療問題的學生的分數也顯著較高。Logistic回歸分析顯示，癲癇與睡眠障礙顯著相關（adjusted odd ratio 7.99, p=0.02）。癲癇與睡眠時間抑制評分較高，入睡延遲和睡眠呼吸障礙有關。肥胖與睡眠呼吸障礙分數較高相關。結論：睡眠障礙在嚴重智力障礙的兒中很常見，其中，癲癇與睡眠障礙顯著相關。建議正確識別睡眠障礙，然後提供改善睡眠的不同方法。

關鍵詞：智力障礙、癲癇、腦性癱瘓、睡眠相關問題

父母社會經濟地位差異對學前兒童發展的影響


目的：本研究調查了父母社會經濟地位差異對香港學前兒童發展的影響。方法：這是一項採用多階段抽樣對911名兒童進行的橫斷面調查。兒童發展結果採用香港學前兒童綜合評估量表進行測量。社會經濟資料通過父母報告家庭收入和父母教育程度來收集。結果：利用主成分分析，社會經濟地位由家庭收入和父母受教育程度構成。Logistic回歸和方差／協方差分析結果表明，社會經濟地位和發展結果之間有顯著的相關性。在總體水平上，社會經濟地位和兒童發展之間的關係類似於劑量—反應模型。結論：我們的研究使用了全港大量樣本，發現社會經濟地位和兒童早期發展之間存在聯繫，這與國際和當地的研究一致。在群體層面擴大基於證據的早期干預計劃，可能有助於解決社會上不平等問題。

關鍵詞：兒童、發展、社會經濟地位
幼兒局部頑固性布魯氏菌病一例

雖然布魯氏菌病在香港並不常見，但在處理和診斷方面是一種具有挑戰性的人畜共患病。在低患病率地區，該病常被忽視和誤診；由於藥物選擇限制和藥物潛在副作用，兒科病人的治療方法也有所不同。我們報告一名30月齡男孩患有頑固性布魯氏菌病，並帶不明原因的發熱病徵。

關鍵詞：羊種布魯氏菌、布魯氏菌病、不明原因發熱

兒童原發血小板增多症伴鈣網蛋白基因突變二例
MMH Cheng, ASC Ling, KFS Leung. Two Cases of Paediatric Essential Thrombocythaemia with Calreticulin Gene Mutation. HK J Paediatr (new series) 2020;25:111-114

原發血小板增多症（Essential thrombocythaemia, ET）是兒科各種血液病中的一種罕見疾病。我們報告兩個有症狀的病例，在香港一所區域醫院接受治療。兩例患者在不同部位均發現鈣網蛋白（calreticulin, CALR）基因突變。一例患者有陽性家族史。這例患者接受抗血小板、細胞減少處理，及干擾素α治療，臨床效果良好。我們的報告強調了這種骨髓增生性疾病的臨床特徵和治療方法，強調了分子研究對診斷的作用。

關鍵詞：鈣網蛋白、原發血小板增多症、干擾素α、骨髓增生性疾病
14歲男孩患類似粟粒性肺結核的甲狀腺乳頭狀癌一例


一名14歲男孩因偶爾發現雙肺有許多結節性病變而轉介到本院。他因踝關節骨折而入院當地醫院，進行骨科治療，其後需取出固定針。術前常規胸片檢查發現多發結節性病變。體檢結果正常。胸部電腦斷層掃描(CT)證實兩肺許多微小的結節病變。痰液和支氣管肺泡灌洗液均未檢出結核分枝桿菌。頸部CT發現右側甲狀腺有一個1.1 cm的模糊結節狀病變伴有鈣化。經甲狀腺細針穿刺及頸部多處轉移淋巴結之組織病理檢查，診斷為轉移性甲狀腺乳頭狀癌。他計劃接受甲狀腺全切除加放射性碘治療。如果在胸片上發現粟粒性浸潤，應考慮包括甲狀腺乳頭狀癌在內的轉移性腫瘤，作為粟粒性肺結核的鑒別診斷，以避免誤診和延誤診斷。

關鍵詞：兒童、粟粒性肺結核、甲狀腺乳頭狀癌

賴文玉醫師

兒童巨大髂腰肌膿腫伴遲發性乙狀結腸穿孔


髂腰肌膿腫在兒童中很少見。已報導的併發症包括感染性休克、腸梗阻和腎積水。作者遇到一例2歲的女孩，左側巨大的髂腰肌膿腫毗鄰乙狀結腸，下行到腹股溝區。膿腫引流術後出現遲發性乙狀結腸穿孔。由膿腫刺激引起的腸壁局部炎症可能是腸穿孔的發病機制。

關鍵詞：兒童、結腸穿孔、髂腰肌膿腫

賴文玉醫師
**MCQs**

**Instruction:**
1. Please use pencil to shade the box for the best and correct answer (only one answer for each question).
2. Send back the answer sheet (see loose leaf page) to the Hong Kong College of Paediatricians. One point will be awarded to each article if ≥3 of the 5 answers are correct. The total score of the 4 articles will be 4 CME points.

(A) **Factors Affecting Health Related Quality of Life and Depression Levels of Mothers in Families Having Children with Chronic Disabilities**

1. Which of the following instruments was used to evaluate Health Related Quality of Life (HRQoL)?
   a. International Physical Activity Questionnaire (IPAQ)
   b. Impact on Family Scale (IPFAM)
   c. Nottingham Health Profile (NHP)
   d. Beck Depression Inventory (BDI)
   e. Mini-Mental State Examination (MMSE)

2. Which of the following findings was not common among families with children with chronic disabilities?
   a. High level of energy
   b. Low level of physical activity
   c. Impaired social relationship
   d. Anxiety
   e. Depression

3. Which of the following factors had a positive relationship with the level of depression?
   a. Presence of medical insurance
   b. Age of the mothers
   c. Level of education of the mothers
   d. Level of education of the fathers
   e. Duration of daily care time

4. Which of the following parameters might be a significant contributing factor to HRQoL?
   a. Level of education of the mothers
   b. The level of total income
   c. Duration of the disorder
   d. The daily care time spent on the child
   e. Age of the mothers

5. What were the recommendations for reducing the effects of children with chronic disabilities on their families?
   a. Provide financial support
   b. Support the establishment of associations and leagues
   c. Provide family rehabilitation
   d. All of the above
   e. None of the above

(B) **Augmentative and Alternative Communication for Children with Autism Spectrum Disorder: A Randomised Study of Awareness and Developmental Language Interventions**

1. In which situation is voice output communication aid (VOCA) is used?
   a. Children who follow typical development
   b. Chronically organic diseases
   c. Epilepsy
   d. Autistic symptoms, language difficulties
   e. Genetic diseases

2. Children with autism spectrum disorder have impaired communication; what could this cause?
   a. Impaired development of social communication
   b. Impaired language skills
   c. Emotion dysregulation
   d. Impaired development of receptive and expressive language
   e. All of above

3. Which is not the target area of VOCA in terms of social interaction?
   a. Requests for social routines and permission
   b. Showing off
   c. Requests for information
   d. Clarifications
   e. Eating

4. Which of the following is the system type for VOCA?
   a. Reading
   b. A touch-sensitive screen-input
   c. Hearing
   d. Medical
   e. A and C
5. How to parents participate in the therapy process?
   a. Shopping
   b. Going to the guests
   c. Taking photos
   d. Providing verbal cues
   e. Going to the zoo with their child

(C) The Risk Factors Associated with Sleep-related Problems in Children with Profound Intellectual Disability

1. Which of the following condition is classified as rapid eye movement parasomnia?
   a. Confusional arousal
   b. Difficulty in sleep initiation
   c. Nightmare
   d. Sleep terror
   e. Sleep walking

2. Which of the following description is correct concerning the use of Children's Sleep Habits Questionnaire (CSHQ) as a screening tool?
   a. Families should be instructed to consider the child's sleeping habit during illness or change of environment
   b. It addresses only on dyssomnias but not on parasomnias
   c. It can be used to diagnose a specific type of sleep disorder
   d. It is divided into 4 sub-scales
   e. It is validated and showed adequate internal consistency for both the community and clinical sample

3. Which of the following contributes to the biological basis of sleep disorders in children with intellectual disability?
   a. Altered perception of different environment (such as light-dark cycle, food schedule)
   b. Excessive physical exertion during the daytime
   c. Normal function in hormonal release (such as melatonin)
   d. Synchronised circadian rhythm
   e. Too little stimulation before bedtime

4. Which of the following description is correct concerning the association between epilepsy and sleep disorder?
   a. Epileptic seizure can affect the sleep state
   b. Sleep deprivation can lower seizure threshold
   c. The relationship between epilepsy and sleep disorder is considered as bi-directional
   d. The use of anti-epileptic drugs can potentially worsen sleep-disordered breathing
   e. All of the above

5. Which of the following description is incorrect concerning sleep disorders in children with intellectual disability?
   a. Clinicians tended to regard the use of medication as the only key to this problem
   b. Management of sleep disorders in these group of children should only focus on ways to improve the sleep architecture, without the need of treating the associated co-morbidities such as epilepsy
   c. Sleep-disordered breathing can worsen obesity in these group of children
   d. Sleep problem is often a significant source of parental stress in these group of children
   e. Use of sedatives in these group of children may potentially worsen the clinical situation

(D) Socioeconomic Difference in Development Among Preschool Children

1. Which of the following statement(s) is/are true about the validity of the present study?
   a. Both multi-stage random sampling and a high response rate have ensured the representativeness of the sample
   b. Results of the study are generalizable to all ethnic groups
   c. The "Hong Kong Comprehensive Assessment Scale - Preschool" is a locally validated individual measure of child development
   d. (a) and (c)
   e. (b) and (c)

2. In the present study, socioeconomic difference in child developmental outcome is observed in all of the following domains of the "Hong Kong Comprehensive Assessment Scale - Preschool", except:-
   a. Motor functions
   b. Cognition
   c. Language
   d. Visual perception
   e. Social cognition
3. The following conclusions about socioeconomic (SE) difference in child developmental outcome have been drawn, except:-
   a. The magnitude of SE difference in child developmental outcome is greater in the lower preschool grades (K1 & 2)
   b. Sex is an important confounder
   c. Preschool education has an "equalizer" (compensatory) effect
   d. SE difference in child developmental outcome is evident as early as 3 years of age
   e. Paternal education, maternal education and family income are components of socioeconomic status

4. Overseas and local literature on socioeconomic difference in child developmental outcome has found the following possible mediators:-
   a. Parental involvement
   b. Use of electronic devices
   c. Sleep deprivation
   d. None of the above
   e. All of the above

5. Which of the following statement(s) is/are true about early intervention?
   a. The Perry Preschool Program has evidence of efficacy in improving long term developmental outcome of disadvantaged children
   b. Local programmes, such as the Healthy Start Home Visit Programme and Parent and Child Enhancement Programme, have short term evidence of positive effect on child learning and behaviour in disadvantaged children
   c. The local early intervention programmes address both parenting and child learning
   d. Effective early intervention programmes are available for local disadvantaged children as young as 2 years of age
   e. All of the above

Answers of January issue 2020

(A) 1. e; 2. e; 3. a; 4. b; 5. c
(B) 1. e; 2. e; 3. d; 4. e; 5. c
(C) 1. c; 2. d; 3. b; 4. a; 5. c
(D) 1. e; 2. a; 3. b; 4. a; 5. c
CLINICAL QUIZ (p122) ANSWER

What is the diagnosis?

The diagnosis of our patient is Klippel–Trénaunay syndrome (KTS).

Diagnosis of KTS is often made clinically, based on the classic triad of capillary malformation (port-wine stain), venous malformation and limb overgrowth with or without lymphatic involvement (discussed below). Sometimes, patients may only present two out of three features. Radiologic evaluation such as ultrasonography and MRI used to characterise vascular anomalies; laboratory testing such as elevated D-dimer level used to identify venous malformation, are also useful in securing a diagnosis.

KTS can also be confirmed by molecular testing of the PIK3CA gene. In our patient, exome sequencing of DNA extracted from the surgical tissue revealed a somatic mosaic mutation in the PIK3CA gene (PIK3CA: p.(Asn1068Lysfs*5), level of mosaicism at 6%). It is a deletion of 11 nucleotides that shifts the reading frame of protein translation (frameshift mutation), which eventually reaches a stop codon five amino acids after the deletion (Figure 2).

Differential diagnosis of KTS includes syndromes associated with vascular malformation such as diffuse capillary malformation with overgrowth (DCMO), Parkes Weber syndrome and other overgrowth syndromes.

What is Klippel–Trénaunay syndrome?

KTS is a rare congenital overgrowth condition that affects the development of soft tissues, blood vessels and bones. There are some key features of KTS:1,2

1. Cutaneous capillary malformation, usually port-wine stains: Port-wine stains are red birth marks typically observed in KTS patients, often on the lateral aspect of the limb. They appear as flat vascular patches; the colour varies from pale pink to dark purple-red. They can be classified into geographic (irregular shape resembling a continent) or blotchy stains.

2. Venous malformation or varicose veins: venous malformation may be present during infancy but are typically more apparent during childhood. Deep venous system can also be affected.

Figure 2  A snapshot of the Integrative Genomics Viewer showing the frameshift mutation, i.e. deletion of 11 nucleotides (indicated by the black arrows) in a proportion of sequencing reads.
3. Abnormal overgrowth of soft tissues and bones: soft tissue swelling and bone hypertrophy of the limbs are commonly observed in KTS patients, which can be progressive.

4. Lymphatic malformation: lymphatic abnormalities may also be present, often characterised by presence of superficial vascular blebs in the area of geographic stains.³

Typically, these congenital malformations affect the lower extremity unilaterally, although there are cases where malformations occur in the upper or multiple extremities.

Because KTS is characterised by the above slow-flow vascular malformations of capillaries, lymphatics and veins, the term ‘capillary-lymphatico-venous malformation (CLVM) with or without overgrowth of the affected limb’ is also used instead of KTS to specify patients with all of three vascular abnormalities.⁴ Meanwhile, the term KTS is applied more broadly to include patients with only one or two vascular anomalies.

What is the genetic basis of Klippel–Trénaunay syndrome?

KTS is one of several overgrowth syndromes, including CLOVES syndrome, which were found to be associated with PIK3CA mutations. These conditions, with overlapping clinical features, are also collectively known as PIK3CA-related overgrowth spectrum (PROS).

PIK3CA encodes phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha, a regulatory subunit of the enzyme phosphatidylinositol 3-kinase (PI3K). PI3K is involved in multiple signalling pathways of cell proliferation and angiogenesis, particularly the PI3K/AKT/mTOR pathway, which is important in regulating the cell cycle. Sustained activation of this pathway has been shown to cause venous malformations due to reduced apoptosis of endothelial cells and defective recruitment of vascular smooth muscles.⁴ Activating mutations in PIK3CA could increase the enzyme's baseline catalytic activity, hence sustained activation of signalling pathways, which are also frequently implicated in human cancer.⁵

Most KTS is caused by postzygotic somatic PIK3CA mutations, meaning that the mutation occurs after conception, usually only found in the affected tissues. Therefore, for patients with disease aetiology of suspected somatic mosaicism, it is important to perform genetic testing in the affected tissues (for KTS it is usually the surgical specimen) rather than peripheral blood, which has very low or no yield of mutation. Correct sampling is the key to the molecular diagnosis.

For the same reason of postzygotic somatic mutation, parents often do not carry the mutation and their future reproductive risk of having another child with the same condition is low.

What are the complications of Klippel–Trénaunay syndrome?

Major complications of KTS include the following: ³⁶

1. Coagulopathy and thromboembolism: KTS patients often suffer from localized intravascular coagulopathy in the areas of venous malformation, thus increased risk of superficial thrombophlebitis, deep venous thrombosis and pulmonary thromboembolism.

2. Bleeding: severity of bleeding in KTS varies from within capillary stain to severe disseminated intravascular coagulation. Intrapelvic and intra-abdominal venous malformation can result in gastrointestinal bleeding, often in the rectum.

3. Chronic venous or lymphatic insufficiency: KTS patients are at risk of chronic oedema in the affected limbs resulting from venous or lymphatic abnormalities.

4. Limb length discrepancy: length discrepancy in the lower limb could have long-term functional impact, with imbalance of the pelvis leading to secondary scoliosis and impaired gait.
5. Skin infection: KTS patients, particularly those with lymphatic abnormalities, are predisposed to recurrent cellulitis and lymphangitis, which in severe cases, could progress to bacteremia.

6. Pain: pain is a common and debilitating problem in KTS patients, which is caused by multiple factors such as chronic venous insufficiency, thrombosis and infection.7

What is the management of Klippel–Trénaunay syndrome?

Management of KTS patients depends on the extent of condition and complications, which requires a multidisciplinary approach involving paediatric dermatology, orthopaedic surgery, vascular surgery and physical therapy etc. For most KTS patients, management is supportive, focusing on relieving symptoms, preventing or managing complications.1 For patients with functional limbs and few or no complications, management is conservative.

Conventional treatment of the slow-flow vascular malformations in KTS include sclerotherapy and surgical resection. Recently, the use of sirolimus (also known as rapamycin), an inhibitor of mTOR, has also been shown to be effective in KTS patients refractory to conventional treatments.4,8 For patients with varices or oedema of extremities, compression stocking, orthopaedic footwear, and pneumatic compression can also be used to control swelling and pain of affected limbs. Port-wine stains usually require no treatment other than laser therapy for cosmetic purpose.

Other medical or surgical interventions may be required depending on the severity of complications, for instance, medications to manage coagulopathy and pain, surgeries to manage limb-length discrepancies, embolic and haemorrhagic events.

References

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**Commentaries** Commentary on current topics is welcome. Length should not exceed 1,200 words; no tables or figures allowed, and references should not be more than 20.

**Clinical Quiz** The clinical quiz should be educational. It should i) include the description of a case in no more than 250 words and 3 clinical photos or figures, and ii) provide answers on the diagnosis, clinical features and findings, and management of the condition in no more than 1,000 words, 10 references, and 3 photos, figures or tables.

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1. Use Arabic numerals for numbers above nine, for designators (e.g. case 5, day 2, etc.) and for units of measure; numbers should be spelled out if below 10, at the beginning and end of sentences, and for fractions below one.
2. Manuscripts should be submitted as a Word document in British English in the following format: Typed double-spaced, page size 22 cm. x 29 cm. (8 1/2 in. x 11 in.), page margins 2.54 cm (1 in), font size 12 pt.
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For original clinical study, authors must state that the protocol for the research project has been approved by the Ethics Committee of the institution within which the work was undertaken. All investigations on human subjects must include a statement that informed consents have been obtained. Patient anonymity must be preserved. Photographs and video clippings need to be prepared to prevent human subjects being recognized unless prior written permission has been obtained. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.

The manuscript should usually be arranged as follows:

**Title page**

This page should include the full names, and affiliations of all authors. A short title of no more than 40 characters should also be given. Up to three academic degrees for each author are allowed. If an author’s affiliation has changed since the work was done, list the new affiliations as well. Limit the number of authors to 4 for case reports and clinical quiz.

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The abstract should be no more than 150 words summarising the purpose, methods, findings and conclusions. Authors should provide no more than five key words to assist with cross-indexing of the paper. Key words should be taken from Index Medicus.

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**Methods**

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**Discussion**

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**Examples of References:**

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