CHAPTER II

Analyzing and Critical Review

Relationship between QOL and disease activity

Since SLE is ever changing and has long-term effects in addition to disease flare, a single HRQOL measurement may not capture the entire burden of the disease. Repeated measurements of HRQOL along with damage and disease activity assessment may be necessary to assess the impact of SLE. General physical health is one of the most compromised domains in SLE patients compared with healthy subjects. Doria A, et al showed *(39)* the relationships between general health and the number of SLE flares or the time to the last relapse, suggest that disease activity, more than disease severity or damage, represents a rapid change in the health status of adult patients. In addition, changes in SLE activity are often unpredictable in terms of flare duration as well as of possible future consequences. Joint pain, with or without a true arthritis, worsens HRQOL either because of the large amount of energy and attention required by the patient to cope with it or because it represents a persistent signal of the disease itself. Ruperto *et al.* assessed HRQOL in 297 children with SLE using the Child Health Questionnaire (CHQ) and found the most affected CHQ domains to be global health, general health perceptions, and parent emotional impact. HRQOL was impacted by both disease activity and accumulated damage, especially in the renal, central nervous, and musculoskeletal systems.*(40)*

Khanna *et al.* examined the relationship between QOL as measured by the World Health Organization Quality of Life-Bref (WHOQOL-Bref) and disease activity as measured by Mexican SLE Disease Activity Index (Mex-SLEDAI) in 73 adults with SLE. Higher SLE activity scores were significantly associated with lower QOL scores in the physical and psychological domains but not with domains of social and environmental QOL. Additionally, age or disease duration did not affect the QOL in any of the domains.*(41)*

In a cross-sectional study of 24 children with SLE, physical function (Childhood Health Assessment Questionnaire – CHAQ) significantly correlated with SLEDAI (rho=0.4, p=0.04), SDI (rho=0.6, p=0.004), and was associated with severity (p=0.03). HRQOL (Pediatric Quality of Life Inventory – PedsQL) did not significantly correlate with above parameters. Higher self-concept and socioeconomic status correlated (p=0.05) with better physical function and QOL. For 19 parents, the only significant correlation was between the SLEDAI and the Worry domain of the PedsQL Rheumatology module (rho=0.5, p=0.01).*(42)* Similar findings were reported by Jolly *et al.*, who found that the SLEDAI and Systemic Lupus International Collaborating Clinics/ ACR Damage Index are poor indicators of HRQOL of SLE patients.*(43)*

Physical functioning and limitations

SLE is associated with pain, bone aches, weakness, and stiffness, multi-systemic effects, and the necessity to comply with medical recommendations and handle increased doctors' visits. Fatigue is part of the disease experience for the vast majority of SLE patients; nearly 80% experience fatigue in adult. Fatigue tends to co-occur with a number of physical and psychological sequelae including muscle and joint pain, fever, anxiety, depression, and poor sleep quality.*(44)* Low scores of QOL are frequently observed in SLE patients, probably because some of them are forced to drastically reduce or even discontinue activities usually considered an essential part of daily life such as work, school or social relationships. Some children reflect a sound understanding of limitations, such as not being able to go out in the sun, and have developed ways of actively minimizing their effects on everyday life, such as using sunblock regularly, dressing appropriately, taking medications and keeping doctors' appointments.*(45)*

Psychological distress and coping

Considerable psychological and social adjustment is required to be able to adapt to such a highly visible, unpredictable and fluctuating disease. Karasz and Ouellette*(46)* reported that SLE negatively affected psychological well-being by causing depression and demoralization because there was impairment of role strain (i.e., inability to fulfill important social roles such as being a wife, mother or working outside the

home). Feelings of uncertainty about the illness, pain and fatigue were domains that patients identified as central to their illness experience. In the cross-sectional study by Dobkin *et al.*, problem-focused coping has been found to be a predictor of low levels of depression, whereas emotion-focused coping has been associated with poorer mental and physical health.*(15)* In the less active state, predictors of better mental health were less stress, less emotion-oriented coping and more task-oriented coping whilst better physical health was predicted by less stress and younger age. In a more active disease state, better mental health was predicted by more education and less emotion-oriented coping whereas better physical health by more emotion-oriented coping.

Children seem to employ different mechanisms to handle SLE. Some focus on their shift in attitude due to SLE, specifically their appreciation of 'the little things in life'. Some reflect the severe emotional impact of SLE, specifically feelings of intense sadness, strong hatefulness towards the disease. SLE significantly and continually evokes anxieties and fear in children about their future, particularly in relation to possible worsening or persistence of disease, shortening of life span, potential effect on progeny, worry about having a family at all, rethinking career goals, and the overall effect upon their life. Some responses evidence a tendency to take control despite the disease affliction.*(45)*

Impact on social and family relationships

Goodman D, et al*(47)* performed the qualitative interviews in 32 adult women who mostly reported many psychological consequences, including relationship breakdowns; loss of the desire and/or ability to form relationships and have children; inability to achieve life goals; feelings of depression and a sense of hopelessness about the future; loss of self-confidence and self-esteem; having to lower personal standards; worry about what other people think; and increased fear and/or loss of adventurous spirit. Almost two thirds of the patients stated that they believed their illness had affected their family and friends. The consequences reported fell into one of four categories: worry about the person with SLE, concerns about the hereditary nature of SLE, having to change activities to accommodate the limitations of the person with SLE, and having to provide physical care for the person with SLE.

Lash*(19)* found that quality of life in SLE was most severely affected by disturbances in alertness and cognitive ability, followed by decreased ability to enjoy and participate in leisure activity. The patients framed their life experiences around the ever-present fatigue that formed a backdrop to their lives and interfered with their ability to enjoy time with family, fulfill role expectations, and, at times, maintain a job.[48] People with chronic health problems resulting in observable physical changes, like SLE, may experience difficulties with their body image and socially perceived attractiveness. Psychological well-being may be damaged by the experience of shame as a result of perceived personal shortcomings. People experiencing shame may see themselves as inferior, flawed and rejectable. Feelings of shame may be associated with disengagement from or avoidance of social interaction and the need to 'disappear' or hide away from others due to the negative impact on self-esteem. Physical disfigurement (such as that arising from skin rashes seen in SLE) resulting in feelings of shame, may also have a negative effect upon physical health and adherence with health-related behaviours.*(49)*

Some children identify social integration, specifically with friends, family and school, as an essential component affected by SLE. The responses imply that in order for these children to handle their disease in a social context, it is crucial for them to be included in activities, and have understanding from family and friends of the limitations imposed upon them by SLE. Their responses reflect awareness of limitations, associated with sadness, a sense of awkwardness due to weight gain secondary to steroids, and the need to wear specific dress ('long sleeves and long pants') when going out.*(45)*

Education, socioeconomic status and quality of life

Candell Chalom et al.*(50)* investigated the vocational and socioeconomic status and quality of life in 64 adults with childhood-onset SLE who were followed for a mean of 13.6 years. Approximately one-third of the patients thought that the disease interfered with their education. Only 25% had full-time employment, and 22% had part-time jobs; the overall income was low. These figures were lower than those reported in patients with juvenile idiopathic arthritis (JIA).*(51)*

Tool measuring HRQOL, QOL and health status

The PedsQL-Generic module version 4.0, a valid and reliable descriptive measure in the form of a brief, easily administered questionnaire, is designed to assess QOL in healthy and sick children between ages two to 18 years.*(52)* The version includes both child- and parent-reports with separate language-adjusted formats for different ages. The PedsQL-Rheumatology module 3.0, formatted similar to the Generic module, comprises of five domains: pain and hurt, daily activities, treatment, worry, and communication.*(53)* Only the domain scores, not the total mean score are reported, thereby limiting its use in pediatric rheumatic studies where sample sizes are often small. The recently developed PedsQL Multidimensional Fatigue Scale with child and parent reports distinguished between healthy children and those with rheumatic diseases and was found to be preliminarily reliable and valid in children seen in the pediatric rheumatology clinic.*(54)* The PedsQL generic, rheumatology and the fatigue scales in conjunction with one another may be suitable for the measurement of QOL in children with rheumatic diseases.

Several QOL scales that are adapted from the adult scales may not account for children's developmental stages that affect cognitive function, autonomy, body image and recall. A widely used global health status measure in children is the CHQ, which was derived along the lines of the SF- 36, a health status tool, and includes domains adapted for children.*(55)* Although there are parent- (for children over five years of age) and child-reports (over 10 years of age), they are not parallel. The CHQ is valid, reliable and has been found to be responsive to clinical changes in children with JIA.*(55, 56)* It has been used widely as a health status measure and is being adapted cross-culturally in different countries.*(55)* The domains of the CHQ are as follows: general health, physical functioning, role/social limitation-emotional/behavioral, role/social physical, bodily pain, behavior, general behavior, mental health, self esteem, general health perceptions, change in health, parental impact emotional, parental impact time, family activities and family cohesion. Although these domains are relevant for all children including those with SLE, further testing is necessary. However, due to the lack of parallel versions and child-report for ages under 10 years, and focus on health status,

additional measures may be required in order to obtain sufficient information to measure global QOL.

The CHAQ is the most extensively administered measure of physical function in children with rheumatic diseases and is modified from the Health Assessment Questionnaire (HAQ).*(36)* The CHAQ comprises brief, easily administered, parallel child- (aged eight to 19 years) and parent-reports (aged two to 19 years), with the chief areas of focus being disability and discomfort. The 30 items estimating disability refer to problems or limitations in the prior week due to illness. The CHAQ was found to be reliable and valid; studies are mixed when addressing its responsiveness.*(36, 57)* The CHAQ is a widely employed functional assessment tool in diverse studies of children with arthritis and has been cross culturally adapted and translated into different languages.*(55)* The minimal clinically important change has been determined for the CHAQ scores to enable prospective follow-up of physical function in children with JIA. CHAQ is additionally valid, reliable, and sensitive to clinical change in children with idiopathic inflammatory myositis.*(58)* The CHAQ may be a useful measure of physical function in children with SLE with avascular necrosis, severe arthritis or fatigue.

The EuroQOL, a generic health utility index widely used in adult studies has demonstrated validity in assessing children with JIA.*(59)* The TNO AZL Children's Quality of Life questionnaire (TACQOL) is a generic QOL instrument in children aged six to 15 years limited by lack of validity in older and younger children.*(60)* This questionnaire assessed the domains of pain and symptoms, basic motor functioning, autonomy, cognitive functioning, social functioning, global positive emotional functioning, global negative and emotional functioning, many of which are affected in children with chronic diseases such as SLE. Quality of My Life Visual Analog Scale has been used for measuring the overall QOL in older children, but the discriminant validity of visual analog scales in young children is questionable.*(61)*

Most of the disease/system-specific instruments such as the Juvenile Arthritis Quality of Life Questionnaire (JAQQ), Childhood Arthritis Health Profile (CAHP), Juvenile Arthritis Functional Assessment Scale (JAFAS), Juvenile Arthritis Functional Assessment Report (JAFAR) and Juvenile Arthritis Functional Status Index (JASI) are developed for

children with arthritis.*(37,62-64)* They may be used to measure the effect of musculoskeletal involvement in children with SLE with severe arthritis where physical function is compromised but they may not adequately assess all aspects of health in children with SLE. There are currently three SLE-specific scales for adults published in the literature: the SLE Symptom Checklist (SSC)*(65)*, the SLE-specific Quality of Life instrument (SLEQOL)*(66)* and LupusQoL*(67)*. The SSC is a useful list of 38 symptoms and their perceived burden to the patients. Because the SSC is purely a symptom scale, the authors concede that it does not evaluate HRQOL in a comprehensive manner. The SLEQOL is an SLE HRQOL measure and its items were derived from health professionals and were subsequently verified by patients who may have been reluctant to challenge the health professionals' ideas. Some of the domains (physical function, pain, burden) are less comprehensively assessed in the SLEQOL than the LupusQoL which comprises of the questions concerning the prognosis and course of disease, body image, effects of treatment, emotional difficulties, inability to plan due to disease unpredictability, fatigue, pain, career prospects and loss of income, memory loss/concentration, reliance on others to assist with everyday tasks, and pregnancy. The SLEQOL contains no items related to body image, which is an important aspect for patients.*(68)* The SLEQOL provides a global score and the LupusQoL provides a profile of domain scores. Both instruments are validated for English- speaking patients in different cultures: the SLEQOL in a Singaporean Chinese population, and the LupusQoL in a predominantly British white population.

A novel pediatric SLE-specific QOL tool titled, Simple Measure of the Impact of Lupus Erythematosus in Youngsters© (SMILEY©) was developed in North America to reflect QOL issues in children with SLE in pediatric practice, and domains of relevant QOL and HRQOL.*(38)* Qualitative research was conducted in children with SLE and their families that yielded important information regarding critical domains affecting QOL in children with SLE.*(45)* Concepts derived from children's responses were categorized as follows: limitations, impact of/on social and family relationships, effect on self and fear of future and long term goals. Concepts derived from the parents' responses were as follows: psychological, accommodating disease, shifting expectations, social support,

worry and medical care. These categories were modified into domains. SMILEY© has parallel child and parent reports five faces-scale for responses. SMILEY© is a valid, reliable and internally consistent pediatric SLE-specific QOL scale.*(38)* However, the questionnaire may be inappropriate for Thai adolescents because of the cultural differences. The indices of the HRQOL in Thai adolescents with SLE have never been evaluated. Of total 26 questions in SMILEY©, there was one about going to school and another about the activities at school which should not be relevant to some adolescents who stop or hold their schooling.