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MINI-SYMPOSIUM: SEVERE ACUTE RESPIRATORY SYNDROME (SARS)

Long-term sequelae of SARS in children

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Summary Severe acute respiratory syndrome (SARS) runs a more benign course in children during the acute phase. Unlike adult patients, no fatalities were reported among the paediatric SARS patients. Published data on long-term sequelae of SARS are very limited. In our follow-up study, although patients have clinically recovered from their initial illness, exercise impairment and residual radiological abnormalities were demonstrated at 6 months after diagnosis. It is important to assess these patients on a regular basis to detect and provide appropriate management for persistent or emerging long-term sequelae in the physical, psychological and social domains.

OUTCOMES

In adults, severe acute respiratory syndrome (SARS) is associated with considerable morbidity and mortality during the acute phase.[1] Worldwide case fatality rate has been reported to be 11% and ranged from 7% to 27% for the most severely affected regions.[2] The course of SARS in adults has been described as triphasic.[3] Patients are relatively stable within the first week, which is the active viral replication phase. In the second week about 80% of the patients will develop progressive pneumonic changes with increasing oxygen requirement ('immune response phase'). About 25% will develop acute respiratory distress syndrome, requiring intensive care unit (ICU) admission. The clinical course in young children is markedly different; they appear to develop a milder form of the disease than adolescents or adults. Two distinct patterns of clinical presentation are noted;[4] teenagers present with symptoms of malaise, myalgia, chills and rigor similar to those of adults, whereas younger children present with cough and runny nose and none had chills, rigor or myalgia. In the recent epidemic, no children of less than 12 years of age required ICU admission and most never developed an oxygen requirement. In contrast, some adolescents may have a more progressive course, though less aggressive than that seen in adult patients. It is also important to note that no fatalities among the paediatric age group were reported.

PSYCHOLOGICAL SEQUELAE

SARS has been perceived as a family crisis that would disrupt daily routines and take away lives suddenly. However, this crisis could be transformed and re-appraised and to some affected children and their caregivers it became a cornerstone of family resilience, cohesiveness and adaptability against hardship in the future.

We carried out psychological assessment on four SARS affected patients, two boys and two girls, aged between 7 and 13 years of age, 5 months after hospital discharge. Both patients and their main caregivers (mother in three cases and grandmother in one) underwent a semi-structured interview that was developed and based on the Resilience Model of Family Stress, Adjustment and Adaptation postulated by McCubbin and McCubbin.[5]

Psychological distress was not found in this small group of SARS affected children. Psychological adjustment and adaptation in children were associated with psychological adaptation of the family instead of the disease-related variables. The main psychological impacts can be differentiated into three domains: illness itself, period of hospitalisation and family responses.

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Psychological impacts of the illness

SARS affected children experienced less bodily symptoms and their clinical course of illness was much less severe than their adult counterparts. Many children have had similar experiences in the past when they had a cold or other 'flu-like' illnesses. As with their previous illness experience, they felt unhappy towards their weakened bodily state but did not experience any emotional distress arising from their illness.

Psychological impacts of hospitalisation

All affected children were isolated during hospitalisation and visitors (including parents) were not allowed in the SARS designated areas. All interviewed children expressed that they were afraid of being left alone but not of the disease itself. During the period of isolation, they could communicate with their family via telephone or video conferencing and all highly valued the time they spent talking to their loved ones and appreciated the parental care and support much more.

Their social support network was also affected during hospitalisation. Even though the children could not meet and play with their classmates and friends, they received lots of encouraging words and 'get well' cards that made them more aware of the importance of school life and friendship.

In the hospital the children learned to be more independent and courageous in interacting with new friends and seeking help for their own needs. Hospitalisation did in fact widen their perspectives.

Psychological impacts of family response

Parental response was found to be highly associated with the emotions and well being of the children. Family members have become more health conscientious and were more anxious about the general health of each other. The children who took part in this interview expressed that they have become more aware of the feelings and emotions of their caregivers. Both parties also expressed that family relationships improved after SARS. The children are now more willing to communicate with other family members and have learned to show empathy and concern to others in the family.

It is encouraging to acknowledge such positive psychological response from SARS affected children and their caregivers. Since this assessment was completed several months after SARS it will need a longer follow-up, with a larger sample population to assess long-term psychological effects of family response and the SARS experience on children.

RADIOLOGICAL, PULMONARY FUNCTION AND EXERCISE TOLERANCE SEQUELAE

Forty-seven serologically confirmed SARS children and adolescents, who had previously received hospital treatment for the condition, were recruited to participate in a follow-up study. Their full cardiopulmonary function (treadmill exercise test, Bruce protocol and lung function which included spirometry, lung volumes and diffusion capacity) and radiological changes, detected by high resolution computed tomography (HRCT) of the chest, were assessed at 6 months after completion of treatment. There were 21 female patients and 26 male patients; their median age was 13.6 years (interquartile range (IR): 9.9–16.0). None of the patients reported any respiratory or exercise intolerance symptoms and all had a normal clinical examination. All were ethnic Chinese and none required readmission following discharge from the hospital for SARS.

Radiological findings

Pulmonary abnormalities were detected on HRCT in 16 (34%) subjects. Abnormal HRCT findings were residual ground-glass opacification (n = 5, 31.2%), air trapping (n = 8, 50%) and a combination of ground-glass changes and air trapping (n = 3, 18.8%). All of the HRCT changes were mild. Three of the five patients who had ground-glass changes on HRCT also had evidence of fibrosis involving a small segment of a single lobe. All three cases with combined air trapping and residual ground-glass changes on HRCT required oxygen supplementation during the course of illness and two of them required ventilatory support.

Based on the presence or absence of abnormal HRCT findings, the subjects were classified into 2 groups (Table 1). There were significant intergroup differences observed in age distribution (p = 0.037), duration of hospitalisation (p = 0.048), requirement of oxygen supplementation (p = 0.003), lymphocyte count on admission and the most abnormal result during the course of illness (p < 0.0001), the need for hydrocortisone (p = 0.004) and for methylprednisolone (p = 0.003). Forward stepwise logistic regression showed that oxygen supplementation (p = 0.02) and a low abnormal lymphocyte count (p = 0.012) were the two significant factors associated with an abnormal HRCT. Both factors were markers of disease severity.

Pulmonary function findings

Thirty-eight patients underwent pulmonary function testing. Four were found to have abnormal lung function, two with a mild obstructive deficit (FEV1/FVC 78%; FEV1/FVC 79%) and two had a mild restrictive deficit (TLC and FVC 76% and 75% predicted respectively; TLC and FVC 77% and 70% predicted respectively). Of the four patients, only one who had a restrictive deficit on lung function also had a concomitant HRCT abnormality.

The pulmonary results stratified according to HRCT findings are shown in Table 2. There were no significant differences in lung function between subjects with either air

Table 1 Comparison of subjects' characteristics stratified according to HRCT results.

	Abnormal HRCT (n = 16)	Normal HRCT (n = 31)	P value
Sex (M/F)	6(37.5%)/10(62.5%)	20(64.5%)/11(35.5%)	0.078
Age (years)	14.4(13.4–16.9)	12.5(5.9–15.2)	0.037
Hospital Stay (days)	26(21–32)	21(20–24)	0.048
Duration of fever (days)	7(7–8)	7(6–8.3)	0.939
Maximum temperature (°C)	40(39.1–40)	39.2(38.6–39.9)	0.090
Oxygen supplement	7(46.7%)	2(6.5%)	0.003
Ventilatory support	2(13.3%)	0(0%)	0.101
Cough	9(60%)	17(56.7%)	1
Malaise	11(73.3%)	13(43.3%)	0.68
Chills	6(40%)	11(36.7%)	1
Runny nose	5(33.3%)	10(33.3%)	1
Myalgia	6(40%)	7(23.3%)	1
Total WBC at admission	5.3(4.2–6.2)	5.3(4.3–7.4)	0.385
Lymphocyte count at admission	0.9(0.6–1)	1.3(1–1.8)	<0.0001
Lowest recorded lymphocyte count	0.4(0.1–0.8)	0.9(0.6–1.1)	<0.0001
Neutrophil count at admission	3.9(3.2–4.7)	2.8(2.2–5.1)	0.260
Highest recorded neutrophil count	12.1(10.4–15.2)	12.5(7.8–19)	0.887
LDH at admission	480.0(270.3–738.3)	371.0(256–563)	0.533
Highest recorded LDH	752.5(401.8–957)	588.0(321.3–859.5)	0.399
CPK at admission	78.5(70.8–106.3)	92.0(67–144)	0.316
Highest recorded CPK	167.0(66.5–467.8)	243.0(88.8–355.8)	0.587
Use of systemic steroids			
Hydrocortisone	11(68.8%)	8(25.8%)	0.004
Prednisolone	14(87.5%)	20(64.5%)	0.168
Methylprednisolone	10(62.5%)	6(19.4%)	0.003

°C - degrees celcius; WBC - white blood count; Lym - lymphocyte; Neutro - neutrophil; LDH - lactate dehydrogenase; CPK - creatine phosphokinase; Numerical data: Median (interquartile range); Categorical data: frequency (%).

trapping or residual ground-glass opacification, subjects with combined abnormalities and those with normal HRCT scans.

Exercise test findings

Seven subjects were too young to perform the exercise test, and six could not achieve their peak exercise level, therefore data from only 34 patients (21 males and 13 females, with a mean (SD) age of 14.7 (2.4) years) were analysed. As a group, subjects that had recovered from SARS had lower peak oxygen consumption (VO2)/kg of body weight compared to normal controls ($p < 0.0005$). Subjects with abnormal HRCT results had significantly lower VO2/kg ($p = 0.008$), and higher ventilatory equivalent for oxygen (minute ventilation (VE)/VO_2) than those with normal HRCT results ($p = 0.048$). There was also a trend of greater impairment in exercise performance with increased HRCT abnormality.

Clinical experience and data from adult physicians indicate that SARS sequelae in other body systems are also being reported, though the extent and severity is as yet unknown. Lymphopaenia appeared to be a transient phenomenon and the cell count returned to normal within a few weeks but whether the functional aspect has also been

Table 2 Lung function stratified according to HRCT findings.

	Normal HRCT	Residual Ground Glass (GG)	Air trapping (AT)	GG + AT	P values
Numbers	22	5	8	3	
% predicted FVC	93.5 (88–101)	82 (73.3–92.3)	96 (78–108.5)	93 (73–108)	NS
% predicted FEV_1	89.5 (81–94)	82 (72.5–87.5)	90.5(74.3–102.8)	97 (79–103)	NS
FEV_1/FVC	89 (80–96)	90 (86.3–94.8)	85.5 (80–93)	97 (88–99)	NS
% predicted $FEF_{25–75}$	88 (64–111)	81 (65–94.5)	83 (57.8–107)	105 (102–126)	NS
% predicted TLC	101 (92.8–108.3)	93 (88.5–102.8)	96.5 (90.5–114.3)	96 (91–102)	NS
% predicted DLco	119 (91.5–141.5)	106 (103.8–119.8)	106 (91–125)	98 (91–102)	NS

Result: median (IR); HRCT: high resolution computed tomography of the thorax; FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; $FEF_{25–75}$: forced expiratory flow rate over the middle 50% of FVC; TLC: total lung capacity; DLco: carbon monoxide diffusion capacity corrected; NS: not statistically significant.

fully restored is unknown. Studies assessing lymphocyte subset and function will give important information on this aspect. Side effects of high dose corticosteroids such as avascular necrosis of the femoral head have been reported. Neurological and psychobehavioural problems such as lack of concentration and poor memory have also been reported by some adult patients.

In summary, despite complete clinical recovery, exercise impairment is evident at 6 months from diagnosis. Some patients have residual radiological changes. Whether such abnormalities will persist and other sequelae, especially psychobehavioural, have yet to emerge can only be answered by following-up these patients and performing comprehensive assessments on a regular basis.

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