Impact of Maternal Diabetes on Retinal Thickness and Vascular Density in Offspring: A Developmental Study

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Introduction

Diabetes affects approximately 10% of the US population. It leads to elevated blood glucose levels which disrupts vital signaling pathways causing complications in the organs. Diabetic retinopathy, which affects half of all diabetic patients, results from dysfunction in retinal endothelial cells and pericytes due to hyperglycemia, increasing blood-retinal permeability. Studies have indicated that maternal diabetes, in particular gestational diabetes can impact retinal thickness, increase the risk of retinopathy and visual impairment in offspring. However, little is known about the impact of maternal diabetes on retinal vasculature of the offspring. Murine retinal vasculogenesis begins postnatally, developing a vascular framework by the third postnatal week. Retinal thickness, indicative of neuronal cell quantity, is known to be reduced in diabetic retinopathy. Our study aims to compare retinal vascular development and thickness in offspring of diabetic versus the offspring of non-diabetic mothers.

Hypothesis

We hypothesize that maternal diabetes contributes to structural and vascular alterations in offspring that may lead to visual impairment. Disparities in developmental patterns, crucial for understanding the risks and mitigating abnormal retinal development in neonates of diabetic mothers.

Methods

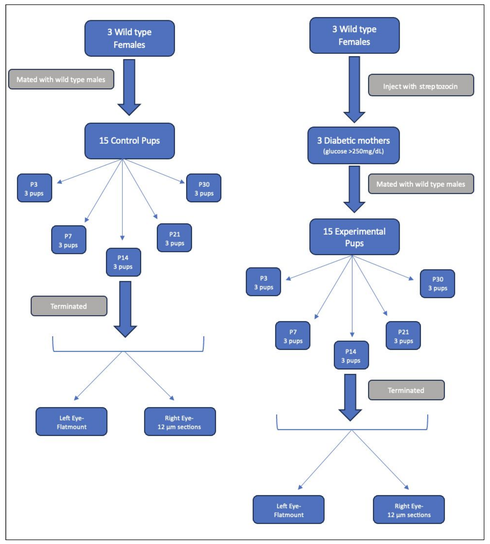

Figure 1. A flow chart explaining the methods used to carry out the experiment.

Results

- Diabetes was induced in female mice via intraperitoneal streptozotocin injections; blood glucose levels ≥250 mg/dL confirmed diabetic status
- Comparison of retinal thickness, both total thickness and inner retinal thickness, and vascular development of pups was done at post-natal days 3, 7, 14, 21, and 30
- Retinal thickness analysis involved cutting frozen samples into 12 µm slices and staining with IsolectinB4 and DAPI
- Retinal vessel analysis involved flat mounting and staining with IsolectinB4
- ImageJ was used to measure the retinal thickness. It was also used to measure the vascular length density by selecting an area of skeletonized vessels and measuring the total length of vessels covering the corresponding surface area and their respective density.

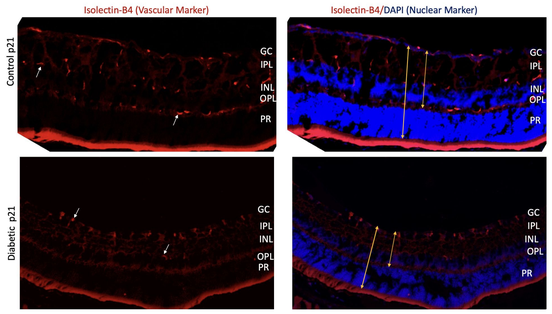

Figure 2. Images of retinal sections at p21 of the control and experimental groups. IsolectinB4 shows as red on the images indicating the retinal vessels. DAPI shows as blue indicating nuclear cells. The yellow arrows on the images on the right show how the retinal thickness was measured, both full thickness and inner layer. The white arrows on the left images point to some of the retinal blood vessels.

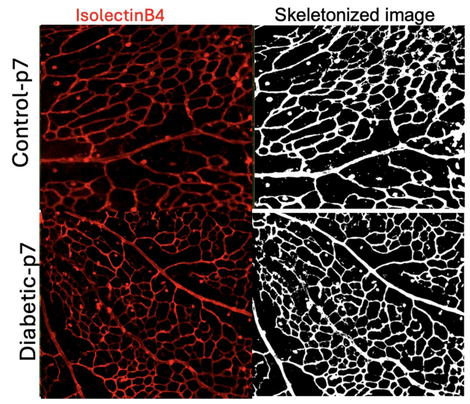

Figure 3. Images of the flat mounts of samples from pups at p7. IsolectinB4 appears in red indicating the retinal blood vessels. The white images are the skeletonized images of the blood vessels which were used to measure the density and length of the vessels.

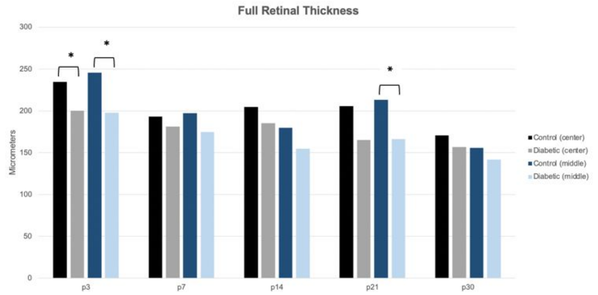

Figure 4. Comparison of full retinal thickness between control and diabetic groups revealed significant reduction in diabetic group p3 in both central and middle part of the retina. Similarly, comparison of full retinal thickness between control and diabetic groups revealed significant reduction in diabetic group p21 particularly in the middle part of the retina. Moreover, there was significant decrease in inner retinal thickness (from the inner limiting membrane to the outer plexiform layer) at p21 in the diabetic group. (*p<0.05, n=3)

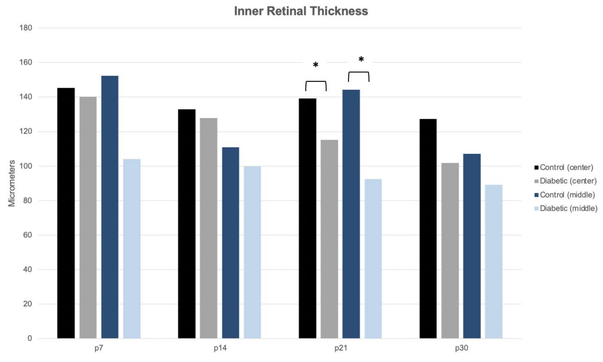

Figure 5. There was significant decrease in inner retinal thickness (from the inner limiting membrane to the outer plexiform layer) at p21 in the diabetic group. (*p<0.05, n=3)

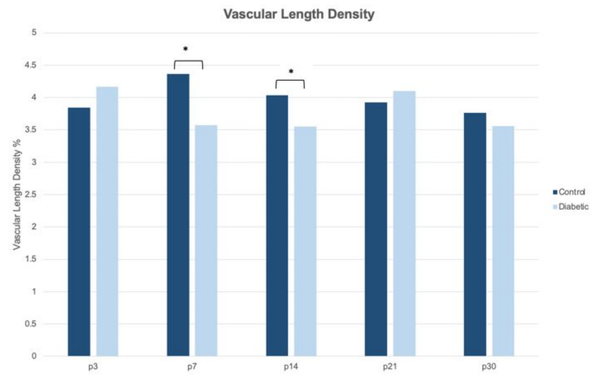

Figure 6. Capillary length density analysis showed a significant decrease in the diabetic group compared to the control pups at p7 and p14 (*p<0.05, n=3)

Discussion

Our study aimed to assess retinal vascular development and thickness in offspring of diabetic mice compared to wild-type counterparts, hypothesizing that maternal diabetes would impede developmental milestones. Analysis at crucial postnatal time points revealed significant reductions in full retinal thickness at p3 and p21 in diabetic offspring, suggesting early structural alterations. Similar patterns were observed in inner neuronal layer thickness, indicating vulnerability to maternal diabetes-induced changes. Vascular density and length density showed reductions at p7 and p14, hinting at vascular abnormalities associated with maternal diabetes, albeit transiently. These findings suggest a potential for structural and vascular abnormalities in offspring, possibly stemming from decreased neuronal cells. Further studies are warranted to confirm this assumption through assessment of retina function and visual acuity using electroretinogram (ERG) and Optokinetic reflex (OKR). Overall, our results highlight the potential impact of maternal diabetes on offspring's retinal development, emphasizing the importance of early detection and intervention strategies to prevent the possibility of visual impairment in offspring of mothers with diabetes.

Conclusion

Maternal diabetes can impact the development of retinal vessels and neurons in offspring, potentially leading to visual impairment. Therefore, early detection and management of maternal diabetes during pregnancy, along with prompt identification of retinal vascular and functional abnormalities or visual impairment in offspring, are crucial for mitigating these risks.

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