Study of progression of diabetic retinopathy in pregnancy & its correlation with glycemic control in a tertiary health care center in state of Odisha

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Abstract
Purpose: The objective of this study is to assess the rapidity of progression of retinopathy in pregnant diabetic women during gestational period with correlation with glycemic control.

Materials & Methods: This was a prospective observational study of patients admitted/visited to the department of Medicine, Endocrinology, Ophthalmology & Obstetrics & Gynecology in a tertiary health care system in State of Odisha during January 2016 to December 2017. The study included total 50 pregnant with diabetes vs 50 non-pregnant diabetes for progression of retinopathy during their gestational period.

Results: At the end of study, 32.5% of cases in the study group showed progression of retinopathy staging during pregnancy as compared to 14% in non-pregnant women. The glycosylated hemoglobin, duration of diabetes, current age was evaluated as risk factors for progression of diabetic retinopathy.

Conclusion: Pregnancy, level of glycemia (HbA1c) & age are risk factors for acceleration of Retinopathy progression.

Keywords: Pregnancy, Diabetic retinopathy, HbA1c.

Introduction
Diabetes mellitus is a disorder in which the level of blood glucose is persistently raised above the normal range.¹ DM is a chronic disorder with multiorgan involvement having many microvascular and macrovascular complications.² Microvascular complications are caused by chronic hyperglycaemia, whereas macrovascular complications are caused by both chronic hyperglycaemia and the consequences of insulin resistance.³ Diabetic Retinopathy (DR) is the most common microvascular complication of Diabetes Mellitus (DM). Pregnancy is a major risk factor for the progression of Retinopathy & is definitely associated with increased prevalence & severity of Retinopathy compared to non-pregnant diabetic women.⁴ The risk factors for the progression of Retinopathy in pregnancy are severity of Retinopathy at conception, glycemic control, duration of diabetes, age of pregnant women, hypertension. Pregnancy itself found to be an independent risk factor.⁵
The objective of this study is to assess the rapidity of progression of retinopathy in pregnant diabetic women during gestational period with correlation with glycemic control.

Materials & Methods
This study conducted as prospective observational study of patients admitted/visited to the Department of Medicine, Endocrinology, Ophthalmology & Obstetrics & Gynecology in a tertiary health care system during January 2016 to December 2017. The study includes total 50 pregnant with diabetes vs 50 non-pregnant diabetes for progression of Retinopathy during their gestational period.

Inclusion Criteria
- Diabetic pregnant women of either 5 years or more duration
- Any type (type-1/type-2/other type of known diabetic women)

Exclusion Criteria
- Other causes of Retinopathy/Prior retinal diseases
- Gestational diabetes

Study Design
In this study minimum 50 numbers of pregnant diabetic of either 5 years or more duration are selected as case. These pregnant ladies are evaluated for glycemic status (FBS, PPBS, HbA1C), any Retinopathy changes by direct & Indirect Ophthalmoscopy, fundus photography as soon as pregnancy is confirmed by Urine pregnancy test.

Diagnosis & Staging of Retinopathy
For retinopathy changes evaluation by direct & Indirect Ophthalmoscopy, fundus photography was done for any fresh changes in Retinopathy during each ANC. Depending upon changes/development of Retinopathy, patients are staged according to International Clinical Diabetic Retinopathy Disease Severity scale for DR.(No apparent retinopathy, mild NPDR, moderate NPDR, severe NPDR, PDR).

Observation
Table-1 No. of Cases with Retinopathy at Baseline

<table>
<thead>
<tr>
<th>DIABETIC PATIENT</th>
<th>PREGNANT</th>
<th>NON-PREGNANT</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>R+</td>
<td>9(18%)</td>
<td>12(24%)</td>
<td>21</td>
</tr>
<tr>
<td>R-</td>
<td>41(82%)</td>
<td>38(76%)</td>
<td>79</td>
</tr>
<tr>
<td>TOTAL</td>
<td>50</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

At baseline only 18% have retinopathy in diabetic pregnant as compared to 24% of non-pregnant.

Table-2 No. of Cases with Retinopathy at Last Visit

<table>
<thead>
<tr>
<th>DIABETIC PATIENT</th>
<th>PREGNANT</th>
<th>NON-PREGNANT</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>R+</td>
<td>22(55%)</td>
<td>15(30%)</td>
<td>37</td>
</tr>
<tr>
<td>R-</td>
<td>18(45%)</td>
<td>35(70%)</td>
<td>53</td>
</tr>
<tr>
<td>TOTAL</td>
<td>40</td>
<td>50</td>
<td>90</td>
</tr>
</tbody>
</table>

At the end of pregnancy, 10 patients could not visit for follow up. At last visit 55% cases had retinopathy as compared to 30% in the control group. On comparison at the end point of study, progression of retinopathy in pregnant diabetic patient is much higher as compared to other.

R- (No retinopathy) R+ (retinopathy) D (lost to follow up)
At start of study 82% of pregnant women had no Retinopathy as compared to 76% of cases in non-pregnant group. At the end of study, 45% of pregnant women had no retinopathy but 55% have various stages of Retinopathy as compared to 30% in the control group.

**Table N0.3. Status of DR at End Point of Study**

<table>
<thead>
<tr>
<th>STATUS OF DR</th>
<th>DIABETIC PREGNANT</th>
<th>DIABETIC NONPREGNANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO PROGRESS</td>
<td>27(67.5%)</td>
<td>47(94%)</td>
</tr>
<tr>
<td>PROGRESS</td>
<td>13(32.5%)</td>
<td>3(6%)</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>50</td>
</tr>
</tbody>
</table>

At the end point of study, 32.5% of the Cases in the study group showed progression of retinopathy staging during pregnancy as compared to 6% in non-pregnant women. So we concluded that pregnancy is a risk factor for acceleration of retinopathy progression.

**Table No.4 Risk Correlation between Retinopathy and HbA1C (Study Group)**

<table>
<thead>
<tr>
<th>Status of DR</th>
<th>MEAN HbA1C</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;8</td>
<td>&gt;8</td>
<td></td>
</tr>
<tr>
<td>NO PROGRESS</td>
<td>24(80%)</td>
<td>3(30%)</td>
<td>27</td>
</tr>
<tr>
<td>PROGRESS</td>
<td>6(20%)</td>
<td>7(70%)</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>10</td>
<td>40</td>
</tr>
</tbody>
</table>

Among diabetic pregnant, patient having HbA1C <8 (80% show no progression of retinopathy). But HbA1C >8 (70% shows progression of retinopathy). So there is significant risk of progression in relation to long term glycemic control.

Graph 1 shows duration of DM Vs retinopathy progression.

Graph 1: Duration of DM Vs retinopathy progression.

P value was 0.143. As the p value >0.05, so there is no significant difference in term of duration diabetes in both group, because of small sample size, very few pregnant cases more than 10 years.
Among age group 25-30 years & more than 30 years progression of retinopathy occurs more frequently as age progresses (43.4% in age group >30 years & 12.5% age group 25-30 years). As p<0.05, so more is age more likely there is progression of retinopathy during pregnancy. Graph 2 shows BMI Vs retinopathy progression.

![Graph showing BMI Vs retinopathy progression.](image)

**Graph 2: BMI Vs retinopathy progression.**
P value was 0.109. As p>0.05, BMI & progression of retinopathy is non-significant.

### Discussion
All the above data collected as per study proforma & analysed by SPSS 21 using chi-square test & unpaired t test to show significant P value.

At base line, 82% has no Retinopathy, 10% had mild Retinopathy & 8% had moderate degree. As the pregnancy proceeds more chance or progression depended upon base line DR & higher grade of Retinopathy. Sampson MJ et al study showed that Progression was more significant in women with moderate and severe forms of retinopathy compared to women with mild or no retinopathy at conception. Maximum progression occurred in end or 2nd trimester or 3rd trimester. At end of study 30% had mild Retinopathy & 12% had moderate Retinopathy. 32.5% had progression of retinopathy staging during pregnancy as compared to 6% in non-pregnant diabetic women. PS Mallika et al although pregnancy does not have any long term effect on DR, progression of retinopathy changes occur in 50%-70% of cases. Pregnant women having HbA1C<8, 20% showed progression of retinopathy, whereas patients having HbA1C >8, 70% showed progression of retinopathy. P <0.043 which significant. So there is strong correlation between glycemic control & retinopathy progression. Mathiesen ER et al stated that low incidence of severe progression of retinopathy during pregnancy observed by us in women reaching an average HbA1c of 5.6% from pregnancy week 20 is reassuring for continuing a strategy of strict metabolic control. Duration of DM & progression of retinopathy in pregnant group for which P value is>0.05, non-significance. In Temple RC et al Progression of retinopathy was significantly increased in women with duration of diabetes 10-19 years compared with duration < 10 years (10% vs. 0%; P = 0.007)

<table>
<thead>
<tr>
<th>Status of DR</th>
<th>No Progress</th>
<th>Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE GROUP (In Year)</td>
<td>20-24</td>
<td>25-30</td>
</tr>
<tr>
<td>No Progress</td>
<td>2(66.7%)</td>
<td>16(66.7%)</td>
</tr>
<tr>
<td>Progress</td>
<td>0</td>
<td>3(12.5%)</td>
</tr>
</tbody>
</table>

Table No.5 Age vs Retinopathy Progression (Study Group)
and in women with moderate to severe background retinopathy at booking (30% vs. 3.7%; P = 0.01). This contradiction study by Temple Rc et al, because of small sample size, few pregnant women>10 years. Age group 25-30 & >30 years progression of retinopathy occur more frequently as the age progresses is 43.4% showed progression in >30 years as compared to 12.5% in 25-30 age group P< 0.05, significant. So more is age more likely there is progression of retinopathy during pregnancy. Kostraba JN et al showed that young age at onset is a protective factor in the long term or whether it only delays the onset of proliferative retinopathy. BMI & progression of retinopathy is non-significant as P>0.05. BMI<24 & >30 there is progression of retinopathy but doesn’t hold good in BMI group 25-29.99. In Klein BE et al study group, the prevalence of being obese was 25.2%.

**Conclusion**
Diabetic retinopathy affects over one- third of all people with diabetes & sss the leading cause of vision loss in working age adults. Maximum changes occurs during 24-30 weeks of gestation though accelerated progression may present throughout pregnancy. There should be proper collaboration between physician, gynecologists & ophthalmologist regarding diabetic retinopathy management in pregnancy.

**References**