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INTERNATIONAL ABSTRACTS BY ORIGINAL AUTHORS

Factors Affecting Fetal Growth and Body Composition

AM J OBSTET GYNECOL

More Than One Previous Cesarean Delivery: A 5-Year Experience with 435 Patients

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Alcohol and Breast Cancer: Results From the Netherlands Cohort Study

AM J EPIDEMIOL

The Effect of Mass Screening on Incidence and Mortality of Squamous and Adenocarcinoma of Cervix Uteri

OBSTET GYNECOL

Comparison of Sperm Preparation Methods

J REPROD MED

MORE ORIGINAL ABSTRACTS INSIDE

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on patients with established mild preeclampsia is unknown.

The aim of this study was to determine whether calcium supplementation prevents progression to severe disease in preterm nulliparous women with mild preeclampsia.

Seventy-five women who were hospitalized at 24-36 weeks of gestation due to mild preeclampsia, were randomized to receive either 2 g/day of elemental calcium (36) or placebo (39). Both groups had similar demographic characteristics, initial blood pressure measurements, and amount of proteinuria. Diagnostic criteria and clinical management for severe preeclampsia were applied consistently.

Of the 36 calcium-treated subjects 18 (50%, 95% confidence interval [CI] 33-67) developed severe preeclampsia, compared with 19 of 39 (48.7%, 95% CI 32-65) in the placebo group (relative risk 1.03, 95% CI 0.64-1.03; p=1.00). Blood pressure values, gestational age at delivery, newborn weights, incidence of low Apgar scores, and umbilical arterial blood gases were similar for the 2 groups.

Calcium supplementation does not prevent severe preeclampsia in preterm patients with mild disease.

Relationship of Blood Rheology to Lipoprotein Profile During Normal Pregnancies and Those with Intrauterine Growth Retardation

J CLIN PATHOL

MUÑOZ, A., UBEROS, J., MOLINA, A., ET AL., J CLIN PATHOL 48:571-574,1995
REPRINTS: AVDA. SALOBREÑA 37, PTAL. 6-4°A,18600 MOTRIL, GRANADA, SPAIN (DR. J. UBEROS)

Changes in lipid concentrations during pregnancy result from the metabolic adaptation of the mother. Mobilization of fat deposits, the increase in free fatty acids, and the relationship between circulating progesterone and estrogen concentrations imply that these hormones are responsible for the lipid changes observed. Placental lactogen favors the release of fats from their deposits and an increase in free fatty acids, both being vital adaptations to ensure the availability of adequate energy substrate to the fetus.

Table 1 - Apolipoprotein and lipid means in pregnant women healthy controls and with intrauterine growth retardation.

Gestation (weeks)	*<17*	*18-24*	*25-32*	*>33*	*IUGR (>33)*
TC (mmol/L)	5.33+ ± SD 0.83	5.45 ± SD 0.95	6.17* ± SD 1.07	6.53 ± SD 1.14	6.41 ± SD 1.03
TG (mmol/L)	1.42† ± SD 0.40	1.45 ± SD 0.52	1.95† ± SD 0.63	2.46 ± SD 0.73	2.11* ± SD 0.59
LDLC (mmol/L)	2.80* ± SD 0.57	2.58 ± SD 0.86	3.27 ± SD 0.83	3.51 ± SD 1.07	3.41 ± SD 0.89
HDLC (mmol/L)	1.72 ± SD 0.40	1.80 ± SD 0.28	1.90 ± SD 0.28	1.78 ± SD 0.38	1.80 ± SD 0.49
FFA (mmol/L)	0.020 ± SD 0.006	0.024 ± SD 0.019	0.025 ± SD 0.014	0.031 ± SD 0.018	0.032 ± SD 0.023
PL (mmol/L)	7.70† ± SD 0.74	7.90* ± SD 1.72	9.40 ± SD 1.51	9.01 ± SD 2.18	9.48 ± SD 1.39
ApoA (g/L)	2.32* ± SD 0.4	2.74 ± SD 0.69	2.99† ± SD 0.62	2.63 ± SD 0.42	2.25* ± SD 0.55
ApoB (g/L)	0.95* ± SD 0.16	1.06 ± SD 0.31	1.20* ± SD 0.35	1.38 ± SD 0.31	1.49 ± SD 0.30

IUGR=intrauterine growth retardation >33 weeks of gestational age; ApoA=apolipoprotein A; ApoB=apolipoprotein B; TC=total cholesterol; TG=triglycerides; HDL=high-density lipoprotein cholesterol; LDLC=low-density lipoprotein cholesterol; FFA=free fatty acid; PL=phospholipid. *p<0.05; †p<0.01, statistical significance observed among the group >33 weeks of gestational age and the groups <17, 18-24, 25-32 weeks of gestational age and the group IUGR (>33).

Table 2 - Ratios of lipoprotein constituents in healthy pregnant controls and in women with intrauterine growth retardation.

Gestation weeks	<17	18-24	25-32	>33	IUGR (>33)
ApoB/ApoA	0.40* ± SD 0.49	0.38* ± SD 0.45	0.40* ± SD 0.56	0.52 ± SD 0.74	0.66† ± SD 0.24
TC/HDL	3.09 ± SD 0.69	3.02† ± SD 0.56	3.24* ± SD 0.85	3.66 ± SD 0.90	3.56 ± 1.27
LDL/HDL	1.62 ± SD 0.53	1.43 ± SD 0.49	1.72 ± SD 0.57	1.97 ± SD 0.82	1.89 ± SD 1.05
HDL/ApoA	0.74 ± SD 0.05	0.65 ± SD 0.07	0.63 ± SD 0.05	0.67 ± SD 0.05	0.80† ± SD 0.1
FFA/TG	0.014 ± SD 0.002	0.016 ± SD 0.005	0.012 ± SD 0.002	0.012 ± SD 0.002	0.015 ± SD 0.002

IUGR=intrauterine growth retardation >33 weeks of gestational age; ApoA=apolipoprotein A; ApoB=apolipoprotein B; TC=total cholesterol; TG=triglycerides; HDL=high-density lipoprotein cholesterol; LDLC=low-density lipoprotein cholesterol; FFA=free fatty acid; PL=phospholipid. *p<0.05; †p<0.01, statistical significance observed among the group >33 weeks of gestational age and the groups <17, 18-24, 25-32 weeks of gestational age and the group IUGR (>33).

Hyperlipidemia is commonly found in the normal population associated with pathologies such as atherosclerosis and hypertension. Increases in total cholesterol (TC), triglycerides (TG), LDL-cholesterol (LDLC) and decreases in HDL-cholesterol (HDL) and apolipoprotein-A (ApoA) have been reported in uncomplicated pregnancies. This would enable us to determine if the changes in the lipoprotein profile during pregnancy imply a greater atherogenic risk with possible repercussions on fetal growth and development. In this study the different lipid fractions in normal pregnancies and in pregnancies with intrauterine growth retardation (IUGR) were determined and related to changes in plasma and serum viscosity. Fifty-nine pregnant women were studied. These were divided into 2 groups. The first group consisted of 35 healthy pregnant women aged between 21 and 38 years (27 [SD 3.5] years) with no previous pathology (with a gestational age of 279 [SD 10] days), and a birthweight of 3345.4 [SD 449.3] g. The second group consisted of 24 pregnant women aged between 16 and 34 years (24.5 [SD 4.9] years) with a gestational age at term of 278 (SD 12) days, with ultrasound-diagnosed IUGR. The diagnosis of

IUGR was made on the basis of a biparietal diameter <2 SD below the mean at 33 weeks of gestational age. The birthweight in the newborn with IUGR was between 1170 g and 2830 g (2305.4 [SD 544.7] g).

The women fasted before blood was drawn. Analytical determinations were carried out in 4 study periods defined at the beginning of the study as: (1) pregnant ≤17 weeks; (2) pregnant 18-24 weeks; (3) pregnant 25-32 weeks; (4) pregnant ≥33 weeks. The following variables were analyzed in all cases: TC, TG, HDL, low density lipoproteins (LDLC), free fatty acids (FFA), phospholipids (PL) by enzymatic microtechnique, ApoA, and apolipoprotein B (ApoB) by simple radial immunodiffusion. Plasma and serum viscosities were measured at 37° C with a Harkness capillary viscosimeter. Statistical analysis included the Shapiro and Wilk's normality test, 1-way analysis of variance (ANOVA), a comparison of means, and Pearson's "r" correlation study.

Table 3 - Proteins, serum and plasma viscosity in healthy pregnant controls and in women with intrauterine growth retardation.

Gestation weeks	*<17*	*18-24*	*25-32*	*>33*	*IUGR (>33)*
Albumin (g/dL)	4.34† ± SD 0.56	3.90† ± SD 0.41	3.66 ± SD 0.34	3.52 ± SD 0.29	3.46 ± SD 0.43
α_1-globulin (g/dL)	0.32 ± SD 0.05	0.28* ± SD 0.04	0.31 ± SD 0.05	0.33 ± SD 0.04	0.42† ± SD 0.19
α_2-globulin (g/dL)	0.68 ± SD 0.1	0.67 ± SD 0.13	0.71 ± SD 0.13	0.72 ± SD 0.13	0.76 ± SD 0.22
β-globulin (g/dL)	0.95 ± SD 0.27	0.90* ± SD 0.21	1.03 ± SD 0.13	1.02 ± SD 0.18	0.99 ± SD 0.21
γ-globulin (g/dL)	0.81 ± SD 0.16	0.76 ± SD 0.19	0.80 ± SD 0.21	0.71 ± SD 0.17	0.79 ± SD 0.30
Total protein (g/dL)	7.12† ± SD 0.7	6.53 ± SD 0.58	6.53 ± SD 0.48	6.31 ± SD 0.50	6.39 ± SD 0.74
Plasma viscosity (mPa.s)	1.09 ± SD 0.08	1.06 ± SD 0.15	1.08 ± SD 0.15	1.12 ± SD 0.12	1.26* ± SD 0.15
Serum viscosity (mPa.s)	0.95 ± SD 0.09	0.96 ± SD 0.13	1.00 ± SD 0.12	0.94 ± SD 0.07	1.03* ± SD 0.13
PV-SV (mPa.s)	0.13 ± SD 0.13	0.09 ± SD 0.2	0.08 ± SD 0.14	0.17 ± SD 0.15	0.22 ± SD 0.2

IUGR=intrauterine growth retardation >33 weeks of gestational age; PV-SV=difference between plasma and serum viscosity. *p<0.05; †p<0.01, statistical significance observed among women >33 weeks of gestational age and the groups <17, 18-24, 25-32 weeks of gestational age and the group IUGR (>33).

TC, TG and LDLC increased progressively during pregnancy and the increase was significant after week 25. HDL and FFA did not change significantly during pregnancy. The PL increased until period 3 then stabilized and decreased slightly. ApoA increased significantly and ApoB increased gradually throughout pregnancy. After 33 weeks the ApoA and triglyceride concentrations were significantly lower in the IUGR group than in the controls, although no differences were observed with the other lipids (tables 1 and 2).

Pregnant women with IUGR had similar total protein values to the control group, with the exception of α_1-globulin which was higher in the IUGR group (table 3). Relationships between HDL and ApoA differed between the groups: the IUGR group had a highly atherogenic HDL/ApoA ratio, significantly greater than that of the control group (table 2). The ApoA concentrations increased significantly between the 25th and 32nd week of pregnancy, although the HDL/ApoA ratio was not significantly different in the

gestational periods considered. Pregnant women with IUGR, however, had modifications in HDL composition (a significantly greater HDL/ApoA ratio).

The ApoB/ApoA ratio was significantly higher than in previous gestational stages. This indicates that the lipoprotein profile in normal pregnancies is more atherogenic in the final stage and is significantly abnormal in women with IUGR (table 2).

The HDL concentration increases, through a rise in ApoA synthesized predominantly in the liver, when estrogen levels are raised. The ApoA level is significantly lower in women with IUGR than in normal pregnancies, but further studies have yet to be carried out to elucidate the mechanisms involved.

The affinity of both ApoB and plasminogen for the same endothelial receptors, leading to competitive inhibition of fibrinolysis, could explain the increase in plasma viscosity observed in the IUGR group.

Table 3 shows that there was significantly higher plasma and serum viscosities in the IUGR group than the values recorded in the same periods in the normal pregnancies.

The difference between these 2 variables is an indirect method of calculating the viscosity effect of the fibrinogen fraction.

The difference between the viscosities in period 4 of the control group, 0.17 (0.15) mPa.s, is not significantly different to that of the IUGR group, 0.22 (0.20) mPa.s, ($t=1.05$; $p=ns$).

The coefficients of variation for the control and IUGR group viscosity differences were 88.2 and 71.4%, respectively. The difference between the plasma viscosity and serum viscosity could be a good index of changes resulting from the fibrinogen fraction. Variation coefficients indicating the difference between the viscosities in the 2 groups in our study were greater than those cited by Ernst et al., and revealed a large variability in the relationships between the viscosity and fibrinogen. This could be explained by increased fibrinolytic activity in pregnant women, which under the circumstances, made the viscosity difference method unreliable.

The ApoB concentrations progressively increase throughout pregnancy. In normal pregnancies, mean ApoA values show a nonsignificant decrease after the 33rd week, whereas in the women with IUGR a decrease to below pregestational levels is observed (table 1).

On the basis of our results we suggest that hemorrheological modifications in the IUGR group, reported by several investigators, are in part secondary to the changes in high density lipoprotein metabolism and the competitive inhibition of fibrinolysis by ApoB which are increased in the pregnant women with IUGR. Although more thorough clinical assays are necessary, changes in ApoA, and more specifically in the ApoB/ApoA ratio, could be good markers for the early detection of IUGR.