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Morphohistometric investigations in placentas of gestational diabetes

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1 Introduction

An increase in perinatal morbidity and mortality demonstrates that maternal gestational diabetes is neither a minor nor harmless variant of diabetes mellitus [1, 8, 15]. Since the high fetal risk factor in the overt form of a diabetes mellitus is partly due to morphologically manifest placental insufficiency [2, 3, 4, 5, 6, 7, 13, 14], we were interested to determine if histopathologic changes also occur in gestational diabetes. To this end, we examined morphometrically the placental terminal villi of 26 patients with gestational diabetes. Results from our previous studies of normal [9] and diabetic placentas [14] served as controls.

2 Material and methods

Twenty-six patients with pathologic blood glucose levels after a positive oral 100 g glucose tolerance test of J. B. O'SULLIVAN [10] form the basis of this study. During pregnancy, 14 patients could be managed on diet alone whereas 12 required insulin therapy. The placentas studied were all from gestations greater than the 37th weeks. Gestational age in all cases was established by early sonographic evaluation. The clinical data of the overt diabetes group demonstrated no marked deviations when compared with the control group. With gestational diabetes, there was a marginally higher incidence of obesity and multiparity.

Placentas were fixed in 10% formalin immediately after delivery, and random sections were taken and stained with hematoxylin and eosin. Fifty terminal villi in the periphery of the placentas or cotyledons were morphometrically studied. Three separate sections were examined for each patient.

The following parameters were determined:

- villous surface area and circumference,
- total surface area, circumference,
- number of villous vessels,
- degree of vascularization,
- number and length of epithelial plates,
- villous circumference coverage by epithelial plates,
- number of vessels directly involved in resorption via epithelial plates.

Statistical calculations were performed on the TR 440 (Siemens) at the computer center of the University of Ulm by analysis of variance.

The study presented is based on the same measurements, methods, and instruments (Kontron, Videoplan) as were the controls. The image analysis system used has a failure rate of < 1%, with an operator's failure rate of 1.5%.

3 Results

The values for the surface areas of terminal villi ($2210 \pm 160 \mu\text{m}^2$) were found to lie almost midway between those for normal placentas ($1977 \pm 190 \mu\text{m}^2$) and those for the diabetic control group ($2484 \pm 296 \mu\text{m}^2$). There is no statistically significant difference (Figure 1). This also holds true for the villous circumference (Table I). The total surface areas of the villous vessels are more reduced in gestational diabetes ($620 \pm 210 \mu\text{m}^2$) compared to overt diabetes mellitus ($631 \pm 217 \mu\text{m}^2$) with a significance of $p < 0.01$ when compared to normal placentas with $706 \pm 230 \mu\text{m}^2$ (Figure 2) as well as the total circumference of

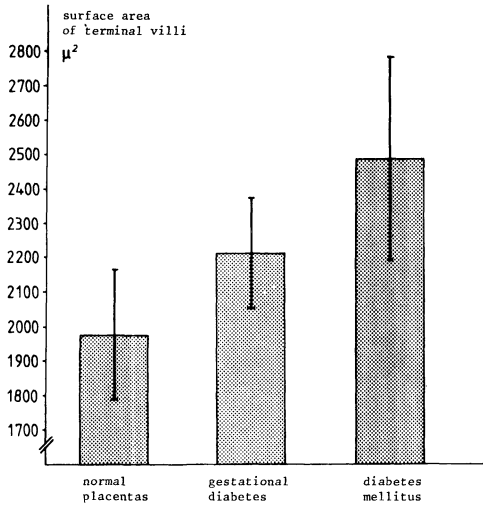


Figure 1. Surface area of placental terminal villi in gestational diabetes versus normal and diabetes mellitus placentas.

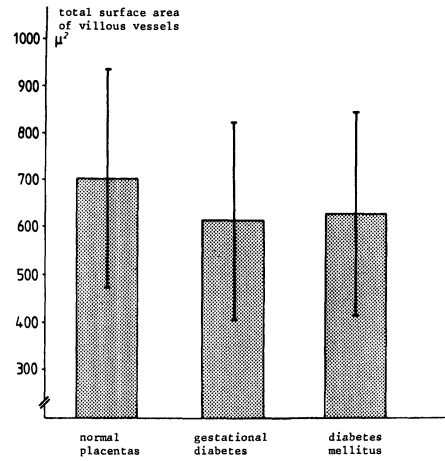


Figure 2. Total surface area of placental villous vessels in gestational diabetes versus normal and diabetes mellitus placentas.

Table I. Parameters of villi and vessels in gestational diabetes as compared to those in normal as well as diabetes mellitus placentas.

	normal placentas (N)	gestational diabetes (G)	overt diabetes mellitus (D)
villous circumference	157 ± 8 μ	163 ± 9 μ NS	183 ± 11.5 μ D/N p < 0.01
total circumference of villous vessels	180 ± 36 μ	165 ± 37 μ G/N p < 0.05	168 ± 35.5 μ D/N p < 0.05
number of vessels	4 ± 0.5	3.5 ± 0.4 G/N p < 0.01	3.5 ± 0.4 D/N p < 0.01

Table II. Parameters of epithelial plates of terminal villi in gestational diabetes as compared to normal as well as diabetes mellitus placentas.

	normal placentas (N)	gestational diabetes (G)	over diabetes mellitus (D)
length of epithelial plates	29 ± 5.4 μ	32 ± 5.3 μ NS	36 ± 8.1 μ D/N p < 0.05
number of epithelial plates	2.5 ± 0.4	2.3 ± 0.6 NS	1.9 ± 0.3 D/N p < 0.001
villous circumference coverage by epithelial plates	18.5 ± 5%	21.1 ± 5% NS	19.6 ± 6% NS
number of vessels with epithelial plates	68 ± 7%	66.1 ± 8% NS	67 ± 9% NS

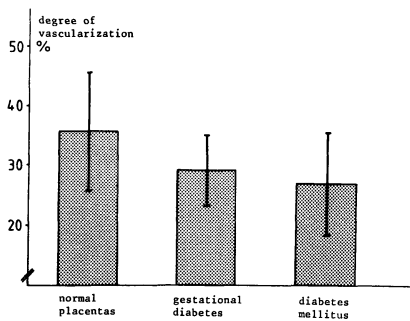


Figure 3. Degree of vascularization of placental terminal villi in gestational diabetes versus normal and diabetes mellitus placentas.

villous vessels (Table I). The number of vessels is reduced compared to the normal group ($p < 0.01$), but corresponds to the values of the diabetic group (Table I). For the degree of vascularization (gestational diabetes: $29.1 \pm 12\%$, overt diabetes $26.9 \pm 8.5\%$, normal: $35.8 \pm 10\%$), the number of vessels involved in reabsorption via epithelial plates as well as the parameters of the epithelial plates were mostly found to lie between the values of normal and diabetic

Abstract

Perinatal morbidity and mortality are increased in both overt and gestational diabetes. Since retardation of placental development has been documented in overt diabetes, we, thus, examined morphometrically the terminal villi of 26 patients with gestational diabetes in order to determine if there is an immaturity of placental development. Investigation of villous surface, degree of vascu-

Keywords: Gestational diabetes, morphometry, placenta.

Zusammenfassung

Morphohistometrische Untersuchungen an Plazenten bei Gestationsdiabetes

Die kindliche Morbidität und Mortalität ist nicht nur bei manifestem Diabetes mellitus, sondern auch bei Gestationsdiabetes erhöht. Bezüglich des manifesten Diabetes muß diese Tatsache zum Teil mit den bekannten Reifungsstörungen der Plazenta erklärt werden.

In einer morphometrischen Studie untersuchten wir deshalb die Terminalzotten der Plazenten von 26 Patientinnen mit Gestationsdiabetes mit der Fragestellung, ob eine Reifungsstörung in den für den materno-fetalen Stoffaustausch essentiellen Terminalzotten vorliegt.

placentas, with only moderate differences between the groups (Table II, Figure 3).

4 Discussion

There is general agreement regarding the retarded maturation of surface areas of terminal villi from diabetic patients [3, 5, 6]. The question whether these pathologic changes are correlated either with the White stages [11, 14, 16, 17] or with blood glucose levels [2, 4] is a controversial issue. Gestational diabetes is characterized by short duration combined with apparently normal blood glucose levels before pregnancy. It usually responds well to therapeutic blood glucose control during pregnancy.

In overt diabetes, retarded maturation is most conspicuous in the placental vasculature [4, 13, 14]. Surprisingly, we observed even lower values in gestational diabetes when compared with diabetic pregnancies which is in accordance with SENFT [12].

The retarded maturation of terminal villi affects the same structures in gestational diabetes as in overt diabetes although less pronounced. Placental insufficiency may occur in gestational diabetes as a result of the retarded vascular maturation.

larization, and development of epithelial plates yielded values lying somewhere between those of non-diabetic patients and those of patients with overt diabetes. Only the surface areas of the vessels were reduced to levels lower than in overt diabetes. Our findings appear to explain the occasional development of acute placental insufficiency.

Die Diagnose Gestationsdiabetes wurde bei allen Patientinnen durch erhöhte Blutzuckerwerte nach einem pathologischen oralen 100 g Glucose-Toleranz-Test gesichert. Während es möglich war, 14 der Frauen durch die ganze Schwangerschaft nur mit Diät alleine zu behandeln, mußten 12 Patientinnen auf Insulin eingestellt werden. Alle untersuchten Plazenten stammten aus der 37. bis 41. Schwangerschaftswoche. Für die Morphometrie benutzen wir das halbautomatische elektronische Bildanalyseverfahren Videoplan, Kontron.

Die Werte für die Zottenquerschnittsflächen und die Zottenumfänge lagen genau zwischen denen bei mani-

festem Diabetes mellitus und denen der normalen Kontrollgruppe ohne signifikante Unterschiede zu beiden. Dasselbe trifft für den Vaskularisationsgrad und die Entwicklung der Epithelplatten zu.

Die Gesamtquerschnittsfläche der Zottengefäße jedoch war sogar noch gegenüber der bei manifestem Diabetes

stark reduzierten Gefäßfläche mit einem Signifikanzniveau von $p < 0,01$ im Vergleich zu den Normalwerten verringert. Unsere Ergebnisse könnten deshalb die gelegentlich bei Gestationsdiabetes auftretende akute Plazentainsuffizienz erklären.

Schlüsselwörter: Gestationsdiabetes, Histometrie, Morphometrie, Plazenta.

Résumé

Explorations morphohistométriques des placentas de diabètes gestationnels

La mortalité et la morbidité fatale périnatale ne sont pas seulement augmentées lors des diabètes patents mais également lors des diabètes gestationnels. On connaît bien le retard significatif du développement placentaire lors de diabètes patents. Toutefois, nous avons examiné de façon morphométrique les villosités terminales chez 26 patientes avec un diabète gestationnel afin de déterminer s'il existe une immaturité du développement placentaire. On a examiné des coupes effectuées au hasard au niveau de la périphérie des cotylédons, ces coupes sont considérées comme représentatives des zones d'échanges fœto-maternelles. Toutes les patientes avaient un test de tolérance au glucose pathologique (100g de

glucose per os). Pendant la grossesse, le régime seul a été suffisant chez 14 patientes alors que chez 12 autres, une insulinothérapie a été nécessaire. Les placentas étudiés étaient tous d'un âge gestationnel supérieur ou égal à 37 semaines. Les études morphométriques ont été réalisées à l'aide d'un système d'analyse d'images électroniques semi-automatique (Kontron-Vidéoplan). Les surfaces villositaires, le degré de vascularisation et le développement des couches épithéliales ont été interprétés comme intermédiaires entre ceux des patientes normales et ceux des patientes avec un diabète patent. Seules les surfaces des vaisseaux étaient plus réduites que celles trouvées lors des diabètes patents. Nos résultats semblent expliquer la survenue occasionnelle d'une insuffisance placentaire aigüe.

Mots-clés: diabète gestationnel, morphométrie, placenta.

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