Relationship between Digit Ratio (2D:4D) and Neck Circumference

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ABSTRACT

Background and Aim: *Ratio between the index and ring fingers (2D:4D) is an indirect evidence of prenatal androgen exposure. Neck circumference (NC), is a simple screening measure reported to be positively correlated with the risk of coronary heart disease (CHD). The current study aims to analyse whether there is a correlation between NC and intra uterine testosterone exposure by using digit ratio as proxy marker.*

Method: *The study population consisted of 150 healthy volunteers in the age group of 18 – 35 years. After eliciting a detailed socio-demographic history from all the subjects, their digit ratio, neck circumference, height and weight were recorded. Pearson's correlation was used to determine the relationship between 2D:4D and NC. Confounding effects of body weight were removed by calculating partial correlations.*

Results: *There was a positive correlation between digit ratio and neck circumference which was significant in males ($p<0.05$) but not in females ($p>0.05$).*

Conclusion: *There exists a possibility that prenatal testosterone exposure is protective against CHD and digit ratio can be considered as an earlier, simple and cost effective method to predict the risk of CHD.*

Key words: *Digit ratio, Neck circumference, Coronary heart disease, Prenatal testosterone*

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INTRODUCTION

Digit ratio is the ratio of the lengths of different digits or fingers typically measured from the midpoint of bottom crease where the finger joins the hand to the tip of the finger[1]. Among the digit ratios 2D:4D (index: ring) digit ratio has been the most extensively studied. 2D:4D is sexually dimorphic. The second digit is typically shorter in both females and males, but the difference between the lengths of the two digits is greater in males than females. In other words, males have a lower ratio compared to females[1].

A number of studies have shown a correlation between the 2D:4D and various physical and behavioral traits and pathological conditions like, hand preference, autism, sperm counts, coronary heart diseases, sports performance and substance abuse[2,3,4,5]. Digit ratio is established very early in life, around 14th week of gestation, and gender differences in digit ratio becomes apparent by two years of age. Moreover, even though there is continuous growth of the digits during development, the ratio seems to be unchanged throughout the life of the individual[6].

According to a previous study, the amount of testosterone produced by the fetus between the 12th and 24th week, as measured by amniocentesis, negatively correlates with 2D:4D[7]. Other methods that have been employed to establish the link between in utero testosterone and digit ratios include, study of 2D:4D in females with congenital adrenal hyperplasia[8], in dizygotic twins of the same and opposite sex[9], in women with polycystic ovary syndrome[10], and in men with Klinefelters syndrome. Breedlove, in his review has concluded that 2D:4D reflects the concentration of and sensitivity to prenatal androgens[11]. Thus, considering all these works, the 2D:4D is considered to be a 'window' to prenatal testosterone exposure and has been used as a proxy marker for the same.

One may wonder that if 2D:4D is associated with testosterone levels it may correlate with risk of coronary artery disease (CAD). Testosterone is one of the protective factors in preventing CAD[12]. Studies have shown that low testosterone is associated with coronary artery disease[13]. In addition, Wu et al have found a positive correlation between 2D:4D and CAD in Chinese males[4]. They observed that a high 2D:4D was predictive of CAD

One of the most important factors contributing to CAD is obesity[14]. There are many methods of assessing obesity. The most commonly used is the Body Mass Index (BMI). Another indicator for obesity which is gradually replacing BMI is the neck circumference (NC). It is an indicator of upper body subcutaneous adipose tissue distribution[15]. Although obesity results in metabolic abnormalities, upper-body obesity is more strongly associated with cardiovascular risk[15]. Thus, NC as a measure of body fat distribution has been reported to

have a high predictive value for cardiovascular risk factors[16].

There has been a study by Fink, Manning and Neave, that showed positive correlation between 2D:4D and NC[17], but no studies so far has been done in Indian population. Bearing these facts in mind, the current study aims to analyze whether there is a correlation between NC and intra uterine testosterone exposure by using digit ratio as proxy marker.

MATERIALS AND METHODS

The study population consisted of 150 healthy individuals (79 males, 71 females, aged between 18 to 35 years). Volunteers were chosen from those who accompanied the patients visiting medicine OPD of Coimbatore Medical College hospital. Subjects with neck swellings, thyroid diseases and malignancies and those on medication for high blood pressure, diabetes and dyslipidemia were excluded from the study. Additionally, those with hand injuries and deformities were also excluded.

Institutional ethical committee approval was obtained. Informed consent was obtained from all participants. A detailed socio-demographic history was taken and a thorough general examination was done.

Anthropometric measurements

Weight was measured using standard weighing scale and height using stadiometer. The BMI was then calculated by using Quetlet index, that is by dividing the weight in kilograms by the square of height in meters (kg/m^2).

Measurement of Neck Circumference

NC was measured in the midway of the neck, between mid-cervical spine and midanterior neck, to within 1 mm, with a plastic tape. In men with a laryngeal prominence (Adam's apple), it was measured just below the prominence. All circumferences were taken with the subjects sitting upright, with the face directed forwards and shoulders relaxed.

Measurement of Digit Ratio

The method described by Neyse & Brañas-Garza[18], was followed. Digital photographs of both hands were taken with palms on flat surface, facing upwards. Precaution was taken to remove any ornaments like ring which may interfere with the clarity of the photograph and measurement of the 2D:4D. Using Adobe Photoshop® the distance between proximal crease to tip of index finger was measured (2D) in pixels. The same was repeated for the ring finger (4D) as shown in Figure 1. The value of 2D is divided by that of 4D to arrive at the ratio.

Figure 1(a): Measurement of Neck Circumference

Figure 1(b): Measurement of Digit Ratio

Statistics

Gender differences in digit ratio were assessed using student t test. Relationships between the 2D:4D and NC were analyzed using Pearson's linear correlation. To rule out the confounding effects of BMI, partial correlation was computed. All analyses were performed using Statistical Package for Social Sciences (SPSS, version 20).

RESULTS

Characteristics of the Population

The study sample consisted of 150 subjects, 79 males, with mean age of 22 ± 5 years and 71 females, with mean age of 26 ± 6 years. The other characteristics are shown in Table1.

Table 1: Population Characteristics

Variable	Males (n=79)	Females (n=71)
Age (years)	22 ± 5	26 ± 6
Digit ratio	0.97 ± 0.02	0.99 ± 0.02
Neck circumference (cm)	34.3 ± 2.7	31.8 ± 3.3
Height (cm)	166 ± 6.6	148 ± 8.0
Weight (kg)	72 ± 13.5	61 ± 12.8
BMI (kg/m^2)	27.3 ± 4.7	26.6 ± 5.2

Gender Differences

The mean digit ratio among males was 0.97 ± 0.02 which was significantly lesser compared to that of females, which was 0.99 ± 0.02 ($p<0.05$). The neck circumference was significantly lower in women, (mean 31.8 ± 3.3cm) when compared to men (mean 34.3 ± 2.7, $p<0.05$).

Correlation of Digit Ratio and Neck Circumference

Mean Digit ratio for men was found to be lower than that of women, whereas mean neck circumference of men was found to be higher than women. Within both the groups, ie, men and women, there was a positive correlation between 2D:4D and NC. As the values of the ratio increased, the neck circumference also increased. This is shown in Figures 2 and 3. For males, the Pearsons coefficient was 0.69 ($p<0.05$) and for females it was 0.56, ($p>0.05$). In order to rule out the confounding effects of BMI, a partial correlation was calculated as seen in Figure4. The Pearson's first order partial coefficient (controlling for BMI) was 0.521, $p<0.05$. This also pointed towards a positive correlation.

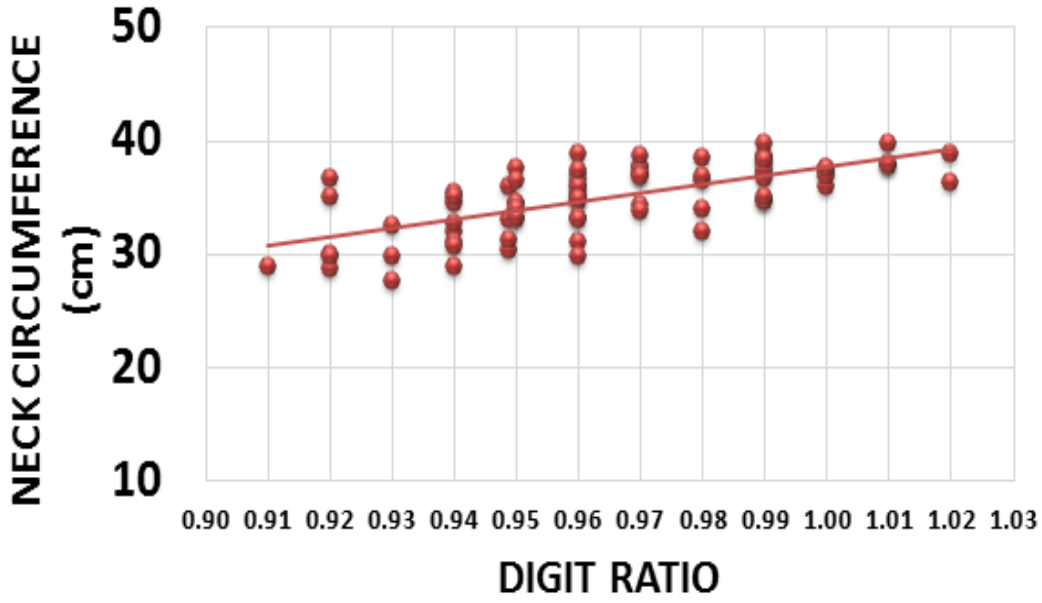

Figure 1: Comparison of 2D; 4D and NC in males (Pearsons coefficient = 0.69, $p<0.05$)

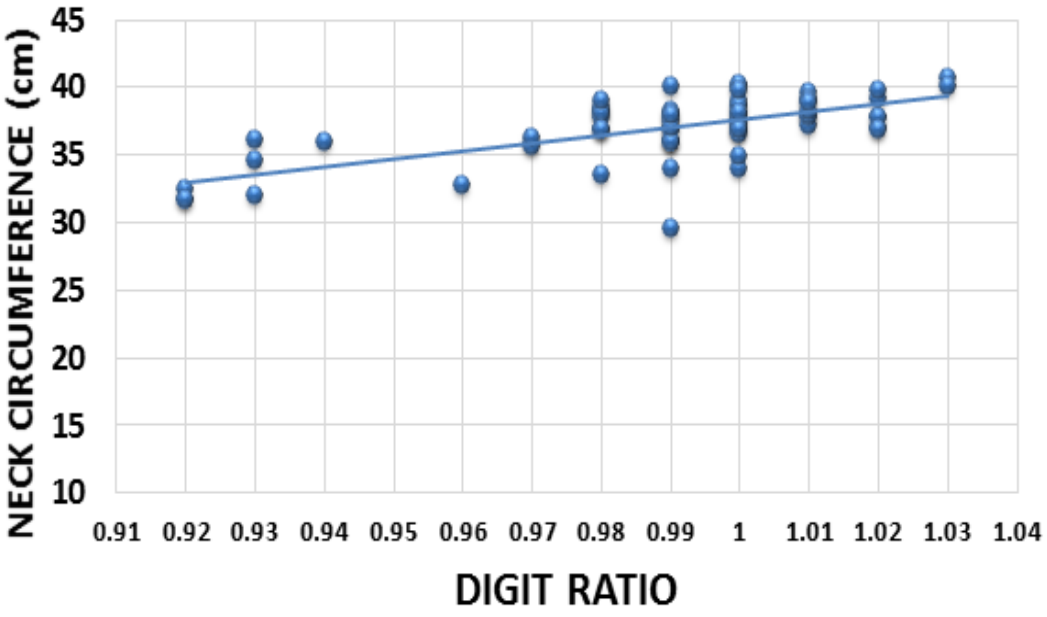

Figure 2: Comparison of 2D; 4D and NC in females (Pearsons coefficient = 0.56, $p<0.05$)

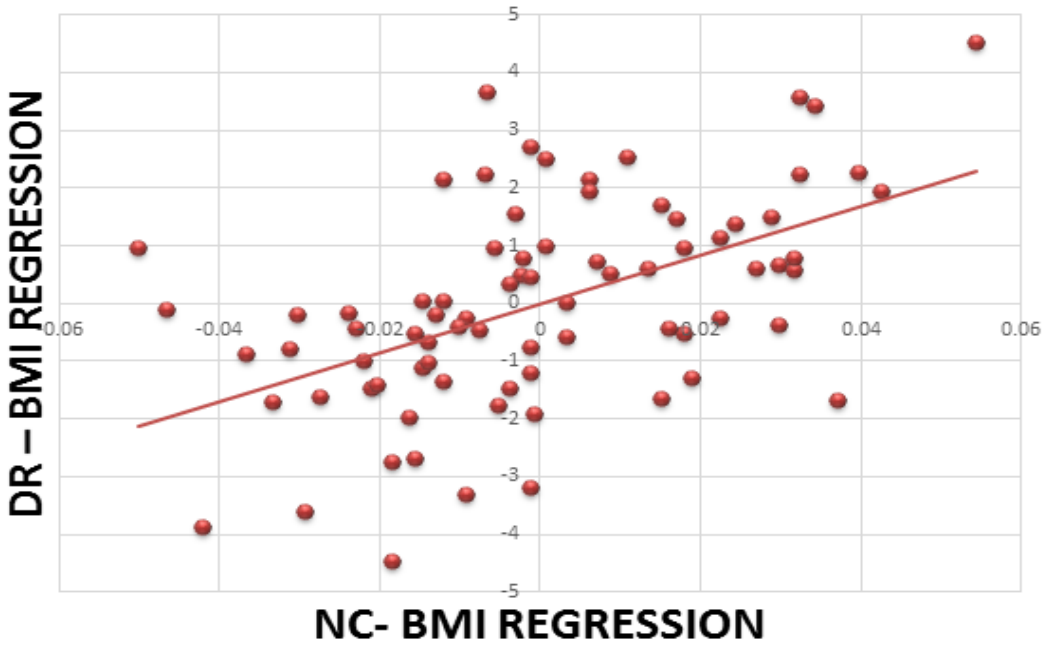

Figure 3 Partial Correlation between 2D:4D and NC by controlling for BMI

DISCUSSION

This study is one of the first attempts in India to address the relationship between Digit ratio and NC. In this study, the digit ratio was found to be lower in males than in females. This finding is in accordance with previous studies by Gillam et all and Lutchmaya el al but contradicts the findings of Park et al[1,7,19]. The probable reason for lower digit ratio in males is a higher level of testosterone exposure prenatally. On the other hand, the neck circumference of males was found to be significantly greater than females. This difference however was found to be negligible when normalised to their height. So the difference between the NC between the genders was negligible ($p>0.05$).

The findings of this study point towards a positive correlation between 2D:4D and NC, when BMI was controlled for. Moreover, the data also suggests that there is a stronger and a significant correlation between digit ratio and neck circumference for males. This relationship however is not significant among females.

Role of prenatal testosterone in establishing Digit Ratio

The underlying hypothesis for digit ratio being indicative of prenatal testosterone exposure is that, a set of genes called Homeobox genes (HoxA and HoxD) form a common factor responsible for the urogenital system differentiation, prenatal androgen synthesis and digit development. In utero testosterone also upregulates another gene called SMOC 1 gene which is responsible for regulation of limb growth[1].

Role of prenatal testosterone in adiposity

Prenatal testosterone exposure increases the sensitivity of β adrenergic receptors to catecho-lamines which mediate the action of hormone sensitive lipase and induce lipolysis and hence decrease adiposity[20]. On the contrary, there have also been evidences in animal models, where prenatal androgen exposure has resulted in increased adiposity, insulin resistance and changes in adipose tissue lipolysis in adulthood[21].

CONCLUSION

The positive correlation in our study suggests low androgen exposure in intra uterine life predisposes to adiposity in adult life and hence increased risk for CAD. This is reflected by an increased NC. The protective role of intrauterine testosterone exposure cannot be asserted as this exposure has been associated with unwanted consequences such as autism, substance abuse, low sperm count, etc as pointed out by previous studies[2,3,5].

Digit ratio is a parameter that can be measured with ease and acts as a proxy marker of intrauterine testosterone exposure, which is constant from birth, and it also correlates well with NC which is a surrogate marker for CAD.

As evidenced by the findings, 2D:4D can be used to provide a quick and inexpensive information about the genetic predisposition for CAD and warrant regular screening from an early age.

REFERENCES:

1. Gillam.L., McDonald.R., Ebling.F. J. P. & T. M. Mayhew (2008). Human 2D (index) and 4D (ring) finger lengths and ratios:cross-sectional data on linear growth patterns, sexual dimorphism and lateral asymmetry from 4 to 60 years of age. Journal of Anatomy 213,325–335 doi: 10.1111/j.1469-7580.2008.00940.
2. Manning J.T, Baron-Cohen.S. & Wheelwright.S. (2001) The 2nd to 4th digit ratio and autism. Developmental Medicine & Child Neurology., 43: 160–164.
3. Manning.J.T., Scutt.D., Wilson.J., Lewis-Jones.D.I., (1998). The ratio of 2nd to 4th digit length: a predictor of sperm numbers and concentration of testosterone, leutinising hormone and estrogen. Human reproduction, 13(11), 3000-3004.
4. Wu.X., Yang.D., Chai.W., Jin.M, Zhou.X., Peng.L. & Zhao.Y(2013). The Ratio of Second to Fourth Digit Length (2D:4D) and Coronary Artery Disease in a Han Chinese Population.International Journal of Medical Sciences 10(11):1584-1588. doi: 10.7150/ijms.6360.
5. Kornhuber.J.,Erhard.G., Lenz.B, Kraus.T.,Sperling.W., Bayerlein.K, Biermann.T. &Stoessel.C.(2011). Low Digit Ratio 2D:4D in Alcohol Dependent Patients. PLoS ONE 6(4): e19332 doi:10.1371/journal.pone.0019332.
6. Garn S.M.,, Burdi.A.R., Babler.W.J. & Stinson.S. (1975) Early Prenatal Rankings and Attainment of Adult Metacarpal-Phalangeal Proportions. American Journal of Physiology and anthropology, 43, 327-332.
7. Lutchmaya.S, Baron-Cohen.S., Raggatt.P, Knickmeyer.P., Manning J.T.(2003) 2nd to 4th digit ratios, fetal testosterone and estradiol. Early Human Development ,77, 23–28.
8. Brown W.M., Hines.M, Fane.B.A, & Breedlove. S.M. (2002). Masculinized Finger Length Patterns in Human Males and Females with Congenital Adrenal Hyperplasia. Hormones and Behavior 42, 380–386, doi:10.1006/hbeh.2002.1830.
9. Anders, S. M., Vernon, P. A., & Wilbur, C. J. (2005). Finger-length ratios show evidence of prenatal hormone-transfer between opposite-sex twins. Hormones and Behavior, 49, 315-319.
10. Cattrall, F. R., Vollenhoven, B. J., & Weston, G. C. (2005). Anatomical evidence for in utero androgen exposure in women with polycystic ovary syndrome. Fertility and Sterility, 84(6), 1689–1692.
11. Breedlove, S. M. (2010). Minireview: Organizational hypothesis: Instances of the fingerpost. Endocrinology, 151(9), 4116-4122.
12. Malkin C.J., Pugh P.J., Morris P.D., Asif.S.,Jones.T.H. & Channer.K.S.(2010). Low serum testosterone and increased mortality in men with coronary heart disease. Heart, 96, 1821-1825. doi:10.1136/hrt.2010.195412.
13. English K.M., Mandour.O., Steeds.R.P., Diver M.J.,Jones T.H. & Channer.K.S. (2000) Men with coronary artery disease have lower levels of androgens than men with normal coronary angiograms. European Heart Journal, 21, 890–894 doi:10.1053/euhj.1999.1873.
14. Coronary Heart Disease Risk Factors (2015), retrieved from National Institutes of Health website : http://www.nhlbi.nih.gov/health/health-topics/topics/hd/atrisk#
15. Hingorjo.M.R., Qureshi.M.A. & Mehdi.A(2012). Neck circumference as a useful marker of obesity: a comparison with body mass index and waist circumference. J Pak Med Assoc. 2012 Jan;62(1):36-40.
16. Zen.V., Fuchs.F.D.,Wainstein M.V., GonçalvesS.C., Biavatti K.,Riedner C.E., Fuchs.F.C.,Wainstein R.V., Rhoden E.L., Ribeiro J.P. &Fuchs S.C.(2012) Neck circumference and central obesity are independent predictors of coronary artery disease in patients undergoing coronary angiography. American Journal of Cardiovascular Diseases.2(4).323-330.
17. Fink.B., Manning.J.T. & Neave.N.(2006) The 2nd–4th digit ratio (2D:4D) and neck circumference: implications for risk factors in coronary heart disease. International Journal of Obesity, 30, 711–71.
18. Neyse.L & Brañas-Garza.P.,(2014). Digit Ratio Measurement Guide, retrieved from http://mpra.ub.uni-muenchen.de/id/eprint/54134.
19. Park.I.N, Yum.H, Lee S.C,Oh J.K & Kim T.B(2014). Second to fourth digit ratio: a predictor of adult lung function. Asian Journal of Andrology,16, (140–145).
20. Pergola G.D.,(2000) The adipose tissue metabolism: role of testosterone and dehydroepiandrosterone. International Journal of Obesity24, Suppl 2, S59-S63.
21. Eisner J.R., Dumesic D.A., Kemnitz J.W.,Colman R.J., & Abbott D.H. (2003). Increased adiposity in female rhesus monkeys exposed to androgen excess during early gestation. Obesity Research, 11(2) 279-286.