Review Article

Evolution of diabetes management in the 21st century: the contribution of quality of life measurement in Asians

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Diabetes mellitus (DM) is a complex and chronic disease with multiple complications leading to increased mortality and poor quality of life. Current studies have shown that lowering glycosylated haemoglobin (HbA1c) confers protection against microvascular complications. However, with more intensive glucose control to achieve HbA1c of less than 6.5%, there seems to be a significant increased risk of mortality and cardiovascular events. The current recommendation worldwide is for “tailoring” of DM management to risk and also quality of Life (QOL) which is a crucial component in determining the success or failure of DM management. In Asia, DM has become a health crisis but there is a lack of QOL assessment tool that is specific for Asians with wide spectrum of ethnicity, languages, religions and socio-economic differences. In this review, we discuss the evolution of DM management over the decade and the issues pertaining to QOL among people living with diabetes in Asia.

Key Words: quality of life, Asians, diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) is a chronic condition associated with multiple complications even at the point of diagnosis. In 2003, the Hoorn Screening Study in the Netherlands reported the following at the point of diagnosis: retinopathy (7.6%), impaired foot sensitivity (48.1%), microalbuminuria (17.2%), myocardial infarction (13.3%), ischemic heart disease (39.5%) and peripheral arterial disease (10.6%). This clearly indicates the insidious onset of organ damage even before diagnosis of DM. Since 1986, glycosylated hemoglobin (HbA1c) has become the standard for assessment of DM control and by 2006, the gold standard for diagnosis of DM. However, guideline recommendations for target HbA1c level still vary across the globe. The UK Prospective Diabetes Study (UKPDS) started in 1977 showed that over 10 years, a difference of HbA1c of 0.9% between the intensively treated versus the conventionally treated group decreased the risk of microvascular complications by 25%; however, no difference was observed for macrovascular complications. The UKPDS also found that for every 1% reduction in mean HbA1c, there was a corresponding 21% reduction in DM complications, 21% reduction of deaths related to DM, 14% reduction of myocardial infarction and 37% reduction of micro-vascular complications. The Kumamoto study found that among Japanese with Type 2 DM on insulin therapy, intensive treatment achieving a mean HbA1c of 7% delayed the onset and progression of microvascular complications. In the Diabetes Control and Complications Trial (DCCT) conducted on subjects with type 1 diabetes for 6 years, a reduction of HbA1c by 2% between the intensively treated to conventionally treated group showed a significant reduction in risk of diabetes complications of about 60%. These studies indicated a strong correlation between improvements of glycemic control as assessed by HbA1c to reduction of diabetes complications.

Post UKPDS follow-up study of 10 years found that the reduction of risk in developing complications remained lower in the intensively treated group compared with the control group despite similar HbA1c levels. Similarly, the EDIC study that followed up subjects with type 1 diabetes post DCCT trial concluded long-term reduction of cardiovascular risk in the intensively treated group despite worsening of the glycemic control comparable to controls. This “legacy effect” or “metabolic memory” threw the diabetes management into a glycemic frenzy stage to reduce HbA1c below 6.5% in order to reduce complications and cardiovascular events. Contradicting the risk reduction results, the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study found that lowering the HbA1c level to less than 6.5% significantly increased the mortality and cardiovascular events in people with type 2 DM. Similar studies to intensive...
ly lower HbA1c have yet to show any beneficial effect of lowering the HbA1c level below 6.5%. Thus, current guidelines support early diagnosis and treatment of DM with ‘tailoring’ of treatment modalities to target glycemic control. DM management “tailoring” is a broad concept involving multiple factors such as duration of disease, symptoms, presence of complications, age, glycemic control, treatment satisfaction, socio-economic background and etc. How do we judge if the management modality is suitable or is the best for the patient? Besides “chasing” after the HbA1c levels, it is important to consider the well being of the patient reflected by the quality of life (QOL).

The impact of diabetes on QOL was elaborately explained by the UKPDS study group between 1977 and 1991 when they performed two cross-sectional studies of patients enrolled in randomized controlled trials of intensive blood glucose control versus conventional control group and tight blood pressure control versus less tight control group. QOL was affected by DM complication but not by the treatment regime. In the United States, a medical survey found that QOL decreased in relation to the number of complications. Male gender, longer duration of DM and patients on insulin regime tended to have a poorer QOL. The American findings were supported by a study in Netherlands suggesting that insulin therapy, obesity and complications of diabetes were associated with poorer QOL regardless of age and gender. The findings are interesting but it is crucial to note that QOL is subjective and is perceived differently by different populations. In both studies a general QOL tool was used which could lead to reduced sensitivity and data loss. A diabetes specific tool would provide a better reflection of QOL. The tool used to measure QOL is also important to ensure accurate data capture. We will discuss QOL in the Asian context, addressing the perception, similarities, differences and the gap in detailed.

**DIABETES IN ASIA**

Asia is divided into 5 regions. Central Asia consisting of Kazakhstan, Kyrgyzstan, Tajikstan, Uzbekistan, Turkmenistan and Xinjiang of western China. The main religions are Islam and Buddhism. East Asia consists of China, Taiwan, Hong Kong, Japan, South Korea and North Korea. The main religions are Confucianism, Buddhism and Christianity. North Asia is made up of Russia and Mongolia with most of the ethnic groups being composed of nomads. South Asia consists of Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka. The main religions are Hinduism, Buddhism, Jainism, Sikhism, Islam and Christianity. South East Asia consists of Burma, Thailand, Laos, Cambodia, Vietnam, Indonesia, Malaysia, Singapore, East Timor, Brunei and the Philippines. The main religions are Islam, Buddhism, Christianity, and Hinduism. South East Asia also has a lot of Western influence due to the legacy of colonialism. West Asia consists of Middle Eastern countries from to Yemen. The predominant religion is Islam.

DM, previously a disease of the West, has now rapidly become a health crisis in Asian countries. The International Diabetes Federation predicted that the number of individuals with DM would increase from 366 million in 2011 to 552 million in 2030. The greatest increase will be contributed by West Asia, India and China. The chronicity and complications of the disease threaten the economic growth of developing countries as the global healthcare expenditure for DM is expected to hit USD490 billion in 2030. A big challenge for Asia is the vast differences in ethnicity, cultures and socio-economic development within Asia, which can affect the clinical presentation, management, prevention of DM and perception of QOL. The Asian population is more diabetogenic compared with the European population. Asians tend to develop DM at a younger age, at lower body mass index and with lesser weight gain. Asians have a greater tendency for abdominal obesity resulting in increased insulin resistance. Another contributing factor is the shift in lifestyle and dietary habits consistent with the rapid economic development experienced by many developing nations in Asia. The many different religions in Asia need to be considered when designing a tool for assessing QOL for Asians as spirituality, religion and personal beliefs are highly correlated to psychological and social domains of QOL. Special attention to ethnicity and language is particularly important in the assessment of QOL not only due to the subjectivity but also the cultural framework essential to the construct.

**WHAT IS QUALITY OF LIFE?**

Quality of life (QOL) is defined by the Constitution of the World Health Organization (WHO) as “an individual’s perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards and concerns”. QOL is an expansive ranging concept that can be affected by the individual’s physical health, psychological state, level of independence, social relationships, personal beliefs and relationship to salient features of his/her environment. The current shift of diabetes care from the traditional “glycemic oriented” to a more “holistic patient care” has made QOL an important outcome measure for interventions, making its accurate measurement crucial. Measurement of QOL also provides a mean for measuring the cost impact of medical interventions from the health economic point of view. DM being a chronic disease, can significantly impact the QOL due to its many complications and to date is still a major cause of mortality, morbidity and high health care expenses. People living with DM often endure great stress, both physically in terms of therapy and psychosocially, which can affect the self-care behavior, glycemic control and QOL.

**IMPACT OF WESTERNIZATION IN ASIA**

In Asia especially South East Asia, there is a strong element of Western culture influence or westernization likely due to the history of colonialism. Westernization represents a lifestyle or behavioral approach to health in epidemiology. DM is considered to be one of the diseases associated with westernization. In an extensive review by Fujimoto in 1992, it was reported that there was a higher prevalence of DM among migrant Asians than in their homeland. This review summarized many of
the prevalence studies of DM in migrant Asian populations as well as in their countries of origin. This strengthens the point that as Asia becomes more westernized; insulin resistance and glucose intolerance will become more common. Westernization is linked to globalization and with globalization and economic growth there is a nutrition shift to high consumption of processed food, increased calories and a more sedentary lifestyle. The combination of excessive calorie intake and reduced energy output leads to increased obesity and insulin resistance.

QUALITY OF LIFE: THE ASIAN PERSPECTIVE
The developments of QOL assessment instruments were not prominent until the late 70’s in North America and Western Europe. Since then, the evolution of QOL measuring instrument development has produced countless well-established and internationally recognized tools. In Asia however, there is a lack of a QOL instrument(s) specifically focused on the diverse ethnic, language, culture, education level, religion and structures of medical care. In view of this complexity, many researchers in Asia chose to translate and adapt instruments developed in Western countries rather than developing a new tool. The question lies in the ability of these translated or adapted tools in accurately reflecting the QOL in the complex Asian population. These well recognized tools including the Appraisal of Diabetes (ADS), Audit of Diabetes Dependent Quality of Life (ADDQoL), Diabetes Health Profile (DHP), Diabetes Impact Measurement Scale (DIMS), Diabetes Quality of Life Measure (DQOL), Diabetes-39 (D-39), Diabetes Specific Quality of Life (DSQOLS), Questionnaire on Stress in Patients with Diabetes Revised (QSD-R), the Well-being Enquiry for Diabetics (WED), Medical Outcome Study Short Form 36 (SF-36), and the World Health Organization Quality of Life Brief Questionnaire (WHOQOL-BREF). These QOL tools were all developed based on the American or European populations. Most of the development process involved focus group discussions to analyze the domains of QOL perceived as important in that population or group of individuals. In the recent years, there is increasing apprehension on the quality of the translation process in the adoption of QOL instruments. The concern is mainly focused on the loss of cultural differences during translation and the assumption that perception of QOL remains unchanged across different population. A critical systematic review of the translation and adaption process of generic QOL measures in Africa, Asia, Middle East, Eastern Europe and South America indicated that among the QOL tools studied including WHOQOL, SF-36, and Euro QOL (EQ5D), only 24.2% of these tools measured local applicability of QOL. The majority of these tools are eager to accept confirmation of validity and reliability as proof of suitability for use in target population without consideration of item equivalent and cultural applicability. Alice Cheng et al in 1999 have provided an excellent example in developing and adapting the Diabetes Quality of Life (DQOL) measure in Chinese population with DM. In this study, a focus group interview of ten elderly Chinese with type 2 DM was undertaken to gain their insight of the DQOL measure. Amendments were made based on the discussion to make the DQOL more culturally appropriate. The first adjustment was the addition of 2 questions on food and eating habits that was deemed important by the focus group. The second was the deletion of two questions on sex life that was considered a taboo subject by the focus group. This new tool is good but there are still a few points that needed highlighting. Firstly, mainly elderly Chinese patients formed the focus group and perhaps because of the age factor, sexual relationships may not be an important factor in determining QOL. This cannot be applied across the different age groups with DM who are sexually active and should be considered before removing this component on sexual relationships. Secondly, it has been well established that diet and food is a major component for Asians especially Chinese, and the addition of 2 questions on food and eating was a positive move by the group albeit not sufficiently reflecting the impact on life satisfaction and QOL. In view of the importance placed on diet and food, more in-depth questions should be allocated.

The best solution to overcome the issue of cultural difference lost in translation is by performing equivalence studies in countries with a significant proportion of residents who are proficient in English and their mother tongues. Countries such as Malaysia, Singapore, Indonesia, Brunei, Hong Kong and Philippines are the most suited, as both versions of the measurement (English and Asian) can be compared within the same social environment and population. A crossover trial involving these bilingual subjects can further strengthen the psychometric properties of the instrument including construct validity. A crossover trial would mean that the same subject who is proficient in English and the translated language is given both sets of questionnaires to answer and this will show if there are any discrepancies between the two languages. A population-based study was previously conducted in Singapore and found that ethnicity remained an important factor influencing QOL in a multi-ethnic sample of Asians with diabetes independent of age, gender and education. However, in this study, the Indian ethnic group was over represented with 47% versus 27% Chinese and 24% Malay. The research question is whether there are any differences across ethnicity and preferred languages with respect to QOL. More studies on multi-lingual Asian populations and perception of QOL are needed. It is undeniable that the Western and Asian population do share commonalities in the domains of physical health, social relationships and life satisfaction. However, the differences in preferences and ranking (i.e. which component of the QOL is more important than others) of certain domains such as social relationships, economic well-being and eating habits must be taken into consideration when adapting or developing a new tool for the different populations in Asia.

REVIEW OF EXISTING QOL MEASURES
A good example of a valid and reliable generic QOL measurement tool would be the World Health Organization’s WHOQOL-BREF questionnaire. This is an abbreviated 26-item version of the WHOQOL-100, which analyzes domains of physical, psychological, social and envi-
population with different degrees of westernization and food habits. Some of the questions are worded in a way that is not commonly used in the local context of various Asian countries and region and hence may be confusing to the subjects. Some choices of answers were based on a Likert scale of 1-6 with choices such as ‘all of the time’, ‘most of the time’, ‘a good bit of the time’, ‘some of the time’, ‘a little of the time’ and ‘none of the time’ were misleading and difficult to differentiate.

The Diabetes-Specific Quality of Life Scale (DSQOLS) comprising 64 items on individual goals, satisfaction and perceived burden of DM was originally developed in Germany. The DSQOLS was affirmed to be a valid and reliable tool as it was able to distinguish between patients with different treatment and detect social inequities. The questionnaire was validated based on patients with type 1 DM; hence, this instrument may not be suitable for people with type 2 DM.

ASIANS AND THEIR EATING HABITS

Why are food and eating habits so important to Asians? In Asia, food and eating have complex meanings and implications for different population but in general the activity of eating is viewed in the context of social bonding and interaction, good health, valued leisure activity often involving close friends and family members. This culture is not only practiced in Asian countries but also strongly rooted in Asian populations living all over the world. This preoccupation with food and eating has led to formation of a strong bond between the ability to eat freely, freedom to participate in such social rituals and life satisfaction. The importance of food is reflected in some Asian cultures for example in Chinese, Taiwanese, Malaysia, Singapore, Indonesia, so much so that when they meet they would usually greet each other with “Have you eaten?” instead of the Western way of “How do you do?” or “How are you?” It is thus crucial to include this component when assessing the QOL of Asians. There are differences in the diet of various Asian region and population versus the Western diet. Generally, Asian populations consume a much higher proportion of carbohydrates that are high in glycemic index such as white rice, noodles and white bread compared with non-Asian populations. This has a detrimental effect on diabetes prevalence and diabetes control as Asians tend to store more fat in the body than individuals in the West. Food and eating habits so important to Asians?

The Revised Diabetes Quality of Life Clinical Trial Questionnaire (DQLCTQ-R) was developed for use in both type 1 and type 2 DM. This questionnaire is a result of focus group and expert discussions across Canada, France, USA and Germany. The strong point of this study is that the validation process is done using the data from clinical trials. This longitudinal data collection appropriately addressed the issue of responsiveness to change that has been understudied in the past due to the cross-sectional method of data collection. The revised version of the questionnaire contains a total of 57 questions addressing 8 domains such as physical function, energy, health distress, mental health, satisfaction, treatment flexibility, treatment satisfaction and frequency of symptoms. It is extremely challenging to develop a QOL assessment tool that can be used accurately and satisfactorily in both type 1 and type 2 DM due to the differences between the two. The DQLCTQ-R is a valid and reliable tool that can be used in both types of DM but in our assessment, the questionnaire may not be suitable in the diverse Asian population with different degrees of westernization and food habits. Some of the questions are worded in a way that is not commonly used in the local context of various Asian countries and region and hence may be confusing to the subjects. Some choices of answers were based on a Likert scale of 1-6 with choices such as ‘all of the time’, ‘most of the time’, ‘a good bit of the time’, ‘some of the time’, ‘a little of the time’ and ‘none of the time’ were misleading and difficult to differentiate.

ECONOMIC WELL-BEING

Economic well-being is strongly linked to good living and life satisfaction and is ranked highly as an important factor in QOL. Out of pocket payment are the principal
means of financing healthcare in most parts of Asia.\textsuperscript{72} Van Doorslaer et al in 2006 estimated the magnitude and distribution of out-of-pocket expenses for health care in 14 countries, amounting to 81\% of Asian populations found heavy reliance on out-of-pocket financing of health care in Asia. The burden of medical cost is often borne by the state government or by the patients themselves. This is especially important for DM because of the chronicity of the disease and the potential to develop multiple arrays of complications incurring exorbitant medical costs in terms of drugs, procedures and disease monitoring. Assessment of financial burden is important and this is especially true with inflation of medical cost leading to high financial burden and affecting QOL. The WHOQOL used the most simple and general question by asking subjects if they have “enough money to meet their ends”, whereas in SF-36 there were no mention of financial component assessment.\textsuperscript{50,51} This is not sufficient to explore the economic stability of the subject and issues of financial constraints of medical costs; worries on future medical costs should be included to accurately reflect the QOL domain.

**PHYSICAL HEALTH ASSESSMENT**

Assessment of physical function remains a very important basic component of all QOL tools available, as the ability to go through daily activities independently and freely is considered a major determinant of QOL. This statement is supported by many studies worldwide and one of the studies on diabetic neuropathy found that patients with chronic symptomatic diabetic peripheral neuropathy has impaired QOL especially in the domains of physical mobility, emotion, energy and sleep.\textsuperscript{73} These questions: “To what extent do you feel that physical pain prevents you from doing what you need to do?” “How well are you able to get around?” and “How satisfied are you with your ability to perform your daily living activities?” were developed by the WHO in the WHOQOL-BREF questionnaire to assess the physical mobility of subjects.\textsuperscript{51}

However, some of the questions were rather confusing; for example, in item 4 “How much do you need any medical treatment to function in your daily life?”, item 9 “How healthy is your physical environment?” and item 13 “How available to you is the information that you need in your day to day life?”, hence making this questionnaire less suitable to be widely used in our Asian population as the patients may not be able to understand the actual meaning of the questions. In SF-36, the questions asked were more detailed about certain limitations to specific activities of daily living that the author deemed important such as running, lifting groceries, climbing stairs, bending, kneeling or stooping. The DSQOLS, a disease-specific QOL tool also incorporated physical function assessment and physical activity satisfaction as part of their domain but being designed for type 1 diabetics, the majority of the questions were aimed at a younger age group and those on insulin treatment.\textsuperscript{47} The DQLCTQ-R assessed the physical functions by asking detailed questions about limitations to perform certain daily activities in the last 4 weeks. However, though more detailed, the questions were more confusing in terms of the different modes of answer choices. Accurate assessment of physical function or limitation is of utmost importance in determining QOL and hence the questions must be simple yet relevant to the local lifestyles.

**PSYCHOSOCIAL ASSESSMENT**

Depression, being one of the most important patient-related co-morbidity of any chronic disease (DM in the context of this study), could significantly affect the patient’s QOL. A much higher prevalence of depression in diabetics (24\%), compared with non-diabetics (17\%) was reported.\textsuperscript{74} A study conducted by the Harvard Medical School in 2008 demonstrated a strong relationship between depression and poor diabetes care.\textsuperscript{75} Nonetheless, this study also showed only a small to medium range of effect of depression on medication concordance.\textsuperscript{75} Over the years, there have been numerous studies eliciting a correlation between depression and poor glycemic control, leading to functional disability in diabetics, highlighting the importance of early detection and proper management of depression in order to maintain the highest possible standards of life in people with diabetes.\textsuperscript{76} Psychosocial and emotional stability of diabetic patients has been identified by studies worldwide as an important domain as it can affect the QOL, compliance, control and outcome of treatment. Most of the QOL assessment tools are aimed at detecting early symptoms of depression or emotional instability. However, the accuracy of such assessment is still questionable as in order to diagnose depression, detailed questions are unavoidable and hence will make the tool too tedious. The SF-36 uses questions such as Item 9A, “Did you feel full of pep in the last 4 weeks?” and item 9F “Have you felt downhearted and blue for the past 4 weeks?” The structure of the sentences and the vocabulary used made these sentences rather difficult for our Asian population to comprehend. Similar questions were also noted in the DQLCTQ-R. In WHOQOL-BREF, only one question was noted asking if subjects have experienced any negative feelings such as “blue mood, despair, anxiety and depression.” In many developing countries in South East Asia, stigmatization against people with psychiatric disorder or mental illness is still very widespread compared with the Western world.\textsuperscript{77} Accurately assessing symptoms of depression becomes extremely challenging, as the subjects are not willing to divulge honest answers due to fear of stigmatization.

**SEXUAL DYSFUNCTION IN ASIANS**

The topic of sex and sexuality is considered a taboo in Asia and is not comfortably discussed in public. However, the prevalence of sexual dysfunction in both genders is significantly higher in Asian population with DM-63.6\% reported erectile dysfunction and 23.3\% in women.\textsuperscript{78,79,76} A study on sexual behavior and dysfunction and help-seeking patterns in urban populations of Asians was carried out in China, Taiwan, South Korea, Japan, Thailand, Singapore, Malaysia, Indonesia and the Philippines, and it was found that although sexual dysfunction was prevalent in the middle age group, socio-cultural factors seemed to prevent the afflicted individuals from seeking treatment.\textsuperscript{80} Self-reported questionnaires are the best way to capture such delicate data from the Asian population.\textsuperscript{79,80} It is vital that this component be included in the QOL mea-
measurement tool to accurately reflect the impact of sexual dysfunction on QOL. The score obtained from the self-reported QOL tool could also help the doctor or health care personnel to detect problems of sexual dysfunction for further action without causing any embarrassment or discomfort to the patient.

CONCLUSION

There is a global shift of diabetes care from “gluco-centric” to holistic approach. The diverse culture, language, religion and complexity of socio-economic differences in Asia possess a big challenge for diabetes prevention, management, education and counseling. There is an increase of diabetes prevalence in Asia but still a lack of QOL assessment tool built specifically for Asians. Most of the available QOL assessment tool are adapted or translated from American or European QOLs. Being constructed for the Western population, the problem of item equivalence and cultural relevance exists and must be addressed in order to get a true reflection of QOL in the Asian population. Different regions of Asia have different population groups and it is recommended that for every population, a focus group consisting of an acceptable number of individuals from different age, culture, religion and socio-economic background is established to assess the perception of QOL in that particular population of Asians. It is important to capture the essence of QOL domains that are important for Asians. In order to overcome translation problems it is recommended that an equivalence study be conducted in bilingual respondents. With such a specific QOL assessment tool constructed based on the multi-lingual Asian population that is stable across the different cultures, ethnicities, languages, religion and socio-economy within Asia, the physician will be at a better advantage to “tailor” the management of DM in Asians.

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二十一世纪糖尿病管理的发展：在亚洲生活质量指标的贡献

糖尿病（DM）是一种复杂的慢性病，它的多种并发症能够导致死亡率增加和生活质量变差。目前的研究表明降低糖化血红蛋白（HbA1c）能够预防微血管并发症。然而，随着更严格的血糖控制使HbA1c低于6.5%，似乎死亡和心血管事件的风险显著增加。当前全世界糖尿病管理的建议是“权衡”风险和生活质量（QOL），这是决定糖尿病管理成功或失败的关键组成部分。在亚洲，糖尿病已经成为一个健康危机，但缺乏针对有很多种族、语言、宗教和社会经济差异的亚洲人的生活质量评估工具。本综述讨论了过去十年糖尿病管理的发展和亚洲糖尿病患者生活质量相关的问题。

关键词：生活质量、亚洲人、糖尿病