ROLE OF FAMILY HISTORY OF DIABETES IN DETERMINING ITS DEVELOPMENT AMONGST INDIANS.

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Abstract: Heredity plays an important role in determining the susceptibility to diabetes mellitus. A significantly greater frequency of diabetes has been found in close blood relatives of diabetic than in the control population. In the total population of 1000 subjects, 107 subjects have the positive family history of diabetes. Out of 107 subjects 61 (57%) subjects are found to be normal and out of these 46 (43%) subjects, 30 (65.2%) subjects are detected as borderline cases and 16 (34.8%) subjects have already developed diabetes. 93 subjects are found to be diabetic from the total 1000 subjects studied. From these 93 diabetic subjects, it has further been inferred that 16 (17.2%) showed the positive family history for this disease. In 38 known and 55 newly detected subjects, 9 (23.6%) and 7 (12.7%) have positive family history of diabetes respectively.

Key Words: Family History; Heredity; Diabetes; Borderline; Newly Detected Diabetes.

Introduction: Genetic susceptibility to type-II diabetes can be unmasked by environmental factors. The wide range prevalence of diabetes is strong indication of the importance of environmental factors in the etiology of diabetes. Since environmental and behavioural factors may be amenable to change and identification of risk factors for diabetes in all populations should be considered a priority (King and Rewers, 1991 and Harrison et al,2003). Diabetes mellitus results from an interaction between genetic and environmental factors (Kirk *et al.*, 1985).Dowse *etal.*(1993) observed a dramatic increase in diabetes prevalence in Melanesians aged over 25 years in Papua, New Guinea which doubled over a 14 year period in an urban settlement, following rapid modernization and sociocultural changes. Available evidence suggests that these groups had a genetic susceptibility to type-II diabetes. Indians have been identified as one of the ethnic groups with a high prevalence of NIDDM (Cheah and Thai, 1993) and high familial aggregation of NIDDM (U.K. Prospective Diabetes Study XII, 1994; Viswanathan *et al.*, 1996). It was consistent that diabetes was linked with "thrifty" genotype in people who were genetically selected through food shortage periods and they were apt to become overweight in normal conditions (Neel, 1962). Indians rank 3rd in the high ethnic susceptibility to diabetes after Micronesian and Pima Amerindians. In this cross-sectional survey it was evident that diabetes was more often diagnosed at a younger age in Indian population. It might be that the genetic mechanisms were stronger in Indians. Most of the population was between 25 and 44 years of age and diabetes at this young age was about half of the overall crude prevalence (Rao *et al.*, 1998).

Materials And Methods: The present epidemiological and biochemical study has been undertaken in the district Sangrur, Punjab (India). The samples survey has been undertaken from the area covered and 1000 subjects were selected randomly for questioning regarding the different aspects of epidemiology. Out of these 1000 samples, 500 are from urban population and 500 from rural population. They were questioned personally, using a questionnaire which is designed for collection of data and also general information regarding family history and various other epidemiological factors. People selected for the survey are invited to a home interview and those who complete the interview are then invited to a mobile clinic for a series of physical and laboratory examinations (assignment to morning or afternoon visits to the clinic is random). This study included adults aged >18 years. Most of them also received a physical examination. The morning sample is important for conditions such as diabetes, for which assessment requires an overnight fasting period. The design of the study, through the use of sample weights, allows for the calculation of national estimates from both the entire interview sample and the morning sample. The total number of cases of diabetes was calculated by adding the previously diagnosed cases to the newly detected cases from the morning sample.

Family history of diabetes was determined with the following question: including living and deceased, were any of your biological relatives, that is, blood relatives, including grandparents, parents, brothers, and sisters. If the answer was "yes," then they were asked, which family member? The possible answers by multiple-choice were mother, father, mother's mother, mother's father, father's mother, father's father, brother, sister, other, refused, or don't know. The risk of diabetes according to family history was stratified in three levels as follows: 1) High: at least two first-degree relatives or one first-degree and at

least two second-degree relatives with diabetes from the same lineage; 2) Moderate: just one first-degree and one second-degree relative with diabetes, or only one first degree relative with diabetes, or at least two second-degree relatives with diabetes from the same maternal or paternal line; or 3) Average: no family history of diabetes or, at most, one second-degree relative with diabetes.

Results: Heredity plays an important role in determining the susceptibility to diabetes mellitus. Diabetes mellitus is multifactorial in its etiology. A significantly greater frequency of diabetes has been found in close blood relatives of diabetic than in the control population. The crude prevalence of diabetes (diagnosed, undiagnosed, and combined) is shown in Table 1. In the total population, 10.7% subjects have the positive family history of diabetes. Subjects showing positive family history of diabetes, 65.2% subjects are detected as borderline cases and 34.8% subjects have already developed diabetes. In total diabetic subjects, it has further been inferred that 17.2% showed the positive family history for this disease. In known and newly detected subjects, 23.6% and 12.7% have positive family history of diabetes respectively (Table-1).Hence in the total population 10.7% have positive family history for this disease. Out of which 3% borderline, 0.7% newly detected, 0.9% known diabetics has a parental history of diabetes and 6.1% are normal (Table-1) .In borderline subjects, 2.2% has first degree relatives (Father, Mother, and Father Mother both) with type-II diabetes, 0.2% has second degree relatives (Grandfather, Grandmother, Uncle) and 0.6% has diabetes in preceding generation (Brothers/Sisters) (Table 2).In diabetic subjects, 0.9%, 0.3% and 0.4% has diabetes in first degree relatives, second degree relative and in preceding generation respectively (Table-2). In borderline subjects fathers (7.05%) have more diabetes (7.05%) than mothers (1.24%). But in total diabetic subjects, there is not significant difference in incidence rate between fathers (3.23%) and mothers (4.30%) (Table-1).

Discussion: In the present study 10.7% subjects have shown positive family history for diabetes. In total diabetic subjects 17.2%hadfamily history of diabetes which is more than the studies of

Sachdeva (1968)	8.7%
Chhetri *et al.* (1975)	16.3%
Thirumorthi *et al.* (1983)	15.4%
Ohlson *et al.* (1988)	12.8%
Oliveira *et al.* (1996)	12.4%
Williams *et al.* (1999)	4.3%

but less than the studies of

Ahuja (1966)	31%
Berry (1966)	36%
Chhetri *et al.* (1975)	22.9%
Bruno *et al.* (1992)	33%
Elbagir *et al.* (1996)	28.3%

The increased prevalence of type-II diabetes in the relatives of affected subjects is likely to reflect genetic predisposition to hyperglcaemia with additional affects from shared environment and life style (Shaw *et al.*, 1999). African Americans with a family history of diabetes were more aware of diabetes risk factors and more likely to engage in certain health behaviors than were African Americans without a family history of the disease (Baptiste Roberts et al, 2007). Individuals with a family history of diabetes are at increased risk for the metabolic consequences of obesity and form an easily identifiable group who may benefit from targeted intervention to prevent the development of obesity through increased physical activity (Sargeant, et al, 2000).Type-II diabetes is recognized to arise from a combination of insulin resistance and impaired beta cell function (Ganada and Soeldner, 1987). One of the most intriguing patterns of familiar aggregation was the sex difference in the prevalence of parental diabetes. Diabetes incidence was strongly related to parental occurrence of diabetes, although no specific mode of inheritance was observed (Knowler *et al.*, 1978).In the present study, borderline subjects (241) also have the positive family history in 30 (12.4%) subjects. In the borderline subjects greater proportion of fathers have diabetes than mothers. A similar trend in diabetic subjects had been noticed from the work of Tuomilehto *et al.*, 1995; Green *et al.*, 1997 and Mitchell *et al.*, 1997. Zimmet (1982) showed that diabetes incidence in the Pima Indians was strongly related to parental occurrence of diabetes although no specific mode of inheritance had been documented. But in Pimas, heredity played an important role in the development of type-II diabetes.

Rema *et al.* (1997) had given the family history in diabetics as below:-

1st degree Relatives	Female	Male	Total
	%	%	%
Father	31.8%	41.6%	37.1%
Mother	31.8%	34%	33.1%
Both Parents	27.3%	15.2%	20.5%
2nd degree Relatives			
Cousins	4.5%	5.3%	50%
Grandparents	1.8%	2.3%	2.1%
Uncle/Aunt	2.7%	1.5%	2%

Ramachandran *et al.* (1997) found percentage with positive family history of diabetes was more in

diabetics than normal groups. A frequently published observation was that diabetic children were more likely to had a father affected than a mother but the mechanism was poorly understood. But it is difficult to explain the preferential transmission from fathers to daughters. Genetic and hormonal factors can be hypothesized but the possible contribution and underlying mechanism remains speculative.

Several studies have reported the prevalence of diabetes in subjects having first degree relatives. Such as – Allen *et al.* (1991), Pociot *et al.* (1993), Lorenzen *et al.* (1994) Shaw *et al.* (1999) and Guttmacher et al. 2004). According to Tuomilehto *et al.* (1999), genetic factors have a major role in the development of type-I diabetes, 85-90% of new cases occur in families with no previous history of type-I diabetes among first degree relatives. By definition a child with type-I diabetes must have inherited the type-I diabetes susceptible genes from one or both parents. Thus the frequency of the disease in the population is a function of the frequency of the susceptibility genes and their penetration in the population. Because the type-I diabetes is not very common in parents of a child with the disease, the number of carriers of the disease susceptibility genes must be relatively high. Grill (1999) also found the association of diabetes with family history in general population of Swedish men. Many investigations showed a preferential maternal effect (Alcolado and Alcolado, 1991 and Riley *et al.*, 1997). Overall, the weighted distribution of the U.S. population according to familial risk of diabetes was as follows: 22.7% were in the moderate and 7.5% in the high familial risk category (Rodolfo et al, 2007). Previous studies have indicated that, versus people without a family history of diabetes, those who have a family history of diabetes are two to six times as likely to have type-II diabetes (Meigs et al.2000 and Hariri et al.2006). More specifically, a recent study based on NHANES data found that family history of diabetes was significantly and independently associated with diabetes in U.S. adults (based on self-reports) and the strength of the association was related to the type and number of relatives involved (Goldfine et al. 2003 and Annis et al. 2005) .This study has unequivocally confirmed this observation in borderline subjects but the mechanism is poorly understood which needs further studies on this aspect and is a new approach for the detection of this disease in borderline subjects and again the trend corresponds well with such studies. In diabetic subjects, 3 subjects have affected father and 4 subjects have affected mothers with diabetes. But the association with prevalence in mothers is weaker and not significant. First degree relatives from various nationalities were genetically more homogenous and shared exposure to environmental risk factors more frequently than unrelated individuals in general population. In the present study, 2.2% have the 1st degree relatives in borderline subjects which are more than the 2nd degree relatives and preceding generation. In total diabetic subjects, 1st degree relatives are again more than the others. Most of the affected subjects in borderline and total diabetic category are males which would be father for next generation. A previous NHANES-based study anticipated the findings of the present study , but this earlier study was not designed to be a direct test of the independence of the association between family history and prevalence of diabetes.

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References:

1. Ahuja, M.M.S., Varma, V.H. and Uma Shankar, J. (1966). A pilot study to determine the prevalence of diabetes mellitus in Delhi. *J. Indian Med. Assoc.,* 46 : 415
2. Alcolado, J., Alcolado, R. (1991). Importance of maternal history of non-insulin-dependent diabetic patients. *BMJ* 302: 1178-1180.
3. Allen, C., Palta, M., Dalessio, D.J. (1991). Risks of diabetes in siblings and other relatives of IDDM subjects. *Diabetes* 40: 831-836.
4. Annis AM, Caulder MS, Cook ML, Duquette D: Family history, diabetes, and other demographic and risk factors among participants of the National Health and Nutrition Examination Survey 1999–2002. Prev Chronic Dis 2:A19, 2005.
5. Baptiste-Roberts K, Gary TL, Beckles GL, Gregg EW, Owens M, Porterfield D, Engelgau MM. Am.J.Public health. 2007 Family history of diabetes, awareness of risk factors, and health behaviors among African Americans. May; 97(5):907-12. Epub 2007 Mar 29.
6. Berry, J.N., Chakravorty, R.N., Gupta, H.D. and Malik, K. (1966) Prevalence of diabetes in a North Indian Town. *Ind. J. Med. Res.,* 54 : 11
7. Bruno, G., Bargero, G., Vuolo, A., Pisu, E. and Pagano, G. (1992). The registry of IDDM in the

province of Turin, Italy. Report on a five year (1984-1988) incidence survey in the age group 0-29 years. A *Diabetologia* 35 : 851-856.
8. Cheah, J.S., Thai, A.C. (1993). Epidemiology of *NIDDM* in ASEAN. *Proceedings of the 7th Congress of the ASEAN Federation of Endocrine Societies.* SCA, (1) : 58.
9. Chhetri, M.K., Raychaudhuri, B. and Bhattacharya Bijan (1975). Epidemiological study of diabetes mellitus in West Bengal. *Jour. Diab. Assoc. India*, XV : 97-104.
10. Dowse, G.K., Zimmet, P.Z., Finch, C.F., Collins, V.R. (1993). Decline in incidence of epidemic glucose intolerance in Nauruans : implications for the 'thrifty genotype'. *Am. J. Epidemiol*, 133: 1093-1104.
11. Elbagir, N. Murtada, Elton A. Mohammed, Elmahadi M.A. Elmahadi Kadam M.S. Ibrahim, Berne Christian (1996). A population based study of the prevalence of diabetes and impaired glucose tolerance in adults in Northern Sudan. *Diabetes Care,* 19 (10) : 1126-1128
12. Ganda, O.P. and Soeldner (1987). Genetic, acquired and related factors in the aetiology of diabetes mellitus. *Arch Intern. Med.,* 137: 461-469.
13. Goldfine AB, Bouche C, Parker RA, Kim C, Kerivan A, Soeldner JS, Martin BC, Warram JH, Kahn CR: Insulin resistance is a poor predictor of type-2 diabetes in individuals with no family history of disease. Proc Natl Acad SciUSA 100:2724–2729, 2003.
14. Green, A., Sjolie, A.K. and Eshoj, O. (1997). *In*: Pickup J.C., Williams, G. The epidemiology of diabetes mellitus. *In* : Pickup J.C., Williams, G. (eds.) Text-book of Diabetes 2nd edn. Blockwell Science, Oxford: 1-16.
15. Grill, V., Persson, G., Carlsson, S., Norman, A., Alvarsson, M., Ostensson, C.-G., Svanstrom, L., Efendie, S. (1999). Family history of diabetes in middle-aged Swedish men is a gender unrelated factor which associates with insulinopenia in newly diagnosed diabetic subjects. *Diabetologia* 42 : 15-23.
16. Guttmacher AE, Collins FS, Carmona RH: The family history: more important than ever. N Engl J Med 351:2333–2336, 2004.
17. Hariri S, Yoon PW, Moonesinghe R, Valdez R, Khoury MJ: Evaluation of family history as a risk factor and screening tool for detecting undiagnosed diabetes in a nationally representative survey population. Genet Med 8:752–759, 2006.
18. Harrison TA, Hindorff LA, Kim H, WinesRC, Bowen DJ, McGrath BB, Edwards KL: Family history of diabetes as a potential public health tool. Am J PrevMed 24:152–159, 2003.
19. King, H. and Rewers, M. on behalf of the WHO Adhoc Diabetes Reporting Group (1991). Global estimates for prevalence of Diabetes Mellitus and impaired glucose tolerance in adults. *Bull. of WHO,* 69 (6) : 643-648.
20. Kirk, R.L., Serjeantson, S.W., King, H., Zimmet, P. (1985). The genetic epidemiology of diabetes mellitus. *Prog. Clin. Biol. Res.,* 194: 119-146.
21. Knowler, W.C., Bennet, P.H., Hamman, R.F., Miller, M. (1978).Diabetes incidence and prevalence in Pima Indians : a 19-fold greater incidence than in Rochester, Minnesota. *Am. J. Epidemiol.* 108: 497-505.
22. Lorenzen, T., Pociot, F., Hougaard, P. and Nerup, J. (1994). Long-term risk of IDDM in first-degree relatives of patients with IDDM. *Diabetologia,* 37: 321-327.
23. Meigs JB, Cupples LA,Wilson PW: Parental transmission of type 2 diabetes: the Framingham Offspring Study. Diabetes 49:2201–2207, 2000
24. Mitchell, B., Valdez, R., Hazuda, H., Haffner, S., Monterosa, A., Stern, M. (1997). Differences in the prevalence of diabetes and impaired glucose tolerance according to maternal or paternal history of diabetes. *Diabetes Care,* 16: 1262-1267.
25. Neel, J.V. (1962). Diabetes Mellitus : a thrifty genotype rendered detrimental by progress ? Diabetes Mellitus Am. *J. Genet.,* 14 : 353-362.
26. Ohlson, L.-O., Larsson, B., Bjorntorp, P., Eriksson, H., Svardsudd, K., Welin, L., Tibblin, G. and Wilhelmsen, L. (1988). Risk factors for Type 2 (non-insulin-dependent) diabetes mellitus. Thirteen and one-half years of follow-up of the participants in a study of Swedish men born in 1913. *Diabetologia* 31 : 798-805.
27. Oliveira, P., Egidio Jose, Milech Adolpho, Franco J. Laercio, The cooperative group for the study of diabetes prevalence in Rio de Janeiro (1996). The prevalence of diabetes in Ride Janeiro, Brazil. *Diabetes Care,* 19 (6): 663-666.
28. Pociot, F., Norgaard, K., Hobolth, N., Andersen, O., Nerup, J. and the Danish Study Group of Diabetes in Childhood (1993). A nationwide population-based study of the familial aggregation of Type 1 (insulin-dependent) diabetes mellitus in Denmark. *Diabetologia:* 870-875.
29. Ramachandran, A., Snehalatha, C., Latha, E., Vijay, V. and Viswanathan, M. (1997). Rising prevalence of NIDDM in an urban population in India. *Diabetologia,* 40 : 232-237.
30. Rao, P.V., Ahuja, M.M.S., Trivedi, B.B., Ramachandran, M., Samal, K.C., Zaini Anuar

Charles Clorence (1998). Age: The most significant risk for diabetes in Indian population. *J. Indian Med. Assoc.,* 96 (5): 155.

31. Rema, N., Parvathi, Easwaran, P. and Kalpana, N. (1997). Development of risk assessment index for diabetes mellitus and cardiovascular diseases. *The Ind. J. Nutr. Dietet.,* 34 : 114-120.
32. Riley, M., Blizzard, C., McCarthy, D., Senator, G., Dwyer, T., Zimmet, P. (1997). Parental history of diabetes in an insulin-treated diabetes registry. *Diabetic Med.,* 14: 35-41.
33. Rodolfo Valdez, Paula w. Yoon ,Tiebin Liu and Muin j. Khoury (2007) .Family History and Prevalence of Diabetes in the U.S. Population: The 6-year results from the National Health and Nutrition ExaminationSurvey (1999–2004) . *Diabetes care* 30(10) :2517-2522
34. Sachdeva Sanjogta (1968). Prevalence of diabetes mellitus in 6000 urban population, Tripuri. M.D., Punjabi University, Patiala.
35. Sargeant, L A, Wareham, N J and Khaw, K-T.2000. Family history of diabetes identifies a group at increased risk for the metabolic consequences of obesity and physical inactivity in EPIC-Norfolk: a population-based study International Journal of Obesity 24, 1333-1339
36. Thirumoorthi, K.V., Narayanan Sankara, K.V. and Moses, G.P. Sam (1983). Glucose tolerance in subjects with family history of diabetes. *Indian J. Med. Res.,* 77: 909-914.
37. Shaw, J.T.E., Purdie,D.M., Neil, H.A.W., Levy, J.C., Turner, R.C. (1999). The relative risk of hyperglycemia, obesity and dyslipidaemia in the relatives of patients with type-II diabetes mellitus. *Diabetologia*, 42: 27-37.
38. Tuomilehto, J., Karvonen, M., Pitkaniemi, J., Virtala, E., Kohtamaki, K., Toivahen, L., Tuomilehto- Wolf, E. and the Finnish childhood type-I diabetes registry group (1999). Record of high incidence of type-I (insulin-dependent) diabetes mellitus in Finnish children. *Diabetologia,* 42: 655-660.
39. Tuomilehto, J., Poder, T., Tuomilehto-Wolf, E. and Virtala, E. (1995). Evidence for importance of gender and birth cohort for risk of IDDM in offspring of IDDM parents. *Diabetologia,* 38 : 975-982.
40. U.K. Prospective diabetes study XII (1994). Difference between Asian, Afrocaribbean and White Caucasian type-II diabetes patients at diagnosis of diabetes.*Diabet Med.,* 11 : 670-677.
41. Viswanathan, M., McCarthy, M.I., Snehalatha, C., Hitman, G.A., Ramachandraan, A. (1996). Familial aggregation of type-II (non-insulin dependent) diabetes mellitus in South India : Absence of excess material transmission. *Diabetes Med.,* 13: 232-237.
42. Williams, E.M. Desmond, Warehem J. Nicholas, COX, D. Brain Byrne Christopher, Hales Nicholas, C. Day, E. Nicholas (1999). Frequent Salad vegetable consumption is associated with reduction in the risk of diabetes mellitus. *J. Clin. Epidemiol.,* 52 (4) : 329-335.
43. Zimmet, P. (1982). Type-II (non-insulin dependent) Diabetes-An epidemiological overview.*Diabetologiaa:399-411.*

Table1-Presence of family history of diabetes in different status of subjects (n=107)

Status of Subjects	F	M	F/M	Gf	Gf/Gm	U	B/S	Total	
Total	n	39	20	8	16	4	2	18	107
Population (N=1000)	%	(3.90)	(2.00)	(0.80)	(1.60)	(0.40)	(0.20)	(1.80)	(10.70)
Normal	n	19	13	4	12	4	1	8	61
(N=653)	%	(2.91)	(1.99)	(0.61)	(1.83)	(0.61)	(0.15)	(1.23)	(9.34)
Borderline	n	17	3	2	2	-	-	6	30
(N=241)	%	(7.05)	(1.24)	(0.83)	(0.82)			(2.47)	(12.44)
Newly detected	n	3	1	-	-	-	1	2	7
(N=55)	%	(5.46)	(1.82)				(1.82)	(3.64)	(12.72)
Known diabetic	n	-	3	2	2	-	-	2	9
(N=38)	%		(7.89)	(5.26)	(5.26)			(5.26)	(23.68)
Hypoglycemic N= (13)	n	-	-	-	-	-	-	-	-
Total diabetic	n	3	4	2	2	-	1	4	16
ND+K(N= 3)	%	(3.23)	(4.30)	(2.15)	(2.15)		(1.08)	(4.30)	(17.20)

F : Father, M : Mother, Gf : Grandfather, Gm : Grandmother, U : Uncle, B : Brother, S : Sister
ND : Newly detected diabetic subjects, K : Known diabetic subjects.
N : Number of subjects in each group, n : Total number of subjects having family history.

STATISTICAL ANALYSIS

TABLE 1A

Status of subjects	X2	DF	p	NS/S
Normal	4.33	3	>0.05	NS
Borderline	3.585	2	>0.05	NS
Newly detected	0.896	2	>0.,05	NS
Known diabetic	6.619	2	<0.05	S
Hypoglycemic	-			-

TABLE 2

Presence of family history of diabetes in Ist degree, 2nd degree relatives and preceding generations in borderline and total diabetic subjects. (N = 1000)

Status of subjects	Ist degree relatives	2nd degree relative	Preceding generations
Borderline subjects	22 (2.2%)	2 (0.2%)	6 (0.6%)
Total diabetic subjects ND+K	9 (0.9%)	3 (0.3%)	4 (0.4%)

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