

A study of palmar dermatoglyphics in type 2 diabetes mellitus in a Bangalore based population

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Abstract

Introduction: Type 2 diabetes mellitus (DM2) is represented by somatic traits of genetic factors like dermatoglyphic patterns. There is a rising incidence of DM2, requiring simple means to identify predisposition to DM2.

Materials and Methods: The study comprised 75 male and 75 female patients of DM2, with positive family history of diabetes, 75 male and 75 female nondiabetics as controls, with no family history of diabetes. The prints were recorded by the Ink Method and analyzed for qualitative and quantitative parameters.

Results: Diabetics of both sexes showed a significantly higher incidence of spiral whorls in both hands except L2, R1 and R4 of male cases and L1 and R5 of females, and nondiabetics of both sexes showed a higher incidence of loops in both hands. Fingertip ridge counts were significantly higher in diabetics of both sexes, except L2 and R1 in males and R5 in females. In males, pattern intensity, TFRC, AFRC and MFRC of both hands were significantly higher in diabetics. In females, the pattern intensity, AFRC, MFRC of both hands and TFRC of the right hand were significantly higher in diabetics. The left hypothenar area showed a significantly higher incidence of open fields in female nondiabetics. The right fourth interdigital area showed significantly higher incidence of open fields in female diabetics. The scores for a-b ridge count, atd angle, distal deviation of t, breadth ratio and main-line index were not statistically significant.

Conclusion: Dermatoglyphics can be used for early and inexpensive screening of individuals at risk for DM2.

Keywords: Dermatoglyphics, Diabetes mellitus, Type 2, Non insulin dependent, Family history, South Indian population, Bangalore.

Introduction

Dermatoglyphics is a branch of Anatomy that is devoted to the study of ridges and their configurations on the skin of the volar surfaces and the application of this science to the fields of criminology and personal identification, as well as to areas of embryology, comparative anatomy, physical anthropology, genetics and medicine.¹

Dermatoglyphic patterns make good material for genetic studies because their arrangement is stable throughout life, unique to the individual, and unlike stature, intelligence and body weight; they are not influenced by age or by post-natal environmental factors.¹

It is a simple, inexpensive, safe and non-traumatic procedure and the taking of a good print makes a permanent and complete record. It can be easily included in the physical examination as a bedside procedure.¹

Type 2 Diabetes Mellitus (DM2) is a global public health crisis, particularly threatening the economies of developing nations² and India is a global leader in diabetes, currently with largest pool of diabetes in the world.³ DM2 is the most common form of diabetes constituting 90% of the diabetic population. The number of patients with diabetes in India is currently around 80-90 million,² 7.3% of the population, and the prevalence of prediabetes is 10.3% (WHO Criteria) or 24.7% (ADA criteria)⁴ and is expected to rise to 101 million by 2030.⁵ Diabetes is slated to be the largest epidemic in human history.²

DM2 has been shown to be associated with certain dermatoglyphic traits⁶ and Indians in particular have been shown to be predisposed to DM2.⁷⁻⁹

Family history of diabetes is a significant risk factor for DM2.¹⁰ The unique feature of the present study was the emphasis placed on the family history of diabetes, thus reducing the effect of a confounding factor in current non-diabetics.

The objective of the present study was to compare dermatoglyphic configurations in patients with DM2 and without DM2 and to determine the significant dermatoglyphic criteria applicable to patients of DM2.

Materials and Methods

After approval from the Institutional Ethics Committee, the study sample for the present study consisted of mainly outpatients and some inpatients attending Rajarajeswari Medical College and Hospital, Bangalore, of age between 35 to 75 years. The case group consisted of 150 patients, 75 males and 75 females diagnosed prior with DM2, and with positive family history of diabetes. The control group consisted of 150 patients, 75 males and 75 females, with no DM2 and with no family history of diabetes. Patients with deformity of hand, and diseases like hypertension, congenital anomalies, neurological disorders, carcinomas and psychiatric diseases were excluded from the study.

In this study, the terminology advocated by Cummins and Midlo (1961)¹ and Penrose (1968)¹¹ has been used.

The materials required were Kores duplicating ink, rubber roller, inking slab- smooth surfaced tile, white paper,

cylinder of appropriate width, cotton puff and spirit, scale, pencil, pen, protractor- to measure the 'atd' angle, set square- to measure breadth ratio, needle with a sharp point for ridge counting, magnifying lens (X5 magnification).

The patterns on both palms were recorded by the Modified Ink Method elucidated by Purvis Smith (1969)¹². The patient is first briefed about the study, the procedure and the need for the hand print. An informed consent form is signed by the patient and the doctor. The hands of the subject are then cleaned with soap and water and dried with a clean cloth. A small amount of ink is placed on the ink slab and spread with the roller to a thin film. The whole of the palm and fingers are smeared with ink by using the roller with light uniform strokes starting from the distal wrist crease to the finger tips, making sure the flexion creases, the ulnar margin, the central hollow of the palm and the finger tips are not devoid of ink. After inking, the palm is brought to the paper kept on the cylinder. The hand is rolled starting from the wrist and moving to the fingers with gentle pressure applied from the dorsal side by the operator. The individual fingertips are rolled from ulnar to radial side to obtain rolled finger prints. The procedure is repeated for the other hand.

Soon after the print is taken, it should be examined for clarity in the different fingers and the palmar areas. The ink is easily removed from the hand by washing with soap and water.

The impressions were analyzed for the following finger and palmar qualitative and quantitative features.

Qualitative dermatoglyphic parameters studied were finger pattern configuration in the fingertips i.e., the area of the terminal phalanx of the finger, and hypothenar, thenar/first interdigital, second interdigital, third interdigital and fourth interdigital pattern analysis, main line formula, presence or absence of Simian line, Sydney line and C-line termination in the palm (Fig.1-4).

Quantitative dermatoglyphic parameters studied were individual finger ridge count for ten fingers, pattern intensity, TFRC, AFRC, MFRC in the fingertips, and a-b count, atd angle, distal deviation of t, breadth ratio and main-line index in the palm (Fig. 4).

The pattern configurations of the fingers were analyzed and recorded in order from the thumb to little finger of left hand numbered in sequence from L1 to L5, and similarly thumb to little finger of right hand numbered in sequence from R1 to R5.

The data was analyzed by two sample t-test for the finger and palmar quantitative parameters. Pearson Chi-square test and Fischer's exact test were used for finger and palmar qualitative parameters. All analysis was carried out using Stata software Version 15.0.

Results and Discussion

The results of the study are as follows

Qualitative Analysis of Finger Pattern Configuration:

There was a higher incidence of spiral whorls in both hands of male and female cases and a higher frequency of loops in both hands of controls. (Table: 1). The difference was

statistically significant in except in L2, R1 and R4 of males and, L1 and R5 of females.

Quantitative Analysis of Finger Ridge Counts: The fingertip ridge counts were higher in cases as compared to controls. The difference was significant for all digits except L2 and R1 in males, and R5 in females (Table 2).

The scores were higher for cases as compared to controls (Table: 3) and the difference was significant in the scores for pattern intensity, TFRC, MFRC and AFRC on both hands in male subjects. There was a significant difference in the scores for pattern intensity, AFRC and MFRC on both hands, and TFRC on the right hand of female subjects.

Palmar Qualitative Analysis: Hypothenar and Thenar/First interdigital areas (Th/ID1): In males, there was a higher incidence of open fields in cases and vestiges in the controls in the hypothenar area. In females, there was a higher incidence of vestiges in both hands and open fields in controls on the left hypothenar area (Table: 4). There was no significant difference between cases and controls in males, and a significant difference in the left hypothenar area of female subjects.

There was a higher incidence of open fields in the right and left Th/ID1 in male controls as compared to cases (Table 4). There was no significant difference was between cases and controls in male or female subjects in either hand.

Interdigital area 2 (ID2), Interdigital area 3 (ID3) and Interdigital area 4 (ID4): In ID2, there was a higher incidence of open fields in cases and vestiges in controls in males, and a higher incidence of distal loops in female cases. There was a higher incidence of open fields in controls in ID3 of males and females in both hands. In ID4 there was a higher incidence of vestiges in male cases and open fields in female cases in both hands. There was a low incidence of true patterns in this area. There was a significant difference in the right ID4 area of female subjects.

There was no significant difference between cases and controls in male and female subjects with respect to C-main line termination, Main-line formula, Simian crease and Sydney line.

Palmar Quantitative Analysis: The palmar quantitative parameters studied were the a-b count, atd angle, distal deviation of t, breadth ratio and main-line index. There was no significant difference in the scores between the cases and controls for these parameters for male and female subjects (Table 6).

Discussion

DM2 is a disease with a long latent period before diagnosis and several long term complications in the major organ systems of the body.¹⁰ The pre-diabetic stage, which lasts for some years is said to be shorter in Indians.⁴ It is in this regard that dermatoglyphics in DM2 can bridge the gap between predisposition, the pre-diabetic stage and the diagnosis.

DM2 has been described as a geneticist's nightmare and the several genetic factors have been linked to the disease in various studies, spanning multiple gene effect¹⁰ at multiple

loci¹³ involving more than seventy genes,^{10,13} with familial tendency with polygenic mode of inheritance, phenotypic expression modified by environmental factors throughout the lifespan.¹⁰ It is therefore difficult to predict the occurrence of DM2 by a specific genetic test.

Several studies have shown that Indians have a higher prevalence of DM2^{3,7} due to genetic predisposition for DM2^{3,8} combined with a predominantly carbohydrate based diet,^{2,3} and the so called "Asian Indian Phenotype" that predisposes Asian populations tend to develop diabetes at younger ages and lower BMI levels than Caucasians.^{3,9} These are some of the factors that have contributed to accelerated diabetes epidemic in Asians.

The genetic basis of dermatoglyphic patterns elucidated by many studies that show the role of several main genes, in conjunction with a number of modifying genes, are responsible for volar patterning, in addition to chromosome 18,21 and the X chromosome.¹⁴⁻¹⁷ Environmental factors affect patterning albeit in the prenatal period only.¹⁸

While questions of genome-wide association studies on DM2 are contemplated on one hand,¹⁹ the burden of the disease on the individual and the healthcare system, on the other, is enormous especially in developing countries like India. In this context, dermatoglyphics is a valuable tool as it can be done by the bedside, in the clinic and at any age, long before the development of significant blood glucose levels.

A unique feature of our study was the emphasis placed on the family history of diabetes in the selection of cases and controls. The possible elimination of this confounding factor in non-diabetics, is in addition an established risk factor for DM2 and thus a supportive factor for cases.

Qualitative Analysis of Finger Pattern Configuration

There is a significantly higher frequency of spiral whorls in male and female diabetics except in L2, R1 and R4 of males and, L1 and R5 of females, and higher frequency of loops in male and female controls. This corresponds with the findings of Sant SM, Vare AM and Fakruddin S,²⁰ Mehta²¹ in both sexes, and Ojha²² in male diabetics. Ahuja YR et al²³ reported a higher frequency of whorls in male diabetics. Vormittag and Weninger²⁴ reported increased frequency of whorls in female diabetics and decreased loops in male diabetics. Whereas, Ravindranath R and Thomas IM²⁵ reported increased frequency of ulnar loops and arches, decreased frequency of whorls in male and female diabetics. Srivastava and Singh²⁶ and Tarigopplula²⁷ reported increased ulnar loops and decreased whorls in diabetics. Floris et al²⁸ and Koliski²⁹ reported increased arches in female diabetics. Chakravarti MR³⁰ reported increased ulnar loops in the 2nd and 3rd digits in diabetics. Nayak V et al³¹ found no significant difference in the incidence of arches, loops or whorls.

Finger Quantitative Analysis

Fingertip ridge counts were higher in cases of both sexes as compared to controls. The counts were significantly

higher in male and female diabetics except L2 and R1 in males, and R5 in females.

Pattern Intensity: It refers to the complexity of ridge configurations. Higher pattern intensity indicates a greater incidence of whorls as compared to loops. Male and female cases show significantly higher pattern intensity than controls on both the hands.

TFRC: The TFRC is significantly higher in male cases for both hands and the right hand of female cases. This corresponds with the studies by Banerjee et al³² and Iqbal et al,³³ Ahuja YR et al²³ and Ojha²² reported an increase in TFRC in diabetics. Vormittag and Weninger²⁴ found low TFRC in female diabetics.

AFRC: The AFRC is significantly higher in male and female cases of both hands. Ojha²² also reported a significantly higher AFRC in both hands of diabetic patients.

MFRC: The MFRC is significantly higher in cases than controls for male and female subjects in both hands.

Palmar Qualitative Analysis

Hypothenar area: In our study female controls showed a significantly higher incidence of open fields in the left hypothenar area. Dzuiba³⁴ found low incidence of hypothenar pattern in female diabetic children.

Thenar/ First interdigital area (Th/ID1): In our study there was a high frequency of open fields in controls though finding was not significant. This corresponds with the findings of Sant SM et al²⁰ and Ahuja YR et al²³ who did not find any significant difference.

Second, third and fourth interdigital areas (ID2, ID3 and ID4): In our study the only 'true pattern' found is the distal loop in both hands of male and female subjects. Female cases showed a significantly higher incidence of open fields in the right ID4 area. It shows cases have less incidence of 'true pattern' in the ID4 area. Eshwariah and Bali³⁵ observed significant decrease in pattern in ID2 of female diabetics. Verbov³⁶ reported a decrease in the frequency pattern in the left ID3 of female type I diabetics. Eshwariah and Bali³⁵ and Tarca³⁷ reported a decreased frequency of patterns in diabetics as compared to controls in ID4. Dastidar³⁸ reported a significantly higher frequency of patterns in diabetics in ID4.

In our study there was no significant difference with respect to Simian crease and Sydney line. Verbov³⁶ reported a difference albeit in type I diabetics.

C-main line termination: Though not significant in our study, Chakravarti MR³⁰ observed a higher frequency of C-line in cases. Eshwariah and Bali³⁵ reported significant differences in C main-line types in diabetics of both sexes. Dastidar³⁸ reported C-main line polymorphism in diabetics.

Palmar Quantitative Analysis

a-b Count: It is higher in cases in both the hands in male subjects. Koliski²⁹ also reported higher a-b ridge count in male diabetics. Floris et al²⁸ Vormittag and Weninger²⁴ reported significant decrease in a-b ridge count in both sexes.

atd Angle: The atd angle is higher, but not significantly, in the both hands of male cases and both the hands of female controls. This corresponds with the studies by Sant SM et al²⁰ and Ahuja YR et al²³ who found no significant difference in the atd angle. Tarigoppula,²⁷ Nayak V,³¹ Srivastava and Singh,²⁶ Vormittag and Weninger²⁴ and Koliski et al²⁹ observed a higher atd angle in diabetics. Floris et al²⁸ found lower atd angles in diabetics.

Distal deviation of t, breadth ratio and main-line index: Though higher in cases as compared to controls the values were not statistically significant. Eshwaraiah and Bali³⁵ reported significant differences in main-line formula in male diabetics.

There were several significant parameters in the results of the present study. This has to be taken in view of the fact that family history of diabetes was a criterion in the selection of cases and controls.

Table 1: Frequency of patterns in fingertips

Digit No.	Pattern	Male							Digit No.	Female						
		Arches		Loops		Whorls				Arches		Loops		Whorls		
		A	A ^t	L ^r	L ^u	W ^s	W ^{dl}	W ^{cp}		A	A ^t	L ^r	L ^u	W ^s	W ^{dl}	W ^{cp}
L1*	Cases	-	1	1	32	26	15	-	L1	-	0	1	38	26	10	-
	Controls	-	3	1	47	12	12	-		-	4	0	50	15	6	-
L2	Cases	-	5	7	36	24	3	-	L2*	-	2	3	30	37	2	1
	Controls	-	6	9	39	18	3	-		-	9	7	40	15	4	1
L3*	Cases	-	3	0	47	23	2	-	L3*	-	2	1	35	33	4	-
	Controls	-	3	2	55	13	2	-		-	7	2	50	15	1	-
L4*	Cases	-	1	-	31	42	1	-	L4 [†]	-	-	-	20	54	1	-
	Controls	-	0	-	41	31	3	-		-	-	-	45	29	1	-
L5*	Cases	1	1	-	49	19	5	-	L5*	-	-	0	40	33	2	-
	Controls	0	0	-	61	13	1	-		-	-	1	50	13	1	-
R1	Cases	-	0	0	38	28	9	-	R1*	-	0	1	41	26	7	-
	Controls	-	2	2	36	26	9	-		-	3	0	50	11	11	-
R2*	Cases	2	1	4	36	28	4	-	R2*	-	2	1	32	32	8	-
	Controls	4	0	10	37	17	7	-		-	13	4	41	13	4	-
R3*	Cases	-	1	1	48	24	0	1	R3*	-	1	1	49	23	1	-
	Controls	-	2	0	57	15	1	0		-	4	0	65	6	0	-
R4	Cases	-	1	1	27	44	1	1	R4 [†]	-	0	-	20	55	-	0
	Controls	-	0	1	34	40	0	0		-	1	-	43	30	-	1
R5*	Cases	-	1	1	50	23	0	-	R5	-	0	-	51	24	0	-
	Controls	-	1	0	59	13	2	-		-	1	-	60	13	1	-

A: Arch, A^t: tented arch, L^r: radial loop, L^u: ulnar loop, W^s: spiral whorl, W^{dl}: double loop whorl, W^{cp}: composite whorl. * Moderately significant (P value: 0.01 < P ≤ 0.05) † Strongly significant (P value: P ≤ 0.01)

Table 2: Comparison of fingertip ridge counts of all fingers

Area	Male		Area	Female	
	Cases	Controls		Cases	Controls
	Mean SD	Mean SD		Mean SD	Mean SD
L1 [†]	19.1 7.1	14.8 7.3	L1*	16.8 6.3	13.9 6.9
L2	13.2 7.5	11.0 7.8	L2 [†]	15.1 7.3	10.2 7.1
L3*	14.2 6.5	11.6 6.5	L3*	14.7 6.9	11.2 6.7
L4*	17.5 6.9	15.0 6.8	L4 [†]	17.3 6.0	14.0 6.3
L5*	13.4 5.8	10.6 4.2	L5*	12.9 4.9	10.8 4.4
R1	20.1 6.7	18.9 7.9	R1*	17.8 6.1	15.5 6.4
R2 [†]	15.0 7.9	11.9 7.5	R2 [†]	15.3 6.3	10.3 6.7

R3	13.9 6.1	12.4 6.7	R3*	13.6 6.0	10.8 5.4
R4*	18.7 6.5	15.8 6.8	R4*	18.0 5.8	14.9 7.3
R5*	14.5 5.7	11.4 4.8	R5	12.6 4.2	11.1 4.7

* Moderately significant (P value: $0.01 < P \leq 0.05$) † Strongly significant (P value: $P \leq 0.01$)

Table 3: Quantitative analysis of fingertip parameters

Parameter	Male		Parameter	Female	
	Case Mean SD	Control Mean SD		Case Mean SD	Control Mean SD
PTN INT RIGHT†	7.1 1.8	6.6 1.7	PTN INT RIGHT†	7.4 1.5	6.0 1.7
PTN INT LEFT†	7.1 2.0	6.3 1.8	PTN INT LEFT†	7.6 1.6	6.1 1.8
TFRC RIGHT*	60.4 13.3	53.0 15.0	TFRC RIGHT*	57.0 11.2	52.2 16.8
TFRC LEFT*	56.7 13.7	49.8 15.0	TFRC LEFT	53.2 10.9	49.4 16.8
AFRC RIGHT†	81.5 26.0	68.3 26.7	AFRC RIGHT†	77.0 20.6	62.4 23.0
AFRC LEFT†	76.7 26.5	62.7 26.0	AFRC LEFT†	75.6 22.8	60.0 24.5
MFRC RIGHT*	16.3 5.3	13.7 5.3	MFRC RIGHT*	15.4 4.1	12.5 4.6
MFRC LEFT*	15.3 5.3	12.6 5.2	MFRC LEFT*	15.1 4.6	12.0 5.0

PTN INT: Pattern intensity, TFRC: Total finger ridge count, AFRC: Absolute finger ridge count, MFRC: Mean finger ridge count. * Moderately significant (P value: $0.01 < P \leq 0.05$) † Strongly significant (P value: $P \leq 0.01$)

Table 4: Qualitative analysis of patterns in Hypothenar area and Thenar/First interdigital area (Th/ID1)

Hypothenar area			A ^t	L ^c	L ^r	L ^u	L ^u /L ^r	O	V	V/O	W
Male	Right	Case	0	2	6	2	0	55	10	0	0
		Control	0	0	8	5	0	45	16	0	1
	Left	Case	0	0	5	3	0	47	19	0	1
		Control	0	0	15	3	0	36	20	1	0
Female	Right	Case	2	1	15	3	0	49	4	0	1
		Control	0	1	10	5	1	48	9	0	1
	Left †	Case	1	1	22	1	5	34	7	0	1
		Control	1	0	8	0	2	48	15	0	1
Thenar/ First interdigital area (Th/ID1)			A ^t	L ^c	L ^d	L ^u	L ^r	L ^r /L ^c	O	V	W
Male	Right	Case	6	2	1	0	0	1	58	7	-
		Control	2	1	0	0	2	0	68	2	-
	Left	Case	7	8	0	0	1	2	53	3	1
		Control	1	6	0	0	4	0	62	2	0
Female	Right	Case	3	4	0	0	0	0	65	3	0
		Control	1	3	0	0	0	0	69	1	1
	Left	Case	3	4	0	1	1	0	63	3	0
		Control	5	4	0	0	1	0	62	2	1

A^t : tented arch, L^c : carpal loop, L^r : radial loop, L^u : ulnar loop, O: open field, V: vestige, W: whorl. * Moderately significant (P value: $0.01 < P \leq 0.05$) † Strongly significant (P value: $P \leq 0.01$)

Table 5: Qualitative analysis of patterns in Interdigital area 2 (ID2), Interdigital area 3 (ID3) and Interdigital area 4 (ID4)

	Pattern		ID2			ID3			ID4					
			L ^d	O	V	L ^d	O	V	L ^d	L ^r	L ^d /L ^d	O [†]	V	W
Male	Right	Case	9	54	19	2	56	10	31	1	-	28	15	0
		Control	3	48	25	2	67	5	34	0	-	32	9	0
	Left	Case	1	41	32	2	67	7	35	1	1	23	15	0
		Control	2	21	52	2	69	4	38	0	3	25	9	0
Female	Pattern		L ^d	O	V	L ^d	O	V	L ^d	L ^r	L ^d /L ^d	O [†]	V	W
	Right	Case	6	45	25	5	65	4	34	-	0	36	5	0
		Control	2	36	39	0	69	4	35	-	1	20	18	1
	Left	Case	3	21	50	4	69	3	34	2	2	30	7	0
Control		0	24	49	2	70	3	40	0	1	20	13	1	

L^d : distal loop, O: open field, V: vestige, W: whorl. * Moderately significant (P value: 0.01<P ≤ 0.05) †Strongly significant (P value: P≤0.01)

Table 6: Palmar quantitative analysis

Parameter	Male		Female	
	Cases	Controls	Cases	Controls
	Mean S.D.	Mean S.D.	Mean S.D.	Mean S.D.
a-b Count Right	29.9 6.2	27.2 5.2	28.1 5.6	29.1 7.3
a-b Count Left	31.3 6.3	28.7 5.0	28.7 6.4	29.9 6.8
atd Angle Right	41.0 8.0	40.3 7.5	40.9 7.0	41.4 6.6
atd Angle Left	41.4 7.4	41.2 6.7	41.4 7.4	42.4 7.5
Distal Deviation of t Right	7.1 1.8	6.6 1.7	16.7 10.3	16.6 11.0
Distal Deviation of t Left	7.1 2.0	6.3 1.8	16.9 10.2	11.1 8.2
Breadth Ratio Right	6.8 0.9	6.7 1.0	6.1 1.1	6.0 1.0
Breadth Ratio Left	6.9 0.9	6.8 1.1	6.0 1.0	5.9 1.1
Main-Line Index Right	14.6 1.8	14.7 1.7	14.4 1.9	14.5 1.8
Main-Line Index Left	13.7 2.0	13.1 1.8	13.3 2.1	13.2 2.0

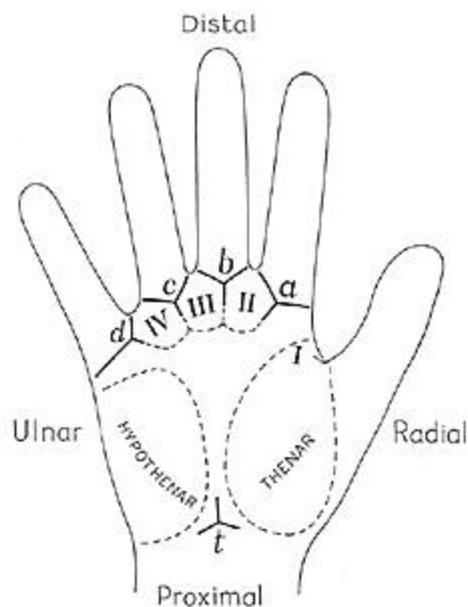


Fig. 1: Palmar dermatoglyphics areas

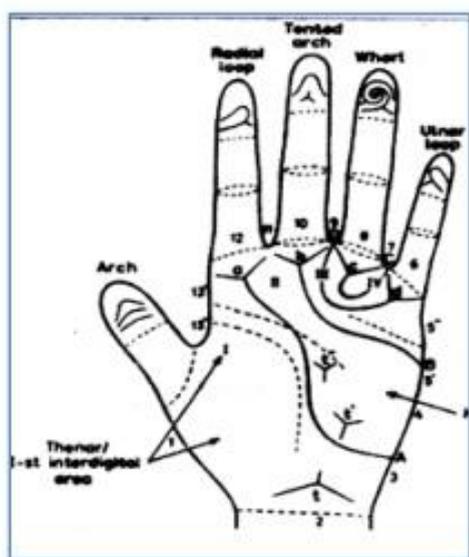


Fig. 2: Dermatoglyphic landmarks

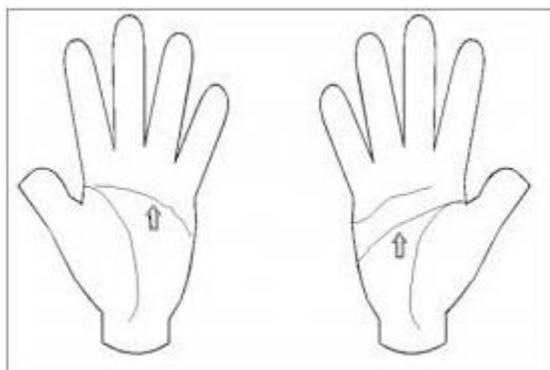


Fig. 3: Simian line and Sydney line



Fig. 4: Analysis of a print, right hand

Conclusion

The present study, with underscoring of family history in the selection of subjects, has determined several significant parameters applicable to type 2 diabetes mellitus in a Bangalore based South Indian population. In a country credited as the ‘diabetic capital of the world’, the use of simple tools involving somatic traits of genetic factors in addition to risk factor analysis will be beneficial to reduce the individual and societal burden of a disease known its several long term complications. There is a need for larger population based studies to standardize the parameters and translate the findings into clinical and public health practice.

Conflict of Interest: None.

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