

Exploring 2d:4d finger length patterns as predictive biomarkers for knee osteoarthritis: Insights from a case-control study

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Abstract

Objective: To evaluate the association and estimation of odds between second-digit-to-four-digit finger length patterns and knee osteoarthritis.

Method: The case-control study was conducted at Liaquat University Hospital, Hyderabad, Pakistan, between December 2019 and December 2022, and comprised confirmed cases of knee osteoarthritis in group A and controls in group B. The second-digit-to-four-digit ratio was visually assessed. The participants placed their hands palm-down on a flat surface with fingers naturally extended and slightly separated. The ratio was determined by comparing the lengths of the index and ring fingers. Data was analysed using SPSS 23.

Results: Of the 949 subjects, 190(20%) were in group A and 759(80%) in group B. Most group B controls (>50%) of both genders had equal index and ring finger lengths, while among group A cases, majority of males (>80%) and females (>70%) had longer ring fingers in both right and left hands, respectively. Significant association between hand finger patterns and knee osteoarthritis was found ($p<0.001$). Type III finger pattern on the left hand was independently associated with an increased risk of knee osteoarthritis (odds ratio: 3.17; 95% confidence interval: 1.31-7.69).

Conclusion: Type III finger pattern of hand strongly correlated with an elevated risk of knee osteoarthritis.

Key Words: Knee osteoarthritis, Finger pattern of hands, Type III finger pattern.

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Introduction

Knee osteoarthritis (KOA) is a degenerative, inflammatory and complicated joint disorder that impairs knee function. During the past two decades, a dramatic increase in the cases of symptomatic OA and knee pain has been observed with a four-fold rise in males and doubled among females.¹ This condition affects men and women almost equally up until age 50, but beyond that, women are twice likely to develop OA.² Bone tissue develops continuously from the prenatal period onwards, and is regulated in part by testosterone and other androgenic hormones.³ Although the rates and severity of KOA differ between genders and age, little is known about the mechanisms underlying this disparity. The structures of the human knee, including articular

cartilage, underlying bone and surrounding muscles, contain oestrogen and testosterone receptors, suggesting that hormonal factors play a significant role in bone formation and degradation, with higher testosterone exposure potentially offering a protective effect.⁴ The second-digit-to-four-digit (2D:4D) ratio correlates with prenatal sex hormones exposure, suggesting that a lower ratio reflects higher prenatal testosterone levels, whereas a higher ratio indicates lower testosterone exposure. Manning et al. in 1998 were the first to propose this theory. Generally, females have either equal in finger length or higher ratio, while males exhibit a lower 2D:4D finger pattern in hands.⁵ These steroidal hormones are not only essential for the growth and maintenance of secondary sexual characteristics, but also have an impact on the development of non-reproductive tissues, especially the skeletal system. Through androgen receptors, testosterone and oestrogen work together to maintain bone metabolism and promote bone development.³ This signifies a crucial role of hormones from the embryonic phase to puberty and adulthood, resulting in the development and maintenance of bodily tissues.⁶ However, fluctuations of androgens or the reproductive hormones can affect the skeletal homeostasis throughout life.⁷

Since estimating foetal androgens is a complex process, most studies recommend using biomarkers, which are

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reliable indicators of the degree of exposure to androgens. The measurement of index and ring finger length (2D:4D) ratio can be used as a surrogate marker or an indicator of testosterone exposure during intra-uterine period.³

Evidence from previous researches links the connection between 2D:4D ratio with numerous health-related problems along with physiological and psychological functions, athletic aptitudes, and skeletal features of the body, like bone mineral density (BMD), osteoarthritis and others.⁸

As KOA is an incurable condition, most research focusses on treatment and managing the symptoms rather than preventing or delaying the disease's progression. Therefore, a deeper comprehension of the underlying aetiology is necessary.² The current study was planned to evaluate the association and estimation of odds between 2D:4D finger length patterns and KOA.

Patients and Methods

The case-control study was conducted at Liaquat University Hospital, Hyderabad, Pakistan, between December 2019 and December 2022. The sample was raised using non-probability convenience sampling technique. To address concerns related to variability in baseline characteristics and a risk of selection bias, and to enhance comparability among the participants, a large sample was recruited. Potential confounding was addressed through the use of multivariable logistic regression models, allowing adjustment for key characteristics that could influence the outcomes.

The sample comprised confirmed KOA cases in group A and controls in group B. the cases were selected from the out-patient department (OPD) of Orthopaedic Surgery and Traumatology, while the controls were recruited from among those visiting the hospital. Approval was obtained from the institutional ethics review committee. The sample size was calculated using Epi-Info version 3.01⁹, taking 78.9% prevalence rate for age <50 years¹⁰ with 95% confidence interval (CI), 2.0 odds ratio (OR).0 and 80% statistical power. To enhance the reliability of data, for every case, four controls were selected with a ratio of 1:4.

Eligibility criteria for the participants required them to be aged at least 30 years regardless of gender. The cases were evaluated on clinical¹¹ and radiographical¹² standards for KOA. The controls were individuals with no history of knee pain or tenderness. The study excluded participants having a history of OA of any kind, rheumatoid arthritis, ankylosing spondylitis, Heberden's node in the hands, knee joint injury, or any congenital

anomaly of the lower limb.

After taking informed consent from the participants, data was gathered using a pre-designed, adapted questionnaire¹³ and permission was obtained to use the Finger Pattern of Hand component of the questionnaire as a data-gathering tool.¹³

The 2D:4D digit ratio was visually assessed following the procedure in line with literature.¹⁴ The participants placed their hands palm-down on a flat surface, with fingers naturally extended and slightly separated. Measurements were performed by matching each hand as closely as possible to the illustrations provided in the questionnaire.¹³ The ratio was determined by comparing the lengths of the index and ring fingers.¹⁴ On the basis of visual assessment, the 2D:4D ratio was determined, and the pattern was classified as Type 1, meaning the ring finger was visually shorter than the index finger,

Type 2, indicating equal length of index and ring fingers, and Type 3, showing the ring finger visually longer than the index finger.¹³

Data was stored in Microsoft Excel, and was then exported for analysis to SPSS 23. For the pattern of fingers on both hands, frequencies and percentages were reported. Pearson's chi-square test was used to assess the relationship among variables of interest. Binary logistic regression analysis was employed with univariate and multivariate models. Age and gender are well-established confounders in Knee Osteoarthritis and were therefore adjusted for in the Multivariate Logistic Regression Model. Both variables were entered as categorical variables using the enter method. To evaluate the association among study variables and outcome, ORs with 95% CIs were worked out. $P < 0.05$ was considered statistically significant.

Results

A total of 949 participants were included, comprising 759 (80%) controls and 190 (20%) cases. Table 1.

Among controls, the majority 417 (54.9%) were aged 30–39 years, whereas among cases, 40.5% were aged ≥ 50 years. This difference in age distribution between cases and controls was statistically significant ($p < 0.001$).

Regarding gender, 513 (67.6%) of controls were male, while 61.6% of cases were female, indicating a significant difference in gender distribution ($p < 0.001$). Table 2.

In univariate analysis, the odds of knee osteoarthritis (KOA) increased with age, being higher in those aged 40–49 years (OR: 1.82, 95% CI: 1.22–2.72) and markedly higher

Table 1: Frequency Distribution of Age Group and Gender among Controls and Cases

Characteristics		TOTAL = 949		p-value
		Controls 759 (80%)	Cases 190 (20%)	
Age Group	30-39 years	417(54.9%)	53(27.9%)	<0.001*
	40-49 years	259(34.1%)	60(31.6%)	
	50 years and above	83(10.9%)	77(40.5%)	
Gender	Male	513(67.6%)	73(38.4%)	<0.001*
	Female	246(32.4%)	117(61.6%)	

Table 2: Odds Estimation of KOA with Age Group and Gender of the study participants.

Characteristics	Univariate Odds Ratio (95% CI)	Multivariate Odds Ratio (95% CI)
Age Group		
40-49 years	1.82*(1.22-2.72)	1.46(0.94-2.26)
50 years and above	7.29* (4.78-11.1)	6.14*(3.78-9.98)
30-39 years	Reference	Reference
Gender		
Female	3.34* (2.40 – 4.67)	2.60* (1.72 - 3.93)
Male	Reference	Reference

in those aged ≥ 50 years (OR: 7.29, 95% CI: 4.78–11.10). After adjustment, the association remained, particularly for ≥ 50 years (OR: 6.14, 95% CI: 3.78–9.98).

Females had higher odds of KOA compared to males in both univariate (OR: 3.34, 95% CI: 2.40–4.67) and multivariate analysis (OR: 2.60, 95% CI: 1.72–3.93).

Of the 949 subjects, 190(20%) were in group A and 759(80%) in group B. Most group B controls (>50%) of both genders had equal index and ring finger lengths, while among group A cases, majority of males (>80%) and females (>70%) had longer ring fingers in both right and left hands, respectively.

Univariate analysis showed that individuals with ring finger longer than index in both hands had substantially higher odds of developing KOA (OR=3.77; 95%CI: 2.16-6.56) for the left hand and OR=3.08; 95%CI: 1.86-5.11 for the right hand). Subjects having the ring and index fingers with equal lengths in both hands exhibited a protective effect (OR=0.30; 95%CI: 0.16-0.55 for the left hand and OR=0.27; 95%CI: 0.14-0.54 for the right hand). Multivariate analysis showed a higher likelihood of KOA risk to be independently associated with ring finger longer than index in the left hand (OR=3.17; 95%CI: 1.31-7.69).

Discussion

In the current study, majority of female cases had ring finger longer than index in both left and right hands

(70.1%, 76.9%). These findings are supported by Shafuzain et al who reported that the majority of female participants had type 3 finger pattern (47%), followed by type 1 (29%) and type 2 (24%).¹⁵ A study conducted on hand osteoarthritis with 802 males and 738 females also reported majority of participants with type 3 finger pattern, suggesting that the type 3 pattern, affected by testosterone during intrauterine period, has some role in the progression and development of OA disease in future life.⁸ Another study on KOA also showed comparable results, where 48% of cases presented with type 3 finger pattern, followed by 28% and 24% with type 1 and type 2. Moreover, the most prevalent type observed among non-osteoarthritis group was type 1 (46%). The study also found statistically significant association between 2D:4D pattern and KOA among females.¹⁵

During foetal development, the ring finger exhibits a greater density of testosterone receptors, reflecting the hormonal exposure in utero. The prenatal hormone levels affect the lengths of digits, mostly second (index finger, 2D) and the fourth (ring finger, 4D), which are compared and used as surrogate marker later in life as 2D:4D ratio. The size of ring finger (4D) is predominantly affected by testosterone, while the development of index finger is under the influence of oestrogen hormone. Increased prenatal testosterone exposure is hypothesised to have significant implications for various health outcomes, potentially influencing susceptibility to a range of health conditions later in life.¹⁶

The current study identified that the odds of disease was likely to be significantly associated with lower 2D:4D ratio. According to a cohort study among 14,511 participants found an association between high 2D:4D ratio and reduced risk of knee joint replacement. This may suggest the role of hormones and digits ratio as a probable proxy indicator towards susceptibility of the disease, and, to fully understand the underlying basis and mechanisms involved in disease causation, further indepth research is recommended.¹⁷ A study on the 2D:4D ratio in correlation with Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and

body mass index (BMI) found a significant positive correlation between WOMAC scores and BMI ($p=0.001$), indicating that obesity or higher BMI are one of the risk factors of KOA. Additionally, the study also revealed the association between BMI and 2D:4D ratio ($p=0.015$) in the context of OA.¹⁵

The current study has limitations. Done in pursuance of an academic thesis, data was collected in December 2022, while the manuscript was submitted in 2025. Although this led to a time gap, the findings remain robust and reliable.

Conclusion

Type 3 was the predominant 2D:4D finger pattern among individuals with KOA, further supporting the association between digit patterns and OA susceptibility, and indicating that the 2D:4D measurement may be useful as a simple, non-invasive screening approach for identifying populations at increased risk.

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AUTHORS' CONTRIBUTIONS:

SRS: Concept, design, data analysis and final approval.

UB: Critically revision.

ML: Data interpretation.

MA: Initial drafting.