

Fluctuating asymmetry in dermatoglyphics of carcinoma of breast

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BACKGROUND: More has been written about the epidemiology of breast cancer than any other form of cancer affecting mankind. The specific breast cancer predisposing genes are BRCA1, BRCA2 and p53. BRCA2, the second breast cancer susceptibility gene, was mapped to chromosome 13q12-q13. The human p53 gene, located on the short arm of chromosome 17, is known to be a tumor suppressor gene that can be inactivated by point mutations.

AIMS: To determine the fluctuating asymmetry and to predict the occurrence of carcinoma of breast in females.

MATERIALS AND METHODS: Rolled finger and palmar prints of 100 female patients of carcinoma of breast were compared with 100 controls. Fluctuating asymmetry measures derived from quantitative parameters (finger ridge counts, *a-b* ridge counts and palmar angles) were analyzed.

RESULTS: Fluctuation asymmetry measures were significantly higher in female patients of carcinoma of breast for the thumb (FA = 2.01), subtotal ridge count (FA = 2.10) and for palmar atd angle (FA = 2.01).

CONCLUSION: These findings suggest that digital dermatoglyphics may have a future role in identifying women at increased risk for breast cancer.

Key words: Breast cancer, dermatoglyphics, fingerprints, fluctuating asymmetry, palmar prints

The study of dermatoglyphics plays an important role in the diagnosis of chromosomal disorder. Dermatoglyphics reveals its significance in Down syndrome, Turners syndrome and in Trisomy 18.^[1-3] Breast cancer is the commonest neoplastic disease in women in the Western world, with a lifetime risk of 11-12% in the general population.^[4-6] The hereditary breast cancers account for 5-10% of all breast cancer cases, wherein about 90% of hereditary breast cancers involve mutation of the BRCA1 and / or BRCA2 genes.^[7] Other cancer-related genes (including myc, c-erb B2, Tsg 101 and Mdg1) are involved in breast carcinogenesis, but they do not give rise to familial breast cancer syndromes.

The fingerprint patterns are also affected in carcinoma of breast.^[8-11]

The dermal patterns once formed remain constant throughout life. Dermatoglyphics is considered as a window of congenital abnormalities and is a sensitive indicator of intrauterine anomalies.^[12] The importance of these markings to the geneticist was not realized until recent years. They have proved to be a helpful adjunct to other diagnostic methods in identifying specific syndromes of genetic origin.

The current status of dermatoglyphics is such that the diagnosis of some illness can now be done on the basis of dermatoglyphic analysis alone, and currently several dermatoglyphic researches claim a high degree of accuracy in their prognostic ability from the hand features.^[13]

In humans, the development of the mammary buds begins to develop during the 6th week as solid down growths of the epidermis into the underlying mesenchyme. These changes occur in response to an inductive influence from the mesenchyme.^[14] The dermal ridges develop in relation to the volar pads, which are also formed by the 6th week of gestation and reach maximum size between 12th and 13th weeks.^[15] This means that the genetic message contained in the genome - normal or abnormal - is deciphered during this period and is also reflected by dermatoglyphics.^[16] Hence these features may serve as proxy markers of altered early development in the breast.^[17,18]

The concept of fluctuating asymmetry (FA), which has been defined as random differences between the right (R) and left (L) sides of a morphological trait.^[19] When the distribution of the 'right minus left' (R-L) differences

in a population sample approximates a normal curve with a mean of zero (or close to zero), the variance of the distributions of R-L difference is a measure of FA.^[19-22] FA has been regarded by many researchers as primarily being an expression of environmental 'noise'^[23,24] disrupting the fidelity of the genetic 'signal.' However, genetic factors may also have a weak link to FA in finger ridge counts^[24] and *a-b* ridge counts.^[23] It has been proposed that the degree of FA in an organism reflects the 'developmental instability' of that organism.^[25,26]

While FA requires that the R-L differences are random and nondirectional, directional asymmetry (DA) involves a significant departure from zero of the normally distributed mean of R-L differences. Examples in humans include the asymmetry of the planum temporal, branching of the bronchi and the distribution of certain internal organs. There is evidence demonstrating rightward DA in finger ridge counts.^[27,28] Studies emphasize that genetic factors affect directional asymmetry.^[24,28]

The aims of the present study were:

1. To find out the quantitative parameters such as ridge count of individual fingers of right and left hands, subtotal finger ridge count of each hand, *a-b* ridge count and palmar angles ('atd', 'dat' and 'adt' angles) of each hand in controls and carcinoma of breast patients.
2. To determine the fluctuating asymmetry of the above-mentioned parameters.
3. To predict the occurrence of carcinoma of breast in females.

Materials and Methods

This study was carried out among 100 female patients of carcinoma of breast attending the Radiotherapy Department of Goa Medical College, Bambolim, Goa. The cases of carcinoma of breast and the normal controls were selected from the Goan population. The Goan population comprises of around 55% Hindus and 45% Christians (Roman Catholics). Both the cases - carcinoma of breast and normal controls - were selected randomly for inclusion in this study. The diagnosis of these patients was confirmed by histopathological

biopsy. These patients were divided into two groups. Group I consisted of carcinoma of breast patients who had no history of any other genetic disorder or heredity diseases. They were matched with 100 controls (Group II) having no family history of cancer breast or any other inheritable diseases. Fingerprints and palmar prints were recorded with cyclostyling ink, and rolled prints of fingers and palms of both hands were taken.^[29]

Ridge counts for each fingertip were calculated from the number of primary dermal ridges that intersected or touched a straight line drawn from the central core of the fingerprint pattern to one or two adjacent triradial points. Consistent with standard methods, fingertips with an arch pattern received a ridge count of zero and fingertips with a loop pattern received a ridge count equal to the number of ridges crossing the single straight line. For fingertip patterns with two triradial points (whorl and double loop pattern), ridge counts equaled counts crossing both the lines. The *a-b* ridge counts (*a-bRC*), which is the number of ridges intersected by a line drawn between the triradius (at the base of the index finger) and *b* triradius (at the base of the middle finger) of the palm in each hand. All measures were assessed by one trained rater who was blind to the subject's group status.

The quantitative parameters observed were:

- i. Ridge counts in individual fingers of both hands
- ii. Subtotal finger ridge count of both hands
- iii. *a-b* ridge counts of both hands
- iv. Palmar angles - 'atd,' 'dat' and 'adt' angles of both hands

Statistical Analysis

Comparisons were made in all the parameters between homologous fingers of the right and left hands using Pearson product-moment correlation coefficients (*r*).^[30] The difference in correlation coefficients between cases and controls was calculated using Fisher's *z*-transformation. '*r*' is a measure of their common variance and $1-r^2$ ^[31] is an estimate of error variance and thus a measure of FA.^[32]

Results

In the present study, fluctuation asymmetry correlation coefficient of finger ridge counts, subtotal ridge counts,

a-b ridge counts and palmar angles are shown. The fluctuation asymmetry correlation coefficient of thumb, subtotal ridge count and atd angle in carcinoma of breast is statistically significant compared to that of controls [Table 1].

It is also seen that the fluctuation asymmetry measures were high in thumb ($Z = 2.01$), subtotal ridge count ($Z = 2.10$) and atd angle ($Z = 2.01$) in carcinoma of breast compared to that of controls [Table 2].

Discussion

This study represents an attempt by the investigators to provide a comprehensive coverage of breast cancer patients. The pattern of dermal ridges and furrows are formed very early in the fetal life. Once formed, they remain unchanged throughout life and vary between the individuals.

The specific breast cancer predisposing genes are BRCA1, BRCA2 and p53. The mutations in BRCA1

account for breast cancer in 50% of families.^[33-36] BRCA2, the second breast cancer susceptibility gene, was mapped to chromosome 13q12-q13.^[37] The human p53 gene, located on the short arm of chromosome 17, is known to be a tumor suppressor gene that can be inactivated by point mutations.^[38] Most BRCA mutation carriers were ascertained by membership in families with a high incidence of breast and ovarian cancers. The actual effects of the gene are likely to be confounded by environmental factors or by contributory activity of other genes. At least one (and possibly several) other major susceptibility gene is likely, since only a fraction of high-risk families have been demonstrated to have mutations in BRCA1 or BRCA2.^[39]

Earlier studies in breast cancer patients were centered on the dermatoglyphic patterns of the fingers in individuals suffering from breast cancer. A pattern of six or more digital whorls was identified more frequently in women with breast cancer than in those without the disease.^[40] Four significantly associated finger patterns were observed with breast cancer: accidentals, transitionals, angled ulnar loops and horizontal ulnar loops.^[8] There has been significant excess of radial loops on the left hand, whereas in premenopausal women with breast cancer, there was increased frequency of ulnar loops on the left hand; and there was an excess of radial loops on the left hand in postmenopausal women with breast cancer.^[10]

Fluctuating asymmetry is the deviation from perfect bilateral symmetry, caused by environmental stresses, developmental instability and genetic problems during development. It is thought that the more perfectly symmetrical an organism is, the better it has been able

Table 1: Fluctuating asymmetry correlation coefficient of finger ridge counts, subtotal ridge counts and atd angle

Parameter	Carcinoma of breast (Group I) 1-r ²	Controls (Group II) 1-r ²
Thumb	0.90	0.36
Index finger	0.60	0.39
Middle finger	0.57	0.5
Ring finger	0.49	0.5
Little finger	0.60	0.61
Sub total finger ridge count	0.55	0.98
<i>a-b</i> ridge count	0.98	0.96
atd angle	0.43	0.74
dat angle	0.88	0.85
adt angle	0.90	0.96

Table 2: Fluctuating asymmetry in carcinoma of breast and control

Parameter	Carcinoma of breast (Group I)		Controls (Group II)	
	Pearsons's r	Fisher's z	Pearsons's r	Fisher's z
Thumb	0.31	0.18z = 2.01, $P < 0.05$	0.79	0.47
Index finger	0.62	0.32	0.77	0.44
Middle finger	0.65	0.34	0.70	0.38
Ring finger	0.71	0.38	0.64	0.33
Little finger	0.60	0.30	0.62	0.31
Sub total finger ridge count	0.66	0.35z = 2.10, $P < 0.05$	0.11	0.04
<i>a-b</i> ridge count	0.12	0.05	0.18	0.08
atd angle	0.74	0.42z = 2.01, $P < 0.05$	0.50	0.24
dat angle	0.33	0.15	0.37	0.17
adt angle	0.30	0.13	0.18	0.07

df = n-1 = 99

to handle developmental stress and has more developmental stability.

The body size is heritable and correlated with fitness, while FA is heritable for females but not males.^[41] Dermal ridge differentiation takes place early in fetal development. The resulting ridge configurations are genetically determined and are influenced or modified by environmental forces.^[12]

It is known that the finger and palm prints are formed during the first 6-7 weeks of the embryonic period and are completed after 10-20 weeks of gestation. Abnormalities in these areas are influenced by a combination of hereditary and environmental factors, but only when the combined factors exceed a certain level, can these abnormalities be expected to appear.^[42,43]

The epidermal ridges of the fingers and palms as well as mammary glands are formed from the same embryonic tissues (ectoderm) during the same embryonic period (6-9 weeks). Since the facial structures like lip, alveolus and palate also develop at 6-9 weeks, the genetic and environmental factors which are responsible for causing cleft lip and palate may also cause peculiarities in the dermatoglyphic patterns.^[44] However, it is quite possible that the mammary glands, which are also developed at 6 weeks, may cause peculiarities in the dermatoglyphic patterns.

Fluctuating asymmetry in dermatoglyphics has been observed in children with cleft lip, alveolus and palate without any other external malformations,^[44,45] wherein a lower frequency of whorl patterns and higher frequency of ulnar loop patterns in the fingers was observed. It was also observed that there was higher percentage of patterns in the third interdigital and hypothenar areas and wider atd angles in the palms. Increased frequency of ulnar loops and higher range of atd angle^[46] and higher percentage of loops and Simian crease and Sydney line were also observed in children with cleft palate.^[47] Fluctuating asymmetry is also observed in cases of schizophrenia and diabetes.^[48,49] Higher fluctuating asymmetry of the index finger ridge count was also observed in men with non-affective psychosis.^[48] Significant results were obtained for 'dat' angle, ridge count of fifth finger in the male and for second finger in the female NIDDM patients.^[49]

Fluctuating asymmetry is defined as the random

differences between two sides of quantitative traits in an individual which increases in parallel to the decreasing buffering ability of an organism and hence inability to maintain developmental homeostasis.^[26] In the case of dermatoglyphics, it is the degree of asymmetry, which will already be present during the early fetal stages, and the magnitude of fluctuating asymmetry that will express the level of developmental homeostasis of the individual.^[26]

Genes in their optimal state are nearly symmetrical. Asymmetry will be illustrated in various human bilateral structures like eyes, teeth, hands, etc., where genes have been damaged.^[26] Thus, as the genetic damage can also be reflected in the hands through the dermatoglyphic patterns, dermatoglyphic analysis can be an extremely useful diagnostic tool for the preliminary investigation into conditions with a suspected genetic base.

On literature review, it was noticed that no studies have been reported on fluctuating asymmetry of dermatoglyphics in carcinoma of breast. In the present study, from quantitative parameters such as ridge count of individual fingers of right and left hands, subtotal finger ridge count of each hand - *a-b* ridge count and palmar angles ('atd,' 'dat' and 'adt' angles) in 100 patients of carcinoma of breast and 100 controls were analyzed. Fluctuating asymmetry in each of these parameters was detected in the Goan population sample. Fluctuating asymmetry correlation coefficients of thumb, subtotal ridge count and atd angle were significant ($P < 0.05$). The positive predicted value associated with the above parameters may have a future role in identifying women either with or at increased risk for breast cancer, such that either risk reduction measures or earlier therapy may be instituted.

Conclusion

The present study concludes that there is a possible genetic influence on the digital ridge patterns in carcinoma of breast patients in whom the digital ridge patterns are otherwise significantly affected. Though a high-risk population is epidemiologically identified, these studies will allow us to detect the possibility of breast cancer so as to enable us to take preventive prophylactic

measures concerning the environmental factors and, in particular, hormonal factors. These relatively noninvasive techniques could reasonably be used on selected nonsymptomatic women (e.g., those with a positive family history) as part of definitive risk assessment strategy. An ability to detect the earliest changes associated with breast tumorigenesis years or decades before the appearance of measurable tumor may allow the introduction of more effective chemopreventive strategies. More precise tools based on techniques of molecular biology, such as microarray analysis, will be needed to assess individual risk for breast cancer. Women who are at high risk for breast cancer can have a variety of options available to them, including watchful waiting, prophylactic surgery and chemoprevention, so as to accurately assess their risk.

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Source of Support: Nil, **Conflict of Interest:** None declared.