Depression, hormonal status and erectile dysfunction in the aging male: results from a community study in Malaysia

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Abstract

Background: Depression and erectile dysfunction (ED) are common in aging and the two conditions often co-exist. These conditions have been shown to be associated with hormonal changes in men. This paper examines the association between depression, ED, and hormonal status of men aged above 50 years in the Klang Valley, Malaysia.

Methods: Five hundred men aged 50 years and above were randomly selected via the electoral roll and invited to participate in a community-based study on men’s health: 351 men responded. Respondents were interviewed individually based on a self-developed questionnaire, which included information on socio-demographic data. Erectile function was measured using the International Index for Erectile Function-5 (IIEF-5) and depression was measured using the 15 item Geriatric Depression Scale (GDS-15).

Results: Sixty-nine percent of the men were diagnosed with ED. Mean GDS score was 3.33 (SD = 3.29). Nineteen percent (n = 67) of the men had abnormal levels of testosterone (<11 nmol/l) and this comprised 73% of men with ED (n = 49) and 27% of men without ED (n = 18). There was no significant association between testosterone level and ED (χ² = 0.68, p = 0.41). Significant association was found between depression (GDS ≥ 5) and men with ED (χ² = 6.07, p = 0.014). Sex hormone binding globulin and luteinising hormone were negatively correlated with erectile function. Results of the multiple linear regression showed that age and depression are predictors of erectile function.

Conclusion: Depression and ED should be screened for when either exists in the male patient and treatment directed accordingly. © 2006 WPMH GmbH. Published by Elsevier Ireland Ltd.

Introduction

The rapid aging of the world’s population is a reality. The United Nations projects that by the year 2050, 1 out of every 5 persons will be aged over 60 years [1]. Health trends in the coming years will be determined mainly by this aging of the world’s population [2]. Depression is a common mental health problem and a public health issue among the elderly [3,4]. As a cause of morbidity, several epidemiological studies have shown that erectile dysfunction (ED) is associated with aging [5,6]. In aging men, depression and ED often co-exist [7,8]. To what extent hormonal alterations associated with aging impact these conditions is speculative.
The Massachusetts Male Aging Study (MMAS) [7] has contributed to knowledge on depression and ED, and remains a commonly cited reference on the subject. An international study on the relationship between somatic symptoms and depression has included some countries in Asia [10] but, to the best of our knowledge, there is no similar collaboration specifically on ED and depression. As 53% of the world’s older persons reside in Asia [1], it is appropriate that a study should be conducted in this part of the world to understand similar issues. The objective of this study was to examine the association between depression, ED and hormonal status among aging men and the factors predicting erectile function in a community of men in Malaysia.

Methods

This was a cross-sectional community-based survey, in 2003, of men living in the Klang Valley, Selangor, which is one of the 13 states of Malaysia. The Klang Valley is an urbanized community. Selection of respondents was based on simple random sampling based on the state electoral list, which constituted the sampling frame. Using 95% power in calculating the sample size, the estimated sample required was 323 respondents. Five hundred letters of invitation were sent to selected men aged 50 years and above. This was followed up by reminder letters and telephone calls. Out of the 500 invitations sent, 351 men responded, giving a response rate of 70%. No significant difference was found between respondents and non-respondents in terms of their age ($t = 1.92, df = 498, p = 0.056$). Written informed consent was obtained from the respondents, and all interviewing was done in the hospital. The ethical approval for this study was obtained from the University of Malaya Medical Centre, Kuala Lumpur.

One to one interviews were carried out by male interviewers based on a self-devised structured questionnaire. Socio-demographic information was obtained from all respondents, the International Index of Erectile Function (IIEF-5) was used to assess the presence of ED and its severity [11]. The IIEF-5 consists of five questions with a Likert scale of 1 to 5 for each one. The scores from the IIEF-5 were categorized into normal ($> 21$), mild ED ($16–21$), moderate ED ($11–15$), or severe ED ($< 11$).

The 15-item Geriatric Depression Scale (GDS-15) is used as a screening instrument for depression in older adults [12–15]. It is well validated in many environments, including both home and clinical settings. The scale was chosen for ease of administration, and it requires no prior psychiatric knowledge [12], which is appropriate as this is a population-based study. The GDS-15 asks about the presence or absence of 15 symptoms over the preceding “few weeks”. Scores from the GDS-15 were divided into normal (0–4), mild/moderate (5–9), and severe depression ($> 10$). The higher the score, the more severe the depression.

Blood samples were taken by nurses, before 11 am in the morning, for analysis of hormonal levels of sex hormone binding globulin (SHBG), prolactin, prostate specific antigen (PSA), luteinizing hormone (LH), testosterone, free testosterone, bioavailable testosterone and insulin growth factor-1 (IGF-1). The blood analyses were carried out by a private laboratory, which uses the ADVIA Centaur Testosterone assay, which is a competitive immunoassay using direct chemiluminescent technology. Calculated free testosterone was done using the formula proposed by the International Society for the Study of the Aging Male (ISSAM) [16]. The results of the blood test were also made known to the respondents.

Data were analyzed using SPSS version 11 statistical software. Descriptive statistics was used and Chi-square was applied to determine the variables that were associated with depression, erectile function, and hormonal status. $T$-tests were also carried out to determine differences in continuous variables between those men with ED (mild, moderate, and severe), and those without. Multivariate regression was performed to determine predictors of erectile function (outcome variable) and age, hormone levels, and GDS score acted as independent variables. All the statistical analyses set a $p$-value of 0.05 for statistical significance.

Results

Table 1 shows the socio-demographic information for men both with and without ED. Overall, mean age ($\pm$standard deviation (SD)) of the men was $58 \pm 7$ years, with a range of from 50
to 93 years old. In terms of ethnicity, 41% were Chinese, 29% Indians, 28% Malays and 3% Others. The distribution of the various ethnic groups is similar to that of the ethnic distribution of the population of Klang Valley, Malaysia. Almost 90% of the men had at least a secondary or higher education, 92% were currently married, and 55% were in employment. Using the IIEF-5, 31% of the men were found to have normal erectile function. The prevalence of ED among these men is as follows: 30.3% had mild ED, 16% had moderate ED and 22.8% had severe ED. Men with ED (mean age = 59.30 years) were significantly older than men without ED (mean = 55.13 years) \( (t = 5.372, \text{df} = 349, p < 0.001) \). Erectile status was also significantly associated with age \( (\chi^2 = 63.48, \text{df} = 6, p = 0.0001) \), educational level \( (\chi^2 = 18.58, \text{df} = 5, p = 0.002) \), and religion \( (\chi^2 = 11.16, \text{df} = 5, p = 0.05) \).

Regarding the prevalence of depression, 14.5% of men were found to have mild/moderate depression (GDS score of 5–9) while 11% of the men screened had severe depression (score of >10). Mean GDS score was 3.33 \( (\pm 3.29) \) (median = 2). Results of the t-test showed a significant difference in prevalence of depression between men with and without ED \( (t = 2.150, \text{df} = 349, p < 0.05) \). Men with ED had significantly higher GDS scores (mean = 3.58) compared with men without ED (mean = 2.77).

Erectile function was significantly associated with depression \( (\chi^2 = 12.89, \text{df} = 2, p = 0.002) \), in that there was a higher proportion of men with ED suffering from depression, as shown in Fig. 1. Among men with mild/moderate depression, 90.2% of them suffered from ED while the remaining 9.8% were without ED. Similarly, among men with severe depression, 61.5% of them had ED compared to 38.5% of men without ED. Pearson correlation showed a negative correlation between GDS score and IIEF score \( (r = -0.163, p < 0.01) \).

Table 2 shows the numbers of men with abnormal levels of hormones and SHBG, based on the reference ranges of the laboratory. Table 3 shows the correlation between the various hormonal levels and IIEF score. Using
the Pearson correlation analysis, only SHBG and LH were significantly correlated with IIEF.

Table 4 shows the mean hormone and SHBG levels in men with and without ED. Mean significant differences were found for SHBG ($t = 2.39, df = 349, p < 0.01$) and LH levels ($t = 2.26, df = 348, p < 0.05$) between those men with and those without ED. Men with ED have significantly higher levels of SHBG than men without ED (mean = 35.02 nmol/l vs. 31.28 nmol/l, respectively; $p = 0.009$), as well as a higher level of LH (mean = 6.36 IU/l vs. 5.04 IU/l, respectively; $p = 0.044$).

Fig. 2 summarizes the proportion of men with and without ED who have abnormal levels of hormones and SHBG. As can be seen...
from this figure, men with ED have a higher proportion of abnormal hormone levels (PSA, SHBG, LH, testosterone, free testosterone, bio-available testosterone, prolactin and IGF-1).

A multiple linear regression model found that age and total GDS score explained 18.2% of the variance in erectile function ($R^2 = 0.182$, Adj. $R^2 = 0.178$, $n = 349$; $F(2/349) = 35.72$, $p < 0.0001$). Independent variables such as testosterone, LH, free testosterone, and SHBG did not predict erectile function (IIEF-5) scores.

**Discussion**

Cross-sectional results from the Massachusetts Male Aging Study (MMAS) showed that male ED was associated with depressive symptoms after controlling for potential confounders and was also a strong predictor of ED in men [7]. Other studies, as well as our present study, have also confirmed this association between ED and depression even though different screening instruments were used [8,17]. We chose the Geriatric Depression Scale because of the ease of its administration and because this scale avoids somatic symptoms, which may be misleading in older persons. The 15-item short form of the GDS, which we used, is highly correlated with the 30-item long form and has the same high sensitivity rates as the long form [18].

We found that men with ED had significantly higher scores on the GDS. The prevalence of depressive symptoms did not vary with age, as found previously [18]. Another study, investigating the prevalence of psychiatric morbidity in patients with ED, found depressive disorders in 25.2% of men [17]. Similarly, in one Asian study [8], it was found that the odds ratio of an association between ED and depression was 2.02.

In our study, we found that men with ED were older than men without ED. This association between aging and ED has also been shown by other workers [7,19, 20]. In the Massachusetts Male Aging Study, the annual incidence rate of ED increased from 12.4 cases per 1,000 man-years for men aged 40–49 years to 46.4 cases per 1,000 man-years for men aged 60–69 years [19]. In the Health Professionals Follow-up Study, 26% of men aged 50–59 years experienced their first erection problems and this increased to 40% in men aged 60–69 years [20]. In the Asian Men’s Attitudes and Life Events Study (M.A.L.E.S.) examining the prevalence of ED among men aged 20–75 years, it was also found that in Korea, Malaysia, and Taiwan, the prevalence rate of ED increased with age [21].

Depression is also common among the elderly. Community studies have shown a positive association between depressive symptoms and the over 65 year age-group [22]. In neighboring Singapore today, depressive disorders are the most commonly seen mental disorders among the elderly [23]. Depression is characterized by symptoms such as low mood, reduced energy, loss of interest and enjoyment, and low libido. The relationship between ED and depression appears to be two-way. Baldwin showed that in comparative studies, depressed patients showed higher levels of sexual dysfunction than non-depressed controls [24]. ED may, thus, be a symptom of depression or, if the man is receiving antidepressant medicines, an adverse effect of antidepressant therapy [25]. However, depression may be secondary to the stress and anxiety that accompany ED [26].
To what extent ED and depression are associated with the age-related decline of testosterone is an unanswered question. It is now generally accepted that aging in men is accompanied by a decline in testosterone levels [27–29]. Penile erection and detumescence are hemodynamic events regulated by corporal smooth muscle relaxation and contraction [30]. The role of testosterone in these events is not fully understood. In treating hypogonadal men who have not responded to sildenafil with adjunctive testosterone, improvement was found, suggesting that testosterone may have a role in augmenting erectile function in hypogonadal men [31]. In the MMAS [7], there was no correlation between total serum testosterone and ED, and our study also showed no significant correlation between ED and total, bioavailable, or free testosterone either. While the effect of testosterone on penile erection still needs to be resolved [32], the positive effects of testosterone on libido and sexual thoughts are well known.

In the MMAS, there was no relationship between total testosterone and depression [7], and our study confirmed this. In the Rancho Bernardo study (RBS), after adjustment for age, there was a weak association between decreasing total testosterone and depression score [33]. However, bioavailable testosterone was 17% lower ($p = 0.01$) in men who were depressed. Our study found no association between depression and bioavailable testosterone.

The difference in our findings with that of the RBS for bioavailable testosterone and depression probably depends on two factors. The first is the difference in the ages of the two populations studied. The mean ($\pm SD$) age of our participants was 58 ($\pm 7$) years, while that of the RBS was 70.2 ($\pm 9.2$) years. In the RBS, total testosterone levels remained at fairly similar levels with increasing age, while levels of bioavailable testosterone fell with increasing age with the lowest levels being in the 80–89 years age-group. The second possibility could lie in the laboratory assay of testosterone. Systematic biases have been found in some of the methods used for the measurement of total serum testosterone in adult men [34]. Coefficients of variation among laboratories using the same instruments or methods could range from 5.1% to 22.7% [34].

In our study, there was a higher proportion of men with ED having abnormal levels of serum hormones and SHBG. No significant differences were found in mean serum follicle stimulating hormone (FSH), LH, testosterone and prolactin in men with and without ED in a prospective study comparing 262 men with ED and 53 healthy men with no ED [35]. In an earlier report from the MMAS, after adjustment for age, a higher probability of ED was correlated with illnesses such as heart disease, hypertension, diabetes, and associated medications [36]. The hormonal milieu in the body is not only a reflection of age-related changes but is also impacted by concurrent medical illnesses and medications. Since normal sexual function in men involves a complex interplay of psychological, neurologic, vascular, and endocrine factors [37], it is not unexpected to see that a higher proportion of men with ED in our study population had abnormal hormone levels.

There was no significant association between prolactin, PSA and IGF-1 with erectile function among our patients. In the MMAS [7], there was similarly no association between prolactin levels and ED. No association was found between ED and PSA and this is not unexpected as PSA abnormalities are more often associated with prostate disease. While serum IGF-1 levels tend to be lower in aging men, the significance of abnormalities of IGF-1 levels in aging is an area of debate [8]. The negative correlation between erectile function and SHBG is likely to be a consequence of the aging process. As noted before, the prevalence of ED increases with age. SHBG is also increased in aging men [33,37]. The negative correlation between SHBG and erectile function thus becomes obvious.

LH was also found to be higher among men with ED in our study, whereas others have shown no significant difference [38]. Luteinizing hormone acts on the Leydig cells to secrete testosterone, which, in turn, feeds back negatively to the pituitary thereby regulating testosterone secretion. In our study, we could not demonstrate any difference in testosterone levels between men with ED and men without ED, and the testosterone levels were generally not low. It is possible that the changes seen in LH in our population of aging men with ED could, as found by Mulligan et al. [39], reflect increased LH pulse frequency. This may be due to the lower responsivity of Leydig cells with age. The compensatory increased LH secretion was thus able to maintain testosterone at the normal levels [39]. However, it remains curious
that ED men had higher LH levels than those without ED, whereas testosterone levels were within the normal range.

While it would be difficult to evaluate the impact of religious ethos on ED, our study has, like the MMAS, found a higher prevalence of ED among men with lower education. Men with higher education are likely to have different health-seeking behaviors to men with lower education, resulting in better general overall health.

Not only was ED associated with depression [40,41], but a link was also found between ED, depression, and cardiovascular disease (CVD) – the DEC Syndrome [41]. While being afflicted with either ED or CVD can make men depressed, depression, in turn, through its neurohormonal alterations impacts on ED and CVD. Interestingly, in a review, it was noted that hypothalamic–pituitary–adrenocortical hyperactivity in depressives leads to increased steroids in the body and an adverse effect of this is injury to vascular endothelial cells [42]. This gives an added perspective to the deleterious effect of hypertension, hypercholesterolemia, and diabetes on vascular endothelium for it is known that endothelial-derived nitric oxide plays an important part in the physiology of erection [43]. Notwithstanding the pathophysiological issues, it must also be remembered that psychological, biological, environmental, and genetic factors – the biopsychosocial factors – are likely contributory factors to the development of depression [22,44] and these share a mutually reinforcing association with the DEC Syndrome.

This study was carried out on an urban population inhabiting the vicinity of two hospitals where the blood tests were performed. It may not be representative of the country as a whole, but is representative of the area researched.

Conclusions

This study has demonstrated a relationship between depression, hormonal status, and ED. The findings indicate that these urban men with ED showed more depressive symptoms. Likely predictors of ED are depression, age, lower education, and poorer health status. In the management of either ED or depression, in addition to screening for the other, CVD should also be screened for. This is a practical course, as these conditions are often missed if either condition is dealt with as an isolated condition. It is of particular significance that by 2025, there will be 322.5 million sufferers of erectile dysfunction (ED) worldwide and 200 million of these men are predicted to come from Asia alone [45]. It has also been projected that depression would be second only to ischemic heart disease as a cause of disability by 2020, which is now less than 15 years away [2]. Attention has to be paid to these issues to meet the challenge they pose to men’s health in the coming years.

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References

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