

Measurement of direct ethanol metabolites suggests higher rate of alcohol use among pregnant women than found with the AUDIT—a pilot study in a population-based sample of Swedish women

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BACKGROUND AND OBJECTIVE

US studies indicate that approximately 3.5% to 22% of pregnant women report alcohol consumption during pregnancy, of whom 0.2% to 1% are classified as heavy drinkers. Among respondents to an anonymous survey in Sweden, some 30% of pregnant women continue to use alcohol while pregnant; 6% report intake of alcohol 2-4 times per month.

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OVERVIEW

Testing for biomarkers of alcohol consumption increased the accuracy of a validated questionnaire in detecting potential users of alcohol during pregnancy.

Detecting alcohol use by pregnant women is an important step toward preventing alcohol-related birth defects. Although several questionnaires have been developed for this purpose, self-reported intake of alcohol during pregnancy is prone to underreporting in terms of both the level of consumption and the number of subjects reporting use. Biochemical markers provide health care professionals with useful additional information.

Currently available biological markers that might be useful for such purposes include a number of nonoxidative direct ethanol metabolites in serum, urine, and hair, including fatty acid ethyl esters (FAEEs), ethyl glucuronide (EtG), and ethyl sulfate (EtS). Each remains positive in serum and urine for a characteristic length of time after the cessation of ethanol intake; for example, FAEEs remain in serum for up to 24 hours and EtG remains in urine for up to 5 days. Moreover, EtG and FAEE can be detected in hair for months, although the deposition of hair is affected by hair care and the use of hair products. Both markers have the potential to distinguish between light, infrequent drinking and heavy, repeated drinking.

EtS, a direct ethanol metabolite, was recently evaluated with promising results. It can be detected in urine up to 36 hours after alcohol intake. Studies evaluating the efficacy of these markers for detecting alcohol use and abuse in pregnant women are lacking.

The purpose of our population-based pilot study was to learn whether biomarkers of alcohol consumption provide more accurate determinations of alcohol use than the use of a validated questionnaire alone.

MATERIALS AND METHODS

Women visiting Uppsala University Hospital for a routine second-trimester ultrasound screening consecutively during the study period were approached and asked whether they would agree to participate in the study. Approximately 97% of pregnant Swedish women undergo routine ultrasound examination at 16-18 weeks of gestation. Because Uppsala has no other ultrasound screening facility, our sample was population based.

Subjects were informed that all data collected in the study would be recorded anonymously. Participants completed the Alcohol Use Disorders Identification Test (AUDIT), a 10-item questionnaire that was developed by the World Health Organization for identifying alcohol use disorders and that has been validated for use in pregnant women. Response options for each item ranged from 0 to 4, resulting in a total possible score of 40. Normally the cutoff point for heavy drinking is set at 8 or greater, but a cutoff point of greater than 5 has been suggested for women. In our study, subjects were asked to respond to conditions present during the current pregnancy.

A urine and hair sample was collected from the participating women. Demographic and behavioral characteristics were recorded, as were neonatal outcome variables. We determined which women had attended the ultrasound screening during the study period and compared demographic variables of included vs ex-



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TABLE
Selected demographic, behavioral, and medical characteristics of included subjects, subjects declining participation, and missed subjects

	Included subjects (n = 100) ^a	Subject not consenting to participate (n = 5)	Subjects missed due to intense patient flow (n = 10) ^a
Age	30.8 ± 5.0	30.2 ± 6.4	27.4 ± 2.5
Body mass index, kg/m ²	24.4 ± 4.3	24.5 ± 2.9	25.1 ± 6.7
Parity	0.9 ± 0.9	1.0 ± 0.7	1.1 ± 0.7
Married or cohabiting	98 (98.0%)	4 (80.0%)	9 (90.0%)
Socioeconomic status			
Professional employee	57 (57.0%)	2 (40.0%)	3 (30.0%)
Laborer	20 (20.0%)	1 (20.0%)	4 (40.0%)
Unemployed/studying	23 (23.0%)	2 (40.0%)	3 (30.0%)
Smokers during pregnancy	4 (4.0%)	1 (25.0%)	1 (11.1%)
Alcohol consumption prior to pregnancy			
Rarely/never	60 (62.6%)	2 (50.0%)	9 (90.0%)
Less than once a week	30 (31.3%)	1 (25.0%)	0
More than once a week	6 (6.1%)	1 (25.0%)	0
Chronic disease	7 (7.0%)	0	0

^a Medical records could not be found for 3 of the included subjects and from 1 of the missed subjects. Certain data from these subjects could be retrieved from other sources. Missing data for alcohol consumption and smoking in the medical records were prevalent in 4-20% of cases; only valid percent is given in the table. No statistical analyses have been performed.

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cluded (whether not asked or not consenting to participate) subjects.

Urine tests were performed for the presence of EtG and EtS. Gas chromatography/ mass spectrometry tests were performed on hair samples for the presence of FAEEs and EtG. For FAEE in hair, the limit of detection was 0.7 pg/mg, and the limit of quantitation was 2.3 pg/mg. For EtG in hair, a cutoff of 7 pg/mg was used to differentiate between teetotalers and social drinkers (up to 40 g alcohol per day) and 25 pg/mg to differentiate social drinkers from excessive and repeated alcohol drinkers.

RESULTS

Of the 120 women found to be eligible for the study, 109 were asked to participate. Eleven women were not approached because the staff was too busy to enroll them when they arrived for their ultrasound

scans. Among the women asked to participate in the study, 1 was excluded because of a missed abortion and 5 declined. Of the latter group, 2 said they consumed no alcohol for religious reasons; 3 gave no reason. Thus, 95.3% of those asked to participate did so. As a result, the study population included 103 women.

The Table provides demographic data. The majority of women (n = 94, 91.3%) stated that they had never consumed alcohol during the current pregnancy; 9 women (8.7%) said they had. Of the latter group, 6 women (5.8%) said they had consumed alcohol once a month or less and 3 (2.9%) that they had done so on 2-4 occasions per month.

Among the 9 women who admitted to alcohol use during the current pregnancy, 7 had consumed the equivalent of 1-2 glasses of wine on each occasion; 1, the equivalent of 3-4 glasses of wine; and 1 did not specify.

Of the 103 urine samples tested, only 1 was positive for EtG. This subject had indicated use of alcohol once or twice per month during the current pregnancy in the AUDIT questionnaire. None of the subjects were positive for urine EtS.

In hair testing, 19 cases tested positive: 16 for EtG and 3 for FAEEs. Among the 16 samples positive for EtG, 12 had values of 7-25 pg/mg, considered to reflect light, infrequent drinking (20-40 g or less ethanol per day). Two of the subjects whose hair was positive for EtG and none of those whose hair was positive for FAEE acknowledged ongoing drinking in the AUDIT questionnaire.

In all, 26 subjects (25.2%) were identified as possible alcohol consumers during pregnancy by the combined use of AUDIT and direct ethanol metabolite test results. Six subjects were positive on AUDIT only; 14 subjects were positive for hair EtG only; 3 for hair FAEEs only; and 3 for both AUDIT and any biomarker (2 had positive hair EtG; 1 was positive for urine EtG). Of the 7 subjects whose hair levels of EtG or FAEE were highly suspicious for heavy drinking, only 1 admitted to ongoing alcohol consumption in the AUDIT questionnaire.

COMMENT

In a population of pregnant women whose alcohol consumption is low and/or limited to rare occasions, the combined use of AUDIT and direct ethanol metabolites could add potentially useful information regarding alcohol use. Furthermore, screening for alcohol consumption with questionnaires and biochemical markers is accepted by most pregnant women, at least when samples are collected anonymously.

In all, our sample identified 25% of subjects as possible alcohol consumers. Of those with positive biomarkers, 3 had acknowledged any alcohol use in the AUDIT questionnaire, although at very low levels. Furthermore, of the 7 subjects in the current study whose EtG or FAEE levels in hair that were highly suspicious for heavy drinking, only 1 had admitted to ongoing alcohol consumption in the AUDIT questionnaire. Clearly, subjects may underestimate their alcohol use

and/or be unwilling to disclose their drinking habits during pregnancy. Although negative results for direct ethanol metabolites are not considered proof of abstinence, we argue that when positive, they provide strong evidence for moderate or excessive drinking.

The findings of our study should be considered in the planning of any future study on adverse alcohol-related fetal outcomes. The combined use of self-reported alcohol consumption and direct ethanol metabolites provides a more accurate evaluation of

maternal drinking patterns than either approach alone. The use of both tests not only identifies more subjects at risk but also can be used to estimate the extent of alcohol consumption in individuals: both FAEE and EtG levels in hair can distinguish between light, infrequent drinking and heavy, repeated drinking.

CLINICAL IMPLICATIONS

- Administering the Alcohol Use Disorders Identification Test questionnaire

and laboratory testing of hair and urine samples for ethanol metabolites detected more potential alcohol users in a population of pregnant women than did any of these tests alone.

- Therefore, we recommend using multiple tests in determining the extent of pregnant women's alcohol ingestion.
- Investigators planning future studies on adverse alcohol-related fetal outcomes should consider this recommendation. ■

Body mass index and weight gain prior to pregnancy and risk of gestational diabetes mellitus

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BACKGROUND AND OBJECTIVE

Gestational diabetes mellitus (GDM), defined as any degree of glucose intolerance with onset or first recognition during pregnancy, complicates 4-7% of pregnancies in the United States.

Few modifiable risk factors for GDM are known. The known risk factors for GDM seem to mirror the established predictors of type 2 diabetes mellitus (T2DM). Obesity is the major identified modifiable risk factor associated with GDM to date. Several studies suggest that weight change, especially during various periods of adult life, is associated

OVERVIEW

Results of a nested case-control study suggest that weight gain during the 5 years before pregnancy is associated with an increased risk of gestational diabetes mellitus.

with increased risk of T2DM. However, data are limited on the role of weight change before pregnancy and risk of GDM.

No prior studies have examined weight change during the years shortly

before pregnancy and risk of GDM. If weight gain shortly before pregnancy increases the risk of GDM, preconception care could include advising women to avoid weight gain, especially those otherwise at high risk of GDM.

In a nested case-control study, we examined the rate of weight change during the 5 years immediately before pregnancy and risk of GDM among women who delivered singleton live infants at a large US group practice prepaid health plan and who received uniform screening and a standardized diagnostic test for GDM.

MATERIALS AND METHODS

The study setting was the Kaiser Permanente Medical Care Program of Northern California (KPMCP-NC), which currently provides comprehensive medical services through 15 hospitals and 23 outpatient clinics to more than 3 million members located in a 14-county region in northern California. The KPMCP-NC membership, which represents approximately 30% of the surrounding population, is demographically, ethnically, and socioeconomically representative of the population living in the same geographic area except in underrepresenting the very poor and the very wealthy.

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