UNIVERSITI PUTRA MALAYSIA

INFLUECNE OF ENVIRONMENT AND GENETICS ON REPRODUCTIVE HEALTH OF TWINS

SHAYESTEH JAHANFAR

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SHAYESTEH JAHANFAR

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Chairman: Prof. Dato' Dr. Lye Munn Sann, MBBS, DrPH

Faculty: Medicine and Health Sciences

Reproductive health is a dynamic part of our lives with a broad spectrum of events. Study of twins can assist to investigate the relationship between environmental and hereditary causes of reproductive diseases, which would otherwise be difficult if not impossible to study. High concordance between twin pairs suggests a strong influence for genetic factors, whereas low concordance indicates a weak influence. Preventive measures can be taken into consideration for those who are at risk of environmental influences if and only when the role of genetic is minor even though gene therapy may minimize the occurrence of genetic disease.

This cross-sectional descriptive study of reproductive health of twins investigated the heritability of qualitative and quantitative measured variables related to reproductive events or behavior of adult twins. Subjects included 156 identical and 110 non-identical twins, 15 years and above who were living in urban areas of Iran and Malaysia. Basic and modern genetic analysis was adopted. Maximum likelihood analysis and model

fitting analysis suggested that birth weight, weight, height, age of menarche, premenstrual symptoms, acne, hirsutism, baldness and infertility are mostly determined by genetic factors while characteristics of menstruation were more likely under the influence of environmental factors. Classical genetic analysis using Falconer's formula suggested higher similarity between monozygotic twins than dyzyotics in relation to reproductive behaviors such as age of first pregnancy and number of pregnancies. Probandwise concordance rate analysis showed higher similarity between identical twins in adopting correct reproductive behavior such as undergoing pap smear and using family planning techniques. Model fitting analysis for the ACE model supported these findings.

Same-sex twins had a higher risk of congenital abnormality, gynecological problem, and irregular menstruation than opposite sex twins. Other reproductive events were not found to be significantly different between the two groups indicating that hormonal transition from male to female may not be a valid explanation for reproductive ill health.

Birth weight was not found to affect reproductive morbidity during adult life as frequency of reproductive event was found to be higher among low birth weight twins compared with normal weight twins. This finding is not consistent with fetal origin hypothesis or thrifty gene hypothesis.

Reproductive ill-health influenced by environmental factors may be minimized using careful primary care evaluation, early detection and prevention while genetic

predisposition can be monitored for those variables under genetic influence. Early reproductive health consultation for adolescents is recommended to avoid complications of reproductive ill-health.

Abstrak tesis yang dikemukakan kepada senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah induk sains

Pengaruh Persekitaran dan Genetik terhadap kesihatan reproduktif pasangan kembar

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August 2009

Pengerusi: Prof. Dato' Dr. Lye Munn Sann. MBBS, DrPH

Fakulti: Peruabatan dan Sains Kesihatan

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pasangan-kembar seiras dalam amalan hal-hal reproduktif yang betul seperti menjalankan ujian pap smear dan perancangan keluarga. Analisa 'model fitting' menyokong hasil kajian ini.

Pasangan kembar jantina serupa adalah lebih berisiko dalam mengalami masalah kongenital tidak normal , masalah-masalah ginekologi dan kedatangan haid yang tidak tetap dibandingkan dengan pasangan kembar jantina tak serupa. Lain-lain hal reproduktif tidak menunjukkan perbezaan yang ketara di antara kedua-dua jenis kumpulan pasangan kembar, seterusnya mencadangkan bahawa transisi hormon lelaki kepada perempuan tidak boleh dianggap sebagai satu penjelasan terhadap kesihatan reproduktif yang kurang baik.

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Pengaruh persekitaran terhadap perihal reproduktif yang tidak sihat boleh diminimakan dengan menggunakan penilaian penjagaan utama yang teliti, pengesanan yang awal dan pencegahan manakala bagi yang dibawah pengaruh genetik dapat diawasi. Perundingan kesihatan reproduktif yang awal bagi remaja adalah disyorkan untuk mengelak daripada komplikasi penyakit reproduktif.

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Take me out later

I certify that an examination Committee has met on 27 August 2009 to conduct the final examination of Shayesteh Jahanfar on her Master of Science degree in Community Health thesis entitled “Influence of Environment and Genetics on Reproductive Health of Twins” in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The committee recommends that the students be awarded the Master of Science.

Members of Thesis Examination Committee were as follows:

Prof. Dr. Syed Tajuddin bin Syed Hassan, PhD

Department of Community Health, Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Name of Examiner 1, PhD
Title: Prof. Madya Dr. Rozita Rosli
Name of faculty: Faculty of Medicine and Health Sciences
University Putra Malaysia
(Internal Examiner)

Name of Examiner 2, PhD
Title: Dr. Shamarina Shohaimi
Name of faculty: Department of Biology, Faculty of Science
University Putra Malaysia
(Internal Examiner)

Name of External Examiner, PhD
Title: Prof. Dr. Rama C. Nair
Name of faculty: Faculty of Medicine
University of Ottawa, Canada

Prof. Dr. Bujang Kim Huat
Professor and Deputy Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

Lye Munn Sann
Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Isthrinayagy A/P S. Krishnarajah, PhD
Faculty of Science
Universiti Putra Malaysia
(member)

HASANAH MOHD. GHAZALI, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 16 November 2009

DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

Shayesteh Jahanfar
Date: August 2009

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List of Abbreviations

A	Additive Genetic Variation
AIC	Akaike's Information Criterion
BMI	Body Mass Index
C	Common Environment Variation
CANDLES	Children of Auschwitz Nazi Deadly Laboratory Experiments Survivors
CDF	Cumulative Distribution Function
D	Dominant Genetic Variation
DNA	Deoxyribonucleic Acid
DSL	Diethylstilbestrol
DZ	Dizygotic
E	Non-shared Environment Variation
FAE	Functional Androgen Excess
FF	Female-Female
FM	Female-Male
GE	Genetic Epidemiology
h^2	Heritability
HDL	High Density Lipoprotein
HPO-Axis	Hypothalamic Pituitary Gonadal- axis
ICPD	International Conference on Population and Development
IQ	Intelligence Quotient
LDL	Low density Lipoprotein
MZ	Monozygotic

NMTR	National Malaysian Twin Registry
OS	Opposite Sex
PCOS	Polycystic Ovary Syndrome
PMS	Pre Menstrual Syndrome
SD	Standard Deviation
SHBG	Sex Hormone Binding Globulin
SPSS	Statistical Package for the Social Sciences
SS	Same Sex
TC	Tetrachoric Correlation
UK	United Kingdom
UniKL	University of Kuala Lumpur
USA	United States of America
WC	Waist Circumference
WHO	World Health Organization

1. INTRODUCTION

Twins play an important role in the study of hereditary risk factors in disease, the on-going quest for knowledge of twins and multiple births, and the search for answers to the profound questions posed by genetic research. A wide range of research projects have been undertaken in conjunction with twins who have registered with twin registries including studies on alcohol and tobacco use; asthma; cholesterol; diabetes; anxiety, stress, and depression; osteoporosis; heart disease; epilepsy; dietary salt; Alzheimer's disease; eating disorders; prostate size; male infertility; premenstrual tension; endometriosis; oral ulcers; attention deficit disorder; and breast cancer (Hurbed, 1978; Phillips, 2001; Baker, 1998; Christensen, 1995; Vagero, 1994).

History of twin studies goes back to year 1876 where Sir Francia Glaton first suggested that the examination of twins can be considered as a method of determining the contribution of heredity and upbringing. His main objective in his research was to find dissimilarities between adult twins as he constantly followed their growth from childhood looking for difference between them with increasing age. Siemen (1924) was the first to conduct the classical twin study where he collected ample representative samples of twins in his study population of school children. He concluded that a trait was under genetic control if monozygotic (MZ) twins were strongly concordant for a trait, while dizygotic (DZ) twins were less concordant (Macdonald, 1993).

Twin studies are therefore traditionally used to estimate the genetic contribution to a trait by comparing MZ twin pairs with DZ twins. Study of twins helps us understand the distinctions between nature (genes) and nurture (environment) in shaping particular individual traits.

The hypothesis behind twin studies is that since MZ twins share 100% of their genes in common, while DZ twins share only 50% of an excess concordance between MZ twin pairs may reflect a greater role of genetic factor (Keith, 1994).

Reproductive health, although very broad in spectrum, is an important part of natural science. It is defined by the World Health Organization (WHO) as a state of mental, physical and social well being related to the reproductive system (WHO, 1999). It is not merely the absence of disease, dysfunction or infirmity. Since the International Conference on Population and Development (ICPD) held in Cairo in 1994 and, more recently, the ICPD+5 Forum in Hague, many organizations and researchers tried to define reproductive health and the way it is measured in order to improve different aspects of reproductive health (Reproductive health strategy, WHO, 2001).

Reproductive health study of twins can assist us to investigate the genetic or environmental causes of reproductive diseases, which would otherwise be difficult or impossible to study. For example, by comparing breast cancer concordance in twin pairs, researchers can estimate the effect of genetics and environment on the development of this type of cancer. High concordance between twin pairs suggests a strong influence for genetic factors, whereas low concordance indicates a weak influence. Preventive measures can be taken in to consideration for those who are at risk of environmental influences if the role of genetics is minor. Gene-gene interaction and

gene-environement interaction for variables are to be studied diligently and future gene therapies can eliminate some light on the type of interventions possible on genetic modifications.

The role of shared environment is extremely important. Even though twins are the same age and usually grow up in the same household, their experiences can differ greatly. Identical twins share all the same hereditary material (DNA), whereas fraternal twins share only about half of the same DNA. Greater similarity for a trait among identical twins than the same trait among fraternal twins implies that the influence of genetic factors may predominate over that of environmental factors.

Investigating the hereditary or environmental nature of reproductive health variables call for an interesting research. As far as the author knows, Malaysian and Iranian twins have never been studied before for reproductive health traits. This study aims at conducting an investigation on various aspects of reproductive health that has some indication of possible heredity. The effect of intra-uterine environment, zygosity and low birth weight on reproductive health was also examined.