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Is moderate alcohol intake in pregnancy associated with the craniofacial features related to the fetal alcohol syndrome?

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Is moderate alcohol intake in pregnancy associated with the craniofacial features related to the fetal alcohol syndrome? Olsen, J. and Tuntiseranee, P. (Steno Institute of Public health, Department of Epidemiology and Social Medicine, University of Aarhus, Building 02C, Nørrebrogade 44, DK-8000 Aarhus C, Denmark).

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Social drinking in pregnancy is common in many countries despite the fact that alcohol in high doses has teratogenic properties. The public health implications would be appreciable if even moderate alcohol consumption were associated with embryonal or fetal maldevelopment.

A presumably sensitive marker of an alcohol effect was used in this study, namely the fetal craniofacial features included in the Fetal Alcohol Syndrome. The study was based upon self-reported alcohol intake and photographs taken at birth or at 18 months of children born to mothers with a low or moderate alcohol intake during pregnancy. These women were selected during pregnancy by a two-stage sampling from all in well defined regions. Data were available concerning 323 pregnant women and some 200 to 220 children. A short palpebral fissure, a short nose to upper-lip distance and a broad root of the nose were expected to be associated with alcohol intake in early pregnancy, but such an association was only seen between binge drinking and a short palpebral fissure. No associations proved statistically significant at the 18-month examination and any association could merely be secondary to the known association between alcohol and birth weight.

Most researchers would recommend abstinence from copious intake of alcoholic beverages during pregnancy, since alcohol in high doses can act as a teratogen. Many would even recommend absolute abstinence from alcohol in pregnancy, as alcohol is at best merely 'empty calories'. Other researchers have presented evidence of a threshold effect below which no harmful consequences are seen. Such a point of view was put forward by the EuroMac Study Group which found no effects of a low to moderate alcohol intake in pregnancy on either birth weight or pediatric development (1). Absence of a 'no effect' dose threshold would imply that preventive measures should be concentrated on women with a high alcohol consumption. Those expectant mothers who drink socially in pregnancy need not feel any guilt or fear of having harmed their unborn baby.

Since alcohol can have a variety of effects, however, it is not enough to demonstrate a 'no effect' level for one or two specific outcomes. One should also be certain that there is no such effect level for any potential side effect related to embryonal, fetal or child development.

One subtle type of congenital malformation affects the development of the facial bones. A typical craniofacial morphology is part of the Fetal Alcohol Syndrome (FAS) and it is perhaps the most specific effect of alcohol exposure, despite a previously published association between tobacco smoking and FAS morphology (3). That particular finding could for example be due to misclassified alcohol data for the smokers. A large number of fetal craniofacial characteristics have been associated with alcohol intake, such as bulging forehead, short palpebral fissure, antimongoloid slant, deep nasal bridge, short nose to upper lip distance, etc.

It was the purpose of this study to correlate craniofacial morphology, as assessed 'blind' from photographs taken shortly after birth or at the age of 18 months, to alcohol consumption during pregnancy. The study was carried out on a group of pregnant women with a low to moderate alcohol consumption in pregnancy. The study was based upon the Danish sample for the EuroMac study (1).

It was expected that alcohol consumption would be correlated to a short palpebral fissure measured for both eyes (Fig. 1) as: $(a-b)/2$ and for the right eye as c. It was also expected that alcohol consumption would reduce the nose to upper lip distance (g/d; Fig. 1) and

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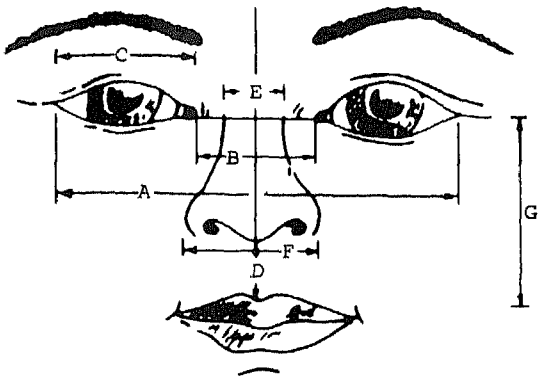

Fig. 1. Measured facial morphology after delivery and at the 18-month examination.

broaden the root of the nose (*e/f*; Fig. 1). These outcome measures are analysed in Tables II to V.

MATERIAL AND METHODS

The study was designed as a longitudinal investigation of alcohol ingestion during pregnancy, of pregnancy outcome,

Table I. *The mother's alcohol, smoking, and coffee habits in pregnancy*

Habit	Category	No.	%
Average alcohol intake/week before pregnancy	0	22	7
	1–4 drinks/w	144	45
	5–9 drinks/w	80	25
	10–14 drinks/w	53	16
	15+ drinks/w	24	7
Alcohol intake in 1st trimester	No	6	2
	Yes	291	98
Binge drinking in 1st trimester (5 drinks or more)	0	216	74
	1–4 times	60	21
	5+ times	15	5
Alcohol intake/week in 1st trimester	0 drinks/w	61	20
	1–4 drinks/w	87	28
	5–9 drinks/w	130	41
	10+ drinks/w	34	11
Average alcohol intake/week in 1st + 2nd trimester	0 drinks/w	61	19
	1–4 drinks/w	184	57
	5–9 drinks/w	55	17
	10+ drinks/w	23	7
Cigarette smoking in 2nd trimester	0 cigarettes/d	183	57
	1–4 cigarettes/d	16	5
	5–9 cigarettes/d	43	13
	10–14 cigarettes/d	54	15
	15+ cigarettes/d	26	8
Coffee drinking in 1st + 2nd trimester	0–3 cups/d	194	62
	4–7 cups/d	96	30
	8+ cups/d	24	8

and of pediatric development. From 1st January 1988 to March 1989, all pregnant women living in a geographically well defined area (Odense Municipality on the island of Funen, Denmark) were given a short self-administered questionnaire at their first visit to the antenatal centre (usually in the 12th week of pregnancy). Altogether 2,880 women (88.9%) completed the questionnaire which was then sent to the Department of Social Medicine, Odense University. Every woman who reported an average consumption of 5 drinks or more per week in the first trimester was enrolled in the EuroMac study (164 women), each one matched 1:1 with a pregnant woman selected from the remainder of the group. Matching was based on the expected date of delivery and the woman's year of birth. The selected women were interviewed by telephone in the 28th week of pregnancy. A personal interview was arranged 18 months after delivery and again 42 months after delivery, by telephone. All interviews were conducted by the same trained female interviewer who did not have access to previous reports when doing the interviewing.

The photographs were taken by a clinical photographer at the hospital shortly after the birth (within a week) or by a specially trained person when the children was 18 months old. The child was placed in a predetermined position in a stereotaxic-frame equipped with a measuring stick and all photos were taken from the same fixed distance. All the 18-month examinations took place in a designated room at the university.

The photographs were then measured 'blind' by a trained person who had no information regarding the alcohol consumption. All measurements were made more than 6 months after the photos were taken, according to the protocol outlined in Ref. (2). Two photos were available for most of the children, one in profile and one *en face*. About one-third of the photos were scored independently by two people and the correlation between these two measurements was used to exclude those profile measures which gave the lowest correlation coefficient between the two measurements. All measurements are expressed as standardized units according to the units indicated on the photographs.

Due to a shortage of clinical photographers at the time, or to a defective camera during a certain period covering the 18-month examination, no photos were available in about one-third of the cases.

Detailed data were collected during pregnancy and after the birth concerning the mother's height, prepregnancy weight, weight gain during pregnancy, social category, school education, working environment, and common life style factors. These potential confounders were integrated into the statistical modelling if they were associated with alcohol consumption or affected the estimated parameters. Analyses of variance and linear multiple regression models were applied to the data.

We have data on 323 pregnant women whose mean age was 29 years at the time of the interview (S.D.) 4.2; min 21 years, max 42 years). Fifty-two percent of their children were boys, whose average birth weight was 3,434 g (S.D. 565 g; min 1756 g, max 5,150 g). Ten percent were born before the 37th week of gestation and 18% had an Apgar score of less than 9.

Table II. *Measured facial characteristics according to different recordings of alcohol consumption in pregnancy. Mean values for newborns. All measurements in standardized units*

Alcohol consumption		Palpebral fissure		Nose upper lip	Root of the nose
		both eyes	right eye		
Alcohol intake before pregnancy drinks/week	0	20.8	21.7	3.3	.38
	1–4	22.3	22.6	3.1	.41
	5–9	22.2	22.5	3.0	.41
	10–14	23.6	23.5	3.0	.42
	15+	21.7	22.1	2.9	.43
p-values		0.01	0.14	0.22	0.45
Binge drinking in first trimester (5 drinks or more)	0	22.7	23.0	3.0	.41
	1–4	22.0	21.8	3.1	.42
	5+	20.4	21.0	2.7	.42
p-values		0.03	0.00	0.09	0.67
Alcohol intake in first trimester (drinks/week)	0	22.4	22.3	3.0	.39
	1–4	22.3	22.9	3.0	.42
	5–9	22.7	22.6	3.0	.41
	10+	21.2	22.1	3.0	.41
p-values		0.09	0.32	0.96	0.38
Alcohol intake in 1st+2nd trimester (drinks/week)	0	21.6	22.1	3.0	.41
	1–4	22.5	22.7	3.1	.41
	5–9	22.3	22.6	3.0	.41
	10+	22.8	23.3	3.0	.41
p-values		0.34	0.34	0.92	0.94
No. of observations	210	210	202	205	

p-values: analysis of variance, between groups

RESULTS

Table I shows that only 2% of the women had not consumed any alcoholic drinks at all during the first trimester. Most women reported a low to moderate intake and only 11% drank on average 10 drinks/week or more. None reported an intake of more than 20 drinks/week (one drink equals about 12 g of alcohol). Seventy-five (26%) had on one or more occasions taken 5 drinks or more in the first trimester. The women reported a lower alcohol consumption during pregnancy than before pregnancy and their consumption had declined after the first trimester. The table also shows that 43% were smokers and 38% drank 4 cups of coffee per day or more.

A short palpebral fissure, a short nose to upper lip distance and a broad root of the nose are some of the facial characteristics in the Fetal Alcohol Syndrome. It was therefore expected that an increasing alcohol consumption would be associated with the measured values presented in Tables II to V.

The results show this expected pattern of binge drinking in early pregnancy and to some extent also for the average alcohol consumption in the first trimester. These associations were weaker at the 18-month examination (Tables II, III).

When checking for potential confounders (smoking, coffee, dietary habits, and mother's age and height) only binge drinking consistently showed the expected signs among newborns. Only one regression coefficient was statistically significant at the 5% level (palpebral fissure – right eye) (Table IV). When birth weight was included in the model, none of the regression coefficients reached statistical significance.

DISCUSSION

Binge drinking in the first trimester was associated

Table III. *Measured facial characteristics according to different recordings of alcohol consumption in pregnancy. Mean values for children at 18 months. All measurements in standardized units*

Alcohol consumption		Palpebral fissure		Nose upper lip	Root of the nose
		both eyes	right eye		
Alcohol intake	0	15.5	16.4	3.1	0.52
before pregnancy	1–4	16.1	16.8	3.1	0.55
drinks/week	5–9	15.9	16.9	3.1	0.53
	10–14	15.7	16.4	3.1	0.54
	15+	16.2	17.2	3.1	0.54
p-values		0.65	0.59	0.99	0.96
Binge drinking in	0	16.1	16.9	3.1	0.55
first trimester	1–4	15.7	16.5	3.0	0.50
(5 drinks or more)	5+	14.9	15.9	3.3	0.59
p-values		0.07	0.15	0.32	0.10
Alcohol intake in	0	16.3	17.0	3.0	0.56
first trimester	1–4	16.2	16.9	3.2	0.53
(drinks/week)	5–9	15.6	16.7	3.0	0.53
	10+	16.1	16.4	3.1	0.59
p-values		0.18	0.63	0.09	0.14
Alcohol intake in	0	16.0	16.9	3.0	0.54
1st + 2nd trimester	1–4	16.0	16.7	3.1	0.54
(drinks/week)	5–9	15.9	16.8	3.1	0.53
	10+	15.1	16.4	2.9	0.56
p-values		0.46	0.86	0.53	0.87
No. of observations	222	222	203	220	

p-values: analysis of variance, between groups

with a short palpebral fissure, and it was the only measure which consistently had the expected association with the other facial morphologies that have been associated with high alcohol consumption. It is believed that above a certain intake, alcohol interacts with the development of the facial bones. All of the women studied were 'social drinkers', most were well educated and lived in reasonable similar social circumstances with good access to health care. None reported drug abuse and none had the appearance of a drug abuser or alcoholic. Quite a large proportion were smokers, but alcohol and smoking habits were not closely correlated.

Among French women with a fairly high alcohol consumption more facial (FAS) characteristics were associated with alcohol consumption (3). Computer analyses of photographs of selected small groups of women with different types of abuse have revealed FAS characteristics among the alcohol users (4). Prenatal cephalometric analyses by ultrasound have indicated that the facial characteristics may be identifiable very early in pregnancy (5).

Landmark analyses of photographs (snapshots) have been shown to have a reasonable sensitivity and specificity in diagnosing FAS (4), but a word of warning is justified. It is extremely difficult to obtain pictures of children under strictly controlled circumstances and to some extent the measurements have to rely upon subjective elements. Even when disregarding the measures based upon photos in profile, a far from perfect correlation was found between the two recorders, despite the use of the same pictures and the same set of instructions. The correlation coefficients between the two independent observers ranged from 0.2 (*e*, Fig. 1) to 0.8 or 0.9 (*a* and *f*, Fig. 1). Without doubt, the magnitude of the effects is vulnerable to random measurement error, which most likely attenuates the associations and reduces the potential of

Table IV. *Association between alcohol consumption in pregnancy and selected facial characteristics. Regression coefficients (B) and their standard error (SE) (Multiple linear regression) Newborns. All measurements in standardized units*

Alcohol consumption		Palpebral fissure		Nose upper lip distance	Root of the nose
		both eyes	right eye		
Alcohol intake before pregnancy drinks/week	B	0.03	0.02	−0.01	0.002
	SEB	0.05	0.04	0.01	0.002
Binge drinking in first trimester (5 drinks or more, no. of times)	B	−0.19	−0.19	−0.01	0.002
	SEB	0.11	0.09	0.02	0.003
Alcohol intake in first trimester (drinks/week)	B	0.01	0.00	0.02	0.000
	SEB	0.08	0.07	0.01	0.002
Alcohol intake in 1st+2nd trimester (drinks/week)	B	0.10	0.05	0.01	0.000
	SEB	0.08	0.07	0.01	0.002

Multiple regression: alcohol variables coded with median values within the categories. Mother's height, age, smoking, coffee, and dietary habits included in the model

the study. Perhaps it would be possible to restrict measurement variation if a rating scale of FAS were used (6).

If the relevant exposure time window is short, the underlying effect of a proper timed alcohol exposure on facial morphology could in fact be very strong.

A previous study has shown that smoking is related to typical FAS morphology (2) but this association was not seen in the present study. Coffee drinking,

Table V. *Association between alcohol consumption in pregnancy and selected facial characteristics. Regression coefficients (B) and their standard error (SE) (Multiple linear regression). 18 months old children. All measurements in standardized units*

Alcohol consumption		Palpebral fissure		Nose upper lip distance	Root of the nose
		both eyes	right eye		
Alcohol intake before pregnancy drinks/week	B	−0.02	0.01	−0.00	0.000
	SEB	0.04	0.04	0.01	0.002
Binge drinking in first trimester (5 drinks or more, no. of times)	B	−0.04	−0.04	0.02	−0.003
	SEB	0.08	0.08	0.02	0.005
Alcohol intake in first trimester (drinks/week)	B	0.05	−0.05	−0.01	−0.006
	SEB	0.05	0.06	0.02	0.004
Alcohol intake in 1st+2nd trimester (drinks/week)	B	−0.06	−0.04	−0.01	−0.002
	SEB	0.06	0.06	0.02	0.004

Multiple regression: alcohol variables coded with median values within the categories. Mother's height, age, smoking, coffee, and dietary habits included in the model

however, was significantly associated with a short nose to upper lip distance. Birth weight was, as expected, closely related to most of the measures in the newborns. After adjusting for birth weight, the association between binge drinking and short palpebral fissure was not statistically significant. Adjusting for birth weight will on the other hand overadjust, since fetal growth is most likely retarded by alcohol exposure (1). It has been suggested, however, that the facial morphology in FAS reflects retarded neural growth, since short palpebral fissures appear to be the most consistent physical feature noted in FAS (7). The eye is neutral and its size may reflect a deleterious effect of alcohol on the developing central nervous system, through it might also reflect a retarded fetal growth, which is also part of FAS.

Missing photographs were a problem in this study but it is very unlikely that they caused selection bias, since their absence was unrelated to alcohol consumption and was most likely unrelated to facial morphology. Regarding newborns, a short stay at the hospital after birth could increase the risk of being unavailable for an appointment with the photographer. In the second stage, the only reason for missing photos was that the camera was out of order during a given period of time.

The facial characteristics found in this sample were indeed minor and will probably never be recognized. None of the children had the FAS diagnosis and in fact the association between facial morphology at 18 months and alcohol in pregnancy was very weak and none of the measures reached statistical significance. However, this could have been due to the fact that age-related changes in facial characteristics tend to mask FAS-related features.

Any marker of child development should nevertheless be taken seriously and the findings do justify a warning at least against binge drinking in pregnancy, a warning that should be possible to heed even early in pregnancy, since most pregnancies nowadays are planned in many countries.

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REFERENCES

1. The EuroMac Study Group. Maternal alcohol consumption and its relation to the outcome of pregnancy and child development at 18 months. Int J Epidemiol 1992; 21, Suppl 1: 1–87.
2. Vitéz M, Korányi G, Gönczy E, Rudas T, Czeizel A. A semiquantitative score system for epidemiologic studies of fetal alcohol syndrome. Am J Epidemiol 1984; 119: 301–8.
3. Rostand A, Kaminski M, Lelong N, Dehaene P, Delestret I, Klein-Bertrand C, Querleu D, et al. Alcohol use in pregnancy, craniofacial features, and fetal growth. J Epidemiol Community Health 1990; 44: 302–6.
4. Sokol RJ, Chik L, Martier SS, Salari V. Morphometry of the neonatal fetal alcohol syndrome face from 'shapshots'. Alcohol & Alcoholism 1991; Suppl. 1: 531–4.
5. Escobar LF, Bixler D, Padilla LM. Quantitation of craniofacial anomalies in utero: Fetal alcohol and crouzon syndromes and thanatophoric dysplasia. Am J Med Genetics 1993; 45: 25–9.
6. Abel EL, Martier S, Kruger M, Ager J, Sokol RJ. Ratings of fetal alcohol syndrome facial features by medical providers and biomedical scientists. Alcohol Clin Exp Res 1993; 17: 717–21.
7. Jones KL, Hanson JW, Smith DW. Palpebral fissure size in newborn infants. J Pediatr 1978; 92(5): 787.

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