

**ASSOCIATION BETWEEN INDEX-TO-RING  
FINGER LENGTH RATIO (2D:4D) IN FEMALE WITH  
KNEE OSTEOARTHRITIS**

**BY**

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## **ABSTRAK**

## HUBUNG KAIT DIANTARA NISBAH PANJANG JARI TELUNJUK DAN JARI MANIS DENGAN PENYAKIT OSTEOARTHRITIS LUTUT DIKALANGAN WANITA

**Pengenalan :** Osteoarthritis merupakan masalah besar kepada kesihatan awam dan memberi impak ketidakbolehan yang paling kerap. Namun begitu, osteoarthritis berlaku pada kadar berbeza di kalangan lelaki dan perempuan terutamanya osteoarthritis lutut yang mana berlaku lebih kerap berlaku di kalangan perempuan. Nisbah angka (2D:4D) bermaksud perbezaan nisbah diantara panjang jari telunjuk dan jari manis. Nisbah angka yang rendah dikaitkan dengan pendedahan hormone testosteron semasa dalam kandungan dan seterusnya di hubung kait dengan sifat agresif, sikap yang berani mengambil risiko serta risiko yang tinggi untuk menjalani pembedahan pertukaran sendi lutu dalam penyakit osteoarthritis.

**Objektif :** Untuk menentukan hubung kait diantara nisbah panjang jari telunjuk dan jari manis di kalangan wanita yang mengalami osteoarthritis lutut dan kalangan wanita yang tidak mengalami osteoarthritis lutut.

**Kaedah kajian :** Satu kajian ‘comparative case control’ di jalankan melibatkan dua kumpulan wanita, dengan jumlah 136 orang yang mengalami penyakit osteoarthritis lutut dan 136 wanita yang sihat dan tidak mempunyai masalah lutut. Ukuran jari diambil dari hujung jari hingga ke lipatan di tapak jari berkenaan. Nisbah antara jari telunjuk dan jari manis dikira dan diklasifikasi kepada 3 jenis. Jenis I (jari telunjuk lebih panjang) pola umum kalangan wanita, Jenis II (sama panjang) pola pertengahan, Jenis III (jari manis lebih panjang) pola umum kalangan lelaki.

**Keputusan :** Kajian ini menunjukkan nisbah angka di kalangan wanita yang mengalami penyakit osteoarthritis lutut kebanyakannya ialah jenis 3, 48% (n=66). Manakala, nisbah angka wanita yang tidak mengalami osteoarthritis lutut kebanyakannya jenis 1, 46%.

Perbezaan ini signifikasi seperti yang ditunjukkan dalam perkiraan statistik ‘Pearson Chi Square test’ ( $p < 0.001$ ).

**Konklusi :** Nisbah angka 2D:4D boleh dijadikan indikasi baru untuk risiko mengalami penyakit osteoarthritis lutut di kalangan wanita. Perihal ini boleh dijadikan pemeriksaan klinikal dan penanda risiko bagi penyakit osteoarthritis.

**Kata kunci :** Nisbah angka 2D:4D, Osteoarthritis lutut, panjang jari, wanita

**ABSTRACT**

## ASSOCIATION BETWEEN INDEX-TO-RING FINGER LENGTH RATIO (2D:4D) IN FEMALE WITH KNEE OSTEOARTHRITIS

**Introduction:** Osteoarthritis (OA) is a major public health problem and the most common cause of disability. There are gender differences in the prevalence, incidence and severity of knee and hip OA, especially knee OA affecting more women than men. Digit ratio (2D:4D) is defined as the ratio of the length of index finger to length of ring finger. Lower digit ratio (2D:4D), is a proxy indicator of in-utero testosterone exposure, which was associated with aggression, risk taking behaviour as well as risk of total knee replacement for osteoarthritis.

**Objective:** To determine the association of index-to-ring finger length ratio (2D:4D) in female with knee osteoarthritis and non-osteoarthritis (control)

**Methods:** Comparative case control study was conducted, in which female patient with Osteoarthritis knees were compared with non-osteoarthritic female (control). Measurements will be taken from the tip of the respective finger to the basal crease. The length of the index finger (2D) will be divided by the length of the ring finger (4D) to obtain the 2D:4D ratio. The ratio was classified into 3 types. Type I (index longer than ring) common female pattern, type II (index=ring) intermediate pattern and type III (index shorter than ring) common male pattern.

**Results:** A total of 136 female patients of OA and non OA each were selected in the study. In the OA, 48% (n = 66) were Type III 2D:4D ratio followed by Type I, 28% (n= 38) and Type II, 24% (n=32). Whereas, among non-osteoarthritis the highest 2D:4D ratio type was Type I which were 46%. With Pearson Chi Square Test, P-value obtained from the test was  $p < 0.001$  which means there was statistically significant difference between 2D:4D ratio in female with knee OA and control.

**Conclusion:** 2D:4D ratio Type III appears to be a associated risk factor for the development of osteoarthritis ; specifically, women with the lower of 2D:4D ratio and should be a part of clinical assessment and risk stratification.

**Keywords:** 2D:4D ratio, osteoarthritis knee, finger length, female gender



# CHAPTER 1

## INTRODUCTION

Osteoarthritis (OA) is a progressive joint disease due to failure in repair of joint damage. It occurs mainly over the tibiofemoral joint (knee joint). However, the aetiology and risk factors of OA have not been fully elucidated, and there is no registered disease modifying drug to halt disease progression. Symptomatic knee OA is currently the fourth leading cause of disability worldwide (Fransen et al, 2011) with an estimated prevalence of 70–80% in the population aged 55 years and older (Enuhumah et al, 2008). An ageing Asia with longer lifespan suggests ever-greater numbers of knee OA, among other chronic conditions (Kim et al, 2010). According to Clinical Practice Guidelines on the Management of Osteoarthritis, Ministry of Health Malaysia, 2010, the point prevalence of knee OA in Malaysia today is estimated to be 10–20% of the total adult population.

The major issue with osteoarthritis of the lower limb is physical disability (Torress et al 2006). It is one of the commonest joint disorders that lead to physical disability in the elderly. Although elderly women experience lower rate of chronic disease and longer life span, it has been reported that they have lower quality of life due to functional limitation and physical disability than male (McAlindon et al 1993).

There are gender differences in the prevalence, incidence and severity of knee and hip OA, especially knee OA affecting more women than men. The incidence and severity of OA has been reported to increase particularly after the menopause. Elderly age and female gender contribute to main risk factor of knee osteoarthritis. Body mass index (BMI) and previous knee trauma are also known risk factor for OA knee (Lawrence et al 1998, Hick et al 2001).

The reason for this sex difference is poorly understood, but a number of potential mechanisms have been speculated, with most of the studies having focused on sex hormones

or alterations in reproductive hormone concentrations that occur with menopause and might contribute to OA pathology. Though several sex hormones, especially the effect of estrogen concentrations have been examined in a number of studies, no clear causal relationship has yet been established (Linn et al, 2012).

Digit ratio is defined as the ratio of the lengths of different digits or fingers, which is measured from the bottom crease or the metacarpo-phalangeal joint to the tip of the finger. It is particularly measured between the 2<sup>nd</sup> Digit (2D) and 4<sup>th</sup> Digit (4D). 2D: 4D of finger length ratio can be classified into three types, 1) type I is when index finger longer than ring finger, 2) type II; index finger equal to ring finger and 3) type III ; index finger shorter than ring finger (Zhang et al 2008). In a study by Zhang et al 2008, they have found that Type III (male pattern) 2D: 4D ratio is associated with OA.

Type III finger length ratio, is a proxy indicator of in-utero testosterone exposure, was associated with an increased risk of total knee replacement for OA but not the risk of total hip replacement for OA. It has been suggested by John T. Manning in his books ‘Digit Ratio: A Pointer to Fertility, Behavior and Health’ that the ratio between these two digits is affected by exposure testosterone while in the uterus (Manning J. 2002). The risk is independent of other major OA risk factors. This is further supported by Ferraro et al 2010, in their study titled ‘Study of Site Specific Osteoarthritis and The Index to Ring Finger Length Ratio’ which concluded that the Type III finger pattern was significantly associated with knee OA and it is also an indicator of OA predisposition.

Generally, males have a ring finger that longer than their index finger while female typically have index finger longer than ring finger or same. Many studies done regarding different between finger pattern in term of sexual ability, physical, athletic ability, sperm count, face shape, aggressiveness and risk for knee OA.

This study was done to identify association between index-to-ring finger length ratio (2D:4D) in female with knee osteoarthritis. Identification of a consistent association between 2D:4D and knee OA could possibly increase our understanding of the disease pathogenesis and possibly provide prevention opportunities.

## **CHAPTER 2**

### **OBJECTIVES OF THE STUDY**

#### **2.1 General Objective**

- a) To determine association of index-to-ring finger length ratio (2D:4D) in female with knee osteoarthritis

#### **2.2 Specific Objectives**

- a) To determine demographic characteristics of the participant of the study
- b) To determine prevalence of 2D: 4D ratio in female with osteoarthritis and control
- c) To determine association between age and 2D:4D ratio in female with knee osteoarthritis
- d) To determine association between BMI and 2D:4D ratio in female with knee osteoarthritis

## **CHAPTER 3**

### **MANUSCRIPT**

#### **3.1 TITLE: ASSOCIATION BETWEEN INDEX-TO-RING FINGER LENGTH RATIO (2D:4D) IN FEMALE WITH KNEE OSTEOARTHRITIS**

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### 3.2 ABSTRACT

**Introduction:** Osteoarthritis (OA) is a major public health problem and the most common cause of disability. There are gender differences in the prevalence, incidence and severity of knee and hip OA, especially knee OA affecting more women than men. Digit ratio (2D:4D) is defined as the ratio of the length of index finger to length of ring finger. Lower 2D:4D, is a proxy indicator of in-utero testosterone exposure, which was associated with aggression, risk taking behaviour as well as risk of total knee replacement for osteoarthritis.

**Objective:** To determine association of index-to-ring finger length (2D:4D) ratio in female with knee osteoarthritis and control

**Methods:** Comparative case control study was conducted, in which female patient with osteoarthritis knees were compared with non-osteoarthritic female (control). Measurements will be taken from the tip of the respective finger to the basal crease. The length of the index finger (2D) will be divided by the length of the ring finger (4D) to obtain the 2D:4D ratio. The ratio was classified into 3 types. Type I (index longer than ring) common female pattern, type II (index=ring) intermediate pattern and type III (index shorter than ring) common male pattern

**Results:** A total of 136 female patients of OA and non-OA each were selected in the study. In the OA group, 48% (n = 66) were Type III followed by Type I, 28% (n= 38) and Type II, 24% (n=32). Whereas, among the non-OA group the highest 2D:4D ratio type was Type I which were 46% (n= 63). The Pearson Chi Square test was  $p < 0.001$ , thus there was statistically significant difference in 2D:4D ratio between the OA and non-OA group.

**Conclusion:** 2D:4D ratio Type III appears to be an associated risk factor for the development of OA knee. Therefore, women with the lower 2D:4D ratio should be a part of clinical assessment and risk stratification for OA knee.

**Keywords:** 2D:4D ratio, osteoarthritis knee, finger length ratio, female gender

### 3.3 INTRODUCTION

Osteoarthritis (OA) is a progressive joint disease due to failure in repair of joint damage. It occurs mainly over the tibiofemoral joint (knee joint). However, the aetiology and risk factors of OA have not been fully elucidated, and there is no registered disease modifying drug to halt disease progression. Symptomatic knee OA is currently the fourth leading cause of disability worldwide (Fransen et al, 2011) with an estimated prevalence of 70–80% in the population aged 55 years and older (Enuhumah et al, 2008). An ageing Asia with longer lifespan suggests ever-greater numbers of knee OA, among other chronic conditions (Kim et al, 2010). According to Clinical Practice Guidelines on the Management of Osteoarthritis, Ministry of Health Malaysia, 2010, the point prevalence of knee OA in Malaysia today is estimated to be 10–20% of the total adult population.

The major issue with osteoarthritis of the lower limb is physical disability (Torress et al 2006). It is one of the commonest joint disorders that lead to physical disability in the elderly. Although elderly women experience lower rate of chronic disease and longer life span, it has been reported that they have lower quality of life due to functional limitation and physical disability than male (McAlindon et al 1993).

There are gender differences in the prevalence, incidence and severity of knee and hip OA, especially knee OA affecting more women than men. The incidence and severity of OA has been reported to increase particularly after the menopause. Elderly age and female gender contribute to main risk factor of knee osteoarthritis. BMI and previous knee trauma are also known risk factor for OA knee (Lawrence et al 1998, Hick et al 2001).

The reason for this sex difference is poorly understood, but a number of potential mechanisms have been speculated, with most of the studies having focused on sex hormones or alterations in reproductive hormone concentrations that occur with menopause and might



contribute to OA pathology. Though several sex hormones, especially the effect of estrogen concentrations have been examined in a number of studies, no clear causal relationship has yet been established (Linn et al, 2012).

Digit ratio is defined as the ratio of the lengths of different digits or fingers, which is measured from the bottom crease or the metacarpo-phalangeal joint to the tip of the finger. It is particularly measured between the 2<sup>nd</sup> Digit (2D) and 4<sup>th</sup> Digit (4D). 2D: 4D of finger length ratio can be classified into three types, 1) type I is when index finger longer than ring finger, 2) type II; index finger equal to ring finger and 3) type III ; index finger shorter than ring finger (Zhang et al 2008). In a study by Zhang et al 2008, they have found that Type III (male pattern) 2D: 4D ratio is associated with OA.

Type III finger length ratio, is a proxy indicator of in-utero testosterone exposure, was associated with an increased risk of total knee replacement for OA but not the risk of total hip replacement for OA. It has been suggested by John T. Manning in his books ‘Digit Ratio: A Pointer to Fertility, Behavior and Health’ that the ratio between these two digits is affected by exposure testosterone while in the uterus (Manning J. 2002). The risk is independent of other major OA risk factors. This is further supported by Ferraro et al 2010, in their study titled ‘Study of Site Specific Osteoarthritis and The Index to Ring Finger Length Ratio’ which concluded that the Type III finger pattern was significantly associated with knee OA and it is also an indicator of OA predisposition.

Generally, males have a ring finger that longer than their index finger while female typically have index finger longer than ring finger or same. Many studies done regarding different between finger pattern in term of sexual ability, physical, athletic ability, sperm count, face shape, aggressiveness and risk for knee OA.

This study was done to identify association between index-to-ring finger length ratio (2D:4D) in female with knee osteoarthritis. Identification of a consistent association between 2D:4D and knee OA could possibly increase our understanding of the disease pathogenesis and possibly provide prevention opportunities.

### 3.4 METHODOLOGY

Comparative case control study was conducted, in which female patient with knee osteoarthritis were compared with non-osteoarthritis. This study was conducted in Orthopaedic Clinic Hospital Universiti Sains Malaysia from September 2016 until May 2017.

Measurement of the 2D:4D ratio was performed to all patient and control recruited. During the follow-up conducted at clinic, the length of the index and ring fingers was measured by using vernier callipers with a resolution of 0.1 mm. Measurements was taken from the tip of the finger to the basal crease. Where two creases were visible at the base of the digit, the crease proximal to the palm was chosen (Lutchmaya et al 2004). The length of the index finger was divided by the length of the ring finger to obtain the 2D:4D ratio. Any features that made measurement difficult or might have affected the validity of the measurements, such as finger deformities potentially due to hand arthritis or injuries, were excluded. For the non-OA group, the data was collected from volunteers that agreed to participate. Sample size for this study was calculated based on study conducted by Veerapen et al, 2007 using Pocok's formula.

The Human Research Ethics Committee Universiti Sains Malaysia approved this study (USM/JEPeM/16080270). All data were managed and analysed by IBM SPSS version 20.0. The continuous variable will be described as mean and standard deviation. Categorical variables will be described in frequency and percentage. Pearson Chi- Square test was applied to determine association between index-to-ring finger length ratio (2D:4D) in female with knee osteoarthritis and control since both variables were categorical variables. One way ANOVA was used to look for significant difference between age and 2D:4D ratio and between BMI and 2D:4D ratio. A  $p \leq 0.05$  was considered as statistically significant for all statistical analyses in this study.

### 3.5 RESULTS

There were 136 female with primary knee osteoarthritis and 136 female without primary knee osteoarthritis (control) who came to Orthopaedic clinic Hospital Universiti Sains Malaysia, Kubang Kerian who are included in this study from September 2016 to May 2017. Every participants fulfilled inclusion and exclusion

The demographic characteristics of the study participants were shown in Table 1. The mean (SD) of patient age in female OA was 61 (7.4) years old meanwhile for non OA was 47 (10.5) years old. However there is no significant different between the 2 group. Majority of patients from the OA group were from Malay ethnic group (86%) followed by Chinese (12.5%) and Siamese (1.5%) similarly in the non-OA group, majority were from Malay ethnic (85%) followed by Chinese (12%), Siamese (2%) and Indian (1%). BMI of participants in female OA 29 (4.5) kg/m<sup>2</sup> was higher compared to non OA which was 27 (3.8) kg/m<sup>2</sup>.

Table 1 also showed the prevalence of 2D:4D ratio in OA and non OA patient. From the result, in OA patient finger pattern Type III was the highest (48.53%) follow by Type 1 (27.94%) and Type 2 (23.53%). Prevalence of 2D:4D ratio in control group showed Type 1 finger was the highest (46.32%) followed by Type 3 (27.21%) and Type 2 (26.47%).

For association between 2D:4D ratio in female with knee OA and control, Table 2 showed the result by using Pearson Chi-Square test. The p-value obtained from the test was  $p < 0.001$  which means there was statistically significant difference between 2D:4D ratio in female with knee OA and control. Type III of finger type was the highest (48.53%) whereas, among control the highest 2D:4D ratio type was Type I which is (46%).

One-way ANOVA test was applied to study association between age and 2D:4D ratio in female with knee OA. From the test, there was no statistically significant difference between age and 2D:4D ratio in female with knee OA with ( $p < 0.629$ ) as shown in Table 3.

Comparison of BMI between 2D:4D ratio in female with knee OA also being studied. This comparison was shown in Table 4. The result showed no statistically significant difference between BMI and 2D:4D ratio in female with knee OA ( $p < 0.089$ ).

### **3.6 DISCUSSION**

Osteoarthritis (OA) is the most common degenerative joint disease, characterized by progressive damage of the articular cartilage, osteophyte formation and alterations in the subchondral bone. OA is associated with an extremely high burden in terms of health and economics on individuals, communities, and health systems.

According to worldwide data, estimates 9.6% of men and 18.0% of women aged over 60 years has symptomatic osteoarthritis (Wolf A.P, 2003). There are gender differences in the prevalence, incidence and severity of knee and hip OA, especially knee OA affecting more women than men. The incidence and severity of OA has been reported to increase particularly after the menopause (Snyder et al, 2000). The reason for this sex difference is poorly understood, but a number of potential mechanisms have been speculated, with most of the studies having focused on sex hormones or alterations in reproductive hormone concentrations that occur with menopause and might contribute to OA pathology (Hussain et al, 2014).

This study shows, the prevalence of type 2D:4D ratio in female with OA has higher Type III or male pattern was higher with the percentage of 48.53% followed by Type I (27.94%) and

Type II (23.53%). However, the prevalence of 2D:4D ratio in control group shows Type I Digit ratio is the highest with 46.32% followed by Type III (27.21%) and Type II (26.47%).

Previous studies by Zhang et al 2008 and Ferraro et al 2010 also showed nearly similar distribution in women with knee OA in their sample. Community database study on radiological assessment in classifying 2D:4D finger pattern in Caucasian adult which involving 1636 man and 1536 female showed that prevalence of definite type III finger pattern on either hand was 37.29% in female and 60.88% in male, Male were nearly 3 times as likely to have type III than women (Zhang et al 2008).

This study shows that there is statistically significant difference between 2D:4D ratio in female with knee OA and control with  $p < 0.001$ . It means there is a significant association between Type III 2D:4D ratio in female with knee OA. The results from this study supports previous case control studies that have shown an association between Type III finger pattern and knee OA (Zhang et al, 2008) and (Ferraro et al. 2009).

The underlying mechanism accounting for the association between type III finger pattern and knee OA is unknown but at least three possible mechanisms may be involved, namely the “posttraumatic”, the “morphometric” and the “hormonal effect”. There is accumulating data that type III finger pattern is positively associated with athletic ability. It has been associated with achievement in many competitive and physically demanding sports (Bennett et al, 2010). Research has also indicated that individuals with type III finger pattern are more active and more likely to take risks (Coates et al, 2009). Perhaps this makes them more prone to injury and repetitive joint microtrauma and that could make them more susceptible to OA.

This is supported by Haugen et al, 2009 who found a higher reported knee injury rate in men with low 2D:4D ratios. Type III finger pattern has been associated with a more masculine type of facial shape (Fink et al, 2006).

Another possible mechanism is hormonal relationship between knee OA and 2D:4D finger length ratio. OA can be related to 2D:4D through physical activity or through hormonal factors. Oestrogen in particular has a complex and possibly protective relationship with the development of OA (Husain et al, 2014). The accelerated vulnerability to OA incidence in postmenopausal women suggests a possible role for sex hormones or the tissue response to sex hormones, particularly oestrogen deficiency, in the systemic predisposition to OA. Majority of the studies to date has examined the association of sex hormones with knee OA, some with hip OA and a couple both knee and hip OA.

The 2D:4D ratio reflects the effects of prenatal sex steroids on 19 skeletogenic genes and skeletogenic SMOC1 gene, suggesting a possible underlying genetic determinant of 2D:4D ratio. Exposure to higher *in utero* parental testosterone and lower estrogen concentrations results in low 2D:4D and there are always consistent finding that men have a lower average 2D:4D than women (Hussain et. al 2014).

From this study and others, we now have convincing evidence that type III finger pattern is associated with knee OA. It was believe that a new risk factor for knee OA has been identified and should be a part of clinical assessment and risk stratification. However, further work is needed to improve our understanding of the mechanism responsible for this association.

The relationship between 2D:4D ratio and age throughout life is currently somewhat uncertain: whilst some cross-sectional studies have provided evidence for an increasing digit ratio with age in children (Williams et al, 2003), and across a considerable range of the lifespan (Gillam et al, 2008) others have reported negative associations in children and young adults. Alternatively, cross-sectional studies of children and adults have indicated that there is no significant association (Manning et al, 1998). According to Richards et al 2017, they

found a significant positive relationship between 2D:4D and age in individuals younger than 18 yrs. However, they identified a significant negative correlation between 2D:4D and age in individuals aged 18 years or older. This confirms with our study also shows that with the mean (SD) age of participants was 61 (7.4) years old there was no association between age and 2D:4D ratio in female with knee OA with  $p < 0.629$ . Mechanisms which may feasibly underlie age-related changes in 2D:4D could include: fluctuations in circulating sex hormones, differential soft tissue growth in the ring and index fingers throughout life, modern influence of endocrine disruptors in the environment, and age-related changes in the ability to fully-extend the relevant digits for accurate measurement.

Obesity is a known association with the risk of knee and hip OA. It has been suggested that obesity induced mechanical stresses on cartilage and subchondral bone result in joint damage. Obesity induced excessive loading might explain the vulnerability of weight bearing joints such as knee and hip joint to OA. Recent advances in the physiology of adipose tissue add further insights in understanding the relationship between obesity and OA. Adipose tissue acts as an endocrine organ by releasing cytokines, such as interleukins and tumour necrosis factor  $\alpha$  (TNF  $\alpha$ ), as well as adipokines, such as leptin, adiponectin, visfatin and resistin . The fact that leptin has a key role in the pathogenesis of OA, has triggered to investigate adipokines as a metabolic link between obesity and OA (Husain et al, 2014).

All of the participants in this study were obese with the mean (SD) BMI for the participant was 29 (4.5) kg/m<sup>2</sup>. The relationship between 2D:4D ratio and obesity, muscle mass has been investigated. According to the study by Golge et al 2015, they found that there was positive association between 2D:4D ratio with BMI. Result from our study failed to support significant association between BMI and 2D:4D ratio in female with knee OA with P-value obtained  $p < 0.089$ .



The result from this study is similar to the study conducted by Ibegbu et al, 2012 in Nigeria that showed the 2D:4D digit ratio has no relationship with BMI of an individual from the people of the Ebira tribe of Nigeria. In addition there are no previous studies that truly look in details for relationship between BMI and 2D: 4D finger length ratio. Further study is needed in order to look further details about this association.

The most important limitation of this study was the relative small number of participant. Future studies should be conducted on larger samples in multicentre which will give a more accurate association. The method of measurement for 2D:4D ratio was by direct measuring from the tip of the finger to the basal crease. This method may less accurate in obese patient. Therefore, radiograph measuring of the phalanx may give better options.

### **3.7 CONCLUSION**

In summary, in this comparative cross sectional study, which was conducted in small community of female with knee osteoarthritis, the prevalence of 2D:4D ratio in female with knee osteoarthritis is Type III, there is significant association between Type III 2D:4D ratio in female with knee OA. Therefore, the Type III 2D:4D ratio appears to be an associated risk factor for the development of OA; specifically, women with type III of 2D:4D ratio and should be a part of clinical assessment and risk stratification

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### 3.9 TABLES AND FIGURES

**Table 1:** Demographics characteristics of study participants

Variables	OA	Non OA	P Value
	Mean (SD) %	Mean (SD) %	
Age (y)	61 (7.4)	47 (10.5)	P < 0.01
BMI (kg/m <sup>2</sup> )	29 (4.5)	27 (3.8)	P < 0.033
Race			
Malay	86%	85%	
Others	14%	15%	
Type I	28%	46%	P < 0.001
Type II	24%	26%	
Type III	48%	28%	

**Table 2:** Association between 2d:4d ratio in female with knee OA and control

Type of OA 2D:4D ratio	OA		Non OA		Pearson Square Test	Chi-
	n	%	n	%	P value	
Type I	38	28	63	46	P< 0.001	
Type II	32	24	36	26		
Type III	66	48	37	28		

**Table 3:** Comparison of age between 2D:4D ratio in female with knee OA

Type	n	Mean (SD)	F	P-value
Type I	38	61.3 (6.9)	0.466	0.629
Type II	32	61.6 (7.2)		
Type III	66	60.2 (7.7)		

**Table 4:** Comparison of BMI between 2D:4D ratio in female with knee OA

Type	n	Mean (SD)	F	P-value
Type I	38	27.3 (4.0)	2.461	0.089
Type II	32	29.3 (4.6)		
Type III	66	29.0 (4.6)		

### **3.10 GUIDELINES/ INSTRUCTIONS TO AUTHORS OF SELECTED JOURNAL**

The selected journal is the Malaysia Journal of medical Sciences

## **CHAPTER 4**

### **STUDY PROTOCOL**

#### **4.1 STUDY PROTOCOL SUBMITTED FOR ETHICAL APPROVAL**

##### **INTRODUCTION**

Osteoarthritis (OA) is a major public health problem and the most common cause of disability. Growing evidence suggests that OA is a disease of the whole joint. However, the etiology and risk factors of OA have not been fully elucidated, and there is no registered disease modifying drug to halt disease progression. Symptomatic knee OA is currently the fourth leading cause of disability worldwide, with an estimated prevalence of 70–80% in the population aged 55 years and older. An ageing Asia with longer lifespan suggests ever-greater numbers of knee OA, among other chronic conditions. The point prevalence of knee OA in Malaysia today is estimated to be 10–20% of the total adult population.

There are gender differences in the prevalence, incidence and severity of knee and hip OA, especially knee OA affecting more women than men. The incidence and severity of OA has been reported to increase particularly after the menopause. Elderly age and female gender contribute to main risk factor of knee osteoarthritis. BMI and previous knee trauma are also known risk factor for OA knee (Lawrence et al 1998, Hick et al 2001).

The major issue with osteoarthritis of the lower limb is physical disability (Toresss et al 2006). It is one of the commonest joint disorders that lead to physical disability in the elderly. Although elderly women experience lower rate of chronic disease and longer life span, it has been reported that they have lower quality of life due to functional limitation and physical disability than male (McAlion 1993).

The reason for this sex difference is poorly understood, but a number of potential mechanisms have been speculated, with most of the studies having focused on sex hormones