Vol.2, No.7, 732-736 (2010)
http://dx.doi.org/10.4236/ns.2010.27091

Natural Science

Familial aggregation and heritability for cardiovascular risk factors: a family based study in Punjab, India

Raman Kumar, Badaruddoza*

Department of Human Genetics, Guru Nanak Dev University, Amritsar, India; *Corresponding Author: doza13@yahoo.co.in

Received 19 March 2010; revised 15 April 2010; accepted 20 April 2010.

ABSTRACT

Background: It is well established that the people with elevated SBP, DBP, BMI and WHR are more prone to cardiovascular disease. However, very few studies have focused on the amount of familial aggregation and heritability of these cardiovascular risk factors in Indian population. Therefore, purpose of this study was to investigate the familial aggregation of blood pressures with respect to certain anthropometric traits and to determine the relative roles of heredity in the etiology of SBP and DBP in a sample of families with three generations. Methods: The study has been conducted through house to house family study among three generations such as offspring, parent and grandparent in a scheduled caste community (Ramdasia) in Punjab. A total of 1400 individuals, constituting 380 families were surveyed for blood pressure, pulse rate, pulse pressure and anthropometric measurements to study familial aggregation and heritability for cardiovascular risk factors. The analysis represents a multivariate model which includes the each individual family data for estimation of familial correlation and heritability. Results: All risk factors showed positive familial correlation but magnitudes are different in various pairs of combination. Correlations generally are higher among genetically close relatives such as brother-sisters or parent-offspring and are lower among spouses. The estimated heritabilities were 22% for systolic and 27% for diastolic blood pressure, 19% for BMI and 17% for WHR. Conclusions: These results indicate a strong familial aggregation of cardiovascular risk factors such as SBP and DBP in this population and also showed that this familial influence can be detected from anthropometric measurements and genetic closeness. Almost all anthropometric variables were found to be significant with blood pressures among three generations.

Keywords: Familial Aggregation; Heritability; Risk Factors; Ramdasia Population; Punjab

1. INTRODUCTION

There is much epidemiological evidence that environmental cofactors and anthropometric characteristics are directly and consistently correlated with cardiovascular diseases in developing countries [1-7]. It has been reported that almost 30% of risk factors for cardiovascular diseases are accounted by genetic heritability and at least approximately 70% of risk factors are of familial in nature [8-13]. However, many authors have contradicted that what extent to which that observed familial aggregation on both systolic and diastolic is due to genetic or environmental reason. Some authors have argued that familial aggregation on diastolic blood pressure is more than systolic blood pressure or vice versa [14]. However, in India the pattern of risk factors for cardiovascular diseases are different to cut across the cultural patterns and geographic regions. Therefore, in Indian context the paucity of family based information and complex etiology of this disease made it difficult for understanding how these factors contribute to the cardiovascular diseases. Hence, the major purpose of this study was to investigate the familial aggregation of blood pressures with respect to certain anthropometric traits and to determine the relative roles of heredity in the etiology of SBP and DBP in a sample of families with three generations such as offspring, parent and grandparent in Punjab, a north Indian state. Our working hypotheses were that there is familial aggregation of blood pressure in the studied families and the association of blood pressure in first degree relatives is more than spouse pairs.

2. MATERIALS AND METHODS

For the present study the population included 1400 indi-

viduals constituting 380 families with three generations. Individuals in the parental generation (N = 780) range in age from 30.5 to 60.7 years. The age of offspring (N = 456) range from 9.5 to 26.7 years. The age of the grandparent generation (N = 164) range from 52.8 to 85.6 years. All families were recruited from Ramdasia community (Ramdasia community is socially and educationally backward from the rest of the population in Punjab) to reduce the confounding effect ethnically determined genetic differences. For recruitment of the subjects family history of heart disease was not the criteria, however, randomly selected families exhibiting a broad cross selection of cardiovascular risk factor levels.

2.1. Phenotypes Measurements

This study was approved by the Ethics Review Committee of Guru Nanak Dev University, Amritsar, India and written consent was obtained from all the participants. Comprehensive and elaborated questionnaires related health, life style, demographic features, socio-economic status and family history were completed by the participants before physical measurement. Blood pressure was measure on the right arm of the subjects in a sitting position after 10 minutes of rest using a mercury sphygmomanometer and a stethoscope with an accuracy of 2 mm Hg by following the recommendations of American Heart Association [15]. On the basis of circumference of the participants arm, a regular adult or large or medium cuff has been chosen. Systolic and diastolic blood pressures were defined at the first and fifth phases of Korotkoff sounds respectively. The pulse rate was measured for 60 seconds. The average of two measurements was used as the estimates of SBP and DBP in the present analysis. Mean arterial blood pressure (MBP) was calculated as DBP + (SBP-DBP)/3 [16]. The pulse pressure was calculated as SBP-DBP.

The other anthropometric measurements were taken from each individual include height, weight, five circumferences (chest, waist, hip, arm and calf) and biceps and triceps skinfolds. All measurements were taken with standard anthropometric techniques [17-18]. Body mass index (BMI) and waist to hip ratio were defined as weight/height^2 (kg/m^2) and waist circumference divided by hip circumferences respectively.

2.2. Statistical Methods

All statistical analyses were performed using SPSS software. The $p < 0.05$ level was selected as the criterion of statistical significance. Heritability estimation was done from regression of offspring on parents.

3. RESULTS

Table 1 shows the summary of data for offspring, parent and grandparent generations with both sexes. The mean ages and standard deviations for different generations are: 18.00 ± 5.12 (male offspring), 17.63 ± 4.95 (female offspring), 41.19 ± 9.12 (male parents), 38.05 ± 9.16 (female parents), 67.52 ± 9.10 (male grandparents) and 62.46 ± 8.72 (female grandparents). In general, maximum mean values of anthropometric measurements such as height, weight and calf circumference for male parent generation; BMI, chest, hip and arm circumferences, biceps and triceps skinfolds for female parent generation; waist circumference, WHR for female grandparent generation have been observed in the present analysis. The maximum SBP, DBP, MBP, pulse rate and pressure have been found in female grandparent generation. On average, offspring generations have lower mean values of almost all measured phenotypes. As shown in the **Table 2** all the means of the measured variables have significant differences ($p < 0.001$) between different intra-generations for all measured variables. However, age, DBP, calf and hip circumferences, and WHR have found maximum intra-generational differences.

Estimates of familial correlations among household members and estimated sample size are presented in **Table 3**. All correlations are positive and maximum familial correlations for almost all the traits were found in close genetically related brother-sister combination. The lowest familial correlations for all the traits were found in spouses. The familial correlations for SBP and DBP are also significantly higher between father-male offspring combination. However, the stronger correlations were found in various traits among different combinations such as for biceps skinfold, chest circumference, pulse pressure between father-male offspring; for arm circumference between father-female offspring; for BMI, WHR and pulse rate between mother-female offspring. Therefore, these risk factors showed the patterns of familial correlation which were stronger among more genetic control relationship and lower in spouse.

Table 4 shows estimated genetic component of variance and heritability for cardiovascular risk factors in this population. The genetic variance included only the additive genetic variance and these are significantly greater than zero for all the risk factors. The genetic effect of these risk factors may be assumed from the square root of these variances. For SBP the genetic effect is 10.56 mm Hg and it contributes 22% (heritability) of the variation in systolic blood pressure. For diastolic blood pressure the genetic effects is 7.28 mmHg and it contributes 27% of the variation in this population. However, the contributions of genetic effects of other variables such as pulse rate, pulse pressure, body mass index (BMI), waist to hip ratio (WHR), biceps and triceps skinfolds, arm and calf circumferences are 10.03 minutes (heritability 10%), 8.75 mm (heritability 30%),

Table 1. Descriptive statistics of measured phenotypes between among different generations.

Variables	Male Offspring		Female Offspring		Male Parent		Female Parent		Male Grandparent		Female Grandparent	
	Mean ± SD	Inter-quartile **range**	**Mean ± SD**	Inter-qua-rtile **range**	**Mean ± SD**	Inter-quartile **range**	**Mean ± SD**	Inter-quartile **range**	**Mean ± SD**	Inter-quartile **range**	**Mean ± SD**	Inter-quartile **range**
Age (yrs)	18.00 ± 5.12	7.00-35.00	17.63 ± 4.95	7.00-30.00	41.19 ± 9.12	21.00-67.00	38.05 ± 9.16	20.00-65.00	67.52 ± 9.10	46.00-96.00	62.46 ± 8.72	40.00-85.00
Height (cm)	157.79 ± 10.6	101.50 − 183.0	150.21 ± 9.98	105.00 − 172.00	167.71 ± 6.44	148.70 − 186.1	154.12 ± 5.5	136.20 − 172.3	164.96 ± 7.1	142.7 − 183.3	152.13 ± 6.23	131.00 − 168.0
Weight (kg)	47.43 ± 11.42	14.00 − 92.00	42.87 ± 10.56	15.00 − 89.00	65.19 ± 10.82	37.00 − 98	59.25 ± 11.9	32.00 − 105.00	55.68 ± 10.2	40.00 − 93.30	56.49 ± 10.58	30.00 − 90.00
BMI (kg/m^2)	18.42 ± 3.56	11.26 − 35.57	18.77 ± 3.82	10.41 − 36.85	23.10 ± 3.75	13.54 − 34.51	24.87 ± 4.70	14.67 − 45.37	20.29 ± 4.05	13.71 − 31.66	24.33 ± 4.67	14.07 − 37.94
Chest circum(cm)	80.19 ± 9.12	52.50 − 116.40	77.32 ± 8.99	52.70 − 112.00	94.31 ± 8.52	73.00 − 120.20	94.81 ± 8.45	70.00 − 130.00	90.23 ± 8.49	77.6 − 113.00	94.65 ± 8.20	71.00 − 119.00
Waist circum(cm)	75.17 ± 10.35	47.80 − 115.00	72.43 ± 9.68	46.5 − 113.00	94.36 ± 8.46	61.60 − 129.90	96.81 ± 9.99	61.00 − 136.00	89.24 ± 10.3	65.40 − 121.0	97.98 ± 9.99	65.00 − 127.00
Hip circum. (cm)	82.16 ± 9.42	52.00 − 112.00	81.78 ± 8.48	47.00 − 121.50	94.12 ± 7.88	73.33 − 122.40	94.66 ± 9.01	72.50 − 130.00	87.89 ± 8.11	76.30 − 106.4	93.94 ± 9.84	72.00 − 121.30
WHR	0.91 ± 0.06	0.71 − 1.10	0.86 ± 0.070	0.69 − 1.09	1.00 ± 0.07	1.253 − 0.759	1.00 ± 0.11	0.07 − 1.88	1.01 ± 0.09	0.804 − 1.269	1.04 ± 0.143	0.10 − 1.294
Arm circum. (cm)	22.87 ± 4.39	13.90 − 37.80	21.97 ± 3.51	13.80 − 33.80	27.11 ± 3.28	18.40 − 37.00	26.78 ± 3.48	18.50 − 38.50	24.00 ± 3.56	17.30 − 33.40	26.08 ± 3.82	17.20 − 35.50
Calf circum (cm)	28.32 ± 4.13	18.00 − 42.00	27.13 ± 3.64	17.40 − 41.50	31.87 ± 3.39	21.00 − 41.80	30.63 ± 3.64	17.80 − 42.50	28.85 ± 3.64	16.40 − 37.60	28.96 ± 3.69	22.20 − 37.30
Biceps skinfold (mm)	6.30 ± 2.57	3.00 − 17.00	7.66 ± 3.42	3.00 − 32.00	7.84 ± 2.91	2.00 − 20.00	10.58 ± 4.05	3.00 − 31.00	5.89 ± 3.04	2.00 − 17.00	9.56 ± 4.38	3.00 − 29.00
Triceps skinfold (mm)	9.94 ± 4.34	4.00 − 17.00	13.50 ± 4.31	4.00 − 42.00	12.49 ± 4.48	3.00 − 32.00	20.10 ± 6.73	3.00 − 31.00	9.72 ± 5.07	3.00 − 28.00	18.37 ± 7.84	4.00 − 4.00
SBP (mm/Hg)	116.47 ± 10.5	90.00 − 150	111.59 ± 9.22	80.00 − 140.00	128.09 ± 9.20	90.00 − 210.00	122.98 ± 9.4	80.00 − 190.00	136.96 ± 9.7	100.0 − 220.0	144.57 ± 10.1	90.00 − 240.00
DBP (mm/Hg)	76.50 ± 7.29	55.00 − 110.00	73.95 ± 6.70	50.00−90.00	82.11 ± 7.80	60.00 − 120.00	78.73 ± 8.15	60.00 − 120.00	82.42 ± 8.08	50.00 − 120.0	85.17 ± 9.97	50.00 − 120.00
MBP (mm/Hg)	89.80 ± 7.68	66.00 − 120.00	86.41 ± 6.79	63.33 − 106.66	97.39 ± 9.19	70.00 − 150	93.45 ± 9.18	66.66 − 140.00	100.26 ± 9.6	66.66 − 153.3	104.76 ± 10.0	63.33 − 160.00
Pulse rate	81.96 ± 8.02	20.00 − 90.00	85.37 ± 8.67	60.00 − 121.00	82.91 ± 9.78	60.00 − 120.00	85.58 ± 10.8	60.00 − 90.00	84.48 ± 8.99	65.00 − 140.0	85.79 ± 8.25	60.00 − 113.00
Pulse pressure	40.49 ± 8.76	54.00 − 132.00	37.87 ± 7.43	20.00 − 60.00	46.13 ± 10.77	10.00 − 90.00	44.29 ± 10.8	20.00 − 95.00	55.16 ± 9.37	10.00 − 20.00	59.14 ± 9.61	20.00 − 130.00

Table 2. T-values with 95% confidence level between intra-generational differences of mean values for all measured phenotypes.

Variables	t	P	95% confidence level of the difference
Age (yrs)	4.715	< 0.005	18.55-63.05
Height (cm)	54.37	< 0.000	150.36-165.28
Weight (kg)	16.49	< 0.000	45.99-62.97
BMI (kg/m^2)	18.67	< 0.000	18.65-24.61
Chest circumference (cm)	27.62	< 0.000	80.34-96.82
Waist circumference (cm)	19.19	< 0.000	75.92-99.40
Hip circumference (cm)	36.09	< 0.000	82.74-95.43
WHR	34.29	< 0.000	0.89-1.04
Arm circumference (cm)	28.16	< 0.000	22.53-27.06
Calf circumference (cm)	42.33	< 0.000	22.53-27.06
Biceps skinfold (mm)	10.72	< 0.000	6.06-9.88
Triceps skinfold (mm)	7.93	< 0.001	9.48-18.56
SBP (mm/Hg)	25.12	< 0.000	113.86-139.82
DBP (mm/Hg)	46.78	< 0.000	75.83-84.19
MBP (mm/Hg)	34.43	< 0.000	88.24-102.48
Pulse rate	160.52	< 0.000	83.35-86.29
Pulse pressure	12.65	< 0.000	37.87-59.16

Table 3. Estimates of familial correlation for cardiovascular risk factors.

Variables	BMI	WHR	BISF	TRISF	AC	CC	PR	PP	SBP	DBP	MBP
Spouse (n = 312)	0.09	0.08	0.05	0.05	0.12	0.07	0.08	0.07	0.04	0.05	0.06
Father-male offspring (n = 270)	0.21	0.12	0.16	0.02	0.11	0.18	0.07	0.13	0.31	0.30	0.25
Father-female offspring (n = 186)	0.15	0.12	0.12	0.05	0.19	0.12	0.07	0.08	0.21	0.20	0.20
Mother-male offspring (n = 270)	0.23	0.14	0.01	0.04	0.18	0.10	0.07	0.04	0.17	0.15	0.14
Mother-female offspring (n = 186)	0.29	0.12	0.03	0.06	0.12	0.13	0.18	0.04	0.20	0.18	0.16
Brother-sister (n = 186)	0.38	0.31	0.15	0.15	0.15	0.12	.21	0.14	0.34	0.31	0.30
Grandfather-male 0ffspring (n = 66)	0.12	0.07	0.07	0.08	0.03	0.14	0.05	0.11	0.16	0.19	0.19
Grandfather-female (n = 66) offspring	0.12	0.13	0.12	0.02	0.18	0.12	0.10	0.02	0.13	0.14	0.14
Grandmother-male offspring (n = 99)	0.10	0.10	0.08	0.06	0.14	0.02	0.0	0.06	0.13	0.17	0.16
Grandmother-female offspring (n = 99)	0.12	0.11	0.13	0.03	0.14	0.09	0.02	0.12	0.14	0.15	0.13

BMI = Body mass index; WHR = Waist-Hip ratio; AC = Arm circumference; CC = Calf circumference; BISF = Biceps skinfold; TRISF = Triceps skinfold; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; MBP = Mean arterial blood pressure; PR = Pulse rate; PP = Pulse pressure.

Table 4. Estimated genetic component of variance and heritability for cardiovascular risk factors.

Risk Factors	Genetic Variance	Heritability
SBP (mm/Hg)	111.72	22%
DBP (mm/Hg)	53.14	27%
MBP (mm/Hg)	58.94	35%
Pulse rate	100.61	10%
Pulse pressure	76.56%	30%
BMI (kg/m^2)	12.67	19%
WHR	0.05	17%
Biceps skinfold (mm)	6.60	21%
Triceps skinfold (mm)	18.83	14%
Arm circumference (cm)	19.36	12%
Chest circumference (cm)	17.05	35%

3.54 kg/m^2 (heritability 19%), 0.22 (heritability 17%), 2.56 mm (heritability 21%), 4.33 mm (heritability 14%), 4.4 cm (heritability 12%) and 4.13 cm (heritability 35%) respectively in this population.

4. DISCUSSION

The analysis from the present studies of three generations families in Punjab, a north Indian state have demonstrated strong familial aggregation of BMI, WHR, SBP and DBP for cardiovascular risk factors. The close genetic relationship such as parent-offspring, brother-sister correlations were significantly higher ($p < 0.05$) than non-genetic or distant genetic relationship such as spouses and grandparents. Overall, heritabilities were estimated to be 22% for SBP, 27% for DBP, 19% for BMI, 17% for WHR and 21% biceps skinfold. Therefore, the present observation suggested that genetically more close relatives have greater chance to aggregate cardiovascular risk factors than non-genetical and distant relatives. Many previous studies have also supported this hypothesis [4,7,10-12,19-21]. The present heritability analysis represents the additive effects of genes. The greater range of heritability for different cardiovascular risk factors have suggested a greater genetic influences in the familial aggregation of SBP, DBP, pulse pressure, BMI, chest circumference and biceps skinfold. However the sample size of three generations strengthens the statistical power to identify the association of cardiovascular risk factors with different relationships.

In this context, the present population due to its homogeneous nature provides a good opportunity to assess the familial determinants of cardiovascular risk factors. Families in this population are sufficiently large and joint in addition to that physical environment and diet contrast are also almost similar. In conclusion, our data suggest a significant familial aggregation of cardiovascular risk factors for SBP, DBP, BMI and WHR.

5. ACKNOWLEDGEMENTS

First author (RK) is thankful to the University Grants Commission, Government of India, for providing Rajiv Gandhi National Fellowship (No. F.16-31/2006 /SA-II) in the Department of Human Genetics, Guru Nanak Dev University, Amritsar, Punjab, India.

REFERENCES

[1] Yu, Z., Nissinen, A., Vartianen, E., Song, G., Guo, Z. and Tians, H. (2000) Changes cardiovascular risk factors in different socio-economic groups: Seven years trends in Chinese Urban population. *Journal of Epidemiology and Community Health*, **54(9)**, 692-696.

[2] Badaruddoza and Afzal, M. (1999) Age specific difference in blood pressure among inbred and noninbred North Indian Children. *Journal of Biosocial Science*, **24(2)**, 177-184.

[3] Badaruddoza and Afzal, M. (2000) Trend of blood pressure in North Indian children. *Indian Journal of Physiology and Pharmacology*, **44(3)**, 304-310.

[4] Wang, X., Wang, B., Chen, C., Yang, J., Fang, Z., Zuckerman, B. and Xu, X. (1999) Familial aggregation of blood pressure in a rural Chinese community. *American Journal of Epidemiology*, **149(5)**, 412-420.

[5] Lasser, U. and Breckenkamp, J. (2005) Trends in risk factors control in Germany 1984-1998: High blood pressure and total cholesterol. *European Journal of Public Health*, **16(2)**, 217-222.

[6] Tomson, J. and Lip, G.Y.H. (2005) Blood pressure demographics, nature on nurture, gene or environment. *BMC Medicine*, **3(8)**, 3-8.

[7] Badaruddoza and Kumar, R. (2009) Cardiovascular risk factor and familial aggregation of blood pressure with respect to anthropometric variables in a schedule caste population of Punjab. *Anthropologischer Anzeiger*, **67(2)**, 111-119.

[8] Brand, F.N., Kiely, D.K., Kanel, W.B., *et al*. (1992) Family patterns of coronary heart disease mortality: The Framingham longevity study. *Journal of Clinical Epidemiology*, **45(2)**, 169-174.

[9] Hopper, J.L. and Carlin, J.B. (1992) Familial aggregation of a disease consequent upon correlation between relatives in risk factors measured in continuous scale. *American Journal of Epidemiology*, **136(9)**, 1138-1147.

[10] Knuiman, M.W., Divitini, M.L., Bartholomew, H.C. and Welborn, T.A. (1996) Spouse correlations in Cardiovacsular risk factors and the effect of marriage duration. *American Journal of Epidemiology*, **143(1)**, 48-53.

[11] Knuiman, M.W., Divitini, M.L., Welborn, T.A. and Bartholomew, H.C (1996) Familial correlations, cohabitation effects, and heritability for cardiovascular risk factors. *Annals of Epidemiology*, **6(3)**, 188-194.

[12] Fuentes, R.M., Notkola, I.L., Shemeikka, S., Tuomilehto, J. and Nissinen, A. (2000) Familial pressure: A population based family study in eastern Finland. *Journal of Human Hypertension*, **14(7)**, 441-445.

[13] Harrap, S.B., Stebbing, M., Hopper, J.L., Hoang, H.N. and Giles, G.G. (2000) Familial patterns of covariation

for cardiovascular risk factors in adults: The Victorian family heart study. *American Journal of Epidemiology*, **152(8)**, 704-715.

[14] Knuiman, M.W., Jamrozik, K., Welborn, T.A., Divitini, M.L. and Whittal, D.E. (1995) Age and secular trends in risk factors for cardiovascular disease in Busselton. *Australian Journal of Public Health*, **19(4)**, 375-385.

[15] American Heart Association, (1981) Report of subcommittee of postgraduate education committee recommendations for human blood pressure determination of sphygmomanometer. *Circulation*, **64**, 510A-599B.

[16] Pérusse, L., Rice, T., Bouchard, C., Vogler, G.P. and Roa, D.C. (1989) Cardiovascular risk factors in the French Canadian population. Resolution of genetic and familial environmental effects on blood pressure by using extensive information on environmental correlates. *American Journal of Human Genetics*, **45(2)**, 240-251.

[17] Singh, I.P. and Bhasin, M.K. (1968) *Anthropometry*, Kamla Raj Enterprises, Delhi.

[18] Weiner, J.S. and Lourie, J.A. (1981) *Practical Human Biology*, Academic Press, London.

[19] Tambs, K., Moum, T., Holmen, J., Eaves, J.L., Neale, M.C., Lund-Larsen, P.J. and Næss, S. (1992) Genetic and environmental effects on blood pressure in a Norwegian sample. *Genetic Epidemiology*, **9(1)**, 11-26.

[20] Rice, T., Rao, R., Pérusse, L., Bouchard, C. and Rao, D.C. (2000) Tracking of familial resemblance for resting blood pressure over time in the Quebec family study. *Human Biology*, **72(3)**, 415-431.

[21] Jee, S.H., Suh, I., Won, S.Y. and Kim, M. (2002) Familial correlation and heritability for cardiovascular risk factors. Y*onsei Medical Journal*, **43(2)**, 160-164.