

RESEARCH

A clinical study of the impact of stressful life events in the aetiology of non insulin dependent diabetes mellitus

Pradip Kumar Thakuria, Punya Dhar Das¹

Associate Professor, Department of Forensic Science Medicine, Fakhruddin Ali Ahmed Medical College Hospital, Barpeta,

¹Retired Professor and Head, Department of Psychiatry, Gauhati Medical College Hospital, Guwahati, Assam, India

Abstract

Background: Since diabetes mellitus was first recognised as a disease, physicians have been aware that emotional factors play an important part in the illness. It was thought necessary that a study on the role of life events as an aetiological factor in non insulin diabetes mellitus (NIDDM) should be conducted in our setup.

Material and methods: Clinically confirmed cases of NIDDM were included in the study. Life events were assessed during the three years to six months period preceding the onset of illness. The control group consisted of 50 subjects which were taken from normal general population. The presumptive stressful life events scale (PSLES) was taken to assess the life events of subjects. Means and standard deviations were taken out and Fisher's 't' test was done in the analysis of life event scoring to see the statistical significance.

Results: Fifty patients with NIDDM were studied. Analysing the relation between total number of life events, it was found that there was significant difference between patients with NIDDM and the control ($P < 0.05$). NIDDM group had more total life event score than the control group but it did not reach the significant level compared to control. On analysing the type of life event which was grouped by area of activity, it was found that financial area was more pronounced and commonest for both the groups.

Conclusion: Although a few statistically significant associations between stressor and illness emerged from this study, it can be concluded that stress might act as an aetiological factor in NIDDM.

Thakuria PK, Das PD. A clinical study of the impact of stressful life events in the aetiology of non insulin dependent diabetes mellitus. *Dysphrenia*. 2013;4(1):71-7.

Keywords: Female. Nuclear family. Marital status. Birth order. Age groups. Education.

Correspondence: kabeript@rediffmail.com

Received on 25 June 2012. Accepted on 11 Dec 2012.

Introduction

Diabetes mellitus is a metabolic syndrome which is usually characterised by a permanent, absolute or relative lack of pancreatic hormone insulin.[1] Between two to six per cent of the general population suffer from this condition[2] which is heterogenous in aetiology and clinical manifestation. The diagnosis of diabetes mellitus is made in patients having fasting blood glucose level greater than 140 mg/100 ml of plasma and a two hour post prandial blood glucose concentration equal to or greater than 200 mg/100 ml. The term type I is often used as a synonym for insulin dependent diabetes mellitus (IDDM) and type 2 has been considered equivalent to non insulin dependent diabetes mellitus (NIDDM).

Since diabetes mellitus was first recognised as a disease, physicians have been aware that emotional factors play an important part in the illness. Thomas Willis, 300 years ago, remarked upon the sweet taste of urine of his

patients and said the disease was caused by 'prolonged sorrow'. [3]

The concept of stress was first introduced in the life science by Hans Selye in 1936.[4] It is a concept borrowed from the natural sciences. The role of stressful life events in the aetiology of various diseases has been a fertile field of research. It is increasingly recognised that stress is one of the components of any disease, not just those labelled 'psychosomatic'. In fact researchers like Holmes and Rahe[5] have established this point beyond doubt that there exist a positive relationship between stressful life events and subsequent illness.

Stress, in engineering, is known as the ratio of the internal force brought into play when a substance is distorted to the area over which the force act.[6] Thus, in physics, stress is a force which acts on a body to produce strain.

In physiology, the various changes in the physiological functions in response to evocative agents denote stress. In physiology, stress refers to a state of the organism resulting from some interaction with the environment. In psychophysiology, stress is that stimulus which imposes detectable strain that cannot be easily accommodated by the body and so presents itself as impaired health or behaviour.

Stress has always been an integral part of human existence. There are stresses which are within the adjustable capacity of human being and these help in a long way in developing human personality. On the other hand there are stressful events which bring about definite change in life pattern of a person requiring for him to make significant readjustment in his life style. Such events have been termed as the life events by modern scientists.

Engel[7] postulated that an emotional state may be associated with the precipitation of disease but that this state is the same for all. He observed that a wide variety of diseases may become manifest following situations of loss and grief that lead to emotional state of helplessness, hopelessness or the giving up-given complex. Engel suggested that the physiological accompaniments of this state may thereby initiate disease. Substantial data also indicate that bereavements, loss, loneliness and depression give rise to adrenocortical activation and increases in catecholamine, uric acid and cholesterol level. More recently several groups have demonstrated impairment in immune functions under these conditions.

Again, Wolf[8] studied the morbidity experience of several hundred people over long periods of time. He found that episodes of physical illness occurred in clusters that appeared to be related to periods of environmental change. Although the study used highly subjective measures of life difficulties, it drew attention to the clustering of illness in the life span.

Holmes and Rahe[9] attempted to introduce quantification in the study of life changes. They compiled a list of 41 life changes concerned with occupation, residence, finance, recreation, religion and family relationship. The items were chosen regardless of whether or not it was under the person's direct control. Each item was given a weighting, according to the estimated extent of the change and of the adjustment required in the individual. Thus, the death of spouse was given a score of 100 life change units, whilst a spell of leave was given 13 life change units. An intensive study in the United States Navy by Rahe *et al.*[9] showed that men with highest scores for life changes developed more illness of all kinds. In other words it appeared that the risk of developing physical illness was greater after a period of physiological or social change than after an uneventful period.

Most of the investigators in India made use of the Social Readjustment Rating Questionnaire (SRRQ) of Holmes and Rahe[5] or scaling of life events[10] with local translations but without any major modifications to suit the Indian population. Sing *et al.*[11] modified the scale of Holmes and Rahe for use in India. They also introduced and rated few items which were significant in our country.

Thus, it was thought necessary that a study on the role of life events as an aetiological factor in NIDDM should be conducted in our setup; in anticipation that, it might provide a lead in our quest for better understanding of stressful life events in precipitating NIDDM.

Aims and objectives

The aims and objectives of the study are:

1. To study the role of stressful life events as an aetiological factor in NIDDM.
2. To study the correlations of sociodemographic variables with life events in NIDDM.
3. To study how the study group and the control group differs in respect of life events in number, scoring and type of life events.

Materials and methods

Place of study: This study was conducted in the Departments of Psychiatry and Endocrinology, Gauhati Medical College Hospital (GMCH). This study was done on the patients attending the diabetic outpatient clinic of the Department of Endocrinology.

Period of study: Study was done during the period from February 1996 to January 1997.

GMCH, situated in Guwahati, is the premier medical college of North Eastern India. Main catchment area of this hospital is the entire lower, middle and part of southern Assam and neighbouring states like Nagaland, Manipur, Meghalaya, Tripura, Arunachal Pradesh and Mizoram. The whole of this region is remarkable for admixture of its various ethnic cultures and traditions.

The average attendance of the outpatient department (OPD) of psychiatry was 50 per day and total number of new cases seen was approximately 5000 per year. As the psychiatry department was a part of the general teaching hospital the mode of admission was voluntary. The department was spacious and well planned and the faculty comprised of seven trained psychiatrists, one psychiatric social worker, resident, supporting secretarial and trained nursing staffs. The Department of Endocrinology had three qualified endocrinologists. Average attendance of patient in the endocrinology OPD was about 40 patients. It ran two OPDs in a week. The

department had its own inpatient unit attached to medical ward.

Definition of the case: NIDDM is a disorder which usually begins in middle life or beyond. The typical patient is overweight. Symptoms begin gradually and the diagnosis is frequently made when an asymptomatic person is found to have elevated plasma glucose on routine laboratory examination. Insulin is detectable in the plasma of nearly all patients in this category and they are therefore less prone to develop ketosis.

Selection criteria: Clinically confirmed cases of NIDDM were included in the study. Cases from both sexes were included. Patients above the age of 40 and below 70 years were taken. Life events were assessed during the three years to six months period preceding the onset of illness.

Exclusion criteria: All cases having the following were excluded—organic brain syndrome, cognitive impairment, history of epilepsy, concomitant alcohol and drug dependence, mental retardation, previous history of head injury, any patient with doubtful history where organicity could not be ruled out.

Control group: The control group consisted of 50 subjects which were taken from normal general population. Persons with presence of diabetes were excluded.

Sampling procedure: Cases were taken using serial sampling procedure i.e. all consecutive 50 cases attending the diabetic OPD of GMCH fulfilling inclusion criteria. All the cases were subjected to detailed physical, neurological and blood sugar and urine sugar estimation. Diagnosis of NIDDM was confirmed in consultation with endocrinologist.

The control group was selected matching with age, sex, educational and social status of the patients as far as possible. They were fully explained about the aims, objectives and procedures of the study.

Description of tool: Sociodemographic data were collected using a standard proforma designed for the study. This proforma was designed and standardised in the Departments of Psychiatry and Endocrinology, GMCH.

The presumptive stressful life events scale (PSLES) of Singh *et al.*[11] was taken to assess the life events of subjects. It was translated from English to Assamese as there was no such questionnaire available in Assamese. Initially the questionnaire was tested upon 20 different individuals by senior consultants including normal persons as well as patients and thus validity of the questionnaire was tested. Test retest and interrater reliabilities of the questionnaire were also then assessed between two consultants before it was finally adopted as tool for this investigation.

Interview procedure: At first informed consent of all the patients were taken. Then all the cases that were selected for the study were interviewed in detail using this tool. Interview pattern was flexible to elicit maximum data. The time spent for each patient ranges between 60 to 100 minutes. While interviewing the patient, if the attention of the patient was found to be diverted, interview was stopped and resumed after a break. For all cases privacy of interview was strictly maintained.

Stressful life events as charted in number if experienced within three years to six months of the onset were assessed. The period of three years to six months were selected to avoid memory distortion as per recommendation of other research workers. Also it was presumed that events which occurred during this period might have direct correlation with onset of illness.

Analysis of data: Data thus obtained was analysed according to number of life events and life event scores as calculated from PSLES. Life events thus obtained were classified again into area of activity. Number of each type of life event was again analysed. Statistical analysis was done whenever required. Means and standard deviations were taken out and Fisher's 't' test was done in the analysis of life event scoring to see the statistical significance. The study was approved by the institutional ethical review board.

Result and Discussion

A total number of 50 cases (patients with NIDDM) and equal number of controls were taken for the study. The sociodemographic variation of the cases and controls are shown in Table 1. As the study was restricted only to the OPD of Endocrinology, GMCH, this study might not reflect the exact picture of the impact of stressful life events in the aetiology of NIDDM community at large. Results are shown in tables 1 to 4 where Table 1 shows socioeconomic variables of the patients with NIDDM (cases) and the controls. Table 2 shows distribution of events grouped by area of activity. Table 3 shows distribution of total number of life events and total life event score. Table 4 shows distribution of life events and socioeconomic variables.

The available evidence suggests that a possibility exists that emotional factors may be important in the onset of diabetes mellitus. While in exceptional instances an emotional trauma may precipitate the symptoms of the disease, it is more likely that the illness will appear in a setting of sustained and chronic emotional conflict. Various authors have emphasised strongly the relationship between stressful life events and illness in adults.[9,12-16] The role of psychological factor in diabetes mellitus has long been a controversial topic. Investigator at one extreme believe in a causal role of psychosocial factor even in the onset of illness and those at other extreme

believe that psychosocial factors play a minimal role in comparison to physical management of the illness. Individual patients often ascribe a very major role to emotional status,[17] but demonstrating this role in well controlled studies has been quite difficult.

Anecdotal case reports abound in the literature as well as in most of our practices. Menninger[18] described

Table 1. Socioeconomic variables

	Case	Control
Sex		
Male	38	35
Female	12	15
Religion		
Hindu	42	30
Muslim	9	20
Locality		
Rural	25	18
Urban	25	32
Socioeconomic status		
Lower	9	8
Lower middle	34	32
Upper middle	7	10
Type of family		
Nuclear	31	30
Joint	18	14
Extended	1	6
Marital status		
Unmarried	4	10
Married	41	30
Widow/widower	3	6
Separated/divorced	2	4
Birth order		
Eldest	15	12
Youngest	11	14
Others	24	24
Age group (in years)		
40-49	26	20
50-59	22	23
60-69	2	7
Educational status		
Illiterate	5	2
Primary	17	20
High school	8	9
College	15	12
Professional	5	7
Occupational status		
Unemployed	2	4
Housewife	8	9
Farmer	7	10
Business	4	4
Service	21	8
Professional	1	3
Daily wage earner	3	6
Skilled labour	1	3
Retired	3	3

a number of patients who developed glycosuria during a period of emotional upheaval, which remitted with psychotherapeutic treatment. Hinkle *et al.*[19,20] closely followed a number of patients with either IDDM or NIDDM and found a close link between psychosocial stressor and the onset and course of illness. A report[21] described the development of transient NIDDM in a Korean physician in the course of his immigration to the United States.

Although studies of life events are subject to recall bias and problems with weighing the importance of a stress, they have provided evidence suggesting a role for emotional factors in the onset of diabetes. In our study, we recorded sociodemographic data in detail to assess the sociodemographic pattern of the cases. We also tried to find out whether stressful life events may be causative factor in NIDDM. For analysis of sociodemographic data we administered Fisher's 't' test.

Number of life events and NIDDM

Analysing the relation between total number of life events, it was found that there was significant difference between patients with NIDDM and the control ($P < 0.05$). Penrose[22] also found more number of stressful life events in three months preceding major physical illness. Robinson and Fuller[23] examined the role of stressful life events in the onset of diabetes by comparing diabetic patients with their siblings and with neighbourhood matched control subjects and found much greater numbers of stressful life events in the parents than in the two control groups.

Life event score and NIDDM

NIDDM group had more total life event score than the control group but it did not reach the significant level compared to control. Our patients with NIDDM also had higher mean life event score as well. Connolly[24] while examining his patients also found mean number of independent events significantly greater than that of matched comparison group during the 12 weeks period to the myocardial infarction.

Table 2. Area of activity

	Case	Control
Type of events	Number of events	Number of events
Bereavement	3	1
Health	12	6
Employment	6	3
Marital	4	2
Financial	22	16
Education	4	2
Legal	3	4
Moves	8	5
Family	5	7
Interpersonal relation	4	8

Table 4. Life events and socioeconomic variables

Socioeconomic variables	Case		Control	
	Total number of life events	Mean life event score	Total number of life events	Mean life event score
Sex				
Male	53	66.63	37	53.2
Female	18	78.5	17	52.93
Religion				
Hindu	61	73.87	33	53.76
Muslim	10	49.44	21	52.15
Locality				
Rural	33	65.68	19	50.05
Urban	38	73.28	35	54.84
Socioeconomic status				
Lower	16	86.77	10	61.62
Lower middle	47	66.23	35	54.5
Upper middle	8	63	9	41.9
Type of family				
Nuclear	45	71.09	34	56.43
Joint	25	69.16	13	38.5
Extended	1	25	7	70.66
Marital status				
Unmarried	4	56	11	58.9
Married	60	68.85	32	51.53
Widow/widower	4	83	6	48.5
Separated/divorced	3	89	5	57.5
Birth order				
Eldest	22	70.2	12	48.41
Youngest	13	57	16	55.64
Others	36	74.7	26	54
Age group (in years)				
40-49	38	75.29	20	51.45
50-59	31	64.77	27	56.39
60-69	2	46	7	47.14
Educational status				
Illiterate	7	74.2	3	68
Primary	29	80	19	45.45
High school	11	67.37	11	57.33
College	19	61.06	12	52.66
Professional	5	57.6	9	66.14
Occupational status				
Unemployed	4	93	5	54.75
Housewife	13	84.37	9	47.22
Farmer	8	61.57	10	47.1
Business	8	80.5	3	41
Service	26	60.8	10	67.5
Professional	1	33	3	57.66
Daily wage earner	5	88.66	5	41.5
Skilled labour	2	87	4	72.33
Retired	4	65.66	5	64

Our study tallies with Singh *et al.*[11] where their female from general population had reported more mean life event score. This could be caused by a variety of factors but the two possibilities of central importance are mental set up due to role characteristics and a 'real' differential in stress responsibility[25] This variation in assignment of weight may be due substantially to social roles in which women are encouraged to admit the stress of life events while men are not.

Regarding religion in our series, 82% of the cases were Hindus and 18% were Muslims. There is no Indian study to our knowledge to compare this data. Though apparently it seems that Hindus are affected mostly by NIDDM, actually it is in conformity with religious composition of this region where Hindus predominate. Hence an association of religion with NIDDM is insignificant. From statistical analysis we found that mean life event score by Hindus

were more than the Muslim group; however, not statistically significant.

Habitational background (locality): Urban group had more number of life events compared to rural. On analysing total life event score urban group reached level of significance ($P < 0.05$) in comparison to control. As the stress and strain along with economic burden and social insecurity are much more in urban areas, it may play a role in influencing life events.

While comparing socioeconomic status with total number of life event, no significant difference could be

Areas of activity

On analysing the type of life event which was grouped by area of activity, it was found that financial area was more pronounced and commonest for both the groups. It again reflects the economic condition of our people.

Socioeconomic variables and life events

Sex and religion: Studying the relation of sex in patients with NIDDM as regards to life events, female had significantly more life event score compared to control.

Table 3. Life events

	Total number of life events	Mean	SD	t	P value	Total life event score	Mean	SD	t	P value
Case	71	1.42	0.70	2.83	<0.05	3474	69.48	34.98	0.026	>0.05
Control	54	1.08	0.48			2656	53.12	26.69		

SD=standard deviation

found; however, mean life event score was highest among lower socioeconomic group. Nothing much could be said about upper middle class because of small number of cases from this category. More acute relation of lower and lower middle group can be explained from the fact that these two categories understandably have more life event because of various social and financial constraints.

Type of family: It was seen that nuclear family had more number of life events. While analysing mean life event score, joint family had statistically significant mean life event score than the control group ($P<0.05$). It can be explained from the fact that persons from nuclear family bears more stress which is distributed to other members in joint family. Regarding extended family type, it is difficult to comment due to small sample size.

Marital status: In analysing the marital status with total number of life events in patients with NIDDM did not show much difference with the control. Again, total life event score showed significant difference between married and control ($P<0.05$) and between widow/widower vs control ($P<0.01$). Though it is difficult to comment, the fact may be that, married people face more stresses while maintaining their family with little resources. As regards to widow/widower, it may be due to the fact that acceptance of this group to social stream is poor and subsequently they experience more life events. About separated or divorced group, sample size is too small to comment.

Birth order: In analysing the birth order with total number of life events, no significant difference was found. While mean life event score was analysed, 'others' group had significant difference than that of control ($P<0.01$). We do not come across any study to compare this finding.

Age group: Total number of life events was higher with age group 40-49 years. Total life event score also showed significant difference ($P<0.05$) in this group compared to the control. It is possible that individual from this age group being more achievement oriented yet unsettled, possibly experience more stressful life events. Singh *et al.*[11] also found from general population older adults (above 35 years) to experience more stressful life events.

Educational status:

Primary level group had highest total number of life events. When total life event score was analysed according to educational status, primary group showed significant difference with control ($P<0.01$).

This finding does not lead to any conclusion and require further study to come to a definite conclusion.

Occupational status: Housewives and service holders had higher number of life events. In an attempt to consolidate the above finding, we separately analysed total life event score as regards to occupational status and found housewife score was statistically significant ($P<0.05$). Our finding that housewife experiences more stress can be explained from the fact that Indian housewife has to bear all the stress of family life including child bearing and rearing, being confined to house and having less chance to neutralise their stress by other social means.

Thus it is obvious that the aetiology of NIDDM from emotional causes remain still a distinct possibility. A long term extensive study in future will impart more knowledge in this field.

Summary and conclusion

This study was an attempt to find out the impact of stressful life events in the aetiology of NIDDM. Most of the significant findings of our study corroborated with previously done studies. In our study we found significant difference between patients with NIDDM and the control in total number of life events. Total life event score analysis did not reveal any significant difference. Analysing the area of activity 'financial' needs special mention. Females were found to be more vulnerable to life events than their counterparts and it reached level of significance. In our study, urban group showed more vulnerability to life events and it also reached level of significance. In case of socioeconomic status lower and lower middle class group of NIDDM manifested more vulnerability to life events.

As a family type, nuclear family reported experiencing more number of life events. Analysing mean life event score joint family had statistically significant mean life event score than the control group. In marital status total number of life event score did not show much difference with the control. Again total life event score showed significant difference between married and control and between widow/widower highly significant with the control. We found significant relationship between birth

order with 'others' group; but, did not come across any study to compare this findings. In our study statistically significant number of life events was experienced by the age group 40-49 years. Analysis of educational status showed subjects with 'primary level' education to experience more number of life events. Again total life event score showed statistically significant difference to the subjects of primary level education group with the control. Finally, housewives showed more total number of life events and statistically significant total life event score.

Although a few statistically significant associations between stressor and illness emerged from this study, it can be concluded that stress might act as an aetiological factor in NIDDM. A number of methodological problems which weaken, if not negate, the findings of a substantial correlation between life events and illness. In our study life events were considered three years to six months with prior to onset of NIDDM. Therefore occurrence of NIDDM within this period and occurrence of stressful events could not be sequenced properly. The number of our subjects was relatively small, hence it does not reflect the community at large.

Proper psychosocial research requires close attention to how stress is defined, how the patient's clinical history is elicited and the control subjects are selected. In summary, it may be concluded that the possibility exists that emotional factor may be important in the onset of NIDDM. Long term prospective studies of individual at high risk for the disease are needed to provide conclusive evidence.

References

1. Labhart A. Clinical demonstrations. *Schweiz Med Wochenschr.* 1974;104:1830-41.
2. Malins JM. Diabetes. *Lancet.* 1974;2:1367-8.
3. Williamson RT. Remarks on the etiology of diabetes mellitus and the diet and conditions of life during the war. *Br Med J.* 1918;1:139-41.
4. Selye H. The stress of life. New York: McGraw Hill; 1956. Rev. ed. 1976.
5. Holmes TH, Rahe RH. The Social Readjustment Rating Scale. *J Psychosom Res.* 1967;11:213-8.
6. Hinkle LE Jr. The concept of "stress" in the biological and social sciences. *Sci Med Man.* 1973;1:31-48.
7. Engel GL. A life setting conducive to illness. The giving-up--given-up complex. *Bull Menninger Clin.* 1968;32:355-65.
8. Wolf S. A new view of disease. *Trans Am Clin Climatol Assoc.* 1962;74:168-75.
9. Rahe RH, Arthur RJ, Gunderson EK, Mahan JL Jr. The epidemiology of illness in naval environments. I. Illness types, distribution, severities, and relationship to life change. *Mil Med.* 1970;135:443-52.
10. Paykel ES, Prusoff BA, Uhlenhuth EH. Scaling of life events. *Arch Gen Psychiatry.* 1971;25:340-7.
11. Singh G, Kaur D, Kaur H. Presumptive stressful life events scale (PSLES) - a new stressful life events scale for use in India. *Indian J Psychiatry.* 1984;26:107-14.
12. Wolf S. The importance of stress in peptic ulcer. *Resen Clin Cient.* 1956;25:147-51.
13. Wolf S. Life stress and allergy. *Am J Med.* 1956;20:919-28.
14. Greene WA Jr, Young LE, Swisher SN. Psychological factors and reticuloendothelial disease. II. Observations on a group of women with lymphomas and leukemias. *Psychosom Med.* 1956;18:284-303.
15. Weiss E, Dolin B, Rollin HR, Fischer HK, Bepler CR. Emotional factors in coronary occlusion. I. Introduction and general summary. *AMA Arch Intern Med.* 1957;99:628-41.
16. Hinkle LE Jr, Christenson WN, Kane FD, Ostfeld A, Thetford WN, Wolff HG. An investigation of the relation between life experience, personality characteristics, and general susceptibility to illness. *Psychosom Med.* 1958;20:278-95.
17. Peyrot M, McMurry JF, Hedges R. Living with diabetes: the role of personal and professional knowledge in symptom and regimen management. In: Roth JA, Conrad P, editors. *Research in the sociology of health care.* Vol 6. Greenwich, CT: JAI Press; 1987. p. 107-46.
18. Menninger WC. Psychological factors in the etiology of diabetes. *J Nerv Ment Dis.* 1935;81:1-13.
19. Hinkle LE Jr, Evans FM, Wolf S. Studies in diabetes mellitus. III. Life history of three persons with labile diabetes, and relation of significant experiences in their lives to the onset and course of the disease. *Psychosom Med.* 1951;13:160-83.
20. Hinkle LE Jr, Evans FM, Wolf S, Conger G, Edwards CJ, Pugh BL. Studies in diabetes mellitus. IV. Life history of three persons with relatively mild, stable diabetes, and relation of significant experiences in their lives to the onset and course of the disease. *Psychosom Med.* 1951;13:184-202.
21. Hong KE, Holmes TH. Transient diabetes mellitus associated with culture change. *Arch Gen Psychiatry.* 1973;29:683-7.
22. Penrose LS. Psychiatric genetics. *Psychol Med.* 1971;1:265-6.
23. Robinson N, Fuller JH. Role of life events and difficulties in the onset of diabetes mellitus. *J Psychosom Res.* 1985;29:583-91.
24. Connolly J. Life events before myocardial infarction. *J Human Stress.* 1976;2:3-17.
25. Horowitz M, Schaefer C, Hiroto D, Wilner N, Levin B. Life event questionnaires for measuring presumptive stress. *Psychosom Med.* 1977;39:413-31.