Delayed fathering and risk of mental disorders in adult offspring

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ABSTRACT

Introduction: Delayed parenting and child bearing at a very young age impose various risks to development of the offspring.
Objective: This study aims to investigate the association between disparities in parental age and increased risk factor for common mental disorders in the progenies during adulthood.
Methodology: The Malaysian Mental Health Survey (MMHS) was analysed for this study. Respondents were asked to estimate the age of their parents at their birth. Presence of common mental disorders (CMD) was determined by referring to the diagnosis given by the Clinical Interview Schedule-Revised (CIS-R) instrument in the Programmed Questionnaire System (PROQSY) format. The association between parental age disparities and CMD was studied using logistic regression.
Result: Fifty three percent (n = 1972) of the MMHS respondents (N = 3666) knew the age of both parents and were included in the study. Three percent (n = 53) had significant disparity in parental age, or a difference of 11 years or more. Respondents born to parents with significant age disparity had a prevalence rate of 24% (95% CI = 22.12–25.89) for CMD in comparison to 6% (95% CI = 5.99–6.11) in their counterparts and 3.4 times higher risk for CMD, after adjusting for demographic factors, paternal age at birth and presence of family history of mental disorders. Amongst those born to older fathers aged 50 and above, the presence of disparity increased the rate for CMD to 42% (95% CI = 39.82–44.18).
Discussion: Disparity in parental age was significantly associated with increased risk for CMD. Various psychosocial factors contributing to age disparity in both the father and the mother could predispose to stress and mental health problems.

1. Introduction

Older mothers and fathers have been associated with increased rate of deformities in the progeny [1]. This is explained by the increased rate of de novo mutation due to increased cell divisions in the germline of older men [2] accompanied by low activity of DNA repair due to reduced activity of antioxidant enzymes in the seminal plasma and spermatozoa of older men [2,3] and also decreased rate of selection process of spematozoas via apoptosis [4]. Deletion in the mitochondrial gene [5] oxidative stress [1] and pre-ovulatory over-ripeness due to endocrine irregularities [1] in the oocytes of older women also contribute to deformities in the progeny.

In mental health, advanced paternal age of 50 and above has been associated with schizophrenia [6–8] and psychosis [9]. Random mutation [9,10] and trinucleotide repeat expansion [10] in the paternal germline, psychological effects of having old parents [11] and early parental loss [8,11] have been used as explanations for the association between delayed fathering and schizophrenia. Increasing maternal age on the other hand has not been established as a cause for these mental disorders.

Our earlier work showed that the association between the risk of common mental disorders (CMD) and paternal age at birth formed a J-shaped curve with an odds ratio of 4.28 (prevalence rate of CMD = 25%) for children born to fathers aged 50 and above and 2.90 (prevalence rate of CMD = 10%) for those born to fathers aged 19 and below in comparison to those born to fathers aged between 20 and 29 years [12] (prevalence rate of CMD = 6%). No significant association was observed between maternal age at birth and CMD [12].

The underlying mechanism for such association between paternal age and risk of CMD has not been studied. There is a growing body of

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evidence on the impact of epigenetic factors, which could explain the moulding of genes by environmental factors and thus leading to altered expression of genes. This paper aims to discuss the association of significant age disparity between parents as a risk factor for the presence of common mental disorders in progenies.

2. Methodology

2.1. Sampling and selection of respondents

Taking the disorder with the least prevalence in the community which is panic disorder with a prevalence of 2% [13] a sample size estimation of 4300 with a confidence level of 90% was made. Multistage cluster sampling method was used with the first stage involving selection of 5 states (clusters) by geographical distribution from a total of 13. The second stage of sampling involved selection of enumeration blocks (EBs) by ethnic distribution. The EBs that consisted of the ethnic groups in the respective states were listed and random selection was made from the list. Households were later selected systematically from each EB. Enumerators visited the listed households, made a list of the eligible respondents in the household and chose two respondents, with the aid of random selection tables provided. All Malaysian citizens aged 16 and above were eligible to participate in the survey with exception of those unable to answer questions due to physical impediments, the elderly (aged 60 and above) who had low scores (0–4) for Elderly Cognitive Assessments Questionnaire (ECAQ) [14], visitors and those who were not at home after three consecutive attempts to contact them. The selected respondents were interviewed upon verbal consent using the instruments in the absence of other family members. A total of 3666 respondents participated in the Malaysian Mental Health Survey of whom 1972 (53%) respondents knew the age of both parents at their birth and were included in the analysis. Amongst the rest, 183 (5%) knew the age of mother alone, 19 (1%) knew the age of fathers and 1492 (41%) did not know the age of both parents at birth.

2.2. Instrument

2.2.1. Assessment of mental disorders
The Malaysian Mental Health Survey (MMHS) data was used for this study. The methodology of the MMHS is also explained elsewhere [15]. Common mental disorder (CMD) was assessed using Clinical Interview Schedule Revised (CIS-R) instrument [16] in Programmed Questionnaire System (PROQSY) format [17]. The CIS-R instrument in PROQSY format generates automatic ICD-10 diagnoses for common mental disorders, namely mixed anxiety and depressive disorder, depressive episode, generalized anxiety disorder, phobic disorders, panic disorder and obsessive compulsive disorder, based on the answers given during the interview. The instrument has 14 subsections, each assessing for an individual symptom and has been validated in the Malaysian population [18].

2.2.2. Explanatory variables for common mental disorders
Socio-demographic factors assessed were age, gender, ethnicity and marital status.

Respondents were assessed for the presence of family history of mental disorders using an item from WHO Mental Health Risk Factor Analysis instrument, which is as follows: "Have any of your parents, siblings or children have ever been diagnosed for mental disorders by a health professional?" The answers were recorded in categories of "Yes", "No", "Don't know" and "Refused to reply".

2.2.3. Parental age disparities
Age of parents at birth of the respondents was determined by the respondents being asked to estimate the parental age as in categories of 19 and below, 20–29, 30–39, 40–49 and 50 and above. Disparity in

parental age was estimated as the difference between the midpoints of the categories. If both parents' age is in the same category, i.e. 20–29 years, there is a possibility of minimum difference of 0 years and maximum of 9 years. The midpoint of the category is 24.5 and the difference between the midpoints is 0. If the ages are one category apart, i.e. 20–29 and 30–39, there is a probability of the age differences being between the minimum of 1 year and a maximum of 19 years. The difference between the midpoints, 24.5 and 34.5 is 10 years. If the ages are two categories away, i.e. 20–29 and 40–49, there is a possibility of the age differences lying between the minimum difference of 11 years and maximum of 29 years. The difference between the midpoints of 24.5 and 44.5 are 20 years. The categories with midpoint differences of 0 and 10 years were grouped together for regression analysis and the midpoint difference of 20 years was used as the indicator for significant parental age disparity, as this category consisted respondents with parents who had a minimum of 11 years age difference.

2.3. Field work

Enumerators for this study, who were college students, medical students and research assistants, were trained in the use of the instruments with mock interviews and only those who showed complete reliability with the trainers in the use of the CIS-R instrument were employed for the survey. The enumerators were closely supervised throughout the data collection process.

2.4. Analysis

Analysis was made using the Statistical Packages for Social Sciences (SPSS) software version 12. Descriptive statistics including chi-square tests were used to study the association between parental age at birth, common mental disorders and parental age disparity. Logistic regression models with enter method were developed to study the impact of parental age disparity on mental health after adjusting for age, gender, ethnicity, presence of family history of mental disorders and paternal age at birth. Likelihood ratio statistics was used to estimate the goodness of fit of the model.

2.5. Ethics approval

Ethical approval was obtained from the National University of Malaysia Ethical Committee.

3. Results

Females formed 61% of the population. Malays formed 54% majority of the population followed by Chinese 26% and Indians, 12%. Mode age group was 30–39 years old (23%) followed by 20–29 years (22%) and 40–49 years (20%). Details on demographic characteristics of the population are as in Table 1. Four percent of the respondents (n = 69) stated that they had first degree family members who had been diagnosed with mental disorders by health professionals. Parental age profiles of the participants of this study are as in Table 2. Almost half of the respondents had mothers aged 20–29 years followed by those aged 30–39 years old. Paternal age profile showed similar mode patterns. Fifty three respondents (3%) had parents with significant age disparity, wits fathers being older.

Respondents born to parents with significant age disparity (defined as age difference of 11 years or above between the parents or a midpoint difference of 20 years) showed 23% (95% CI = 22.12–25.89) prevalence for CMD which is higher than that of their counterparts, who had a prevalence rate of 6% (95% CI = 5.99–6.01) (Table 3). In the absence of disparity the rate of CMD was highest amongst the respondents born to fathers aged 19 and below (9%). Progeny of fathers aged 50 and above did not display a remarkable