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Original Article

# Chronic stress, sense of coherence and risk of type 2 diabetes mellitus

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ABSTRACT

*Aims:* The study was conducted to ascertain whether chronic stress and sense of coherence are associated with risk of type 2 diabetes mellitus.
*Methods:* Stress questionnaires - Presumptive Stressful Life Events Scale (PSLES), Perceived Stress Scale (PSS) and Sense of Coherence (SOC) - were administered to 500 Newly Detected Diabetes Mellitus (NDDM) cases and 500 Normal Glucose Tolerance (NGT) controls recruited following 75 g OGTT. Assessment of stress was completed before the diagnosis of diabetes was revealed to them.
*Results:* PSLES and PSS scores were significantly higher and SOC score was significantly lower in NDDM subjects compared to those with NGT. PSLES and PSS correlated positively with anthropometric parameters (waist circumference, BMI), glycemic parameters (FPG, 2 hPG, A1C) and HOMA-IR and inversely with HOMA-β whereas SOC correlated inversely with glycemic parameters (FPG, 2 hPG, A1C) and HOMA-IR and positively with HOMA-β. In stepwise logistic regression analysis, SOC emerged as the strongest independent predictor of diabetes (OR: 0.774) after HOMA-IR (OR: 1.621) and BMI (OR: 1.288). Other significant predictors included PSS (OR:1.153), PSLES-LT (OR: 1.005) and HOMA-β (OR: 0.894).
*Conclusion:* Chronic stress and low sense of coherence are associated with a higher risk of type 2 diabetes mellitus.



## 1. Introduction

The aetiology of diabetes includes genetic as well as life style factors. Urbanization has adversely affected our lifestyle in many ways. Besides changing the dietary and physical activity patterns, urbanization has also led to psychological stress which can be an important risk factor associated with diabetes, hypertension and coronary artery disease [1–3]. The stress experience has been assessed in earlier studies by various instruments [4–6]. Objective measures of the stress experience such as presumptive stressful life events scale (PSLES) have traditionally been used in research aimed at assessing the role of psychosocial and environmental stressors in physical illness [7]. The perceived stress scale (PSS) is a global subjective measure of perceived stress which lays emphasis on the perception of a situation by the individual as stressful [8].

The sense of coherence (SOC) scale was developed by Antonovsky [9] as a tool to assess successful coping with stressful situations. It seeks to explain why some people despite experiencing major stressors and stressful life events stay healthy while others do not [10]. Persons with low SOC are more likely to deal unsuccessfully with stressors and individuals with high SOC are more likely to cope effectively with stressful life events. Sense of coherence could thus be a moderator of stress related risk of diabetes Mellitus.

Direct evidence supporting a significant role for stress in the development of human diabetes has come only from recent studies. These studies have evaluated the stress experience as well as SOC in the context of diabetes mellitus. Mooy et al. [11] confirmed the association of chronic psychological stress and diabetes in a cross sectional study while Novak et al. [12] reported that self perceived stress is an independent predictor of incident diabetes through long term follow up studies. Similarly, low decision latitude at work place [13,14] and low sense of coherence (SOC) has also been linked to type 2 diabetes mellitus in Swedish women [13]. The whitehall II

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study demonstrated that psychosocial stress at work place was associated with a 2 fold increased risk of type 2 diabetes after 15 years of follow up in women but not in men [15]. A prospective occupational cohort study with a 17 year follow up found that low SOC was associated with 46% increased risk of diabetes in working male employees of the study population [10].

Despite the emerging evidence on the association of stress and risk of diabetes there are some limitations. Some of the studies evaluated work related stress only, while others have used only a single question [12] or a single questionnaire to assess stress [10,13]. None of the studies used both objective and subjective indicators of stress to comprehensively evaluate the stress experience.

There are few studies which have reported the role of SOC as a moderator or mediator between stress and chronic symptoms or disease states [16–18]. The interaction of chronic stress and SOC may be important in determining the risk of diabetes as differences in SOC can modify the way individuals react to stressful experiences. Whether SOC moderates and or mediates the effect of chronic stress on diabetes risk has not been investigated so far.

We hypothesize that high levels of chronic stress and low SOC are independently associated with a higher risk of diabetes. Further, we hypothesize that SOC moderates the effects of chronic stress on diabetes risk such that this association is stronger in those individuals with a low SOC. The purpose of the present study therefore was to examine whether there is an association between chronic stress and risk of type 2 diabetes mellitus and whether SOC mediates or moderates this association.

## 2. Methods

The study was conducted after approval by the institutional ethical committee for human research. It compared stress measures viz PSLES over life time and over the past 1 year, PSS over last 1 month and SOC, in 500 newly detected diabetic patients and 500 subjects with NGT in a case control design.

### 2.1. Recruitment

Subjects were recruited from apparently healthy individuals of either sex, if they were aged above 30 years and consented for the study. The decision on who was "apparently healthy" and could be recruited was made by a physician/Endocrinologist after a thorough clinical evaluation. Several questions were asked from subjects such as history of any chronic symptoms or chronic diseases including diabetes and history of prolonged use of any medication. In addition, subjects were also assessed by a detailed physical examination for evidence of any systemic illness before declaring them apparently healthy for recruitment.

A standard 75 g OGTT [19] was performed in all eligible subjects who were then divided into normal glucose tolerance (NGT), impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and newly detected diabetes mellitus (NDDM) patients based on standard WHO criteria [20]. The diagnosis of NDDM was confirmed by a second OGTT. Subjects with NDDM and NGT were enrolled in the study while those with IGT and IFG were excluded.

Self reported cases of previously diagnosed diabetes mellitus were excluded from the study. Subjects were also interrogated for classic symptoms of diabetes such as polyphagia, polyuria and polydipsia. If they said yes, their medical records were also checked to confirm whether they were indeed diabetic based on WHO diagnostic criteria [20]. All such cases confirmed to have diabetes from medical records were also excluded and so were pregnant/lactating women and subjects with a history of smoking or alcohol consumption, any chronic illness/on medications and mental retardation.

### 2.2. Matching of cases and controls

NDDM cases and NGT controls were matched for age and sex. Matching of controls (NGT) with cases (NDDM) for age and sex was performed progressively over time until 500 new cases of NDDM were detected. Of the total number of subjects called on a particular day for OGTT that constituted a batch, those detected as NGT were matched with those detected as NDDM in the same batch by a "batch processing method" wherein controls who matched the NDDM cases in every batch of OGTT performed were recruited. (see Fig. 1).

### 2.3. Anthropometric and clinical assessment

A predesigned proforma was filled in all recruited subjects containing demographic data, details of family history of diabetes, anthropometry and other physical examination. Height was measured by a stadiometer with subjects standing upright without shoes and with their back against the wall and their head in the Frankfurt plane [15]. Weight was measured on electronic balance with subjects in light clothing and without shoes [21]. BMI was calculated as weight in kilograms divided by height in meter square [22]. Waist circumference was measured as the minimum circumference between lowest rib and iliac crest at the end of expiration and hip circumference was measured at level of great trochanters [23]. Anthropometric indices were used as measures of obesity and central obesity to study the relationship between stress and obesity.

### 2.4. Assessment of chronic stress

The assessment of chronic psychological stress was made by administering the following stress questionnaires viz presumptive stressful life events (life time & last 1 yr) [7], modified perceived stress scale (last 1 month) [8] and sense of coherence ([9,24]) by personal interview and subject responses were then entered in the questionnaires.

#### 2.4.1. Presumptive stressful life events scale (PSLES)

This scale measures 51 stressful events that have occurred in an individual's life span or over last 1 year with a weighted score for each item that add up to give a total stress score over lifetime (PSLES-LT) or last 1 year (PSLES-1yr). It has been well validated in

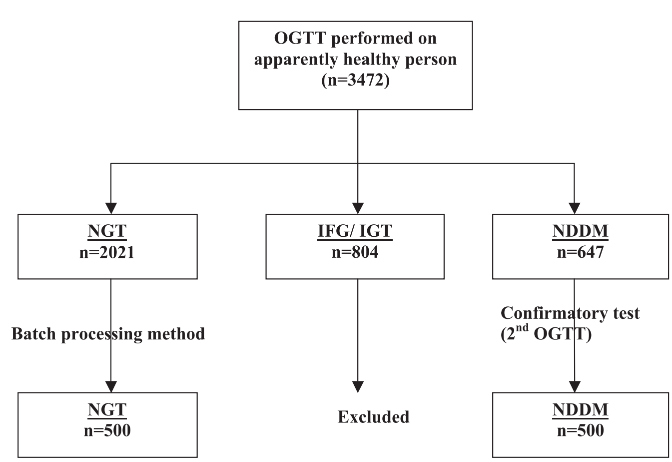


**Fig. 1.** Flow chart of recruitment of subjects.

India [5,6,25,26] with a reliability of 0.80 [27].

*2.4.2. Perceived stress scale (PSS)*

Perceived stress scale measures the degree to which an individual perceived a particular situation in the previous month as stressful. The modified version of this scale (PSS-10) was used which has 10 items with 5 point likert scale [5]. Responses on all items of the scale were summed up to get the total PSS score. PSS has been used in several studies [4] and its internal reliability coefficient (cronbach alpha) has been reported as > 0.70 [28].

*2.4.3. Sense of coherence (SOC)*

Sense of coherence is a scale developed to measure the ability of persons to cope well with stressful situations and represents a global orientation that facilitates successful coping [29]. The modified version of this scale (SOC-13) was used which had 13 items with a 5-point likert scale [5,24,30]. SOC-13 contains five questions on comprehensibility, four questions on manageability and four questions on meaningfulness [31]. Responses to all items of the scale are summed up to get the total SOC score. The internal reliability coefficient (cronbach alpha) of this scale was 0.76 in Indian subjects [32].

Validation of all questionnaires were carried out before they were used in the present study. None of the subjects were aware of their glucose tolerance category at the time of assessment of stress and the result of the OGTT was revealed only after completion of all stress questionnaires. This was to ensure that stress evaluations were valid and unaffected by any stress resulting from a new diagnosis of diabetes.

*2.5. Biochemical assessments*

Fasting blood samples were collected for glycated hemoglobin (A1C) estimations and the serum separated and stored at −-70 °C for estimation of insulin.

*2.5.1. Oral glucose tolerance test (OGTT)*

OGTT was performed in all subjects 3 days after they were asked to consume a diet without any restriction of carbohydrates [19]. On the day of OGTT, fasting blood sample was drawn in a vacutainer for plasma glucose through a venepuncture. Immediately after the fasting blood sample was drawn, subjects were instructed to drink 75 g of anhydrous glucose dissolved in 300 ml of water over 5 min. For the next 2 h, subjects were not allowed to take anything except small amount of water, if necessary. Exactly after 2 h of ingestion of glucose drink, another blood sample was drawn for estimation of plasma glucose i.e. 2 h PG.

*2.6. Other biochemical estimations*

Glucose was estimated in plasma by the method of glucose oxidase (Glucose Kit, Accurex Biomedicals, India). A1C was estimated by ion-exchange high performance liquid chromatography (HPLC) using analyser D-10 (BioRad, USA) which is traceable to the reference methods of both diabetes control and complications trial (DCCT) and the international federation of clinical chemistry and laboratory medicine (IFCC). Serum insulin was measured by radioimmunoassay method (Immunotech, Beckman Coulter, USA). Insulin resistance and pancreatic β-cell function were assessed as HOMA-IR and HOMA-β respectively by homeostasis model assessment (HOMA) [33] as follows:

$$\mathrm{HOMA-IR} = \frac{\text{Fasting insulin } (\mu\mathrm{IU/ml}) \text{ x fasting glucose } (\mathrm{mmol/L})}{22.5}$$

$$\mathrm{HOMA}-\beta = \frac{20 \text{ x fasting insulin } (\mu\mathrm{IU/ml})}{\text{Fasting glucose } (\mathrm{mmol/L}) - 3.5}$$

*2.7. Sample size calculation*

Sample size was calculated as for case control studies based on an anticipated probability of exposure of stress for those with diabetes ($P_1$) of 0.387, an anticipated probability of exposure of stress for those without diabetes ($P_2$) of 0.243 and an anticipated adjusted odds ratio of 1.5 at a confidence level of 95% and relative precision of 25% which came out to 457 for each group. Therefore, for the two study groups (NDDM and NGT) a total of 914 has been rounded off to a figure of 1000 subjects and 500 subjects recruited in each of the two study groups.

*2.8. Statistical analysis*

Statistical analysis was done by using SPSS package version 17.0. Group comparison of baseline parameters was obtained using unpaired “t” test. Group comparisons of stress scales to detect any gender differences were done by two-way analysis of variance (ANOVA) followed by post-hoc analysis using Tukeys test [34]. This was done keeping in view some of the earlier studies which had reported significant gender differences in the levels of stress [16,35]. Measures of effect size were estimated by using partial eta square ($\eta^2$p) [36,37]. Stepwise logistic regression analysis was carried out to obtain the significant predictors of diabetes in the presence of other potential parameters by calculating the odds ratio (OR) and 95% of confidence intervals (CI).

The mediating or moderating effect of SOC on the relationship between chronic stress (PSLES-LT, PSS) and risk of type 2 diabetes mellitus was examined by applying a logistic regression model. The raw data of all variables were centred by subtracting the average from each observed value of the variable [38] before performing stepwise logistic regression analysis. In step I, the independent chronic stress variables (cPSLES-LT or cPSS) were entered along with the dependent variable (NDDM) (model I). In step II, the mediator variable cSOC was added to model I along with the independent chronic stress variables to assess any mediation effect (model II). A mediation effect of cSOC was concluded if the significant effect of the chronic stress scales (cPSLES-LT or cPSS) in the first step diminished or disappeared in step II. In step III, interaction terms of the moderator and independent variables (cSOC x cPSLES-LT or cSOC x cPSS) were also entered simultaneously to model II to assess any moderation effect of cSOC (model III). A moderating effect of SOC was concluded if either of the interaction terms were significant or if there was a change in beta coefficient of the respective stress score [16,39]. Further analysis was performed to illustrate the moderation effect by distributing the cSOC into low cSOC (<50% percentile) and high cSOC (≥50% percentile) on the basis of percentile [17].

## 3. Results

A total of 3472 apparently healthy subjects underwent OGTTs to enrol 500 subjects each of NDDM and NGT. The mean age (NGT: 48.01 ± 8.44 yrs, NDDM: 47.03 ± 9.22yrs) and gender distribution (Male/female ratio: NGT-193/301 and NDDM- 193/307) of the subjects was similar in both the study groups. BMI (27.25 ± 4.47 vs 24.80 ± 3.98, $p < 0.001$), WC (Male: 91.20 ± 12.58 vs 83.94 ± 12.58, $p < 0.001$; Female: 89.36 ± 11.07 vs 83.98 ± 9.54, $p < 0.001$), FPG (9.27 ± 4.16 vs 4.73 ± 0.41, $p < 0.001$), 2 hPG (17.03 ± 4.84 vs 5.93 ± 0.97, $p < 0.001$), A1C (8.81 ± 2.26 vs 5.51 ± 0.49, $p < 0.001$), HOMA-IR*10_log (1.36 ± 0.33 vs 0.93 ± 0.36, $p < 0.001$) were found to be significantly higher in NDDM subjects as compared to NGT subjects whereas HOMA-β_log (1.39 ± 0.46 vs 1.83 ± 0.37, $p < 0.001$) was significantly lower in NDDM subjects.

### *3.1. Comparisons of psychological stress scales*

The scores of stress scales such as PSLES-LT_log, PSLES-1yr_log and PSS were significantly higher and scores of stress coping scale SOC were significantly lower in NDDM subjects when compared with NGT subjects (Table 1). The significant differences in different stress scales were noted both in male and female study subjects.

### *3.2. Logistic regression analysis*

In logistic regression analysis, SOC along with PSLES-LT and PSS emerged as independent predictors of diabetes when family history of diabetes, BMI, WC, HOMA-IR_10, HOMA-β and stress scales namely PSLES-(LT & 1yr), PSS, SOC were included in the model (Table 2).

### *3.3. Mediation and moderation effects of SOC*

Addition of centred (c) SOC to model II (step II) of logistic regression did not change the significance of the relation between cPSLES-LT and diabetes as beta coefficient remained the same indicating that SOC did not have any mediating effect on PSLES-LT. In case of association of cPSS and diabetes risk, there was a significant increase in beta coefficient after addition of cSOC in the model II. This indicates mediation by SOC to the extent that the risk of diabetes associated with PSS increased when SOC was controlled.

Similarly, to assess the role of cSOC as a moderator, when the interaction term was introduced in the logistic regression model (model III), the beta coefficient for cPSLES-LT did not change indicating no moderation. In the case of cPSS, there was a significant increase in beta coefficient in model III suggesting that SOC was moderating the effect of PSS on risk of diabetes mellitus (Table 3).

**Table 2**
Step wise logistic regression analysis of parameters for prediction of newly detected diabetes mellitus (NDDM).

| Parameters | β-coefficient | p-value | Odds Ratio | 95% CI |
|---|---|---|---|---|
| BMI | 0.253 | ˂0.001 | 1.288 | 1.166–1.422 |
| HOMA-IR_10 | 0.483 | <0.001 | 1.621 | 1.464–1.795 |
| HOMA-β | - 0.112 | <0.001 | 0.894 | 0.874–0.914 |
| PSLES-LT | 0.005 | <0.001 | 1.005 | 1.002–1.008 |
| PSS | 0.143 | <0.001 | 1.153 | 1.086–1.224 |
| SOC | −0.256 | ˂0.001 | 0.774 | 0.709–0.846 |

Variables entered in the model: F/h, BMI, WC, HOMA-IR_10, HOMA-β, PSLES-LT, PSLES-1yr, PSS, SOC.

**Table 3**
SOC as a mediator or moderator between chronic stress and newly detected diabetes mellitus analysed by logistic regression.

| | PSS | |
|---|---|---|
| | β coefficient | p-value |
| Model - I | 0.111 | <0.001 |
| Model - II | 0.126 | <0.001 |
| Model - III | −0.002 | 0.587 |

Model I: cPSS variable entered.
Model II: cPSS + cSOC (mediation test).
Model III: cPSS + cSOC + (cSOC x cPSS) (moderation test).

**Table 4**
Low SOC and high SOC as a moderator between chronic stress and newly detected diabetes mellitus (NDDM).

| | PSLES-LT | | PSS | |
|---|---|---|---|---|
| | β coefficient | p-value | β coefficient | p-value |
| Low SOC (<50% percentile) | 0.004 | <0.001 | 0.147 | <0.001 |
| High SOC (≥50% percentile) | 0.008 | <0.001 | 0.107 | <0.001 |

Further moderation analysis performed by comparing individuals who scored low SOC (<50% percentile) and high SOC (≥50% percentile) (Table 4) revealed that the association between PSS and diabetes was significantly higher among those with low SOC (beta coefficient - 0.147) as compared to those with a high SOC (beta coefficient - 0.107). In the case of PSSLES-LT there was only a small change in the association between PSLES-LT and diabetes whose effect size was also very small.

## 4. Discussion

We found significantly higher chronic psychological stress and significantly lower SOC level in newly detected diabetic mellitus (NDDM) subjects as compared to those with normal glucose tolerance (NGT). Both NDDM (cases) and NGT (controls) subjects were recruited from the same pool of apparently healthy

**Table 1**
Comparative data of chronic psychological stress scales in NGT (n: 500, male: 193 and female: 307) and NDDM (n: 500, male: 193 and female: 307) subjects.

| Parameters | Group | | | | Group | Significance (Tukey's test at 5%) | |
|---|---|---|---|---|---|---|---|
| | NGT (Mean ± SD) | | NDDM (Mean ± SD) | | η2p (Effect size) | Male (NGT vs NDDM) | Female (NGT vs NDDM) |
| | Male | Female | Male | Female | | | |
| PSLES-LT_Logŧ | 2.66 ± 0.11 | 2.59 ± 0.11 | 2.73 ± 0.10 | 2.68 ± 0.11 | 0.115€ | S | S |
| PSLES-L1 yr_Logŧ | 1.64 ± 0.29 | 1.71 ± 0.27 | 1.80 ± 0.31 | 1.79 ± 0.31 | 0.039€ | S | S |
| PSS | 10.68 ± 5.66 | 11.40 ± 5.58 | 14.49 ± 6.43 | 15.58 ± 6.31 | 0.095€ | S | S |
| SOC | 24.36 ± 4.28 | 25.11 ± 4.13 | 22.06 ± 4.68 | 20.24 ± 4.97 | 0.129€ | S | S |

Significant €($p < 0.001$) by 2-way ANOVA. €Tukey's test applied to all significant parameters and was found to be significant (S) ($p < 0.05$) in males and females both. $\eta^2_p$, partial eta square; PSLES, Presumptive stressful life events scale; PSS, Perceived stress scale; SOC, Sense of coherence.ŧDue to skewed nature of these parameters, log transformation has been applied to normalize them.

individuals not previously known to have diabetes. We also found significant independent associations between objective (PSLES) as well as subjective (PSS) indicators of chronic stress and risk of diabetes mellitus. SOC emerged as the strongest predictor of diabetes risk with significant independent protective effects. However, our results provide limited support to a moderating effect of SOC on stress related risk of diabetes.

We used different stress scales to fully characterize psychological stress. These included subjective indicators of stress that assessed perceived stress (PSS) as well as sense of coherence (SOC), objective indicators such as presumptive stressful life events scale (PSLES). We believe that such a comprehensive evaluation of chronic psychological stress in the context of diabetes mellitus has not been carried out earlier. Also, newly detected diabetes was diagnosed on the basis of oral glucose tolerance tests. Both these approaches allowed for a much more robust conclusion on the association of chronic psychological stress and risk of diabetes.

The PSLES scales have been successfully used in earlier studies in Indian population to objectively assess stress in different disease conditions [6,25,26]. Recent studies [4,5,28] have focused on PSS as an important instrument to assess stress because it takes into account the individual's perception of a particular situation in life as stressful rather than merely listing all life events which are presumed to be stressful. More weightage is placed in this scale to the individual's interaction with the environment and therefore characterizes stress better. However, this scale is applied only for a short time period and accurately assesses the psychological stress of the past 1 month only [8].

Sense of coherence (SOC) scale specifically takes into account the ability of individuals to meet stressful challenges rationally by utilizing all available resources rather being overwhelmed by the same. It examines the question why some people regardless of encountering stressors and stressful life events stay healthy while others do not [10,13,14].

The significantly higher presumptive stressful life events scale (PSLES) and perceived stress scale (PSS) scores and lower sense of coherence (SOC) score in NDDM subjects observed in this study indicate that individuals experiencing more stressful life events or major changes in their life and those having a generally lower ability to cope with stress are at higher risk of developing diabetes.

Logistic regression analysis revealed that the odds of being detected with diabetes was significantly greater in the presence of higher levels of antecedent stress and lower levels of SOC suggesting that higher stress and an impaired ability to deal with stressful situations are both independently associated with a greater risk of type 2 diabetes mellitus.

Sense of coherence was the strongest independent predictor of diabetes with an odds ratio of 0.77 that translates to a 23% lower risk of diabetes. This points to significant independent protective effects of SOC on diabetes risk. In other words, individuals with a higher SOC who are able to deal effectively with stressors have a reduced associated risk of diabetes mellitus. Previous studies have also reported that SOC is associated with lower risk of diabetes [10,13,14]. However, these studies examined the effects of SOC in relation to occupational stress and risk of diabetes and did not evaluate SOC outside the workplace.

Our results also support a mediating as well as a moderating effect of SOC on PSS based perceived stress and risk of diabetes. However, there was no significant mediation or moderation of the association of PSLES-LT and diabetes. The mediating effect of SOC on chronic stress was supported to the extent that the independent effects of PSS on diabetes risk were significantly increased when SOC was controlled. In other words, PSS and SOC influenced diabetes risk in opposing manners and the enhancing effect of PSS on diabetes risk was being counteracted by the protective effect of SOC.

The moderating effect of SOC on the association of PSS and Diabetes risk was further illustrated by subgroup analysis. Those individuals with low SOC and therefore with generally lower capabilities to deal with stressful situations displayed greater effects of perceived chronic stress on diabetes risk than those with high SOC which confirmed the moderation effects of SOC.

Future prospective cohort studies are required to confirm and further clarify the independent protective role as well as the specific mediating/moderating effects of SOC on stress related risk of diabetes mellitus.

Whether stress is causally linked to diabetes cannot be said from our study as cohort studies are required for any such interpretation and randomized controlled trials are required to conclusively prove causality. We used a case control design and therefore no conclusions on causality can be drawn with certainty. However, useful information to suggest a possible causality can also be provided from case control studies such as ours. We believe that the association between stress and diabetes observed in our study is likely to be causal due to a number of reasons. Firstly, stepwise logistic regression analysis clearly suggests that chronic psychological stress is an important significant factor that predicts newly detected diabetes. Secondly, the fact that increased stress levels in NDDM subjects in the current study was demonstrated in the preceding month (PSS), year (PSLES-1 year) and lifetime (PSLES-life time) of these subjects, would suggest that it is stress that contributed to the risk of diabetes in them and not vice versa. Thirdly, we had excluded all known diabetes subjects from this study so that the contribution of diabetes itself to the stress can be significantly reduced. Also, stress assessments were made before glucose tolerance categories were revealed to the study subjects to further ensure that even the knowledge of a fresh diabetes diagnosis does not affect them. However, the possibility of diabetes having contributed to stress cannot be completely ruled out from our study. This is because NDDM patients could have had a period of unrecognised diabetes prior to detection in this study about which they remained unaware. Only cohort studies which detect incident diabetes can eliminate the contribution of diabetes to stress altogether.

It would appear that chronic stress could result initially in redistribution of body fat and central obesity [ [13] [40] [41]] with associated insulin resistance. This is believed to be the result of chronic activation of the HPA axis causing elevation of cortisol level which in-turn is responsible for central adiposity and insulin resistance [42]. Cortisol is also believed to have a direct suppressive action on the beta cell to decrease insulin secretion [43,44]. Whether HPA axis dysfunction and the resultant chronic immune suppression have any role in the inflammation that could underlie obesity, insulin resistance and diabetes is unclear. Persistent or repeated exposure to stressful stimuli that are accompanied by suboptimal coping could be associated with progressive increase in insulin resistance, dysglycemia, glucotoxicity, beta cell dysfunction and later type 2 diabetes.

Our study has certain limitations. Firstly, we could not exclude all cases of preexisting diabetes as some of them could have remained undetected and study subjects may have been unaware of it. Some of the patients included in the study and were detected as newly diagnosed DM following OGTTs, could have been diabetic even earlier. While this effect may only be small it does not rule out some effect of diabetes on stress. Also, as mentioned above, ours was not a cohort study and conclusions on causality have to be made with caution.

## 5. Conclusion

This study demonstrates that high chronic stress is associated with a greater risk of diabetes mellitus. More importantly, sense of coherence reflecting the ability of persons to cope well with stressful situations is a stronger independent protective factor associated with reduced diabetes risk. Also, SOC significantly mediated and moderated the effects of perceived chronic stress on the risk of diabetes mellitus.

## Conflicts of interest

The Authors declare that they have no conflict of interest.

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