ANNALS
ACADEMY OF MEDICINE, SINGAPORE
COMMITTED TO SPECIALIST EDUCATION AND TRAINING SINCE 1957

VOLUME 48 | NUMBER 12 | FREE PAPERS | DECEMBER 2019 MCI (P) 040/07/2019

"We win justice quickest by rendering justice to the other party."

Mahatma Gandhi (1869 – 1948)
Indian leader

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Free Papers

Editorial

The Greying Pandemic: Implications of Ageing Human Immunodeficiency Virus-Positive Population in Singapore

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Human immunodeficiency virus (HIV) remains a global public health issue. It is estimated that there are 37.9 million people living with HIV (PLHIV) today.[1] With advances made in efficacy and tolerability of combination antiretroviral therapy (ART) and increased access to health services in developed and developing countries, PLHIV are now living longer, healthier lives. Consequently, there is a global demographic shift in the epidemiology of HIV including Singapore.

In 2002, 18.1% of PLHIV in Singapore were ≥50 years old; by 2018, the figure had increased to 23%.[2] The increase is attributed to 3 factors. First, ART has effectively reduced morbidity and mortality that are associated with HIV. Second, life expectancy of PLHIV who achieved durable viral suppression on ART is now comparable with that of the general population.[3] Third, there is a decreasing incidence of HIV in younger adults and this has led to a visible shift in disease burden to older adults. The trend towards a growing number of older HIV patients is a global phenomenon: approximately 20% of PLHIV ≥50 years old live in Central and Western Europe and North America.[1]

Effective HIV treatment, viral suppression and immune recovery have led to a shift in care priorities to include a focus on physiological and psychological health and quality of life for PLHIV of all ages. Treatment recommendations for adolescents and adults infected with HIV are also appropriate for older adults with HIV. However, there are unique challenges faced by older patients that include low perception of HIV risk (leading to reduced testing and delayed diagnosis and presentation to care), coexisting health issues, disease stigma and discrimination. In this article, we highlight aspects and challenges of HIV management in older adults in Singapore and offer some recommendations to address them.

HIV and Comorbidities

Morbidity that is typically associated with ageing—such as chronic cardiovascular, kidney and liver diseases; bone loss and increased fracture risk; cognitive impairment; and cancer—is more common in HIV-positive individuals. Additionally, frailty—a syndrome characterised by reduced strength and endurance and diminished physiologic function that leads to increased risk of adverse health outcomes—may pose a particular risk in older PLHIV since HIV is a chronic, multisystemic disease. The onset of these age-related syndromes may also present at least a decade earlier than is typically observed in comparable HIV-negative populations.[4]

The reasons for "accelerated" ageing in PLHIV are complex. They include chronic inflammation and immune activation, drug toxicity and response to ART, lifestyle and social factors that persist even with highly effective ART and viral suppression.[5] The situation is worsened when adherence is compromised in individuals who have several concomitant chronic conditions—including neuropsychiatric conditions associated with HIV infection—or when they face poverty and food insecurity that are not uncommon in older PLHIV. These non-communicable comorbidities, consequent polypharmacy and frailty can threaten the functional ability, intrinsic capacity and quality of life of PLHIV as they age, and the overall effect may be potentially greater than conditions associated with acquired immune deficiency syndrome (AIDS).

HIV and Polypharmacy

Polypharmacy is defined as the concurrent use of ≥5 medications, and PLHIV have a higher polypharmacy rate than their HIV-negative peers. Typically, ART involves the use of 3 antiretroviral drugs. With increasing age, the medications can also include non-ART drugs. In the Multicenter AIDS Cohort Study which compared the prevalence of polypharmacy in PLHIV and HIV-negative participants over a 12-year period, Ware et al[6] found that PLHIV had a higher polypharmacy rate of 24.4% compared to 11.6% in the HIV-negative group (P <0.0001). In its examination of polypharmacy and epidemiology

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of non-AIDS diseases in 8444 PLHIV, the Swiss HIV Cohort Study[7] found that antihypertensives were the most commonly prescribed non-ART medications followed by lipid-lowering agents, antiplatelet drugs and diabetes medications. This finding highlighted the higher risk for age-associated comorbid diseases in these patients.

Polypharmacy is associated with decreased medication adherence, serious adverse drug events (ADE) that require hospitalisation and increased mortality. Ageing PLHIV may be more susceptible to ADE due to diminished organ system reserves, chronic inflammation and immune dysfunction and metabolic changes that can precipitate a vicious cycle of end-organ injury and frailty.[8]

Additionally, polypharmacy increases the risk of drug-drug interactions that may result in increased treatment-associated toxicities or reduced treatment efficacy. The risk of non-adherence, discontinuation or reduced efficacy of ART is of particular concern since it is crucial to maintain viral suppression and immune reconstitution in PLHIV.

Behavioural, Mental Health and Psychosocial Aspects of HIV and Ageing

Ageing is associated with a multitude of psychosocial challenges that can affect mental health and neurocognitive function in older PLHIV.[9] The incidence of neurocognitive disorders is intrinsically higher in PLHIV than in HIV-negative individuals, and 50% of PLHIV develop some degree of HIV-associated neurocognitive disorder (HAND).[10] ART may not be sufficient to prevent milder forms of HAND such as asymptomatic neuropsychological impairment. However, access to cognitive rehabilitation and behavioural interventions that can improve or maintain societal and environmental mastery is lacking. Depression, substance abuse and unemployment are higher in PLHIV and despite evidence that supports a need for mental health services, older PLHIV are less likely to receive such services than younger counterparts.

Studies suggest that older PLHIV are less happy, less resilient, have poorer attitudes towards ageing and report earlier and more rapid decline in health and independence than their HIV-negative peers.[11] As they age, PLHIV are forced to grapple with issues such as impending retirement from the workforce, disengagement and/or uncertainty about their role in society, finances and long-term housing with their own increasing care needs. Although efforts were made to promote "successful ageing" in Singapore, the prospects of living with HIV—a stigmatised chronic condition—can heighten anxiety and uncertainty over the ageing process.

In HIV-positive individuals, disease stigma and social isolation increase with age. The fear of discrimination and social stigma attached to HIV can predispose PLHIV to poorer social connectedness that leads to poor social support later in life.[12] This is a disconcerting issue since HIV disproportionately affects single, older men and men who have sex with other men in Singapore who may lack traditional social support networks in their later years. In Singapore, sociocultural norms such as family and filial piety that provide some semblance of safety in old age may not necessarily be true for PLHIV.

Challenges and Recommendations for "Greying" PLHIV in Singapore

Singapore faces several potential challenges to care for her ageing PLHIV population. First, her HIV and infectious diseases physicians are not trained to handle the specific needs of the geriatric population. Her geriatricians and family physicians may also not be familiar with the care of PLHIV. There is a need for her medical practitioners to learn to manage holistic health issues that are beyond their chosen field of work and to work closely with one another to provide community-based care and support for ageing PLHIV.

Second, sexual health education that includes HIV prevention and community support for PLHIV traditionally targets a younger demographic. With more "greying" PLHIV, health services can target prevention of HIV and sexually transmitted infections in older adults. Additionally, community services such as smoking cessation and physical activity programmes for HIV patients can be enhanced to support ageing PLHIV. PLHIV with chronic medical conditions can also be supported in the community with, for example, the setting up of dialysis centres that are equipped to handle the needs of HIV patients. Such initiatives will require a concerted effort to drive service enhancement that includes educating service providers on ageing and HIV-specific issues, engaging primary care providers and equipping eldercare and long-term care facilities to care for older PLHIV.

Third, older PLHIV may face stigma of a nature which is unique to that faced by younger PLHIV; however, this is not well understood in the local context. Consequently, there is a need for more awareness and training on mental health and social support by frontline workers, health providers and policymakers to provide programmes and services that mitigate the unique challenges faced by ageing PLHIV.

Conclusion

The community, health providers and stakeholders involved in the care of PLHIV must appreciate and understand the experience of ageing with HIV. As her society matures, Singaporeans must learn to be kinder and more accepting and tolerant. An adage comes to mind: "Grow old along with me, the best is yet to be". This may yet hold true for the current generation of older PLHIV in Singapore.

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Original Article

Relationship Satisfaction Mediates the Association Between Emotional Expressiveness and Depressive Symptoms Among Asian Women

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Abstract

Introduction: Few studies in Asia have examined the association among depressive symptoms, relationship satisfaction, sexual dysfunction and emotional expressiveness. Examining the role of emotional expressiveness in the context of depression and relationships is important as it can be a point for therapeutic intervention. Materials and Methods: Guided by the Marital Discord Model of Depression and based on data from partnered women in Singapore (n = 193), we conducted a path analysis to examine the mediating role of relationship satisfaction and sexual dysfunction in the link between difficulty in emotional expression and depressive symptoms. Results: Controlling for age and health, lower relationship satisfaction (β = -0.213; *P* <0.001), higher sexual dysfunction (β = 0.139; *P* = 0.010) and greater difficulty in emotional expression (β = 0.908; *P* <0.001) were associated with increased depressive symptoms. Relationship satisfaction partially mediated the association between emotional expressiveness and depressive symptoms (indirect effect, 0.169; 95% confidence interval, 0.043–0.379). Conclusion: The findings suggest the importance of effective communication in mitigating relationship- and self-distress.

Ann Acad Med Singapore 2019;48:396–402

Key words: Emotional expression, Marital Discord Model of Depression, Sexual dysfunction

Introduction

Marital relationship satisfaction accrues many benefits for both men and women, including greater physical and psychological well-being.[1–4] Conversely, marital relationship dissatisfaction has been reported to be associated with negative outcomes such as psychiatric morbidity, poor health and decreased work satisfaction.[5–7] Marital well-being affects not only the spouses involved but also children, family and society as a whole.[8–9]

The Marital Discord Model of Depression (MDMD) posits that marital distress is a significant antecedent to depression for those who are married.[10] Although the literature has been consistent in showing a relationship between marital distress and depression,[11,12] most of the studies have been conducted in Western cultural settings and little is known about marital relationship satisfaction and its consequences in other cultural settings including Asia. One study that examined 391 couples living in 2 major cities in China reported that husbands' and wives' marital satisfaction significantly predicted their depressive symptoms.[3] In Singapore, it has been reported that those who are divorced/separated were significantly more likely to report suicidal attempts compared to those who are single.[13] A recent qualitative study using thematic analyses found

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that having relationship issues was an important precipitant for suicide.[14] These studies lend support to MDMD.

Nevertheless, there continues to be a paucity of studies examining relationship satisfaction from an Asian cultural context where the expectations of, attitudes towards and communication styles within a marriage may be different from Western romantic relationships (which the majority of studies are based on). Examining the role of emotional expressiveness in the context of depression and relationship distress is important as it can be a point of therapeutic intervention.

The literature suggests that sexual engagement and well-being are associated with relationship satisfaction and psychological well-being.[2,15,16] The literature also suggests that the ability to self-disclose and communicate one's emotions is a stable, individual characteristic that is related to relationship satisfaction, sexual well-being and ultimately psychological health.[17–21] These specific aspects of a marital relationship are important to understand as they offer opportunity for problem-focussed couples intervention. However, these constructs have not been explored in Asian cultural settings.

Singapore is a small nation in Southeast Asia with a developed economy and high per capita income.[22] Due to fast economic growth, the shape and dynamics of the family have changed in the last generation with an increase in dual-income families, later marriages, fewer children and higher divorce rates.[23,24] Local studies have reported that marital status—specifically being divorced or widowed—is associated with psychiatric morbidity.[25] Like many other countries in the region, Singapore is experiencing a shift in openness in discussing one's marital and sexual relationships.[26,27] It is thus timely and important to examine the state of the different aspects of romantic relationships and their association with psychological well-being in this population.

The aim of our study was to examine the associations among depressive symptoms, relationship satisfaction, sexual dysfunction and emotional expressiveness as well as the extent the relationship between emotional expressiveness and depressive symptoms is accounted for by relationship satisfaction and sexual dysfunction in a sample of women in Singapore. Understanding the mediating relationships among the study variables can help to identify treatment intervention targets for couples. We expected that depressive symptoms will be negatively associated with relationship satisfaction and emotional expressiveness, and positively associated with sexual dysfunction. Specifically, we hypothesised that relationship satisfaction (hypothesis 1) and sexual dysfunction (hypothesis 2) would mediate the relationship between emotional expressiveness and depressive symptoms. The findings will help elucidate the relationships among these constructs in an Asian cultural setting that will in turn have implications for clinical practice and further research.

Materials and Methods

Participants

We conducted a cross-sectional study. A total of 193 women who were married/romantically-partnered were recruited from the waiting rooms of a public hospital for women in Singapore. This study sample is a subset of a larger project where women with no history of gynaecological cancer were recruited to serve as a control comparison group. Eligibility criteria for the study participants were: 1) no history of gynaecological cancer, 2) female, 3) ≥21 years old, 4) living in Singapore, and 5) able to read and understand English.

Procedures

Eligible participants filled up an anonymous survey that took approximately 10 minutes to complete. Electronic data collection was conducted using the Qualtrics platform. Participants were exempted from signing informed consent as no identifying information was collected. Approval for the study was obtained from the SingHealth Centralised Institutional Review Board (reference: 2015/2888).

Measures

Depressive symptoms were measured using the depression subscale of the Hospital Anxiety and Depression Scale (HADS).[28] The HADS was designed for detecting clinically significant levels of depression in an outpatient setting and has been validated for use in Singapore.[29–31] There are 7 items measuring depressive symptoms (e.g., "I feel as if I am slowed down") and participants reported their responses on a 4-point scale with higher scores indicating greater symptoms. The internal reliability of the subscale in this study was $\alpha = 0.71$.

Relationship satisfaction was measured using the Dyadic Adjustment Scale-4 (DAS-4).[32] The DAS-4 is a brief 4-item version of the original 32-item Dyadic Adjustment Scale[33] that measures satisfaction in a romantic relationship. Higher scores indicate greater relationship satisfaction (e.g., "Do you confide in your partner?"). The internal reliability of the scale in this study was $\alpha = 0.68$.

Sexual dysfunction was measured using the Arizona Sexual Experience Scale[34] which consisted of 5 items. Responses were reported on a 6-point scale with higher scores indicating greater problems with sexual drive, arousal, lubrication, ability to reach orgasm and sexual satisfaction. The internal reliability of the scale in this study was $\alpha = 0.88$.

Emotional expressiveness was measured using 2 items from the Ambivalence over Emotional Expressiveness Questionnaire (AEQ)[19] that inquired about general difficulty in expressing one's emotions: "It is hard to find the right words to indicate to others what I am really feeling" and "I often cannot bring myself to express what I am really feeling". Responses are reported on a 5-point scale (Never – Frequently). In the current study, the mean of the 2 items was calculated, with higher scores indicating greater difficulty in emotional expression. The internal reliability of the 2 items in this study was $\alpha = 0.87$.

Demographic questions that were asked included the participant's age, race/ethnicity, highest education, work status, marital status and number of children aged ≤21 years old. Participants also indicated any chronic illness they may have using a checklist. Covariates that were included into the model included age (entered as a continuous variable) and health (which was a dichotomous categorical variable indicating the presence of a chronic illness).

Analysis

Demographic characteristics of the sample were presented descriptively. We conducted a path analysis to evaluate whether the association between difficulty in expressing emotion and depressive symptoms was mediated by relationship satisfaction and sexual dysfunction, controlling for age and health (coded as yes/no to having a chronic illness) using Mplus v8.[35] The model fit was examined using the χ^2 test, comparative fit index (CFI), Tucker-Lewis index (TLI), root mean square error of approximation (RMSEA) and standardised root mean square residual (SRMR). Values >0.90 for CFI and TLI represent an acceptable model.[36–38] RMSEA and SRMR values ranging between 0.08–0.10 indicate fair fit and values >0.10 suggest model rejection.[36,38,39] The indirect effect, which refers to the product term between the path coefficient of predictor-mediator relationship and that of mediator-outcome relationship was examined. Bootstrapping (2000 samples) was employed to address the significance level of the indirect effect. A 95% bias-corrected bootstrap confidence interval (CI) that does not include zero indicates that the indirect effect is significant.

Results

Participant Characteristics

Participant demographic characteristics are presented in Table 1. Majority of the sample are ethnic Chinese with mean age of 37 years. Majority have at least 12 years of education, are currently working full-time and have a monthly household income of >S$3000 per month. Majority of the sample are also currently married and have at least 1 child. Nearly 30% of our study participants reported a diagnosis of a chronic illness.

Table 1. Characteristics of Study Sample (n = 193)

Variable	Mean ± SD	n (%)
Age (years)	37.21 ± 8.72	
Ethnicity		
Chinese		108 (56)
Indian		40 (21)
Malay		34 (18)
Others		11 (6)
Religion*		
Buddhism/Taoism		50 (26)
Christianity		29 (15)
Hinduism/Sikhism		28 (15)
Islam		46 (24)
Free-thinking/atheism		34 (18)
Others		2 (1)
Highest education (years of education)		
Primary school or lower (≤6 years)		5 (3)
Secondary (10 years)		35 (18)
JC/polytechnic/ITE (12 years)		71 (37)
University and above (16 years)		82 (42)
Work status*		
Full-time		118 (61)
Part-time		16 (8)
Retired/not working		5 (3)
Homemaker		50 (26)
Monthly household income*		
<$999		12 (6)
$1000 – 2999		34 (18)
$3000 – 4999		45 (23)
≥$5000		98 (51)
Marital status		
Married		182 (94)
In a relationship but not married		11 (6)
Have children <21 years old?		
Yes		120 (62)
Chronic illness		
Cancer		2 (1)
Cardiovascular disease		0 (0)
Chronic lung disease		12 (6)
Diabetes		14 (7)
Hypertension/hyperlipidaemia		12 (6)
Liver disease		1 (0.5)
Others		18 (9)

ITE: Institute of Technical Education; JC: Junior college; SD: Standard deviation
*Does not add up to 193 due to missing data.
Percentages may not add up to 100% due to rounding or missing data.

Depressive Symptoms, Relationship Satisfaction and Sexual Dysfunction Characteristics

Table 2 presents the mean (standard deviation) and number of participants who met the cutoff criteria for depression,[40] relationship satisfaction[32] and sexual dysfunction.[34] The mean scores did not meet any of the recommended cutoff criteria. Nevertheless, 15%, 18% and 26% of the sample met the recommended cutoff for depression, relationship satisfaction and sexual dysfunction, respectively.

Path Analysis Findings

Our path model fit the data well: χ^2 (3) = 2.332; *P* = 0.506; CFI = 1.000; TLI =1.000; RMSEA = 0.000; SRMR = 0.019 (Fig. 1). All significant individual paths and indirect effects were in the expected direction. The model indicated that controlling for age and health, difficulty in emotional expression was negatively associated with relationship satisfaction (β = -0.791; standard error [SE] = 0.259; *P* = 0.002) and increased depressive symptoms were directly predicted by decreased relationship satisfaction (β = -0.213; SE = 0.054; *P* <0.001), increased sexual dysfunction (β = 0.139; SE = 0.054; *P* = 0.010) and increased difficulty in expressing emotion (β = 0.908; SE = 0.201; *P* <0.001). Bootstrapping procedures showed that the indirect effect of difficulty in emotional expression on depressive symptoms via relationship satisfaction was significant (indirect effect, 0.169; 95% CI, 0.043–0.379). This indicates that relationship satisfaction partially mediated the linkage between emotional expressiveness and depressive symptom, which supported our hypothesis 1 (27.3% in the variance of depressive symptoms was explained by the model).

Sexual dysfunction was not significantly predicted by difficulty in expressing emotion (β = 0.492; SE = 0.352; *P* = 0.162). Hence, sexual dysfunction did not emerge as a mediator for the relationship between difficulty expressing emotion and depressive symptoms (indirect effect, 0.069; 95% CI, -0.032–0.260). Hypothesis 2 was not supported. Also, relationship satisfaction and sexual dysfunction were not related (r = -0.622; SE = 1.151; *P* = 0.589).

Table 2. Mean (SD) of Study Outcomes and Number of Participants Who Met the Recommended Cutoff Scores

Variable	Aggregate	Mean ± SD	Recommended Cutoff Score	Number Who Met Cutoff Score (%)
Depression (Hospital Anxiety Depression Scale)	193	4.140 ± 2.999	≥7	29 (15)
Relationship satisfaction (Dyadic Adjustment Scale-4)	191	15.440 ± 3.509	≤12	34 (18)
Sexual dysfunction (Arizona Sexual Experience Scale)	156	14.990 ± 4.134	≥19, 1 item ≥5 or 3 items ≥4	41 (26)

SD: Standard deviation

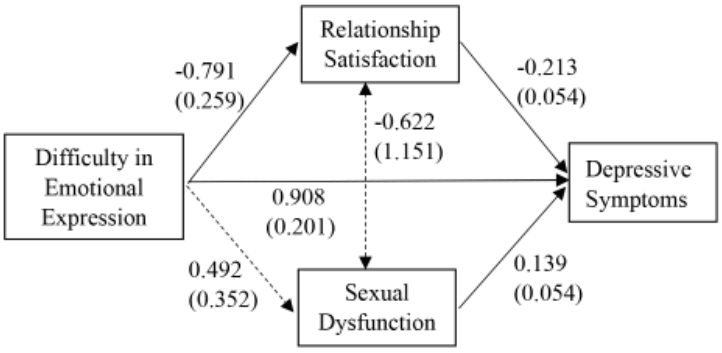

Fig. 1. Estimated unstandardised coefficients (standard errors) for the fitted path model controlling for age and health. Solid line represents significant relationship; dotted line represents non-significant relationship.

Discussion

The aim of the current study was to examine the associations among depressive symptoms, relationship satisfaction, sexual dysfunction and emotional expressiveness. The extent association between emotional expressiveness and depressive symptoms was accounted for by relationship satisfaction and sexual dysfunction. Our sample included 193 adult women who were married/ romantically-partnered in Singapore. Approximately 1 out of 7 women (15%) met the cutoff score for depression, 1 out of 5 women (18%) for marital dissatisfaction and 1 out of 4 (26%) for sexual dysfunction. Although clinician-interviews are needed for formal diagnoses, these numbers may be helpful as a tentative gauge of the prevalence of the issues under study in our sample of women.

As hypothesised, the path analysis model indicated that higher levels of depressive symptoms were predicted by lower relationship satisfaction, higher sexual dysfunction and greater difficulty in emotional expressiveness, controlling for age and health. This is consistent with the findings from previous studies that support MDMD[3,41] and other studies that have found depression to be associated with sexual dysfunction[15,42] and emotional expressiveness.[17,43] Our data suggest that just like their Western counterparts, Asian women who have problems expressing themselves and their needs and who face marital or sexual difficulties have a higher risk of being distressed.

We further found that the relationship between depressive symptoms and emotional expressiveness was partially mediated by relationship satisfaction. Our finding underscores the fact that being able to communicate one's emotions affects both an individual's romantic relationship and psychological well-being. Although seemingly intuitive, our findings add to the body of knowledge by showing that the ability to express one's self is important even in a society where open communication between spouses or romantic partners is stereotypically not always expected and may not be highly valued. In many Asian cultures, a couple who are experiencing distress/discord may choose to suppress their emotions to maintain harmony within the larger family. However, this may come at a cost. Further, this behaviour is perpetuated across generations as parental socialisation of emotions is predictive of a person's emotional regulation and expression.[44]

Contrary to expectations, sexual dysfunction was not associated with relationship satisfaction or emotional expressiveness. A possible explanation is that sexual function—which affects the physical aspects of a romantic relationship—is given less importance as a measure of satisfaction in Asian romantic relationships. One epidemiological study conducted in 10 Asian countries has reported that >30% of women reported at least 1 sexual dysfunction[45] and another worldwide epidemiological study reported that lack of interest in sex for women in Asia is higher than in European and non-European Western countries.[46,47] It may be that sexual well-being is not necessarily a significant predictor of marital success, especially in a cultural setting where other aspects of marriages may be considered more important such as parental responsibilities, harmonious relationships with the larger family, etc. Given this explanation, it follows that communicating and expressing one's self has small bearing on sexual difficulties faced.

From a clinical standpoint, it is important that individuals who present with distress be assessed comprehensively, including in the areas of relationship happiness, sexual functioning and interpersonal effectiveness (i.e., being able to express themselves verbally to others). In particular, we may extrapolate that interventions aimed at increasing an individual's awareness of their emotions and expressing them effectively may be helpful for their relationship satisfaction and psychological well-being. The challenge will be how to intervene. There continues to be a lingering societal taboo surrounding participation in psychological therapies or marital counselling, which is unfortunate given the increasing levels of stress reported in the nation. It is hoped that the findings from the current study can spur further research on ways to mitigate distress through communication training and emotional expressiveness in a culturally appropriate manner.

Limitations

Although our proposed model posits that decreased relationship satisfaction, sexual dysfunction and decreased emotional expressiveness give rise to depressive symptoms, the causal direction of the relationship cannot be confirmed using our cross-sectional data. It is possible that individuals who are depressed have poorer interactions with their spouses that negatively affected their relationship and sexual well-being. Other limitations include not using a full version instrument to measure emotional expressiveness (we had used a subset of items of the AEQ as that was our best option available). We did not assess the length of romantic relationship and menopausal status in this study which are potentially important to consider. The study also included only women. Additionally, although we controlled for study participants having chronic illness, we did not examine specific illness subgroups (e.g., diabetes) that may place individuals at higher risk for poorer mood and sexual functioning. Future studies are needed to consider longitudinal designs and include both partners, as well as consider disease-specific factors in further investigations on the interplay among elements of romantic relationships and psychological well-being.

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Original Article

Renal Transplant Outcomes in Spousal and Living-Related Donors in Malaysia

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Abstract

Introduction: Studies have shown that a compatible human leukocyte antigen (HLA) match can confer a favourable effect on graft outcomes. We examined the outcomes of HLA matching in renal transplant donors in Malaysia. Materials and Methods: A total of 140 patients who had compatible ABO blood type with negative T-cell lymphocytotoxicity crossmatch were included in the study and 25% of them were spousal transplant donors. No remarkable differences in acute rejection rate, graft survival, patient survival and serum creatinine level were observed between the spousal and living-related donor groups. Results: The spousal donor group had a higher degree of HLA mismatch than the living-related donor group. HLA-A mismatch was associated with increased rejection risk at 6 months (odds ratio [OR], 2.75; *P* = 0.04), 1 year (OR, 2.54; *P* = 0.03) and 3 years (OR, 3.69; *P* = 0.001). It was also observed in the deleterious effects of HLA-B and HLA-DQ loci when the number of antigen mismatches increased. The risk was 7 times higher in patients with ≥1 mismatch at HLA-A, HLA-B and HLA-DR loci than those who did not have a mismatch at these loci at 6 months (*P* = 0.01), 1 year (*P* = 0.03) and 3 years (*P* = 0.003). Conclusion: A good match for HLA-A, HLA-B, HLA-DR and HLA-DQ can prevent acute rejection risk in renal transplant patients. Consequently, spousal donor transplants could be a safe intervention in renal patients.

Ann Acad Med Singapore 2019;48:403–11

Key words: Graft survival, Human leukocyte antigen incompatibility, Immunosuppressant, Patient survival

Introduction

Renal transplantation has substantial benefits for patients with end-stage renal disease (ESRD). Not only is it cost-effective in the long run, it also confers better patient survival and quality of life compared to dialysis treatment.[1] However, the success of any transplantation programme is highly dependent on availability of donors,[2] accessibility to infrastructure and trained personnel, technological advances in histocompatibility tests,[3] use of potent immunosuppressants[4] and sound health policy.[5]

Generally, living donor kidney transplants (LDKTs) have better outcomes than deceased donor kidney transplants and have been attributed to factors such as higher quality of initial renal function and shorter cold ischaemic time of the organ.[6] According to the International Registry of Organ Donation and Transplantation, countries that have legislated "presumed consent" on organ donation include Belgium, France, Italy and Spain. Since every resident in these countries is considered a donor, they consistently ranked among states with the highest number of donors worldwide.[7]

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Malaysia, on the other hand, has an "opt in" legislation on organ donation and her residents are required to provide informed consent to donate various organs and tissues in the event of sudden and untimely demise.[8] Although the country's living donor transplant policy stipulates that organ donation from emotionally or genetically related donors is acceptable, the number of organ donations in the country remain low. Moreover, any donation by unrelated living donors (except for spousal transplants) must be approved by the Unrelated Transplant Approval Committee and only when no suitable cadaver and related donors are available.[9]

In its 11th report, the National Transplant Registry of Malaysia reported that the number of kidney transplants in the country had declined from 6 individuals in 2005/2006 to 3 individuals in 2014 in 1 million residents.[10] As more Malaysians head overseas for a kidney transplant, the number of dialysis cases in the country doubled in the last 10 years,[11] reflecting a growing need for donors. Current legislations on organ donation in Malaysia would only widen the gap between the number of available donors and patients who are awaiting a kidney transplant.[12]

In its 13th report, the National Transplant Registry[13] reported an increase in the number of living donor transplants in 2016 and approximately half of them were LDKTs. However, they involved mostly living donors who were genetically related and only 7.4% were spousal donors. On the other hand, the rate of cadaveric local transplantations continued to fluctuate through the years and accounted for only 11% of all transplants performed in 2016.

These findings have prompted Malaysia to promote living donor transplants including spousal transplants. Since she has a multiracial population comprising Malays (68.6%), Chinese (23.4%), Indians (7%) and other ethnicities (1%),[14] inter-racial marriages are common and have a recognisable effect in the distribution of human leukocyte antigen (HLA) alleles among her residents. Consequently, spousal donor transplants can predispose patients to increased rejection risk when there is greater HLA disparity between donors and patients.

In the literature, there is a dearth of reports on the degree and impact of HLA disparity on the outcome of spousal donor transplants in Malaysia. A crucial question that must be addressed is whether such transplants can be considered a safe option to improve patients' eligibility for organ transplantation in the country. To address this issue, in this study we compared the long-term outcomes of spousal and other living-related kidney transplants and examined the clinical relevance of HLA mismatch in patients.

Materials and Methods

The records of 146 patients who received their first renal allograft between March 1996 and April 2014 at the University Malaya Medical Centre (UMMC) were retrieved and retrospectively reviewed. Thirty-two patients were spousal donor transplants and 109 were living-related donor transplants. Five cases of living non-related donor transplants were excluded due to lack of data. Recipients of combined transplants and paediatric patients were also excluded from this study.

The immunosuppression regimen included triple immunosuppressants of either cyclosporine, mycophenolate acid and steroid or mycophenolate acid, steroid and tacrolimus. According to the transplant protocol of UMMC, cyclosporine (Neoral®) was administered at a starting dose of 4–6 mg/kg/day and titrated at 150 ng/mL and 300 ng/mL for 3 months based on trough concentrations, and then at approximately 150 ng/mL thereafter. For tacrolimus (Prograft®), the initial dose was 0.2 mg/kg/day and it was titrated at 8–15 ng/mL based on its trough levels in the first 3 months, 5–12 ng/mL in the first year and 5–10 ng/mL thereafter.

All donors and patients had the same blood type—ABO blood group—and had tested negative for T-cell lymphocytotoxicity crossmatch. HLA typing was performed with polymerase chain reaction–sequence-specific oligonucleotide technique or serology. Since the introduction of the transplantation programme in UMMC, HLA class I typing was performed routinely; HLA class II typing was commenced for HLA-DR and HLA-DQ in 2002 and 2006, respectively. When needed, HLA antibodies were detected by serology and solid-phase assay (Luminex®).

The number of antigen mismatch for HLA-A, HLA-B, HLA-Cw, HLA-DQ and HLA-DR was defined as the number of donor HLA that differed from those in recipients according to the guidelines on HLA values and split equivalences of the Organ Procurement and Transplantation Network.[15] Graft failures included death of patient and resumption of dialysis; graft rejection was diagnosed based on clinical presentation and/or biopsies. Biopsies were performed to detect early graft rejection and when patients experienced altered graft function that suggested acute rejection. Data on rejection types—such as antibody-mediated, cellular, glomerular or vascular—was not available.

Statistical analysis was performed using SPSS Statistics for Windows version 21.0 (IBM Corp., Armonk, NY, USA) to compare baseline characteristics and HLA mismatch between donors and recipients. Graft rejection and continuous variables were analysed using chi-square test and student's t-tests, respectively. Predictors of acute rejection were modelled by binomial logistic regression. Results were expressed as odds ratio (OR) and 95% confidence interval (CI). A value of $P < 0.05$ was considered statistically significant. This study was approved by UMMC Ethics Committee in accordance with the Helsinki Declaration.

Results

The baseline characteristics of donors and graft recipients are shown in Table 1. In spousal donor grafts, the mean age of graft recipients and donors were 38.48 ± 13.85 years and 32.47 ± 15.45 years, respectively; in living-related donor grafts, it was 33.16 ± 12.48 years and 42.87 ± 15.96 years, respectively. Spousal donors were younger than donors in living-related grafts, but the age difference was not statistically significant ($P = 0.54$).

There were more female donors in living-related grafts than spousal grafts (61% vs 23%, $P > 0.37$), but more men were transplant recipients in spousal grafts than living-related grafts (75% vs 25%, $P = 0.39$). The distribution of Malays, Chinese and Indians was similar in both spousal donor and living-related donor grafts (65%, 19% and 12% vs 67%, 15% and 16%, respectively; $P = 0.74$). All patients were on triple immunosuppressants and medication types were similar in both groups ($P = 0.74$); most patients were on cyclosporine, mycophenolate acid and steroid or mycophenolate acid, steroid and tacrolimus.

The main aetiologies of ESRD in spousal and living-related donors were bilateral small kidneys, hypertensive nephropathy and immunoglobulin A nephropathy (Table 2); >60% of renal failure was attributed to these diseases. No mortality was reported at 3 years post-transplantation. At 6 months, all 33 transplant recipients in the spousal donor group were well but 2 of the 109 transplant recipients in the living-related donor group had resumed dialysis (100% vs 98%, $P = 0.44$). At 1 year post-transplantation, 3 recipients in each group required dialyses (91% vs 97%, $P = 0.10$); at 3 years post-transplantation, 4 and 7 recipients in both groups, respectively, were on dialysis (Fig. 1). In our study, graft survival in the spousal donor group was comparable to the living-related donor group (88% vs 94%, $P = 0.26$).

At 1 year and 3 years post-transplantation, 8 and 12 patients in the spousal donor group experienced at least 1 acute rejection episode, respectively. At 1 year post-transplantation, 3 and 6 rejection episodes were observed in husband-to-wife and wife-to-husband transplantations, respectively. The rejection rates in the spousal donor group were not higher than the living-related donor group at 6 months (22% vs 18%, $P = 0.66$), 1 year (25% vs 22%, $P = 0.72$) and 3 years (38% vs 39%, $P = 0.84$) (Fig. 2).

Table 1. Baseline Characteristics of Spousal and Living-Related Renal Donors and Recipients Between March 1996 and April 2014

Variable	Spouse (n = 32)	Living-Related (n = 109)	*P* Value
Age at transplant (mean ± SD, years)			
Recipient	38.48 ± 13.85	33.16 ± 12.48	0.30
Donor	32.47 ± 15.45	42.87 ± 15.96	0.54
Recipient gender (%)			0.39
Male	24 (75)	73 (25)	
Female	8 (25)	36 (18)	
Donor gender (%)			0.37
Male	8 (16)	41 (39)	
Female	19 (23)	64 (61)	
Ethnicity (donor and recipient, %)			0.74
Chinese	21 (65)	73 (67)	
Indian	4 (12)	18 (16)	
Malay	6 (19)	17 (15)	
Immunosuppressant (%)			0.74
Cyclosporine, mycophenolate acid	6 (19)	15 (14)	
Tacrolimus, mycophenolate acid	21 (66)	73 (67)	
Cyclosporine, mycophenolate mofetil	2 (6)	10 (9)	
Tacrolimus, mycophenalte mofetil	1 (3)	1 (1)	
Cyclosporine, azathioprine	2 (6)	6 (5)	
Tacrolimus, azathioprine	0 (0)	4 (4)	

SD: Standard deviation

Table 2. Clinical Outcomes in Spousal and Living-Related Renal Donors

Variable	Spouse (n = 32)	Living-Related (n = 109)	*P* Value
Aetiology of ESRD (%)			0.48
Hypertensive nephropathy	7 (21)	27 (25)	
Diabetic nephropathy	3 (9)	10 (9)	
Glomerulonephritis	4 (12)	17 (15)	
Bilateral small kidneys	8 (24)	22 (20)	
Idiopathy	2 (6)	11 (10)	
IgA nephropathy	6 (18)	7 (6)	
Polycystic kidney disease	2 (6)	4 (5)	
Others	1 (3)	11 (10)	
Graft survival (%)			
6 months	32 (100)	107 (98)	0.44
1 year	29 (91)	106 (97)	0.10
3 years	28 (88)	102 (94)	0.26
Acute rejection (%)			
6 months	7 (22)	20 (18)	0.66
1 year	8 (25)	24 (22)	0.72
3 years	12 (38)	43 (39)	0.84
Creatinine level (mean ± SD, μmol/L)			
1 month	121.9 ± 58.50	198.6 ± 26.50	0.238
6 months	116.38 ± 17.72	148.28 ± 8.03	0.108
1 year	108.00 ± 13.61	137.85 ± 6.16	0.052
3 years	112.88 ± 13.19	139.39 ± 5.98	0.074

ESRD: End-stage renal disease; IgA: Immunoglobulin A; SD: Standard deviation
Note: There is no mortality at 6 months, 1 year and 3 years post-transplantation.

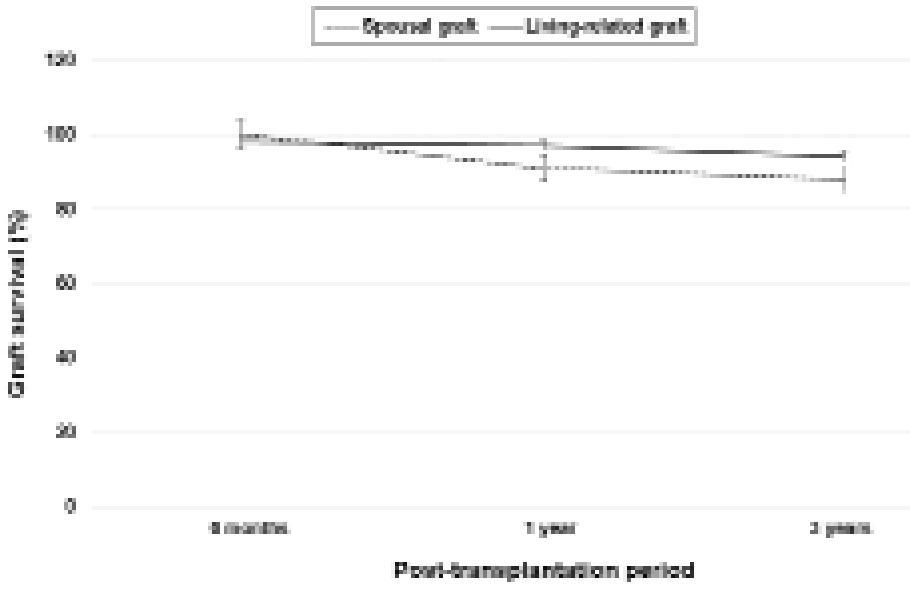

Fig. 1. Renal graft survival in spousal and living-related donor groups at 6 months, 1 year and 3 years post-transplantation.

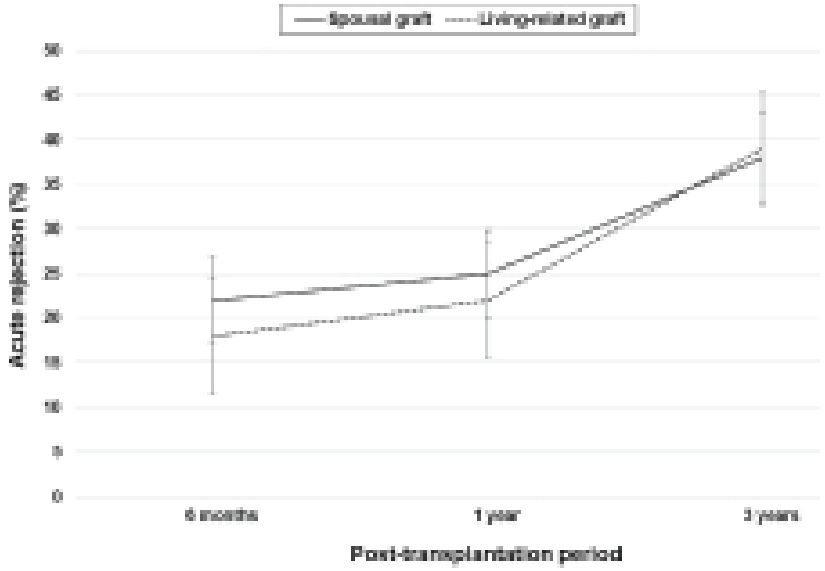

Fig. 2. Incidence of acute renal rejection in spousal and living-related donor groups at 6 months, 1 year and 3 years post-transplantation.

At 6 months, 1 year and 3 years post-transplantation, mean serum creatinine levels in graft recipients in the spousal donor group were 116.38 ± 17.72 µmol/L, 108.00 ± 13.61 µmol/L and 112.88 ± 13.19 µmol/L, respectively; in the living-related donor group, the levels were 148.28 ± 8.03 µmol/L, 137.85 ± 6.16 µmol/L and 139.39 ± 5.98 µmol/L, respectively (P >0.05). At 3 years post-transplantation, no significant difference was observed in renal function in both groups.

Generally, spousal donors have a higher incidence of HLA mismatch than living-related donors (Table 3). For HLA-A, the number of spousal grafts with 2 HLA mismatches were significantly higher than living-related grafts (26% vs 3%, P = 0.0004). The number of spousal donor grafts with ≥1 HLA mismatch was significantly higher than living-related donor grafts for HLA-B (90% vs 70%, P = 0.039) and HLA-Cw (87% vs 58%, P = 0.012) loci. More patients (57%) in the spousal donor group had 2 HLA-B mismatches than patients (12%) in the living-related group (P = 0.0002). For HLA-Cw locus, 67% of patients in the spousal donor group had 1 antigen mismatch and 20% had 2 antigen mismatches; in the living-related donor group, 56% of patients had 1 HLA-Cw mismatch and only 2% had 2 antigen mismatches. The same finding was observed in HLA-DR and HLA-DQ loci. There was a higher incidence of 2 HLA-DR mismatches in the spousal donor group than the living-related donor group (44% vs 3%, P = 0.004). The incidence of mismatch that involved at least 1 HLA-DQB1 was also higher in the former than latter (80% vs 45%, P = 0.033).

There was a significant association between acute rejection risk and HLA mismatch regardless of donor type (Table 4). Although no antigen mismatch was observed in HLA-A, HLA-B and HLA-DR in 19 patients, none of them experienced graft rejection at 6 months post-transplantation. They also experienced the lowest rejection rates of 5% and 11% at 1 year and 3 years post-transplantation, respectively. Patients with ≥1 HLA mismatch have an increased risk of early graft rejection, and 24% of our patients experienced rejection episodes at 6 months post-transplantation (P = 0.01). Also, our study showed that the risk of rejection was 7 times higher at 1 year (29%, P = 0.03) and 3 years (46%, P = 0.003) post-transplantation.

Univariate analysis of each HLA locus showed the deleterious effects of antigen mismatch on HLA-A and HLA-B. Graft rejection rates in patients with HLA-A mismatch were 26% (OR, 2.69; P = 0.04), 31% (OR, 2.54; P = 0.03) and 51% (OR, 3.22; P = 0.002) at 6 months, 1 year and 3 years, respectively. In patients with HLA-B mismatch, the rejection rates were 25% (OR, 3.25; P = 0.06), 29% (OR, 2.56; P = 0.07) and 47% (OR, 2.68; P = 0.02) over the same period. The rejection risk was comparable between patients with and without mismatch for HLA-Cw at 6 months (21% vs 18%, P = 0.64) and 1 year (28% vs 20%, P = 0.35), but it was higher at 3 years in patients with HLA-Cw mismatch (48%) than those with a match (31%). However, the difference was not statistically significant (OR, 2.0; P = 0.07).

Table 3. HLA Mismatch in Spousal and Living-Related Renal Donors

HLA Type and Mismatch	Relationship Type		*P* Value
	Spouse (%)	Living-Related (%)	
HLA-A			
None	7 (23)	44 (41)	–
1	16 (51)	61 (56)	NS
2	8 (26)	3 (3)	0.0004
≥1	24 (77)	64 (59)	NS
HLA-B			
None	3 (10)	32 (30)	–
1	10 (33)	63 (58)	NS
2	17 (57)	13 (12)	0.0002
≥1	27 (90)	76 (70)	0.039
HLA-Cw			
None	3 (13)	41 (42)	–
1	16 (67)	54 (56)	0.035
2	5 (20)	2 (2)	0.001
≥1	21 (87)	56 (58)	0.012
HLA-DRB1			
None	3 (19)	15 (45)	–
1	6 (37)	17 (52)	NS
2	7 (44)	1 (3)	0.004
≥1	13 (81)	18 (55)	NS
HLA-AB			
None	1 (3)	17 (16)	–
1	3 (10)	37 (34)	NS
2	10 (33)	45 (42)	NS
≥3	16 (54)	9 (8)	0.002
≥ 1	29 (97)	91 (84)	NS
HLA-DQB1			
None	3 (20)	17 (55)	–
1	7 (47)	13 (42)	NS
2	5 (33)	1 (3)	0.008
≥1	12 (80)	14 (45)	0.033
HLA-ABDR			
None	1 (3)	17 (16)	–
1	3 (10)	30 (28)	NS
2	7 (23)	41 (38)	NS
≥3	19 (63)	20 (18)	NS
≥1	29 (97)	91 (84)	NS

HLA: Human leukocyte antigen; NS: Non-significant

Table 4. HLA Mismatch and Risk of Acute Renal Rejection at 6 Months, 1 Year and 3 Years Post-Transplantation

HLA Type and Mismatch	6 Months		1 Year		3 Years	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
HLA-A						
1	2.75 (1.02 – 7.40)	0.04	2.70 (1.11 – 6.59)	0.03	3.69 (1.71 – 7.97)	0.001
2	2.35 (0.50 – 11.02)	NS	1.69 (0.38 – 7.51)	NS	1.37 (0.36 – 5.19)	NS
>1	2.69 (1.02 – 7.11)	0.04	2.54 (1.06 – 6.09)	0.03	3.22 (1.52 – 6.81)	0.002
HLA-B						
1	2.98 (0.81 – 10.99)	NS	2.62 (0.90 – 7.63)	NS	3.0 (1.24 – 7.24)	0.01
2	3.91 (0.95 – 16.11)	NS	2.42 (0.72 – 8.21)	NS	2.06 (0.73 – 5.77)	NS
>1	3.25 (0.91 – 11.53)	NS	2.56 (0.91 – 7.20)	NS	2.68 (1.15 – 6.24)	0.02
HLA-Cw						
1	1.20 (0.46 – 3.10)	NS	1.41 (0.57 – 3.46)	NS	1.83 (0.84 – 3.99)	NS
2	1.85 (0.30 – 11.30)	NS	3.0 (0.56 – 15.87)	NS	5.54 (0.96 – 32.08)	0.04
>1	1.25 (0.49 – 3.17)	NS	1.52 (0.63 – 3.66)	NS	2.0 (0.93 – 4.32)	NS
HLA-DRB1						
1	2.67 (0.47 – 15.13)	NS	3.29 (0.59 – 18.27)	NS	1.30 (0.34 – 4.94)	NS
2	2.67 (0.30 – 23.43)	NS	4.80 (0.61 – 37.35)	NS	2.60 (0.46 – 14.63)	NS
>1	2.67 (0.50 – 14.22)	NS	6.67 (1.22 – 36.22)	0.01	1.56 (0.44 – 5.47)	NS
HLA-AB						
1	–	NS	4.76 (0.56 – 40.64)	NS	5.44 (1.11 – 26.78)	0.03
2	–	0.01	9.5 (1.18 – 76.73)	0.02	10.2 (2.15 – 48.46)	0.001
3	–	0.03	6.3 (0.71 – 56.29)	NS	5.84 (1.12 – 30.55)	0.04
4	–	0.03	9.0 (0.78 – 103.73)	NS	6.8 (0.95 – 48.69)	NS
≥1	–	0.01	7.28 (0.94 – 56.45)	0.03	7.30 (1.62 – 32.88)	0.003
HLA-DQB1						
1	5.94 (0.62 – 56.20)	NS	9.5 (1.05 – 82.26)	0.02	1.50 (0.39 – 5.84)	NS
2	12.67 (0.86 – 186.91)	0.03	19.0 (1.45 – 248)	0.01	6.00 (0.83 – 42.29)	NS
>1	17.1 (1.89 – 154.85)	NS	11.18 (1.29 – 96.65)	0.01	2.06 (0.58 – 7.35)	NS
HLA-ABDR						
1	–	NS	3.72 (0.41 – 33.52)	NS	5.02 (1.00 – 25.32)	0.0001
2	–	0.003	10.8 (1.33 – 87.91)	0.007	10.93 (2.27 – 52.65)	0.0007
3	–	0.04	6.6 (0.79 – 55.48)	NS	6.02 (1.23 – 29.57)	0.0008
4	–	NS	9.0 (0.78 – 103.73)	NS	10.63 (1.48 – 76.08)	0.02
5	–	0.01	18.0 (1.37 – 235.70)	0.03	8.5 (0.97 – 74.43)	NS
>1	–	0.01	7.38 (0.95 – 57.11)	0.03	7.27 (1.62 – 32.65)	0.003

CI: Confidence interval; HLA: Human leukocyte antigen; NS: Non-significant; OR: Odds ratio

With the recent introduction of HLA class II typing, data on HLA-DR and HLA-DQ were available in a third of our patients. HLA-DR mismatch was associated with increased rejection risk at 1 year (31%, $P = 0.01$), but not at 6 months and 3 years. Patients with HLA-DQ mismatch were predisposed to early rejection risk at 6 months ($P = 0.05$) and 1 year ($P = 0.01$).

Discussion

Living-related kidney donors are more common than spousal kidney donors in Malaysia. To the best of our knowledge, this is the first study in Malaysia that reported on the potential of spousal donors as a safe option in renal transplantation despite a higher incidence of HLA mismatch than living-related donors.

In the literature, the benefits of spousal and other living-related donor transplantations have been reported in different populations.[16,17] Terasaki et al[18] reported that patient survival in spousal grafts were similar or even higher than grafts from parents with 1 HLA haplotype mismatch or other living donors. Our study found out that acute rejection episodes, graft function and patient survival at 6 months, 1 year and 3 years in recipients of spousal grafts were comparable to other living-related donor grafts. Additionally, Terasaki et al[19] showed that—in the absence of pregnancy—the survival rate in wife-to-husband grafts was similar to husband-to-wife grafts. Due to the small number of spousal grafts and incomplete pregnancy data in our study, we could not replicate this finding.

Several reports have documented the viability of spousal transplantation in different Asian populations. For example, Tang et al[20] showed that despite a numerical difference between spousal and other living-related grafts in a Chinese population, the incidence of delayed graft function, acute rejection episodes, changes in serum creatinine level and graft or patient survival at 5 years did not reach statistical significance (P >0.05). A recent Korean study on graft and patient survival in renal transplantation had shown comparable rates between spousal and living-related grafts.[17] Kute et al[5] also reported that recipients of living donor allograft from their spouses in India experienced an improvement in their marital, parent-child and sexual relations and family psychodynamics.

A comparative analysis of renal transplantation outcomes over a 20-year period had reported the influence of HLA mismatch on transplant function rate.[21] This finding was corroborated by our study that showed a correlation between HLA mismatch and acute rejection risk regardless of donor types. However, our study also showed that not all classes of antigen mismatch are equally detrimental since HLA-Cw mismatch was not significantly associated with graft rejection up to 3 years post-transplantation. Instead, our study showed that HLA-A and HLA-B mismatch had a substantial negative effect on patient outcomes.

HLA class II antigens are reported to have lower levels of tissue expression compared to HLA class I antigens.[22] However, findings on HLA-DR have shown that it plays an important role in renal transplantation. For example, Moore et al[23] have shown that increased HLA-DR mismatch is associated with increased acute rejection risk and lowered graft survival. In acute rejection, expression of HLA-DR is induced on renal tubular epithelial cells by cytokines.[24] A multi-centre analysis of HLA matching has shown a steady fall in graft survival when the number of HLA mismatch increases—in combination with HLA-DR mismatch—to 6.[25] Additionally, logistic regression analysis in another study reported that HLA-DR mismatch is an independent predictor of subclinical inflammation after renal transplantation.[26] Our study found that HLA-DR mismatch poses a significant risk for the development of acute rejection at 1 year post-transplantation.

HLA disparity is not the only determinant of graft outcomes in spousal and other living-related renal transplantations. Factors such as graft quality,[27] HLA presensitisation,[28] cold ischaemic time,[29] age difference between donor and recipient[30] and compliance with immunosuppressant intake[31] may also contribute to postoperative complications. In our centre, all transplantations are performed as scheduled procedures to prevent prolonged cold ischaemic time and immunosuppressants are initiated prior to surgery. Kuo et al[32] reported that antibody induction was associated with a modest salutary effect on post-transplant acute rejection. Like most transplant centres, the immunosuppressive protocol in our centre comprise a calcineurin inhibitor (cyclosporine or tacrolimus), antimetabolite (mycophenolate mofetil) and steroid (prednisolone) that were administered during the maintenance period. Since most recipients of spousal renal grafts live with their donors, it may address the issue of non-compliance to immunosuppression medication-taking that is associated with negligence and postoperative depression.

Conclusion

Our study showed that HLA mismatch remains a valuable predictor of acute graft rejection in renal transplant patients in Malaysia. Although spousal donors have a higher incidence of HLA mismatch, overall no significant differences were observed in graft rejection risk, function and survival of living-related donor grafts. Consequently, spousal donors are a safe option and can address the shortage of kidney donors in Malaysia.

Acknowledgements

The authors would like to thank the patients for their participation in the study and the nurses and transplant team for their assistance with retrieval of patients' data. This study was supported by the University of Malaya UMRG grant RG506-13HTM.

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Original Article

Sun Exposure and Sun Safety Habits Among Adults in Singapore: A Cross-Sectional Study

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Abstract

Introduction: Sun exposure increases skin cancer risk. Studies have shown that demographic factors influence sun safety behaviour but there is a paucity of such data in Singapore. We aimed to identify sociodemographic predictors of sun safety habits in Singapore. Materials and Methods: A total of 2328 adults participated in a cross-sectional survey on time spent under the sun and sun safety habits (using protective headgear, body attire, umbrellas and sunscreens). A composite Sun Protection Score (higher scores represented better habits [range, 0–15]) and the average daily hours (ADH) of sun exposure were derived from the data. The relationship between the Sun Protection Score and ADH of sun exposure with sociodemographic factors was analysed using univariate (Mann-Whitney U or Kruskal-Wallis tests), multiple linear and logistic regression analyses. Results: The following statistically significant variables predicted a lower Sun Protection Score: men (β = -1.48, *P* <0.001), Indians (β = -1.04, *P* <0.001), history of diabetes (β = -0.60, *P* = 0.007) and people who do not consume alcohol (β = 0.31, *P* = 0.03). Younger adults (β = -0.2, *P* <0.001), men (β = 0.80, *P* <0.001), darker skin type (β = 0.27, *P* <0.001) and lower education level (β = -0.18, *P* <0.001) were statistically significant variables that predicted a longer ADH of sun exposure. Conclusion: The study has identified sociodemographic predictors of sun safety habits in Singapore.

Ann Acad Med Singapore 2019;48:412–28

Key words: Skin cancers, Ultraviolet radiation

Introduction

Exposure to solar ultraviolet radiation (UVR) is a major risk factor for skin cancers.[1,2] Although Asians have a lower risk of melanoma,[3] there has been a steady increase in the overall incidence of skin cancers from 7.4/100,000 in 2003–2006[4] to 19.3/100,000 (for men) and 14.4/100,000 in 2011–2015 (for women).[5]

Singapore is located near the equator and receives solar exposure all year. Studies have shown that demographic factors influence sun safety behaviour. For instance, white women are more likely to use tanning beds, men are more likely to get sunburned and the young tend to spend more time outdoors under the sun. Women tend to have better sun safety habits such as seeking shade and wearing protective clothing, hats or sunscreen.[6–11] However, clear cultural differences exist between countries and there is a paucity of such data in Singapore.

In this study, we aimed to identify sociodemographic predictors of sun safety habits and examine if there were any correlations between these habits and other health behaviours such as smoking and alcohol consumption in Singapore residents.

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Materials and Methods

Study Population

A total of 2328 Singapore citizens and permanent residents aged 18–79 years old were recruited under the Singapore Health (SH) study from August 2012 to March 2013. The SH study is a nationally representative cross-sectional survey designed to estimate the prevalence of chronic diseases and specific health behaviours.[12] Information on umbrella, sunscreen, headgear and protective attire use was obtained. Demographic data such as age, gender, ethnic group, Fitzpatrick skin type, marital status, employment status, smoking history, alcohol consumption, body mass index (BMI), education level, household income, history of diabetes mellitus, hypertension and hyperlipidaemia were obtained in the same interview session. In line with local clinical practice guidelines for obesity,[13] BMI >23 was considered overweight (instead of the World Health Organization's classification of 25). Interviewers were asked to classify the Fitzpatrick skin type of the participant using a chart.[14] Consent was obtained from all participants. The study was approved by the ethics review board of the National University of Singapore.

Sun Protection Score

A composite Sun Protection Score was formulated from the responses with a higher score representing better habits (range, 0–15). Three points were each allocated to the following categories: headgear use, umbrella use, habits at work, habits at leisure time where shade is available, and habits at leisure time where shade is not available. The latter 3 categories were divided into 3 sub-questions to examine upper body attire, lower body attire and sunscreen use during each period. Only participants who applied sunscreen with a sun protection factor (SPF) of ≥30 were awarded a point. This is because using a sunscreen of SPF of ≤30 is more likely to provide inadequate sun protection as studies have shown that SPF values on product labels are often overestimated and that many individuals apply less than half the recommended amount of sunscreen.[15–17]

Average Daily Hours (ADH) of Sun Exposure

Participants were asked how many hours they spent under direct sun exposure on work days and on rest days. The average number of hours spent under the sun in a day, or average daily hours (ADH), was calculated using the number of days the participant reported to work per week.

Statistical Analysis

Univariate analysis was performed (with Sun Protection Score and ADH as dependent variables) using the Mann-Whitney U test for independent variables with 2 groups and the Kruskal-Wallis test for independent variables with multiple groups. *P* values were calculated to test the null hypotheses of no significant difference of Sun Protection Score and ADH with the variables of interest.

Multiple linear regression analysis was then performed with Sun Protection Score and ADH hours as continuous dependent variables and age, gender, ethnic groups, Fitzpatrick skin type, marital status, employment status, smoking history, alcohol consumption, BMI, education level, household income, history of diabetes mellitus, hypertension and hyperlipidaemia as independent variables. Beta coefficient (β) and *P* values were calculated to test the null hypotheses of no significant association between the variables of interest with Sun Protection Score and ADH. Multicollinearity between the independent variables was assessed using variance inflation factor.

Multiple logistic regression analysis was performed with the individual sun safety habits ("umbrella use", "protective headgear use", "sunscreen use", "wearing of protective upper body attire", "wearing of protective lower body attire", "wearing of protective attire at any time") dichotomised into "yes" or "no" responses as the dependent variables and age, gender, ethnic groups, Fitzpatrick skin type, marital status, employment status, smoking history, alcohol consumption, BMI, education level, household income, history of diabetes mellitus, hypertension and hyperlipidaemia as independent variables. Odds ratios (ORs), 95% confidence intervals (CIs) and *P* values were calculated to test the null hypotheses of no association between variables of interest and sun safety habits.

A two-sided $P < 0.05$ was considered statistically significant. Statistical Package for Social Sciences (version 25) was used to conduct the analysis.

Results

The mean age of the participants was 42.6 ± 15.1 years and 48.5% were male. There was an overrepresentation of Malays, Indians and other races compared to the racial make-up in Singapore. The majority of participants had either Fitzpatrick type 3 or 4 skin. The mean ADH was 1.45 ± 1.59 hours (range, 0–12 hours), of which 1.39 ± 1.95 hours (range, 0–12 hours) were spent at work and 1.52 ± 1.57 hours (range, 0–12 hours) were spent on rest days.

Few participants engaged in regular sun safety habits. Only 14.2% of participants wore protective headgear, 18.8% used umbrellas regularly and 23.9% applied sunscreens with an SPF of ≥30. Less than half wore protective upper or lower body attire at any time (Tables 1 and 2; Supplementary Table 1 provides a detailed breakdown analysis on use of upper and lower body protective attire). The mean Sun Protection Score was 3.31 ± 2.44 (range, 0–13).

Table 1. Logistic Regression Model With Protective Headgear and Umbrella Use as Dichotomous Dependent Variables

Variable	Protective Headgear Use						Umbrella Use					
	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value
Age (years)	-	-	1.01	0.99	1.02	0.11	-	-	1.03	1.01	1.04	<0.001
Gender												
Male	187	770	2.26	1.58	3.25	<0.001	35	922	0.08	0.05	0.12	<0.001
Female	94	932	1.00	-	-	-	338	688	1.00	-	-	-
Race												
Chinese	76	218	1.00	-	-	-	151	543	1.00	-	-	-
Malay	98	422	2.06	1.34	3.18	0.001	74	446	0.60	0.41	0.92	0.02
Indian	37	397	0.72	0.43	1.20	0.21	69	365	0.70	0.51	1.23	0.29
Fitzpatrick skin type												
1	2	32	1.00	-	-	-	10	24	1.00	-	-	-
2	17	103	2.62	0.54	12.7	0.23	37	83	1.51	0.46	3.35	0.43
3	154	1088	1.76	0.40	7.75	0.45	260	982	1.02	0.34	2.00	0.96
4	89	355	3.00	0.67	13.5	0.15	53	391	0.99	0.29	1.96	0.98
5	19	118	1.88	0.39	9.20	0.43	13	124	0.67	0.21	2.01	0.52
6	0	6	0	-	-	0.99	0	6	0	-	-	0.99
Marital status												
Married	208	1141	1.16	0.81	1.62	0.41	279	1070	1.54	1.20	2.23	0.01
Single/divorced/widowed	72	554	1.00	-	-	-	90	536	1.00	-	-	-
Employment status												
Employed	213	1182	1.16	0.80	1.67	0.43	214	1181	0.65	0.57	0.99	0.05
Unemployed	67	512	1.00	-	-	-	156	423	1.00	-	-	-
Ever smoked												
Yes	138	565	1.15	0.80	1.63	0.43	50	853	0.61	0.43	0.95	0.02
No	142	1131	1.00	-	-	-	320	953	1.00	-	-	-
Ever drank alcohol												
Yes	151	910	1.05	0.75	1.49	0.76	180	881	1.48	1.04	1.96	0.02
No	129	786	1.00	-	-	-	190	725	1.00	-	-	-
Body mass index (>23)												
Yes	171	988	0.89	0.66	1.21	0.47	190	969	0.93	0.70	1.22	0.62
No	109	708	1.00	-	-	-	180	637	1.00	-	-	-

CI: Confidence interval; GCE: General Certificate of Education; OR: Odds ratio; PSLE: Primary School Leaving Examination
The variance inflation factor values ranged from 1.138–2.318.

Table 1. Logistic Regression Model With Protective Headgear and Umbrella Use as Dichotomous Dependent Variables (Cont'd)

Variable	Protective Headgear Use						Umbrella Use					
	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value
Hypertension												
Yes	49	304	0.87	0.58	1.31	0.51	71	282	1.08	0.68	1.49	0.72
No	228	1375	1.00	-	-	-	297	1306	1.00	-	-	-
Diabetes mellitus												
Yes	27	161	0.75	0.44	1.29	0.30	28	160	0.50	0.30	0.83	0.04
No	248	1522	1.00	-	-	-	340	1430	1.00	-	-	-
Hyperlipidaemia												
Yes	74	419	0.93	0.65	1.34	0.70	74	419	1.24	0.93	1.84	0.22
No	195	1218	1.00	-	-	-	195	1218	1.00	-	-	-
Education						0.07						0.09
PSLE or below	60	285	1.00	-	-	-	76	269	1.00	-	-	-
GCE Ordinary or Normal level	95	644	0.65	0.43	1.01	0.05	145	594	1.43	0.92	2.14	0.09
GCE Advanced level or diploma	72	375	1.02	0.62	1.7	0.93	58	389	1.28	0.73	2.15	0.36
University degree and above	52	391	0.84	0.47	1.49	0.55	91	352	1.88	1.05	3.11	0.02
Household income per month						0.52						0.68
<$2000	59	282	1.00	-	-	-	65	276	1.00	-	-	-
$2000 – 3999	86	493	0.84	0.56	1.26	0.39	109	470	1.12	0.73	1.67	0.59
$4000 – 5999	51	353	0.73	0.45	1.16	0.18	73	331	0.98	0.61	1.53	0.96
≥$6000	60	415	0.72	0.44	1.17	0.18	89	386	0.87	0.52	1.37	0.57
Total, n (%)	281 (14.2)	1702 (85.8)					373 (18.8)	1610 (81.2)				

CI: Confidence interval; GCE: General Certificate of Education; OR: Odds ratio; PSLE: Primary School Leaving Examination
The variance inflation factor values ranged from 1.138–2.318.

Table 2. Logistic Regression Model With Wearing of Protective Body Attire and Sunscreen Use as Dichotomous Dependent Variables

Variable	Wearing of Any Form of Protective Attire At Any Time*						Sunscreen Use					
	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value
Age (years)	-	-	0.97	0.96	0.98	<0.001	-	-	1.00	0.99	1.02	0.55
Gender												
Male	689	163	1.38	0.98	1.95	0.07	82	770	0.14	0.10	0.20	<0.001
Female	675	194	1.00	-	-	-	330	539	1.00	-	-	-
Race						<0.001						<0.001
Chinese	495	86	1.00	-	-	-	177	404	1.00	-	-	-
Malay	372	92	0.98	0.64	1.50	0.92	88	376	0.58	0.38	0.87	0.009
Indian	258	117	0.43	0.28	0.66	<0.001	67	308	0.39	0.25	0.62	<0.001
Fitzpatrick skin type						0.20						0.54
1	21	4	1.00	-	-	-	9	16	1.00	-	-	-
2	88	13	0.89	0.17	4.58	0.89	34	67	1.10	0.36	3.33	0.87
3	891	183	0.68	0.15	3.08	0.62	282	792	0.99	0.36	2.74	0.99
4	281	120	0.45	0.09	2.08	0.31	70	331	1.47	0.51	4.25	0.48
5	79	37	0.46	0.09	2.20	0.33	17	99	1.32	0.40	4.36	0.64
6	4	0	0	-	-	0.99	0	4	0	-	-	0.99
Marital status												
Married	642	707	0.77	0.54	1.09	0.14	281	883	1.03	0.75	1.42	0.85
Single/divorced/widowed	257	369	1.00	-	-	-	130	420	1.00	-	-	-
Employment status												
Employed	976	238	1.12	0.82	1.53	0.48	286	928	1.22	0.90	1.65	0.20
Unemployed	384	115	1.00	-	-	-	125	374	1.00	-	-	-
Ever smoked												
Yes	486	140	0.66	0.47	0.94	0.02	91	535	0.95	0.67	1.36	0.78
No	875	214	1.00	-	-	-	320	769	1.00	-	-	-
Ever drank alcohol												
Yes	763	165	1.33	0.97	1.84	0.07	230	698	1.35	0.98	1.86	0.07
No	598	189	1.00	-	-	-	181	606	1.00	-	-	-
Body mass index (>23)												
Yes	787	210	1.25	0.94	1.66	0.13	200	797	0.89	0.67	1.12	0.41
No	574	144	1.00	-	-	-	211	507	1.00	-	-	-

CI: Confidence interval; GCE: General Certificate of Education; OR: Odds ratio; PSLE: Primary School Leaving Examination
The variance inflation factors ranged from 1.138–2.318.
*See Supplementary Table 2 for a detailed breakdown analysis of the use of upper and lower body protective attire (as dependent variables).

Table 2. Logistic Regression Model With Wearing of Protective Body Attire and Sunscreen Use as Dichotomous Dependent Variables (Cont'd)

Variable	Wearing of Any Form of Protective Attire At Any Time*						Sunscreen Use					
	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value
Hypertension												
Yes	220	72	1.08	0.73	1.58	0.71	57	235	0.91	0.60	1.37	0.64
No	1130	275	1.00	-	-	-	353	1052	1.00	-	-	-
Diabetes mellitus												
Yes	104	49	0.72	0.46	1.13	0.15	24	129	0.61	0.40	1.08	0.09
No	1246	299	1.00	-	-	-	384	1161	1.00	-	-	-
Hyperlipidaemia												
Yes	315	90	1.26	0.89	1.79	0.19	96	309	1.19	0.83	1.69	0.34
No	1010	245	1.00	-	-	-	308	947	1.00	-	-	-
Education						0.23						0.001
PSLE or below	175	94	1.00	-	-	-	42	227	1.00	-	-	-
GCE Ordinary or Normal level	516	140	1.45	0.99	2.12	0.06	166	490	2.37	1.49	3.77	<0.001
GCE Advanced level or diploma	338	63	1.30	0.81	2.12	0.27	90	311	1.82	1.05	3.14	0.03
University degree and above	331	57	1.56	0.92	2.64	0.09	113	275	2.48	1.41	4.35	0.02
Household income per month						0.22						0.16
<$2000	199	86	1.00	-	-	-	58	227	1.00	-	-	-
$2000 – 3999	289	110	1.20	0.82	1.73	0.35	100	399	0.82	0.64	1.24	0.35
$4000 – 5999	293	68	1.31	0.86	2.00	0.21	88	273	0.99	0.63	1.54	0.97
≥$6000	360	61	1.64	1.03	2.60	0.04	129	292	1.26	0.80	1.99	0.32
Total, n (%)	1364 (79.3)	357 (20.7)					412 (23.9)	1309 (76.1)				

CI: Confidence interval; GCE: General Certificate of Education; OR: Odds ratio; PSLE: Primary School Leaving Examination

The variance inflation factors ranged from 1.138–2.318.

*See Supplementary Table 2 for a detailed breakdown analysis of the use of upper and lower body protective attire (as dependent variables).

Univariate Analysis

A lower Sun Protection Score was associated with male gender (P <0.001), Indian ethnicity (P <0.001), high BMI (P<0.001), darker skin type (P<0.001), smokers (P<0.001), current employment (P <0.001) and history of diabetes mellitus (P = 0.003). A longer ADH was associated with an older age (P <0.001), male gender (P <0.001), Malay ethnicity (P<0.001), smokers (P<0.001), darker skin type (P <0.001), participants without hypertension (P = 0.006) and without hyperlipidaemia (P <0.001). More educated participants also tended to have longer ADH, although those with a university degree abstained more from the sun (P <0.001). These findings are presented in Table 3.

Multiple Linear Regression Analysis

By using multiple linear regression analysis to adjust for the independent variables, the following were statistically significant and predicted a lower Sun Protection Score: men (β = -1.43, P <0.001), Indians (β = -1.03, P <0.001), diabetics (β = -0.56, P = 0.007) and people who do not consume alcohol (β = 0.31, P = 0.03). The relationships between BMI, skin type, smoking history and employment with Sun Protection Score seen in univariate analysis were no longer statistically significant when adjusting for all covariates.

On the other hand, the statistically significant variables of younger age (β = -0.02, P <0.001), male gender (β = 0.80, P <0.001), darker skin type (β = 0.27, P <0.001) and lower education level (β = -0.18, P <0.001) predicted longer ADH in the multiple linear regression model. The relationships between Malay ethnicity, smoking history, hypertension and hyperlipidaemia with ADH seen in univariate analysis were no longer statistically significant when adjusting for covariates. These findings are presented in Table 4. Supplementary Table 2 compares the average number of hours spent under the sun at work and on rest days.

Multiple Logistic Regression Analysis

In the multiple logistic regression model, dichotomous individual sun safety habits comprised the dependent variables and demographic variables comprised the independent variables. Malays (OR = 2.06, P <0.001) and males (OR = 2.26, P <0.001) were more likely to use headgear. Males (OR = 0.08, P <0.001), Malays (OR = 0.60, P = 0.02), diabetics (OR = 0.50, P = 0.04), unmarried individuals (OR = 0.65, P = 0.01), smokers (OR = 0.61, P = 0.02), people who do not consume alcohol (OR = 0.68, P = 0.02) and those without a university degree (OR = 0.53, P = 0.02) were less likely to use umbrellas. Sunscreen use was less likely in males (OR = 0.14, P <0.001), Indians (OR = 0.39, P <0.001) and in those who had received Primary School Leaving Examination education or below (P = 0.001). Indians (OR = 0.43, P <0.001), smokers (OR = 0.66, P = 0.02) and those who earned an income of <$6000 per month (OR = 0.61, P = 0.04) were less likely to wear protective clothes at any time. There was no evidence of multicollinearity between the independent variables in the linear or logistic regression models.

Determinants of Risky Sun Exposure and Safety Habits

This study has identified 4 vulnerable demographic groups. First, males are at greater risk because they spent an average of 53 more minutes under the sun per day (71 more minutes at work and 23 more minutes on rest days). In addition, they had an average score that was 1.5 points lower on the Sun Protection Score. Men had 86% and 92% lower odds of using sunscreen and umbrellas, respectively. Second, younger adults spent more time under the sun—both during work and on rest days—but did not compensate by having better sun safety habits. Third, Indians and individuals with dark skin demonstrated riskier behaviour. Indians scored an average score that was 1 point lower than the Chinese in the Sun Protection Score, had 57% lower odds of wearing any form of protective attire and 61% lower odds of using sunscreen compared to the Chinese. Those with darker skin type were more likely to spend more time under the sun (especially at work). Fourth, participants who had less education spent more hours under the sun (especially at work) and were less likely to use sunscreen and umbrellas.

Discussion

This is the first study to examine sun safety habits in Singapore. The multiracial make-up of Singapore's population presents a good opportunity to compare the differences between the racial groups and skin phototypes. The findings suggest that most do not regularly engage in sun safety habits as evidenced by the majority's reluctance to use umbrellas, wear headgear, apply sunscreen and wear adequate protective clothing. A lack of awareness about the harmful effects of sun exposure or fear of discomfort in the hot and humid climate may explain the reluctance among the local population.

It is not surprising to find men and young adults at greater risk as they are more likely to perform manual labour, work outdoors or engage in outdoor sports. Many other studies worldwide have similarly found that men[9,18–20] and young adults[6,8–11,18,19] are at greater risk. More emphasis on educating men and young adults on the risk of skin cancers may be needed.

Indians and individuals with dark skin also demonstrated riskier behaviour possibly due to the belief that dark skin gives them natural protection from the sun. Other ethnicity-specific or cultural practices may be additional reasons why dark-skinned individuals demonstrated poor

Table 3. Univariate Analysis Examining the Relationship Between Sun Protection Score and ADH With Demographic Variables

Question	Option	Distribution (%)	Mean Sun Protection Score	*P* Value	Mean ADH	*P* Value
Age (years)				0.43		<0.001
	<40	804 (40.5)	3.24		1.74	
	≥40	1179 (59.5)	3.35		1.25	
Gender				<0.001		<0.001
	Male	1130 (48.5)	2.55		1.91	
	Female	1198 (51.5)	4.06		1.03	
Race*				<0.001		<0.001
	Chinese	798 (34.3)	3.61		1.21	
	Malay	599 (25.7)	3.24		1.71	
	Indian	535 (23.0)	2.61		1.51	
	Others	389 (16.7)	3.71		1.46	
Fitzpatrick skin type				<0.001		<0.001
Interviewers were asked to classify the participant's skin type using a chart	1. Never tans, always burns, pale white skin	34 (1.5)	4.24		0.76	
	2. Tans poorly, burns easily, fair skin	120 (5.2)	4.17		1.04	
	3. Tans after initial burn, darker white skin	1242 (53.4)	3.52		1.30	
	4. Tans easily, burns minimally, light brown skin	444 (19.1)	2.77		1.85	
	5. Tans darkly easily, rarely burns, brown skin	137 (5.9)	2.29		2.07	
	6. Tans darkly easily, never burns, dark brown or black skin	6 (0.3)	2.25		0.87	
Marital status†				0.34		<0.001
	Married	1554 (66.8)	3.35		1.33	
	Unmarried	766 (32.9)	3.22		1.71	
Currently working‡				<0.001		0.11
	Yes	1618 (69.5)	3.19		1.49	
	No	692 (29.7)	3.61		1.37	
Smoking history§				<0.001		<0.001
Have you ever smoked cigarettes?	Yes	843 (36.2)	2.71		1.82	
	No	1478 (63.5)	3.65		1.25	

ADH: Average daily hours
*Seven missing. "Others" comprised Burmese, Javanese, Filipinos, Sikhs, Indonesians, Eurasians, Boyanese, Japanese, Malayalees, Persians and Thai.
†Eight missing.
‡Nine missing.
§Nine missing.

Table 3. Univariate Analysis Examining the Relationship Between Sun Protection Score and ADH With Demographic Variables (Cont'd)

Question	Option	Distribution (%)	Mean Sun Protection Score	*P* Value	Mean ADH	*P* Value
Alcohol history[‖]				0.51		0.12
Have you ever consumed alcohol?	Yes	1236 (53.1)	3.27		1.51	
	No	1085 (46.6)	3.35		1.39	
Body mass index				<0.001		0.05
	<23	961 (41.3)	3.56		1.37	
	≥23	1360 (58.4)	3.13		1.51	
Education[¶]				0.16		<0.001
What is the highest level of education that you have attained?	Primary School Leaving Examination or below	414 (17.9)	3.09		1.25	
	General Certificate of Education Ordinary or Normal level	871 (27.6)	3.33		1.56	
	General Certificate of Education Advanced level or diploma	521 (22.5)	3.21		1.73	
	University degree and above	509 (22.0)	3.53		1.15	
Household income[#]				0.08		0.74
Over the last 12 months, what is the average earnings (S$) of the household per month?	<$2000	423 (18.2)	3.21		1.44	
	$2000 – 3999	667 (28.7)	3.15		1.57	
	$4000 – 5999	465 (20.0)	3.19		1.37	
	≥$6000	546 (23.5)	3.61		1.35	
History of diabetes mellitus[**]				0.003		0.31
Have you ever been told by a doctor (western trained) that you have diabetes?	Yes	223 (9.6)	2.76		1.34	
	No	2076 (89.2)	3.37		1.47	
History of hypertension[††]				0.46		0.006
Have you ever been told by a doctor (western trained) that you have high blood pressure?	Yes	412 (17.7)	3.22		1.25	
	No	1886 (81.0)	3.34		1.50	
History of hyperlipidaemia[‡‡]				0.72		<0.001
Have you ever been told by a doctor (western trained) that you have high cholesterol or lipids?	Yes	556 (23.9)	3.38		1.23	
	No	1680 (72.2)	3.33		1.55	

ADH: Average daily hours
[‖]Seven missing.
[¶]Ten missing.
[#]Two-hundred-and-twenty-seven missing (participants either refused to reveal or did not know their average household income per month).
[**]Twenty-nine missing.
[††]Thirty missing.
[‡‡]Ninety-two missing.

Table 4. Linear Regression Model With Sun Protection Score and Average Daily Hours as Dependent Variables

Variable	Sun Protection Score					Average Daily Hours Under the Sun*				
	Mean Score	β	95% Lower CI	95% Upper CI	*P* Value	Mean Hours	β	95% Lower CI	95% Upper CI	*P* Value
Age (years)	-	0.005	-0.006	0.02	0.41	-	-0.02	-0.02	-0.016	<0.001
Gender										
Male	2.55	-1.43	-1.70	-1.14	<0.001	1.91	0.80	0.62	0.97	<0.001
Female	4.06	-	-	-	-	1.03	-	-	-	-
Race										
Chinese	3.61	-0.10	-0.47	0.26	0.58	1.21	-0.21	-0.43	0.02	0.07
Malay	3.24	-0.24	-0.61	0.12	0.19	1.71	0.10	-0.13	0.33	0.39
Indian	2.61	-1.03	-1.42	-0.64	<0.001	1.51	-0.19	-0.43	0.05	0.13
Fitzpatrick skin type	-	-0.10	-0.28	0.08	0.27	-	0.27	0.16	0.38	<0.001
Marital status										
Married	3.35	0.15	-0.14	0.44	0.32	1.33	-0.11	-0.28	0.07	0.23
Single/divorced/widowed	3.22	-	-	-	-	1.71	-	-	-	-
Employment status										
Employed	3.19	-0.15	-0.43	0.12	0.28	1.49	-0.09	-0.26	0.08	0.29
Unemployed	3.61	-	-	-	-	1.37	-	-	-	-
Ever smoked										
Yes	2.71	-0.24	-0.53	0.06	0.11	1.82	0.07	-0.11	0.25	0.45
No	3.65	-	-	-	-	1.25	-	-	-	-
Ever drank alcohol										
Yes	3.27	0.31	0.03	0.58	0.03	1.51	0.03	-0.14	0.21	0.71
No	3.35	-	-	-	-	1.39	-	-	-	-
Body mass index (>23)										
Yes	3.13	-0.02	-0.27	0.23	0.90	1.51	0.08	-0.08	0.23	0.33
No	3.56	-	-	-	-	1.37	-	-	-	-

β: Beta coefficient; CI: Confidence interval

The variance inflation factor values ranged from 1.132–2.317.

*See Supplementary Table 1 for a detailed breakdown analysis of average daily hours at work and rest days (as dependent variables).

Table 4. Linear Regression Model With Sun Protection Score and Average Daily Hours as Dependent Variables (Cont'd)

Variable	Sun Protection Score					Average Daily Hours Under the Sun*				
	Mean Score	β	95% Lower CI	95% Upper CI	*P* Value	Mean Hours	β	95% Lower CI	95% Upper CI	*P* Value
Hypertension										
Yes	3.22	0.09	-0.25	0.44	0.59	1.25	-0.09	-0.30	0.12	0.41
No	3.34	-	-	-	-	1.50	-	-	-	-
Diabetes mellitus										
Yes	2.76	-0.56	-1.03	-0.16	0.007	1.34	0.06	-0.20	0.32	0.65
No	3.37	-	-	-	-	1.47	-	-	-	-
Hyperlipidaemia										
Yes	3.38	0.08	-0.23	0.39	0.62	1.23	-0.13	-0.32	0.06	0.17
No	3.33	-	-	-	-	1.55	-	-	-	-
Education	-	0.15	-0.002	0.29	0.53	-	-0.18	-0.27	-0.08	<0.001
Household income	-	0.04	-0.09	0.17	0.54	-	0.003	-0.08	0.081	0.94

β: Beta coefficient; CI: Confidence interval
The variance inflation factor values ranged from 1.132–2.317.
*See Supplementary Table 1 for a detailed breakdown analysis of average daily hours at work and rest days (as dependent variables).

sun safety habits. Although having dark skin is protective to a certain extent, experimental studies have confirmed the presence of deoxyribonucleic acid (DNA) damage in dark skin after UVR exposure.[21] A local health survey in 2003 had found that 50% of Malay and >50% of Indian children had suffered sunburns in the first 10 years of life.[22] Considering their riskier behaviour, potential for misdiagnosis and poorer overall prognosis from skin cancer,[1,23,24] it will be prudent for clinicians to have a higher index of suspicion for skin cancer when dark-skinned individuals present with skin lesions.

A lower education level is associated with more sun exposure at work but not on rest days. This may imply that lower educated individuals are more likely to work in outdoor environments. Despite this, they were also less likely to wear protective lower body attire, use umbrellas or sunscreen—a common finding also seen in other studies.[8,25,26] Those who earned <$6000 per month were also less likely to wear protective clothes at any time. Studies have shown that the risk of non-melanoma skin cancer increases when people work outdoors.[27] There is a need to encourage sun safety habits if it is not possible to avoid the sun at work.

Diabetic individuals have an overall lower Sun Protection Score than non-diabetic individuals and were less likely to use an umbrella. Similarly, smokers were also less likely to use an umbrella and wear protective attire (especially of the upper body). Conversely, alcohol consumers seemed to be more conscious of sun safety (higher Sun Protection Score) and used umbrellas more frequently. Interestingly, married people spent less hours under the sun on their rest days and used more umbrellas. Interpretation of these findings is limited but may reflect clustering of health behaviours or from residual confounders.

The local population spent a mean duration of 1.45 hours per day exposed to direct sun—with more time spent under the sun on their rest days than work days—which may suggest that people enjoy outdoor activities and seek the sun for leisure. In comparison, Caucasian populations spent longer average durations under the sun in summer (up to 3 or 4 hours a day).[28] This may, to some extent, reflect differences in beauty ideals between Asian and Western societies—with Asian societies valuing "white skin" while their Western counterparts value "tan skin".[29]

The effects of UVR on the skin are complex. Absorbed UVR damages DNA and causes mutations, ultimately leading to skin tumours, photoageing and pigmentary disorders.[30] On the other hand, exposure to ultraviolet B radiation is important for the endogenous production of vitamin D that is important for skeletal and muscular health. Exposing the arms and legs for 5 to 30 minutes between the hours of 10 am to 3 pm twice a week is generally adequate to obtain sufficient vitamin D while minimising photodamage.[31] Despite a mean ADH of 1.45 hours found

in this study, the local prevalence of vitamin D deficiency is high at 42% in a healthy population[32] and 57.5% in those who suffered a hip fracture,[33] which may suggest that there are other more important factors that contribute to vitamin D deficiency such as diet or physical inactivity.[34]

There are several limitations in this study. Information obtained by self-reporting during the interviews may result in recall or social desirability bias. Due to the study design, we were unable to examine cause-and-effect relationships and found that several statistically significant results were likely explained by residual confounders. The Sun Protection Score was designed to capture general sun safety habits but is not a validated scoring system. Further studies that examine factors such as indoor and outdoor tanning, family history of skin cancer, incidence of sunburn and attitudes towards change may provide more information to guide more effective health initiatives.[35]

Conclusion

This study revealed that although our local population spends less time under the sun as compared to Western populations, sun safety habits are not widely practised. The study has identified that men, young adults, Indians, dark-skinned individuals and those with lower education are most vulnerable to poor sun safety habits and prolonged sun exposure, and may benefit the most from sun safety health promotions. Future research may include longitudinal studies to examine sun exposure trends among the local population over time and determine the effectiveness of health initiatives.

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Supplementary Table 1. Logistic Regression Model With Breakdown Analysis of the Wearing of Protective Upper and Lower Body Attire as Dichotomous Dependent Variables

Variable	Wearing of Protective Upper Body Attire at Any Time						Wearing of Protective Lower Body Attire at Any Time					
	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value
Age (years)	-	-	1.02	1.01	1.03	<0.001	-	-	0.95	0.94	0.96	<0.001
Gender												
Male	387	570	0.99	0.78	1.27	0.95	609	243	2.89	2.11	3.96	<0.001
Female	515	511	1.00	-	-	-	382	487	1.00	-	-	-
Race						<0.001						<0.001
Chinese	248	446	1.00	-	-	-	467	114	1.00	-	-	-
Malay	287	233	2.91	2.13	3.99	<0.001	186	278	0.14	0.09	0.21	<0.001
Indian	200	234	2.18	1.56	3.05	<0.001	181	194	0.14	0.09	0.22	<0.001
Fitzpatrick skin type						<0.001						0.64
1	21	13	1.00	-	-	-	12	13	1.00	-	-	-
2	57	63	0.51	0.20	1.31	0.16	64	37	1.64	0.48	5.60	0.43
3	604	638	0.42	0.18	0.99	0.05	633	441	1.91	0.63	4.82	0.25
4	161	283	0.21	0.08	0.50	0.01	214	187	2.22	0.71	6.99	0.17
5	56	81	0.22	0.08	0.60	0.02	64	52	2.58	0.77	8.66	0.13
6	3	3	0.29	0.04	2.30	0.24	4	0	0	-	-	0.99
Marital status												
Married	642	707	0.84	0.66	1.09	0.16	281	883	0.73	0.53	1.02	0.07
Single/divorced/widowed	257	369	1.00	-	-	-	130	420	1.00	-	-	-
Employment status												
Employed	645	750	1.49	1.17	1.91	0.02	286	928	1.15	0.85	1.55	0.38
Unemployed	254	325	1.00	-	-	-	125	374	1.00	-	-	-
Ever smoked												
Yes	262	441	0.68	0.53	0.88	0.03	415	211	1.05	0.76	1.45	0.78
No	637	636	1.00	-	-	-	574	515	1.00	-	-	-
Ever drank alcohol												
Yes	400	661	0.70	0.55	0.90	0.03	683	245	2.13	1.61	2.83	<0.001
No	499	416	1.00	-	-	-	306	481	1.00	-	-	-
Body mass index (>23)												
Yes	561	598	1.15	0.92	1.42	0.22	551	446	1.06	0.81	1.39	0.68
No	338	479	1.00	-	-	-	438	280	1.00	-	-	-

CI: Confidence interval; GCE: General Certificate of Education; OR: Odds ratio; PSLE: Primary School Leaving Examination
The variance inflation factors ranged from 1.138–2.318.

Supplementary Table 1. Logistic Regression Model With Breakdown Analysis of the Wearing of Protective Upper and Lower Body Attire as Dichotomous Dependent Variables (Cont'd)

Variable	Wearing of Protective Upper Body Attire at Any Time						Wearing of Protective Lower Body Attire at Any Time					
	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value	Yes	No	Adjusted OR	95% Lower CI	95% Upper CI	*P* Value
Hypertension												
Yes	181	172	1.21	0.90	1.63	0.20	144	148	1.01	0.69	1.48	0.96
No	712	891	1.00	-	-	-	837	568	1.00	-	-	-
Diabetes mellitus												
Yes	93	95	0.90	0.62	1.31	0.59	61	92	0.73	0.45	1.17	0.19
No	800	970	1.00	-	-	-	921	624	1.00	-	-	-
Hyperlipidaemia												
Yes	253	240	1.07	0.83	1.40	0.59	205	200	1.00	0.72	1.40	0.98
No	617	796	1.00	-	-	-	756	499	1.00	-	-	-
Education						0.05						0.11
PSLE or below	179	166	1.00	-	-	-	85	184	1.00	-	-	-
GCE Ordinary or Normal level	318	421	1.01	0.73	1.39	0.98	259	297	1.65	1.10	2.49	0.02
GCE Advanced level or diploma	178	269	0.97	0.66	1.42	0.86	273	128	1.49	0.92	2.41	0.10
University degree and above	223	220	1.45	0.96	2.19	0.08	271	117	1.66	0.98	2.78	0.06
Household income per month						0.97						0.03
<$2000	156	185	1.00	-	-	-	128	157	1.00	-	-	-
$2000 – 3999	260	319	1.01	0.40	1.36	0.80	263	236	1.05	0.72	1.53	0.81
$4000 – 5999	176	228	1.05	0.75	1.47	0.61	217	144	1.19	0.79	1.79	0.42
≥$6000	223	252	1.10	0.77	1.56	0.21	300	121	1.77	1.14	2.74	0.01
Total, n (%)	902 (45.4)	1081 (54.6)					730 (42.4)	991 (57.6)				

CI: Confidence interval; GCE: General Certificate of Education; OR: Odds ratio; PSLE: Primary School Leaving Examination
The variance inflation factor values ranged from 1.138–2.318.

Supplementary Table 2. Linear Regression Model With Breakdown Analysis of the Average Number of Hours Spent Under the Sun at Work and on Rest Days as Dependent Variables

Variable	Average Number of Hours Spent Under the Sun at Work					Average Number of Hours Spent Under the Sun on Rest Days				
	Mean Hours	β	95% Lower CI	95% Upper CI	*P* Value	Mean Hours	β	95% Lower CI	95% Upper CI	*P* Value
Age (years)	-	-0.02	-0.04	-0.02	<0.001	-	-0.23	-0.03	-0.02	<0.001
Gender										
Male	1.91	1.05	0.81	1.30	<0.001	1.76	0.42	0.24	0.60	<0.001
Female	0.72	-	-	-	-	1.38	-	-	-	-
Race										
Chinese	1.08	-0.27	-0.57	0.04	0.08	1.37	-0.19	-0.41	0.03	0.10
Malay	1.90	0.24	-0.09	0.56	0.14	1.57	0.02	0.21	0.25	0.89
Indian	1.35	-0.41	-0.75	-0.07	0.02	1.66	-0.002	-0.24	0.24	0.90
Fitzpatrick skin type	-	0.35	0.20	0.50	<0.001	-	0.04	-0.07	0.15	0.50
Marital status										
Married	1.36	0.08	-0.18	0.33	0.56	1.34	-0.31	-0.48	-0.13	0.001
Single/divorced/widowed	1.47	-	-	-	-	1.92	-	-	-	-
Employment status										
Employed	-	-	-	-	-	1.60	0.05	-0.12	0.24	0.54
Unemployed	-	-	-	-	-	1.34	-	-	-	-
Ever smoked										
Yes	1.93	0.15	-0.10	0.40	0.24	1.73	-0.09	-0.27	0.09	0.33
No	1.03	-	-	-	-	1.48	-	-	-	-
Ever drank alcohol										
Yes	1.41	-0.01	-0.24	0.23	0.96	1.64	0.09	-0.10	0.25	0.38
No	1.36	-	-	-	-	1.45	-	-	-	-
Body mass index (>23)										
Yes	1.49	0.01	-0.21	0.23	0.93	1.54	0.08	-0.06	0.25	0.22
No	1.23	-	-	-	-	1.49	-	-	-	-

β: Beta coefficient; CI: Confidence interval
The variance inflation factor values ranged from 1.132–2.317.

Supplementary Table 2. Linear Regression Model With Breakdown Analysis of the Average Number of Hours Spent Under the Sun at Work and on Rest Days as Dependent Variables (Cont'd)

Variable	Average Number of Hours Spent Under the Sun at Work					Average Number of Hours Spent Under the Sun on Rest Days				
	Mean Hours	β	95% Lower CI	95% Upper CI	*P* Value	Mean Hours	β	95% Lower CI	95% Upper CI	*P* Value
Hypertension										
Yes	1.32	0.008	-0.28	0.30	0.96	1.22	-0.07	-0.27	0.14	0.54
No	1.40	-	-	-	-	1.59	-	-	-	-
Diabetes mellitus										
Yes	1.48	0.07	-0.33	0.46	0.74	1.23	0.06	-0.21	0.32	0.67
No	1.38	-	-	-	-	1.56	-	-	-	-
Hyperlipidaemia										
Yes	1.47	-0.08	-0.34	0.17	0.52	1.24	-0.001	-0.19	0.19	0.90
No	1.38	-	-	-	-	1.63	-	-	-	-
Education	-	-0.26	-0.39	-0.13	<0.001	-	0.04	-0.05	0.13	0.36
Household income	-	-0.03	-0.15	0.08	0.59	-	0.05	-0.02	0.13	0.17

β: Beta coefficient; CI: Confidence interval

The variance inflation factor values ranged from 1.132–2.317.

Marital Status and Positive Mental Health of Psychiatric Outpatients

Dear Editor,

Marriage has been associated with positive effects for individuals—a stronger sense of self-identity, improved psychosocial outcomes, increased economic resources and companionship especially during stressful life events.[1] The social and emotional support experienced by married individuals may be an important catalyst for greater life satisfaction and better coping mechanisms against the hardships of life, leading to improved psychological well-being.[2] In particular, married individuals with anxiety, mood and substance abuse disorders reported lower prevalence of mental health issues such as depression or alcoholism, lower rates of suicide and fewer admissions to psychiatric facilities.[3] The protective effects of marriage have been attributed to companionship that serves as a stress buffer and imparts feelings of happiness, life satisfaction, purpose and belonging.[3]

Jahoda[4] first introduced the concept of positive mental health (PMH) as a "personal matter involving humans" and a "condition of an individual human mind" that concentrates on the individuals' attitude towards themselves, the way they perceive the world around them and their ability to take life as it comes. PMH introduces a wide range of emotional and cognitive aspects that are essential for the well-being of individuals, their family and society.[5] In addition, the beneficial effects of PMH in individuals with mental illness have been associated with decreased clinical symptoms and better recovery.[5] Many studies have examined the relationship between marital status and psychological well-being in patients with mental illness. However, a majority of these studies involved Western populations. Hence, there is a need for local studies to examine the differences especially in a multiethnic country such as Singapore. This study aimed to investigate the differences and associations between marital status and PMH total and domain scores among outpatients with schizophrenia, depressive and anxiety disorders.

Materials and Methods

From January 2014 to June 2015, a total of 308 outpatients with clinical diagnosis of schizophrenia spectrum, depressive and anxiety disorders (according to the International Classification of Diseases, 9th Revision)[6] from the Institute of Mental Health were recruited for the study. Participants were: 1) aged 21–65 years old, 2) from the Chinese, Malay and Indian ethnic groups, 3) literate in the English language, and 4) able to self-complete the questionnaires. Those with intellectual disabilities, who were attending the clinic on their first visit or unable to read English were excluded from the study. Written informed consent was obtained from all participants. The study was approved by the relevant ethics committee (Domain Specific Review Board of the National Healthcare Group, Singapore).

Sociodemographic information was collected using a structured questionnaire. Clinical information such as psychiatric diagnosis was collected through a review of medical records. Participants' functional status was evaluated using Global Assessment of Functioning (GAF) which was administered by trained interviewers. The PMH instrument and Satisfaction With Life Scale (SWLS) were self-administered questionnaires completed by participants.

The 47-item PMH is a self-administered instrument that was developed and validated in Singapore to measure levels of PMH in the local general population[7] and among the psychiatric population.[5] It contains 6 domains: 1) General Coping (GC), 2) Emotional Support (ES), 3) Spirituality (S), 4) Interpersonal Skills (IS), 5) Personal Growth and Autonomy (PGA), and 6) Global Affect (GA). Higher total scores indicate greater levels of PMH. An earlier article has reported detailed information on the study methodology.[5]

The 5-item SWLS[8] is an instrument used to assess global cognitive judgement of satisfaction with one's life. The items in the SWLS subscale are scored on a 7-point scale from "strongly disagree" to "strongly agree". Higher total scores on the SWLS indicate greater life satisfaction.

The GAF[9] was used to evaluate the psychological, social and occupational functioning of the participants using a 100-point single-item rating scale for overall psychosocial functioning during the past 1 month. An accurate description of functioning for each participant is reached as per the rater's judgement. Higher total scores on the GAF indicate greater levels of individual functioning.

Results

Sociodemographic and clinical characteristics of the participants are shown in Table 1. Among the participants,

Table 1. Sociodemographic and Clinical Characteristics of Never-Married and Married Outpatients With Mental Disorders (n = 308)

Variable	Overall Sample		Never-Married		Married		*P* Value*
	n	%	n	%	n	%	
Age (years)							<0.001
21 – 39	169	54.9	135	67.5	34	31.5	
40 – 65	139	45.1	65	32.5	74	68.5	
Marital status							
Never-married	200	64.9					
Married	108	35.1					
Gender							0.01
Male	163	52.9	116	58.0	47	43.5	
Female	145	45.1	84	42.0	61	56.5	
Ethnicity							0.14
Chinese	134	43.5	92	46.0	42	38.9	
Malay	87	28.2	49	24.5	38	35.2	
Indian	87	28.2	59	29.5	28	25.9	
Education							0.39
Some formal/primary	26	8.40	14	7.00	12	11.1	
Secondary/junior college/pre-university	204	66.2	132	66.0	72	66.7	
Vocational	36	11.7	27	13.5	9	8.30	
Tertiary/postgraduate	42	13.6	27	13.5	15	13.9	
Employment status							0.86
Unemployed	167	54.2	109	54.4	58	53.7	
Employed	140	45.5	90	45.0	50	46.3	
Diagnostic group							<0.001
Depressive disorders	108	35.1	58	29.0	50	46.3	
Anxiety disorders	74	24.0	43	21.5	31	28.7	
Schizophrenia spectrum disorders	126	40.9	99	49.5	27	25.0	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Global Assessment of Functioning	51.8	16.4	51.2	16.6	52.8	15.9	0.41
Satisfaction With Life Scale	19.7	7.93	18.7	8.09	21.7	7.25	<0.001
Positive Mental Health scores							
Positive Mental Health total	3.94	0.96	3.84	0.98	4.12	0.88	0.01
General Coping	3.82	1.15	3.75	1.19	3.95	1.07	0.15
Emotional Support	4.01	1.31	3.86	1.33	4.28	1.22	0.01
Spirituality	3.95	1.48	3.86	1.50	4.13	1.41	0.12
Interpersonal Skills	4.25	1.03	4.11	1.05	4.48	0.95	<0.001
Personal Growth and Autonomy	3.92	1.17	3.79	1.19	4.15	1.09	0.01
Global Affect	3.70	1.17	3.67	1.17	3.75	1.16	0.55

SD: Standard deviation
*Derived from independent t-test and chi-square test for continuous and categorical variables.

majority (43.5%) was Chinese, had secondary/junior college/pre-university education (66.2%) and was diagnosed with schizophrenia spectrum (40.9%), depressive (35.1%) and anxiety disorders (24.0%). The mean GAF score was 51.8 (standard deviation [SD] = 16.4) and the mean SWLS score was 19.7 (SD = 7.93). The married sample scored significantly higher in PMH total and domain scores, and in GAF and SWLS scores (compared to the never-married sample).

After adjusting for sociodemographic characteristics and diagnosis in multivariate analyses, marital status remained significantly and positively associated with PMH total scores and ES and IS domains (Table 2).

Table 2. Relationship Between Marital Status and Positive Mental Health After Adjusting for Sociodemographics and Diagnostic Group

Positive Mental Health and Domain Score	β	95% CI	*P* Value*
Positive Mental Health total	-0.31	-0.55 – -0.07	0.01
General Coping	-0.21	-0.50 – 0.08	0.16
Emotional Support	-0.46	-0.80 – -0.13	0.01
Spirituality	-0.24	-0.60 – 0.13	0.20
Interpersonal Skills	-0.39	-0.66 – -0.12	<0.001
Personal Growth and Autonomy	-0.28	-0.58 – 0.01	0.06
Global Affect	-0.28	-0.57 – 0.01	0.05

β: Beta coefficient; CI: Confidence interval
*Derived from multiple linear regression analyses by using Positive Mental Health total and domain scores as dependent variable, other sociodemographic (age group, ethnicity, gender, marital status, education, employment status) and diagnostic group as independent variables.

In Table 3, among the never-married sample, Malay ethnicity (vs Chinese) was found to be significantly and positively associated with higher PMH total score (β = 0.45) and domain scores (PGA, [β = 0.55]; IS, [β = 0.43]; S, [β = 0.93]; and GC, [β = 0.54]). Those with some formal/ primary education (vs tertiary/postgraduate) reflected lower IS (β = -0.73). On the other hand, those with anxiety disorder (vs schizophrenia spectrum disorder) had significantly lower GA (β = -0.54), S (β = -0.64) and GC (β = -0.43) scores. The GAF score was significantly and positively associated with PMH total score (β = 0.02) and domain scores for GA (β = 0.02), PGA (β = 0.02), IS (β = 0.02), ES (β = 0.02) and GC (β = 0.01).

Among the married sample, those with depressive and anxiety disorders (vs schizophrenia spectrum disorders) had significantly lower GA (β = -0.63 and β = -0.98, respectively) (Table 3). Additionally, those with secondary/junior college/ pre-university education (vs tertiary/postgraduate) reflected higher PGA score (β = 0.63). Similarly, Malay and Indian ethnicities (vs Chinese) were found to be significantly and positively associated with higher S scores (β = 1.18 and β = 1.01, respectively). Lastly, GAF was associated with significantly higher scores in GA (β = 0.01), PGA (β = 0.01), ES (β = 0.02) and GC (β = 0.02).

Discussion

Similar to earlier studies,[10,11] our study revealed that married individuals had higher mean scores for PMH total and domain scores. A significant association was also found between PMH total scores and marital status. Such differences have been attributed to marriage-related gains such as long-term social support that has in turn been associated with increased economic resources.[1] Possible reasons posited include combined accumulation of resources leading to higher levels of financial satisfaction, health and self-esteem contributing to a higher level of life satisfaction, better coping skills and psychological well-being.[1]

As expected, ethnic differences in PMH were observed in both married and never-married individuals. The never-married Malay participants had higher PMH total, PGA, IS and GC scores compared to Chinese participants (Table 3). One possible explanation is related to religious beliefs, practices and values (e.g., meaning in life) that are more deeply held among Muslims (the Malay population is predominantly Muslim).[12] In addition, Radzi et al[13] have also found significant relationship between higher spirituality and its positive effect on mental well-being.

The current study also found that never-married patients with depressive and anxiety disorders had lower GA, S and GC scores, while married patients with depressive and anxiety disorders showed a negative association only with GA domain. Fagan[14] has proposed that marriage is associated with low prevalence of mental illness and likely mitigates health-damaging effects due to advantages conferred through psychosocial support and economic resources thus buffering the impact of adverse life events and allowing married individuals to have better relationship stability, religious participation, coping skills and lower risk of depression.[1]

Lastly, SWLS scores for both never-married and married samples were significantly associated with PMH total and all domain scores. Holt-Lunstad et al[15] have proposed that marriage per se may not be beneficial—instead, the quality of the relationship is important to influence individuals' life satisfaction. Hence, individuals in non-marital but committed relationships may also be able to receive a feeling of purpose, social identity and social integration.[15] However, these findings need to be confirmed by further studies.

To the best of our knowledge, this is the first study to investigate the relationship between marital status and the components of PMH among mental health service users. However, the study has some limitations. Firstly, the study excluded individuals who were once married but divorced or separated at the time of the study (due to their relatively small sample size). Secondly, the study did not collect information on outpatients who were not married but in a stable relationship or were in a relationship at some point in time (which presents another sample of similar social environment). Thirdly, only outpatients who were literate in English and capable of self-administering the PMH instrument were recruited. Lastly, the self-report responses by the participants might be influenced by social desirability bias. However, we tried to minimise this by having self-administered questionnaires completed in a private setting and asking participants to return their responses within the next 3 days in a sealed envelope.

Table 3. Factors Significantly Associated With Positive Mental Health Total and Domain Scores in Never-Married and Married Outpatients With Mental Disorders

Positive Mental Health and Domain	Never-Married			Married		
	β*	95% CI	*P* Value	β*	95% CI	*P* Value
Positive Mental Health total score						
Ethnicity						
Malay	0.45	0.20 – 0.71	0.00			
Indian	0.17	-0.07 – 0.42	0.16			
Chinese	Reference					
Satisfaction With Life Scale	0.06	0.05 – 0.08	0.00	0.06	0.04 – 0.08	<0.001
Global Assessment of Functioning	0.02	0.01– 0.02	0.00			
Global Affect						
Diagnostic group						
Depressive disorders	-0.43	-0.74 – -0.13	0.01	-0.63	-1.11 – -0.14	0.01
Anxiety disorders	-0.54	-0.87 – -0.21	0.00	-0.98	-1.50 – -0.46	<0.001
Schizophrenia spectrum disorders	Reference			Reference		
Satisfaction With Life Scale	0.07	0.05 – 0.09	0.00	0.07	0.05 – 0.10	<0.001
Global Assessment of Functioning	0.02	0.01 – 0.03	0.00	0.01	0.00 – 0.03	0.03
Personal Growth and Autonomy						
Age (years)						
21 – 39	-0.45	-0.75 – 0.16	0.00			
40 – 65	Reference					
Gender						
Male				0.46	0.03 – 0.88	0.04
Female				Reference		
Ethnicity						
Malay	0.55	0.22 – 0.87	0.00			
Indian	0.42	0.11 – 0.73	0.01			
Chinese	Reference					
Education						
Some formal/primary				0.38	-0.41 – 1.18	0.34
Secondary/junior college/pre-university				0.63	0.06 – 1.19	0.03
Vocational				0.69	-0.14 – 1.51	0.10
Tertiary/postgraduate				Reference		
Satisfaction With Life Scale	0.06	0.05 – 0.08	0.00	0.07	0.04 – 0.10	<0.001
Global Assessment of Functioning	0.02	0.01 – 0.03	0.00	0.02	0.00 – 0.03	0.01
Interpersonal Skills						
Ethnicity						
Malay	0.43	0.11 – 0.75	0.01			
Indian	0.19	-0.12 – 0.49	0.23			
Chinese						
Education						
Some formal/primary	-0.73	-1.37 – -0.08	0.03			
Secondary/junior college/pre-university	-0.13	-0.52 – 0.25	0.49			
Vocational	-0.04	-0.53 – 0.45	0.88			
Tertiary/postgraduate	Reference					
Satisfaction With Life Scale	0.05	0.04 – 0.07	0.00	0.04	0.02 – 0.07	<0.001
Global Assessment of Functioning	0.02	0.01 – 0.03	0.00			

β: Beta coefficient; CI: Confidence interval
*Derived using multiple linear regression analyses using backward stepwise method after adjusting for all covariates.

Table 3. Factors Significantly Associated With Positive Mental Health Total and Domain Scores in Never-Married and Married Outpatients With Mental Disorders (Cont'd)

Positive Mental Health and Domain	Never-Married			Married		
	β*	95% CI	*P* Value	β*	95% CI	*P* Value
Spirituality						
Ethnicity						
Malay	0.93	0.46 – 1.41	0.00	1.18	0.52 – 1.85	<0.001
Indian	0.15	-0.02 – 0.61	0.50	1.01	0.26 – 1.76	0.01
Chinese	Reference			Reference		
Education						
Some formal/primary				0.04	-1.09 – 1.78	0.94
Secondary/junior college/pre-university				0.68	-0.13 – 1.48	0.10
Vocational				1.15	-0.02 – 2.33	0.05
Tertiary/postgraduate				Reference		
Diagnostic group						
Depressive disorders	-0.53	-1.03 – -0.05	0.03			
Anxiety disorders	-0.64	-1.15 – -0.14	0.01			
Schizophrenia spectrum disorders	Reference					
Satisfaction With Life Scale	0.06	0.03 – 0.08	0.00	0.05	0.01 – 0.09	0.01
Emotional Support						
Age (years)						
21 – 39				0.69	0.22 – 1.17	<0.001
40 – 65				Reference		
Gender						
Male	-0.38	-0.70 – -0.07	0.02			
Female	Reference					
Satisfaction With Life Scale	0.07	0.05 – 0.09	0.00	0.09	0.06 – 0.12	<0.001
Global Assessment of Functioning	0.02	0.01 – 0.03	0.00	0.02	0.01 – 0.04	<0.001
General Coping						
Ethnicity						
Malay	0.54	0.17 – 0.90	0.00			
Indian	0.38	0.03 – 0.73	0.03			
Chinese	Reference					
Diagnostic group						
Depressive disorders	-0.16	-0.53 – -0.21	0.40			
Anxiety disorders	-0.43	-0.82 – -0.04	0.03			
Schizophrenia spectrum disorders	Reference					
Satisfaction With Life Scale	0.05	0.03 – 0.71	0.00	0.04	0.01 – 0.07	0.01
Global Assessment of Functioning	0.01	0.00 – 0.02	0.00	0.02	0.00 – 0.03	0.01

β: Beta coefficient; CI: Confidence interval
*Derived using multiple linear regression analyses using backward stepwise method after adjusting for all covariates.

Conclusion

This study has made a preliminary yet valuable contribution to the understanding of the relationship between marital status and psychological health in people with mental disorders. It highlights the importance of further research on how marriage may influence mental health in different ways and promote better PMH in this population. The findings could also contribute to policy-making and mental health practices such as interventions or treatments designed to facilitate positive and holistic approaches for patients' recovery and improvement of their quality of life.

Acknowledgement

The study was funded by Singapore Ministry of Health's National Medical Research Council under the Centre Grant Programme (Grant No.: NMRC/CG/004/2013). The funding source had no role in the study design, collection, analysis, interpretation of data and in the writing of this article.

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Ventricular Assist Device Support in End-Stage Heart Failure From Cardiac Amyloidosis

Dear Editor,

A 46-year-old female presented with recurrent heart failure admissions over 3 months. Clinical examination revealed bilateral pleural effusions, raised jugular venous pressure and bilateral swelling of the lower limbs. During her initial admission, a transthoracic echocardiogram showed moderate concentric left ventricular (LV) hypertrophy with moderate global hypokinesia. Left ventricular ejection fraction (LVEF) was moderately impaired. The left ventricular end-diastolic diameter (LVEDD) was 3.5 cm, with restrictive LV filling pattern. There was concomitant moderate to severe tricuspid regurgitation. Her electrocardiogram showed sinus tachycardia and small voltas in the praecordial leads. Serum high-sensitive troponin T was 279 pg/ml (normal: <14 pg/ml) and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) 24,800 pg/ml (normal: <150 pg/ml). Computed tomography (CT) coronary angiogram demonstrated normal coronary arteries. Cardiac magnetic resonance imaging (MRI) confirmed depressed LVEF of 39% and a concomitant reduced right ventricular (RV) ejection fraction of 30%. T1-weighted scout image showed that the myocardium could not be nulled. Together with global diffuse subendocardial late gadolinium enhancement seen on late images, the MRI findings were strongly suggestive of cardiac amyloidosis. While an endomyocardial biopsy was not performed, amyloid deposits were detected on a rectal biopsy sample. Serum electrophoresis did not show the presence of a monoclonal band, but immunofixation detected a monoclonal lambda band with serum free light chain assay showing lambda free light chain concentration of 400 mg/L (normal: 5.7–26.3 mg/L) while the kappa free light chain was within normal limits. A subsequent bone marrow biopsy was also not diagnostic of multiple myeloma. She was diagnosed with Mayo stage IV light chain (AL) amyloidosis and commenced on a chemotherapy regime involving bortezomib, dexamethasone and cyclophosphamide.

Although the serum lambda free light chain levels returned to normal following 2 cycles of chemotherapy, she continued to have recurrent heart failure symptoms despite medical treatment. Her low blood pressure (BP) (systolic BP: 70s) precluded the use of any renin-angiotensin-aldosterone-system inhibitors or beta blockers. A low dose of loop diuretics frusemide resulted in the development of acute kidney injury.

She was wheelchair-bound within 3 months of her initial heart failure presentation and was hospitalised 3 times for decompensated heart failure. She was 1.51 metres tall and weighed 41 kg. Her body surface area (BSA) was 1.32 m^2. Preoperative right heart study showed cardiac index of 1.27 L/min/m^2, RV stroke work index of 60.5 mmHg.ml/m^2 and pulmonary vascular resistance of 3.3 Wood units. After extensive discussion, she decided to undergo a high-risk left ventricular assist device (LVAD) implantation. Via median sternotomy, we modified the LVAD inflow cannula implantation by fashioning a conduit out of a 20 mm Gore-Tex® (WL Gore & Associates, Arizona, United States of America [USA]) interposition graft, implanting one end to the interatrial septum and the other end to the anterior right atrial wall. The HeartWare™ HVAD™ (HeartWare International, Massachusetts, USA) inflow cannula was connected to the Gore-Tex® graft on the right atrial wall (Fig. 1). The outflow graft was trimmed and subsequently connected to the ascending aorta. The tricuspid valve was bicuspidised by closing off the posterior leaflet by stitching between the adjacent commissures. At the end of the procedure, the HVAD was anchored to the right-sided rib cage before the chest was closed. Figures 2 and 3 show the position of the LVAD anterior to the right atrium as seen on CT scans.

Postoperatively, the patient was nursed in the intensive care unit (ICU) and extubated on the second postoperative

Fig. 1. The Heartware™ HVAD™ inflow cannula was connected to the Gore-Tex® graft that was sewn in the interatrial septum.

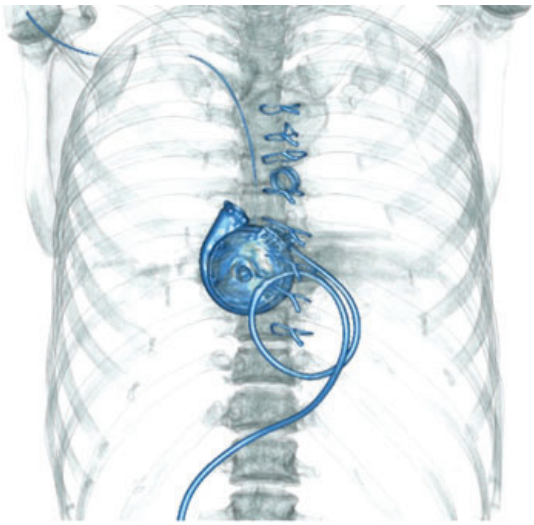

Fig. 2. Computed tomography scan image of the position of the left ventricular assist device shows it was positioned anterior to the right atrium.

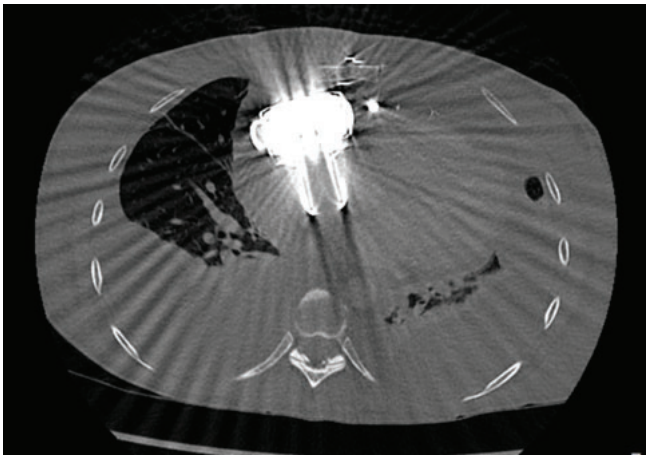

Fig. 3. Computed tomography scan image shows the left ventricular assist device anterior to the right atrium. It is connected to the left atrium through the right atrium via a Gore-Tex® conduit.

day (POD). Perioperative RV failure was managed with judicious inotropes. She was transferred to the general ward after 7 days in the ICU and high dependency unit. She was discharged back to her home on POD 21.

The patient's HeartWare™ HVAD™ pump speed was initially set at 2500 rpm at a pump flow of 3.0 L/min immediately at the end of surgery. It was subsequently increased during the hospital stay to 2640 rpm at a pump flow of 4.0 L/min at discharge. She was anticoagulated with aspirin (100 mg) every morning and warfarin titrated to an international normalised ratio of 2.0–3.0. Her other medications included sildenafil (25 mg) that was taken 3 times a day, and spironolactone (25 mg) and frusemide (80 mg) that were taken every morning. At 90 days after hospital discharge, she has not had any LVAD complications nor hospital readmission and is community-ambulant and undergoing outpatient cardiac rehabilitation.

Discussion

The outcome of patients with AL amyloidosis is highly dependent on the spectrum and severity of organ involvement, especially cardiac involvement.[1] Amyloid deposition in the heart results in rapidly progressive heart failure because of restrictive cardiomyopathy (RCM).[2] The ventricular walls are concentrically thickened with normal or reduced cavity size. The ventricular ejection fraction can be normal or only slightly decreased, but impaired ventricular filling limits cardiac output.[3] The severity of organ involvement—especially the heart—usually determines early outcome with cardiac biomarkers such as cardiac troponin T and NT-ProBNP that strongly predict 1-year mortality.[4] Long-term outcomes are more likely to be determined by factors related to the underlying clonal disorder.[5]

The Mayo staging system based on cardiac biomarkers and clonal markers is a widely accepted staging method for AL amyloidosis.[5] The median overall survival from diagnosis for those with stages I, II, III and IV disease was 94.1, 40.3, 14.0 and 5.8 months, respectively. Our patient was stage IV at the time of diagnosis and could not tolerate most heart failure medications due to low BP. The typical course of treatment would be palliative care. However, in view of the patient's wishes to pursue treatment to extend her survival and improve her quality of life despite high perioperative risks, the option of using LVAD to treat her refractory heart failure secondary to RCM was discussed and subsequently undertaken.

Although LVAD is primarily implanted in patients with advanced heart failure with reduced ejection fraction, it is also a feasible, life-saving therapy for end-stage heart failure related to RCM.[6] In a retrospective study involving 28 patients with end-stage RCM receiving LVAD implantation, the 1-year survival rate for patients with LVADs without transplantation was 64%.[7] This rate was not significantly different between amyloidosis and non-amyloidosis patients. Prior to LVAD implantation, our patient had persistent lower limb swelling, New York Heart Association (NYHA) IV functional class, was home-bound and could ambulate only a few steps. After LVAD implantation, she improved to NYHA II functional capacity and has not had a hospital admission 90 days after discharge.

A major concern with implanting LVADs in patients with end-stage RCM is the association of smaller LV with worse LVAD outcomes.[8,9] These studies reported that an LVEDD of <64 mm was associated with an increased

30-day morbidity and mortality and RV failure. Most patients recruited in these studies were indicative of dilated cardiomyopathy in aetiology. Possible reasons for poorer outcome in patients with smaller LV sizes include: 1) the risk for "suck-down" events due to the ventricular septum or LV walls resulting in ventricular arrhythmias or reduced LVAD preload, 2) shifting of the ventricular septum to the left leading to altered right ventricle geometry, hence worsening RV function, and 3) small LV cavity presenting technical challenges to optimal inflow cannula implantation, hence suboptimal device placement and inadequate LVAD support.[7] In our patient, we anticipated that postoperative LVAD inflow cannula obstruction was likely as the LVEDD was only 3.5 cm. She also had a small body size (BSA: 1.32 m^2). We used a modified approach for the implantation of the LVAD inflow cannula, previously described by Maeda et al[10] in a paediatric patient with hypertrophic cardiomyopathy. This transatrial left atrial cannulation technique removed the risk of the inflow cannula sucking down on the LV walls. It also limited surgery to the low-pressure chambers of the left and right atrium, avoided surgery to the high-pressure left ventricle, thereby potentially reducing the risk of postoperative bleeding. Our patient did not experience postoperative bleeding nor re-opening despite having concomitant thrombocytopaenia with a nadir of 44 × 109 U/L preoperatively.

In the same series of LVAD in RCM patients described by the Mayo Clinic group, the mean hospitalisation time was 24 ± 18 days, while the most common postoperative complication was RV failure.[7] Postoperative recovery of our patient was also not different from the typical course of LVAD patients of dilated cardiomyopathy aetiology. She was discharged 21 days after surgery. Postoperative RV failure in our patient was initially treated with intravenous dopamine, followed by levosimendan infusion. She was also subsequently put on sildenafil (25 mg) 3 times a day for RV afterload reduction.

While short-term outcome was achieved in our patient, long-term prognosis remains guarded—limited largely by potential complications while on LVAD support. Prior to the LVAD, she was ineligible for multi-organ transplant in view of her frailty and renal impairment. With the LVAD implanted, her clinical condition has much improved, making it possible to bridge her to a potential sequential heart and autologous bone marrow transplantation[11] or novel anti-amyloid therapy that may reverse the infiltrative cardiomyopathy. Several treatment regimens that aid in the clearance of amyloid deposits in end organs are actively being investigated. One such treatment regime is with the drug (R)-1-[6-[(R)-2-carboxy-pyrrolidin-1-yl]-6-oxo-hexanoyl] pyrrolidine-2-carboxylic acid followed by an antiserum amyloid protein antibody that has been shown to safely trigger clearance of amyloid deposits from the liver and other tissues in a phase 1 clinical trial.[12]

Conclusion

LVAD is a feasible therapy for end-stage restrictive cardiomyopathy secondary to cardiac amyloidosis. A modified surgical technique of implanting the LVAD inflow cannula into the left atrium via a conduit/ baffle may reduce the risks of postoperative LVAD complications and can be considered in patients with small left ventricles.

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Unusual Atlantoaxial Stenosis Adjacent to Long Segment Cervical Spinal Fusion

A 79-year-old man presented to our clinic with a history of unsteady gait and loss of hand dexterity for many years. He had undergone decompression and fusion without instrumentation at C2–C6 >20 years ago. Three months prior to presentation, his symptoms worsened considerably and he was forced to ambulate with a walking aid. He also complained of neck stiffness and intermittent bilateral hand numbness. On examination, he could not perform tandem gait and had bilateral upper limb weakness (C5–T1) that was more pronounced in the left limb. Hoffmann's reflex and inverted supinator jerk were positive. Deep tendon reflexes in lower and upper limbs were exaggerated. A comprehensive radiologic evaluation that included dynamic radiographs, magnetic resonance images (MRI) and computed tomography (CT) scans was performed.

What are the 2 pathologies that cause stenosis at the atlantoaxial region?

A. Ossification of posterior longitudinal ligament
B. Ossification of ligamentum flavum
C. Ossification of transverse ligament of atlas
D. Hypoplastic posterior arch with ligamentous thickening
E. Bony hypertrophy of posterior arch

Findings and Diagnosis

Dynamic radiographs did not show instability (spondylolisthesis) at C1–C2 complex (Fig. 1) and MRI revealed the previous C2–C6 decompression site. Sagittal MRI showed anterior and posterior compression of the spinal cord at the level of C1–C2 with an anteroposterior diameter of 0.42 cm (Fig. 2A). Axial MRI showed a thickened ligament—likely the posterior atlantoaxial ligament—that caused compression from the posterior aspect (Fig. 2B).

CT images suggested C2–C6 fusion that patient underwent earlier (Fig. 3A) and atlantoaxial fusion (Fig. 3B). Axial CT image demonstrated ossification of transverse ligament of atlas (OTLA) and hypoplastic posterior arch with only flecks of bone (Fig. 3C); inner diameter of spinal canal on axial CT image was 1.63 cm.

Based on these radiologic findings, a diagnosis of cervical myelopathy attributed to atlantoaxial spinal stenosis caused by anterior OTLA and posterior ligamentous thickening was made. Patient was offered posterior decompression and instrumentation but he declined surgery. At follow-up 2 years later, his condition and symptoms remain stable and he continues to ambulate with the aid of a quadstick.

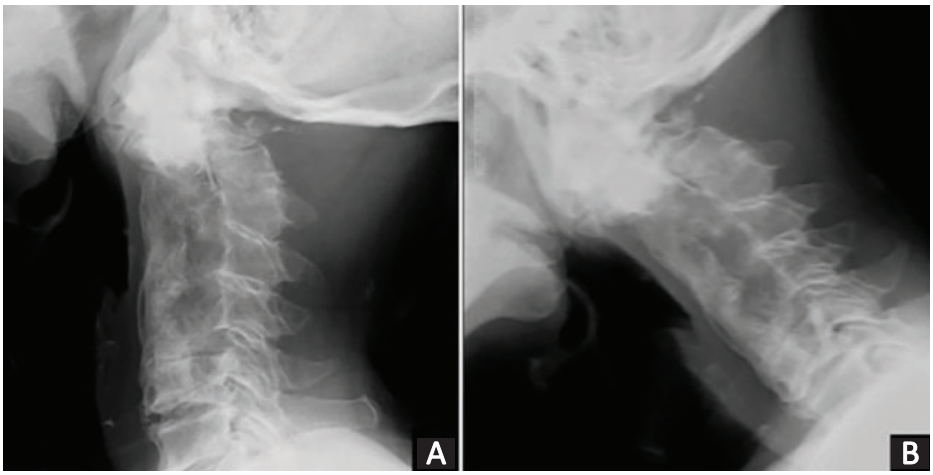

Fig 1. Extension (A) and flexion (B) lateral view radiographs showed fusion of C1–C6 with no signs of instability.

Answer: C and D

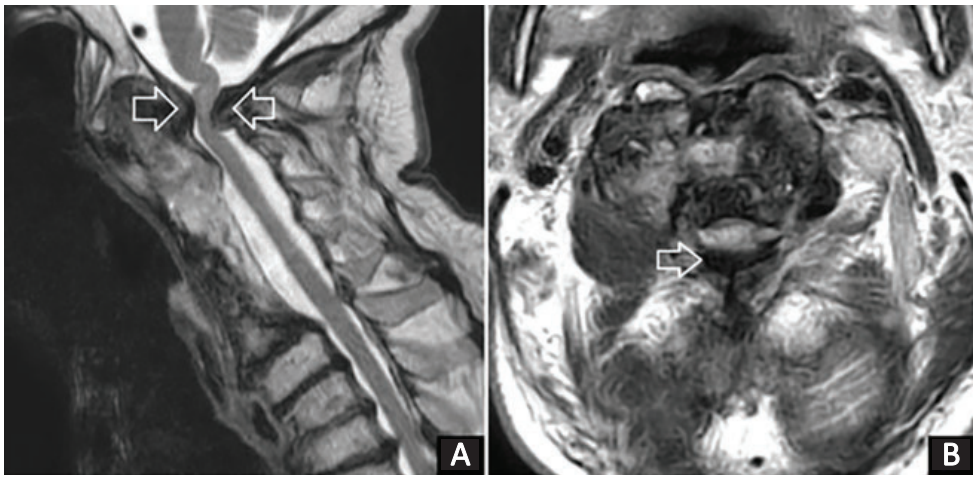

Fig. 2. A: Sagittal T2-weighted magnetic resonance image (MRI) showed previous decompression site (C2–C6) and stenosis (arrows) at C1–C2 level. B: Axial T2-weighted MRI showed cluttered fusion and posterior ligamentous thickening (arrow) at C1–C2 level.

Discussion

Adjacent segment disorders—such as degeneration and instability—following spinal fusion are common. However, reports of ossification of spinal ligaments adjacent to fusion levels are rare. Although ossification can occur naturally due to increased stress on ligaments, additional mechanical load on lower and upper levels adjacent to the fusion can accelerate this process.

Below the axis (C2) level and throughout the spine, the posterior longitudinal ligament or ligamentum flavum (yellow ligament) can become ossified.[1-4] However, since these ligaments are not found at the atlantoaxial level,

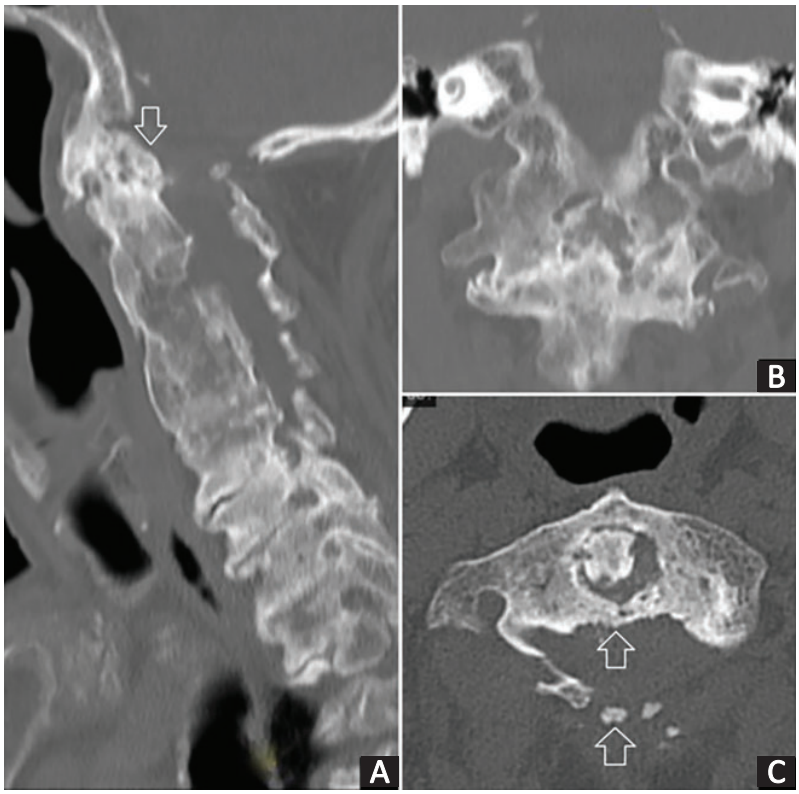

Fig. 3. A: Sagittal computed tomography (CT) image showed atlantoaxial (C1–C2) fusion (arrow) in addition to previous C2–C6 fusion (arrow). B: Coronal CT image showed bilateral fusion of atlantoaxial joints. C: Axial CT image showed ossification of the transverse ligament of atlas (upper arrow) and a hypoplastic posterior arch with flecks of bone (lower arrow).

transverse ligament of the atlas (a strong band that crosses the ring of the atlas and maintains the odontoid process by being in contact with the atlas) or atlantoaxial ligament can become ossified.[5-9]

In this patient, MRI findings were suggestive of anterior and posterior stenosis of the spinal canal that could be attributed to ossification on both sides. However, CT scans showed only anterior OTLA and a hypoplastic posterior arch with mere flecks of bone, thus ruling out the possibility of posterior bony hypertrophy or ligamentous ossification. Given its anatomical location, the posterior element of the compression was considered a thickened posterior atlantoaxial ligament.

As seen in our patient, posterior ligamentous thickening and OTLA can potentially cause cord compression that can lead to myelopathy.[10] Consequently, a definite diagnosis of cervical myelopathy attributed to anterior and posterior atlantoaxial spinal canal stenosis was made.

Since our patient has a history of C2–C6 fusion, it was hypothesised that the upper adjacent C1–C2 level was subjected to increased stress that led to OTLA, posterior ligamentous thickening and atlantoaxial fusion. In our patient, it is debatable whether this phenomenon occurred secondary to adjacent segment degeneration or from natural degeneration secondary to ageing irrespective of the adjacent segment stress. Even so, this presentation is extremely rare and emphasises the possibility of symptomatic OTLA and/or posterior ligamentous thickening occurring in patients with prior fusion involving C2 and below.

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The Annals Gold Awards give special recognition to reviewers for both quality and number of reviews, adherence to the Annals' guidelines (in particular, being fair and supportive to authors), and providing helpful advice to the Editorial Board. In 2019, the Gold Reviewers who completed 3 or more reviews were (in alphabetical order):

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Annals, Academy of Medicine, Singapore
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