Diabetes - Increased Risk for Cancers through Chromosomal Aberrations?

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Abstract

Diabetes, a comprehensive genetic disease, is principally due to the deregulation of glucose levels in the blood. In addition to contemporary epidemiological studies, systematic substantiation suggests that long-term diabetes leads to cancers due to a variety of reasons. In this study, blood samples were collected with informed consent from confirmed type I diabetic (T1DM, n=25) and type II Diabetic patients (T2DM, n=25) with equal numbers of controls. Further depending on the lifestyle habits they were subdivided into smokers/non-smokers and alcoholics/non-alcoholics. Chromosomal assays were performed for these cases and it was found that there was a significant increase in chromosomal aberration frequency in diabetic patient groups who are exposed to smoking and alcohol than that of normal diabetic groups (T1DM and T2DM). On the other hand, patient groups who were non-smoking and non-alcoholics also showed higher chromosomal aberrations when compared to that of controls. While the mechanisms for these increased chromosomal aberrations in diabetic groups are not clear, they may be due to increased oxidative stress leading to oxidative damage and resulting in genomic instability, which in turn may contribute to an increased risk for cancer.

Keywords: Oxidative damage - diabetes - cancer - chromosomal aberrations - lifestyle habits
Chromosomal aberration assay was carried out for all the samples. Peripheral blood samples collected were cultured as follows. 0.5 ml of heparinised blood was added to 6 ml of RPMI (Hi Media), 1.2 ml of fetal bovine serum (Hi Media) and 0.3 ml of phytohemagglutinin (GIBCO®) and allowed for lymphocyte division upto 72 hours. CO₂ was released by unscrewing the culture vial cap for every 24 hours. At 72nd hour, cells were arrested by adding colchicine (0.6µg/ml) and treated with hypotonic solution (0.075M KCL). The cells were fixed on the microscope slides and stained with giemsa (4%) after air drying. Chromosome preparations were made by modified method of Hungerford, 1965. Well spread 100 metaphases were scored for chromosomal aberration assay.

Statistical analysis
For different data obtained from the patient groups and the control groups, Student’s t-test was analysed using Graph pad prism 5 software. A p value of <0.05 with confidence limit of 95% was defined as statistically significant. Numerical data are presented as Mean±SE.

Results
The slides were analysed blindfold for chromosomal aberrations. In this study the diabetic patients were grouped as smokers/alcoholics and non-smokers/non-alcoholics for analyses. Interestingly in our study although we did not find any specific chromosome breaks, an increased random chromosomal aberrations in both the diabetic patient groups were observed. A drastic significant increase in chromosomal aberrations was observed in smokers/alcoholics in T1DM (1.4±0.42) and T2DM (2.8±1.16) when compared to controls (0.22±0.14) and diabetic groups with non-smokers (1.0±0.33) /non-alcoholics (1.2±0.31) (Table 1).

Table 1. The Chromosomal Aberration Frequencies in Diabetic Groups and Controls

<table>
<thead>
<tr>
<th>Study Groups</th>
<th>Mean±SE</th>
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</thead>
<tbody>
<tr>
<td>Controls</td>
<td>0.22±0.14</td>
</tr>
<tr>
<td>T1DM (non-smokers &amp; non alcoholics)</td>
<td>1.0±0.33</td>
</tr>
<tr>
<td>T1DM (smokers &amp; alcoholics)</td>
<td>1.4±0.42</td>
</tr>
<tr>
<td>T2DM (non-smokers &amp; non alcoholics)</td>
<td>1.2±0.31</td>
</tr>
<tr>
<td>T2DM (Smokers &amp; alcoholics)</td>
<td>2.8±1.16</td>
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</tbody>
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Discussion
An increase in cancer risk due to diabetes is documented but the underlying mechanism is not clearly understood till date. Although many risk factors are shared between cancers and diabetes patients, an increased oxidative stress is well documented which contribute to genomic instability (Limoli and Giedzinski, 2003) directly or indirectly. Also several studies reported an increased oxidative damage in diabetes patients using cytogenetic tests (Dominguez et al., 1998; Sardas et al., 2001; Cinkilic et al., 2009). However, they were inconclusive. In the present study, it is observed that a significantly high frequency of chromosomal aberrations in T1DM and T2DM indicates that diabetics may be at a higher risk for developing cancers than the control subjects (without diabetes). Chromosomal aberration assay may be used as a marker to evaluate the genomic instability in the lymphocytes of diabetes patients.

Recently Nefic and Handzic (2013) reported the DNA damage to be correlated with life style factors and micronuclei frequency in smokers. Our results also show an increase in chromosomal aberrations in smokers and alcoholics than that of controls (diabetics without smoking and alcoholics). As it is known that smoking and alcohol consumption triggers cancer (Goa et al., 2013; Shahdoust et al., 2013) this study also confirms that alcohol and smoking will increase the chances of cancer risk in these diabetic patients.

In conclusion, certain diabetic therapies were also found to be cytotoxic in nature and as literature shows medications (Bonnefond et al., 2013) could be one of the reasons for high chromosomal aberrations. This study has been extended to in vitro study to assess the relationship between drugs and chromosomal aberrations, which may help in understanding the role of diabetes, drugs and cancers.
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References


