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Is there a fetal effect with low to moderate alcohol use before or during pregnancy?

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Abstract

***Study objective*—The aim was to investigate the effect of low or moderate alcohol consumption upon fetal outcome.**

***Design*—This was a prospective randomised cohort study with mother and infant follow-up sample stratified on level of maternal alcohol intake.**

***Setting*—A large maternity hospital in Western Australia.**

***Participants*—2002 randomly selected pregnant women were recruited over a 3 year period for questionnaire survey (19 mothers refused participation). From 665 women in a stratified subsample selected on the basis of prepregnancy alcohol consumption, 605 newborns were available for study.**

***Investigation and main results*—All 2002 women completed a comprehensive questionnaire on demographic, lifestyle (including diet), health, and obstetric factors. Of the 665 mothers who were followed through pregnancy, 605 liveborns were available at birth for measurement and detailed clinical evaluation. Low to moderate prepregnancy maternal alcohol intake was not associated with any untoward effect upon weight, length, head circumference at birth, or clinical well-being as indicated by Apgar score, respiratory distress syndrome, and overall clinical state. Other factors, particularly nicotine, were of much greater importance.**

***Conclusions*—This study fails to show any significant relationship between low to moderate prepregnancy maternal alcohol intake and newborn clinical status. The outcome suggests that cautionary advice to pregnant women warning that *any* alcohol taken during pregnancy is potentially harmful to the fetus is inaccurate and therefore probably counterproductive.**

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Much evidence has recently accumulated to indicate that heavy drinking mothers have offspring with proportional pre- and postnatal growth retardation, reduced intellect, a characteristic pattern of facial dysmorphisms, and many congenital malformations, the so-called "fetal alcohol syndrome".[1 2] Some authors have reported that alcohol effects also extend to the offspring of moderate or socially drinking mothers, with diminished fetal growth and increased neonatal risk factors such as respiratory distress.[3–7]

Many problems and complexities are inherent in assessing factors that influence pregnancy outcome in moderately drinking women. Self reporting of alcohol intake, variability of drinking patterns, and multiple beverages of differing strength complicate alcohol quantitation.[8] Other confounding variables include physiological features such as body weight, maternal smoking environment, other drugs and beverages consumed, diet, general lifestyle, maternal health, and obstetric factors.[7 9–13] Despite such acknowledged methodological difficulties several authoritative medical bodies have issued unequivocal statements saying that abstinence is the best policy and any alcohol taken in pregnancy is potentially harmful to the fetus.[14–18] It is probably unlikely that such warnings have any effect on the at risk heavier drinking group of mothers.[19–24] Such cautionary policy is not supported by the available scientific evidence and may have the effect of inducing or promoting guilt and suffering in a group of light or social drinking mothers, particularly when there has been a poor pregnancy outcome.[12 25–29]

The following prospective study was undertaken to investigate in detail a representative Australian population, mainly of moderate and social drinking pregnancy women, and to follow them through pregnancy. Newborn morphological data, birthweight, length and head circumference, and clinical status were used to evaluate birth outcome in relation to prepregnancy maternal alcohol consumption.

Methods

A full description of the method has been given elsewhere and a summary is provided here.[30]

SUBJECTS

Between January 1982 and December 1984 inclusive, 2002 consecutive pregnant women attending the public antenatal clinic of the main maternity hospital in Western Australia were recruited voluntarily to take part in the study. The women were not aware that the study was specifically related to alcohol consumption. Only 19 refused to participate. The majority (58%) were in the first trimester of their pregnancy at the time of recruitment, 33% were in the second trimester, and 8% were in the third trimester. The demographic characteristics of the selected cohort were compared with the Western Australian general obstetric population.[31] The sample contained a higher proportion of single mothers but otherwise was similar to the population of child bearing women in Western Australia. Subsequently, a sample of 605 mother-infant pairs was selected for follow up to obtain a

resulting cohort of alcohol abstainers through to more heavily drinking women.

QUESTIONNAIRE PROCEDURE AND CONTENT

A questionnaire was completed by those 2002 mothers entering the study.* The aims and purpose of the study and confidentiality of answers were explained to respondents. A study researcher was available if required to help respondents with the questionnaire. Answers to the smoking and drinking items were retested in 50 mothers four to six weeks after completing the first questionnaire. Reliability coefficients of 0·87 and 0·85 respectively on those items were thought acceptable.

The questionnaire consisted of items assessing demographic characteristics, prepregnancy height and weight, past obstetric history and information on "life style" factors which included details of diet, smoking, drugs and medicines. Alcohol intake information was obtained to enable quantification of alcohol measures. The average amount of beer, wine and spirits consumed by each woman in the study was calculated. These volumes, when added together, resulted in the absolute alcohol score,[32] and could also be used to derive Calahan's quantitative frequency-volume (QFV) and volume variability (VV) scores.[33] As a guide, two drinks of spirits, two glasses of wine, or two cans of average strength beer contain about 28 ml (1 oz) of absolute alcohol.

Questions on smoking required the women to report how many cigarettes per day and which brand they usually smoked. Daily intake of nicotine (mg) was then calculated.

SELECTION OF OBSTETRIC AND INFANT FOLLOW UP GROUPS

On the basis of stratifying by alcohol intake *prior* to pregnancy, 665 pregnant women were selected from the cohort of 2002 to represent a wide spectrum of drinkers. Of the 665 pregnant women, 60 were lost to follow up because of miscarriage (n=42), stillbirth (n=12), or neonatal death (n=6). We have already shown that there were no significant differences in mean cigarette and mean absolute alcohol consumption in women who had spontaneous abortion and stillbirths versus those with livebirths.[30]

Extensive maternal obstetric and medical details were obtained.[30] Newborn clinical information, morphological data, and birth details were obtained by the same paediatrician, who was unaware of the maternal drinking status. Both physical examination and neurobehavioural assessment were performed between 24 and 72 h after birth unless the infant was preterm, in which case evaluation took place at the appropriate postconceptional age.

DATA PREPARATION AND ANALYSES

The major dependent variables of interest in this study included: birthweight, head circumference, birth length, Apgar scores at one and five minutes, and respiratory distress syndrome. The major control variables include: gestational age, parity, prepregnancy maternal weight, height, age and education, and nicotine consumption. The independent variable was recalled total daily absolute alcohol intake before pregnancy. The table shows the distribution of these variables.

In our study design and analyses, we attempted to anticipate potential problems in constructing statistical models due to measurement and specification error, multicollinearity and heteroscedasticity.[34 35] The statistical treatment of choice was ordinary least squares multiple regression.[34 35]

The distributions of the independent variable (daily absolute alcohol consumption) and each dependent and control variable were examined for normality primarily to locate extreme cases and outliers. The distribution of absolute alcohol and nicotine was positively skewed owing to the number of women who abstained from drinking (n=145) and smoking (n=422). However, given the sample size and the relative robustness of multiple regression to violations of normality, we undertook no transformation of the data distributions.[35 36]

All models reported were further examined for possible multicollinearity by examining the tolerance of the independent variables entered in the model. The presence of heteroscedasticity was examined through analysis of residuals. We were satisfied that our data met the assumptions for analysis by multiple regression.

Each multiple regression proceeded in two steps. In step one the variance in the dependent variable of interest explained by the control variables was removed, and in step two absolute alcohol was entered.

Results

ADEQUACY OF FOLLOW UP SAMPLE

Several comparisons were made of the characteristics of the 665 mothers selected into the

Summaries of study variables

	Mean	SD	Median	Minimum	Maximum
			Dependent variables		
Birthweight (g)	3421·9	498·9	3390·3	2075	5290
Head circumference (cm)	34·8	1·4	35·0	32·5	43·3
Birth length (cm)	49·7	2·3	50·0	40·0	60·0
			Control variables		
Gestational age (weeks)	39·5	1·4	39·8	35	43
Parity (number)	2·2	1·3	1·9	1	7
Maternal weight (kg)	57·1	9·5	56·0	35·4	98·0
Maternal height (cm)	162·9	7·1	162·9	120	194
Age (years)	26·0	5·5	25·8	14	50
Education (level)*	4·6	1·0	4·6	2	6
Nicotine (mg)	34·9	66·9	0·5	0	385
			Independent variables		
Absolute alcohol	0·45	0·89	0·14	0	11·2

* A six level ordinal scale was used

** Copies of the questionnaire are available by contacting the first author (IW)*

follow up cohort compared with those who were not selected. Significantly more of those followed up were married as opposed to single ($\chi^2 = 22{\cdot}45$; df = 3; $p < 0{\cdot}001$). Otherwise there were no significant differences in maternal height, weight, age, educational level, number of previous pregnancies, rate of cigarette smoking, and ethnicity for those chosen for follow up and those not chosen. In addition there were no significant differences in the level of alcohol consumption both before and during pregnancy for the mothers of children followed versus those not followed.

Overall we were satisfied that our sampling procedure yielded a follow up group that was representative of the population of women presenting at a major metropolitan maternity hospital.

OUTCOMES

Absolute alcohol

The table shows the distribution of the absolute alcohol score in the 605 selected women. In practical terms, 24% of the women were abstainers, 50% had daily average alcohol consumption of less than one drink, 12% consumed one to two drinks per day, 5% consumed two to three drinks per day, 4% had three to four drinks, and 4% had over four drinks per day.

Birthweight

There was a significant association between birthweight and both maternal weight and nicotine consumption ($F_{7356} = 22{\cdot}8$; $p < 0{\cdot}0001$; $R^2 = 0{\cdot}22$), and when the effects of these variables were removed, there was no significant association between birthweight and absolute alcohol consumption ($F_{change} = 1{\cdot}9$; $p > 0{\cdot}05$; $R^2 = 0{\cdot}23$).

Birth length

There was a significant association between birth length and gestation, maternal weight, and nicotine consumption ($F_{7536} = 13{\cdot}9$; $p < 0{\cdot}0001$; $R^2 = 0{\cdot}15$). When the effects of these variables were removed, there was no significant association between birth length and absolute alcohol consumption ($F_{change} = 1{\cdot}49$; $p > 0{\cdot}05$; $R^2 = 0{\cdot}15$).

Head circumference

There was a significant association between head circumference and maternal weight and gestation ($F_{7536} = 14{\cdot}5$; $p < 0{\cdot}0001$; $R^2 = 0{\cdot}15$). When the effects of these variables were removed there was no significant association between head circumference and absolute alcohol consumption ($F_{change} = 0{\cdot}003$; $p > 0{\cdot}05$; $R^2 = 0{\cdot}15$).

Apgar scores

No significant associations were found between Apgar scores at one and five minutes and absolute alcohol consumption when adjusted for the control variables.

Respiratory distress

Fifty three infants were recorded as having mild to moderate respiratory distress (none was severe). There was a significant association between respiratory distress syndrome and gestation and nicotine consumption ($F_{7536} = 4{\cdot}13$, $p < 0{\cdot}001$; $R^2 = 0{\cdot}05$). When the effect of these variables was removed, there was no significant association between respiratory distress syndrome and level of absolute alcohol consumption ($F_{change} = 0{\cdot}03$; $p > 0{\cdot}05$; $R^2 = 0{\cdot}05$).

Type of beverage

Each of the above models was studied using the individual beverage scores for beer, wine or spirits in an attempt to determine whether type of beverage consumed had any specific effects on the reported dependent variables. As before, two step multiple regressions were employed adjusting for control variables, and then entering the beverage of interest.

No significant associations between birthweight, head circumference, birth length, Apgar scores and respiratory distress syndrome with beverage type were found.

Discussion

The data presented here indicate that newborns of mothers who drank light or moderate amounts of alcohol show no detrimental effects which can be attributed to such exposure. Public policy advising mothers that even small quantities of alcohol taken during pregnancy may potentially damage the fetus cannot be scientifically sustained and is likely to be counterproductive.

In excessive maternal alcohol intake it has long been observed that pre- and postnatal growth failure of weight, length, and head size are frequently seen, with an array of birth defects including a characteristic facies and psychomotor delay.[2 37 38] Reduction of in utero fetal growth is greater if heavy drinking is continued throughout pregnancy.[39–41] Chronically alcohol dependent women who are more likely to have clinically evident alcohol affected newborns also have a high morbidity and mortality associated with an advanced stage of alcohol related disease.[42–44] This present study, along with most other reports, fails to show any significant relationships between light and moderate maternal alcohol intake and fetal growth effect. These observations strongly support the views of Fabro who proposed that the adverse effects of alcohol in human fetal development follow a dose-response standard for teratogens.[45]

Of the cohort reported here, 49% were abstainers or light drinkers, 38% were moderate drinkers, and 13% consumed more than 28 ml (1 oz) of absolute alcohol daily. This is similar to other Australian studies of obstetric populations.[46 47] It is within the latter group of mothers who drink excessively that real fetal risks exist.

BIRTHWEIGHT AND LENGTH

This and a number of other studies of moderate drinking mothers have not shown alcohol to have a significant impact on fetal growth. These studies have several different methodologies, particularly in relation to alcohol quantitation, timing of interview, and the way in which potential confounding factors are treated.[12 46–56]

In this study cofactors such as smoking and maternal weight prior to pregnancy were significantly related to fetal growth, whereas low to moderate maternal alcohol consumption was not. Smoking has been found to be a significant contributor to reduced fetal growth, although there is debate as to whether its effect is additive or potentiates the effects of higher alcohol consumption.[47 49 51]

Few studies have shown that light to moderate alcohol intake produces significant intrauterine growth retardation. A widely quoted study by Little[6] which concluded that an average maternal consumption of one ounce (28 ml) of absolute alcohol daily would produce lower birthweight babies has been criticised on the basis that alcohol abusers could have accounted for most of the relationships discovered by the author.[27] A later study by the same author reported similar more striking reductions in fetal growth with as little as 10 g of absolute alcohol per day prior to pregnancy. The results have not been reproduced in other studies and the authors stated the sample to be small and unusual.[3]

HEAD CIRCUMFERENCE

This study found that moderate maternal alcohol consumption was not associated with reduced head circumference and that maternal weight before pregnancy and gestation were the important variables. This has been true of other studies, and smoking has often been cited as another significant variable.[12 46–48 50 51 54–56]

Davis *et al* studied 973 white women attending a Warwickshire antenatal clinic and who completed a self administered questionnaire on social class, smoking, and consumption of a number of beverages, including alcohol during pregnancy.[5] While admitting the limitations of the study methods, the authors still claim significantly reduced newborn head circumference in mothers who drank more than 20 ml of alcohol per day. They also recommended abstention from alcohol as the only safe measure in pregnancy.

NEWBORN CLINICAL STATUS

Newborn infants in our study were fully evaluated. Apgar scores, respiratory distress syndrome, and the absence of any significant correlation with maternal alcohol consumption were chosen for particular comment. Nicotine was found to be significantly associated with untoward effects on the newborn, as has previously been reported. Others have reported a statistically significant, though clinically irrelevant, association with lower Apgar scores in the newborn of mothers who consumed more than two drinks a day.[48 54]

CONCLUSION

In the attempt to tease out the aetiological association between alcohol and birth outcome, numerous methodological problems arise. They include many confounding variables such as maternal smoking, parity, ethnicity, gestation, socioeconomic status, weight at conception, diet, drug use and abuse, and medical and obstetric history.[3 10 30 37 46 57] Of these factors, smoking is undoubtedly the most powerful and consistent predictor of low birthweight, and often the most difficult to control statistically because it is strongly related to alcohol consumption. We believe that the data presented in this study have addressed most of the above problems, particularly by being prospective, population based, and by considering the major possible outcome variables in detail.

With no specific biological alcohol marker, the problems of alcohol quantitation, pattern of drinking, and differences in beverages, which are all dependent upon self reporting, are well recognised.[30] Heavy drinkers tend to underreport so that if fetal outcome of maternal alcohol drinking is observed against a sliding scale of rate of drinking this should mean merely a shift to left and not a loss of effect, if there is one to be observed. In this study alcohol quantitation was reliable, as it was assessed by retesting a cohort subgroup and by evaluating alcohol intake at a time when recall should have been more accurate and uninfluenced by a knowledge of outcome.

This study, like most similar studies, fails to show any significant relationship between low to moderate maternal alcohol intake and fetal outcome. Whether total abstinence is the best advice to pregnant mothers is therefore questionable. Where this knowledge or advice has been widely and successfully imparted to the community, those mothers in the heavier drinking groups continue to drink,[3 9] while unnecessary guilt and anguish is engendered in light and occasional drinking women.[12 26 29 40 41 51]

To recommend responsible drinking habits is not to advocate drinking in pregnancy. It is better to promote the idea that women should avoid binge and heavy drinking if they are planning for pregnancy. There should be greater emphasis on detecting the heavier drinking obstetric patient. Evidence indicates that appropriate early intervention can be effective in improving the prognosis for fetus and mother.[40 51]

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