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Estimated Prevalence of Harmful Alcohol Consumption in Pregnant and Nonpregnant Women in Saxony-Anhalt (NorthEast Germany) Using Biomarkers

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Background: Alcohol consumption is commonly accepted in Western societies and is a known risk factor in pregnancy, which could lead to fetal alcohol spectrum disorders (FASDs). Prevalence of alcohol consumption during pregnancy is mostly unknown. Prevalence estimates in publications based on questionnaires are limited by possible underreporting due to social stigmatization. The aim of this study was to estimate the prevalence of harmful alcohol consumption in a large cohort of pregnant women using different biomarkers related to alcohol consumption and compare the findings with those of nonpregnant women

Methods: Routine parameters known to be influenced by alcohol consumption (γ-glutamyltransferase, GGT; carbohydrate-deficient transferrin, CDT/%CDT; mean corpuscular/cell volume, MCV; combined parameter of GGT and %CDT, GGT-CDT) were analyzed in serum samples of 2,182 pregnant women and 743 non-pregnant, age-matched females. Data were tested for (i) differences between pregnant and non-pregnant women and (ii) changes across the 3 trimesters of pregnancy.

Results: Prevalence rates differ greatly according to the parameter and cutoff, which reflects the limitations of assessing alcohol consumption with biomarkers. The prevalence of harmful alcohol consumption on the basis of a single or several elevated parameters was 13.8% (95% CI: 12.4 to 15.2) in pregnant women and 18.6% (95% CI: 15.8 to 21.4) in non-pregnant women, though 85.0% of the elevated measurements were attributable to an isolated elevation in %CDT only. Using GGT-CDT as the parameter with the highest specificity according to the literature, the estimated prevalence of harmful alcohol consumption in pregnancy is 0.5% (95% CI: 0.2 to 0.7).

Conclusion: Estimated prevalence rates differ greatly with respect to the biomarkers and cutoffs used. The use of CDT/%CDT alone appears to overestimate harmful alcohol consumption during pregnancy.

Key Words: Alcohol, Pregnancy, Prevalence, %CDT, GGT, GGT-CDT Ratio.

ALCOHOL CONSUMPTION IS commonly accepted in Western societies. 66.5% of the female population in Germany reported consumption of alcohol in the last 30 days (Atzendorf et al., 2019), 24.6% reported binge drinking (5 or more drinks (>70 g ethanol [EtOH]) in one day, in the last 30 days), and 19.7% consumed 12 g EtOH or more every day. Consumption of alcohol is not just known to be a risk factor for diseases such as liver cirrhosis, hepatocellular carcinoma, or pancreatitis (GBD, 2016 Risk Factors Collaborators, 2017), and it is also known to cause fetal alcohol spectrum disorders (FASD) if consumed during pregnancy (Kraus et al., 2019). FASD summarizes all teratogenic effects of intrauterine alcohol exposure, where fetal alcohol syndrome (FAS) is the most severe form, comprising typical facial dysmorphias, neurodevelopmental and growth deficits, and variable congenital malformations (Kraus et al., 2019). The underlying pathophysiological mechanisms of FASD are still incompletely understood. It seems that EtOH enhances the formation of reactive oxygen species (ROS), which leads to "macromolecular oxidative damage," causing DNA, RNA, and histone modifications as well as dysfunctional proteins. All these alterations could lead to

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teratogenesis resulting in FASD and FAS (Bathia et al., 2019). The prevalence of alcohol consumption in pregnancy, FASD, and FAS is widely unknown or was estimated in the past using questionnaires, which are showing difficulties based on possible underreporting due to social stigmatization (Göransson et al., 2003). Popova et al. estimated a global prevalence of alcohol consumption in pregnancy of 9.8% (European estimate: 25.2%, 95% CI: 21.6–29.6) and a prevalence of FAS of 15 per 10,000 (European estimate: 37.4 per 10,000, 95% CI: 24.7–54.2) (Popova et al., 2017). Another systematic review estimated a global prevalence of FASD of 77 per 10,000 (Europe estimate: 198 per 10,000) (Lange et al., 2017). Several laboratory markers are associated with alcohol consumption and therefore are used routinely to monitor drinking behavior. The most used biomarkers are carbohydrate-deficient transferrin [as absolute concentration (CDT) and in relation to total transferrin (% CDT)], gamma-glutamyltransferase (GGT), and mean corpuscular/cell volume (MCV). Elevated measurements of %CDT were found in people with a daily alcohol consumption of 50–80 g for at least 1 week (Stibler, 1991) and may also be able to detect binge drinking (Howlett et al., 2017). For GGT, Hietala et al. found significantly higher concentrations in case of 40 g or more alcohol ingestion per day (Hietala et al, 2005). Notably, these biomarkers differ greatly with respect to sensitivity and specificity. GGT is reported to have sensitivity of up to 95% for the detection of ingestion of 60g or more per day for several months (Andresen-Streichert et al., 2018), which is higher than the sensitivity of %CDT (46-90%). Under the same circumstances, %CDT was reported to be more specific for the detection of alcohol consumption than GGT (70–100% vs. 18–93%) due to GGT elevation in cases of nonalcoholic liver diseases or toxic effects of different drugs (Andresen-Streichert et al., 2018). To elevate sensitivity without losing specificity, the combined parameter GGT-CDT was established (Hietala et al., 2006). For assessing the capability of these parameters for estimating the prevalence of alcohol consumption in pregnancy, Shipton and colleagues (2013) conducted a pilot study and showed that CDT is able to detect and monitor "hazardous" alcohol consumption in pregnancy. Howlett and colleagues (2020) measured %CDT and GGT in 600 random blood samples of women in early pregnancy in northeast England and estimated a prevalence of elevated measurements of 1.7% (95% CI: 0.7 to 2.9) based on %CDT and of 4.2% (95% CI: 2.6 to 5.9) based on GGT. In order to evaluate the prevalence of harmful alcohol consumption during pregnancy in Saxony-Anhalt (North Germany), 5 laboratory biomarkers (CDT, % CDT, GGT, MCV, and GGT-CDT) were analyzed in 2,182 pregnant and 743 non-pregnant age-matched females and statistically compared between (i) pregnant and non-pregnant women and (ii) for changes in the 3 trimesters of pregnancy.

MATERIALS AND METHODS

Study Design and Study Population

Study design was composed of retrospective and prospective parts. Frozen backup serum samples from pregnant women (undergoing toxoplasma gondii serology testing), which were stored for 12-15 months at −20°C, were sorted out for enough specimen volume, visible icteric, lipemic, or hemolytic staining and for the measurement of MCV from the same venipuncture (Fig. 1). Specimens that met these requirements were used for analyzing GGT, CDT, and %CDT. Each sample also received a Hemolysis-Icterus-Lipaemia-Check (HIL-Check) to exclude preanalytical interferences by these 3 conditions. Values for MCV were taken from the measurement of the corresponding blood sample at day of sample entry (12 to 15 months in the past; 05/2016–09/2017). Elevated MCV values were further assessed by the measurement of holotranscobalamin (HTC) to rule out vitamin B12 deficiency. Borderline or reduced HTC concentrations, indicating vitamin B12 deficiency, resulted in exclusion of the case from study cohort. Samples whose measurements were not possible or incomplete were also excluded from study cohort. All samples were barcoded at 2 levels to ensure anonymous setting of the analysis as recommended by the Local Ethics Committee of the Land Saxony-Anhalt in its approval (No. 56/17). According to this approval, no declaration of consent by participants was necessary. In total, 2,182 samples from pregnant women could be measured and further analyzed statistically. The control samples were selected from age-matched women from whom MCV was analyzed and pregnancy was excluded by laboratory parameters. The number of control samples (n = 743) was chosen to match the average sample numbers of pregnant women in the different trimesters. Control samples were frozen to −20°C to get the same preanalytical conditions as the samples of pregnant women. According to the approval of the Local Ethics Committee of the Land Saxony-Anhalt, no declaration of consent was obtained from this cohort either. All together, serum samples of 2,182 pregnant women and 743 non-pregnant age-matched females were analyzed (details presented in Table 1). Information about drinking habits or preexisting chronic diseases was not available.

Measurement Methods

CDT and transferrin were measured using the immunonephelometric N Latex CDT and the N Antisera to Human Transferrin assay on BN ProSpec analyzer platform by Siemens (Siemens Healthcare Diagnostics Products, Marburg, Germany); %CDT was calculated automatically. For quantification of GGT, the standardized (IFCC/Szasz) GGT-2 kinetic assay on Roche cobas c analyzer was applied (Roche Diagnostics, Mannheim, Germany). Calculation of MCV (from measured hematocrit and erythrocyte count) was done using the fully automated routine hematology analyzers by Sysmex (Sysmex, Germany, Norderstedt, Germany). Equation of GGT-CDT was done using the formula published by Hietala et al. (2006) as follows: GGT-CDT = 0.8 * ln(GGT) + 1.3 * ln(% CDT).

Cutoffs

Cutoffs used to estimate the prevalence rate of harmful alcohol consumption on the basis of biomarkers were selected from 2 publications by Niemelä et al that used the same test kit to measure % CDT as used in this study (Niemelä et al., 2016b; Niemelä et al., 2016a). The cutoff for %CDT (≥ 1.79) reflects the mean + 2 standard deviations from women not consuming alcohol. Due to the high degree of international standardization of GGT assays, using cutoffs derived by studies based on the same test kit was refrained. For GGT and GGT-CDT, the cutoffs with the highest specificity were selected.

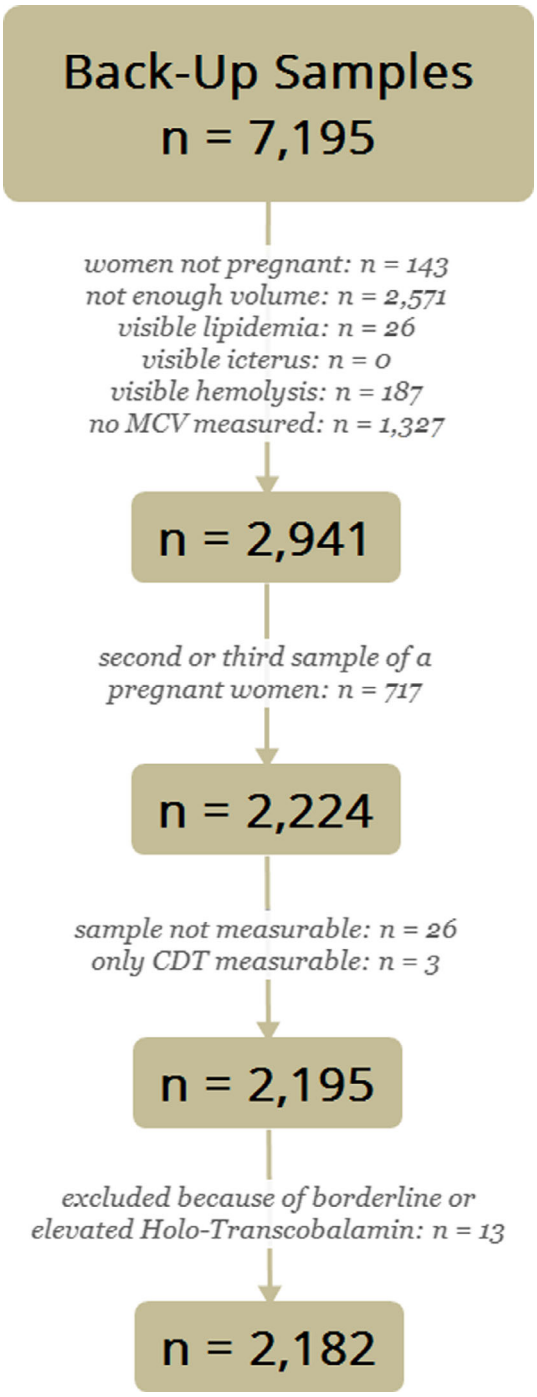

Fig. 1. Selection of specimens. Numbers of backup samples sorted out for enough specimen volume, visible icteric, lipemic, or hemolytic staining, measurement of MCV from the same venipuncture, exclusion of multiple measurements from one woman, not or incompletely measurable samples, and holotranscobalamin concentrations indicating vitamin B12 deficiency.

Statistical Analysis

Statistical analysis was done using R (version 4.0.3; Vienna, Austria). Testing for normal distribution was performed by using the Shapiro–Wilk test. Since none of the parameters analyzed were normally distributed, non-parametrical tests were used. Prevalence rates were compared by using the chi-squared test. Calculation of confidence intervals was done by using the normal approximation. For comparisons of means between 2 independent groups, the Mann–Whitney U-test was applied. For comparison of means between more than 2 independent groups, the Mann–Whitney U-test with correction using the Bonferroni adjustment method was used. The level of significance was set to 0.05 ($p < 0.05$ was considered statistically significant). Due to the exploratory character of the study, no further adjustment for considering several endpoints in parallel has been applied.

Table 1. Study Population Characteristics

Characteristics	Pregnant women	Non-pregnant women
Evaluable samples (*n*)	2,182	743
Age range (years)	14 to 46	15 to 43
Age mean (years)	29.5	29.8
Age standard deviation (years)	4.8	5.2
Gestational age (*n*) (reported or estimated)	First trimester: 1,356 Second trimester: 551 Third trimester: 275	-

Trimester were defined as first trimester from 1st to 13th gestational week, second trimester from 14th to 26th gestational week and third trimester from 27th gestational week to delivery.

RESULTS

The analysis of 5 alcohol consumption-associated biomarkers in both groups revealed highly significant differences for 4 parameters, whereas MCV was found to be similar with a tendency of higher values for pregnant compared with non-pregnant women (Table 2). MCV values were therefore not further evaluated.

Prevalence rates of harmful alcohol consumption based on biomarkers were calculated for both pregnant and non-pregnant women on the basis of previously published cutoffs as shown in Table 3. Estimates show prevalence rates between 0.5% and 11.9% for pregnant women and between 3.8% and 11.4% for non-pregnant women (details presented in Table 3). 301 pregnant (13.8%) and 138 (18.6%) non-pregnant women demonstrated at least one elevated biomarker (Tables 3 and 4). Various constellations of one or more elevated biomarker for the prevalence estimates are shown in Table 4.

Trimester-specific analysis of biomarkers

Further analysis estimated prevalence rates based on biomarkers for each trimester of pregnancy. GGT and GGT-CDT values showed a decreasing trend, whereas % CDT values were found to be increased (Table 5). The cutoff for %CDT showed a higher prevalence of elevated measurements in the second and third trimesters in comparison with the first trimester. Furthermore, a significant increase in % CDT values for the second trimester compared with the first trimester (mean: 1.43% vs. 1.57%, $p < 0.001$, *U*-test) was demonstrated, whereas the second trimester and the third

Table 2. Values of Alcohol Consumption-Associated Biomarkers in Pregnant and Non-pregnant Women

Characteristics	Pregnant women (n = 2,182)	Non-pregnant women (n = 743)	p-value
CDT median (range)	**44.5** (21.5 to 99.8)	**39.7** (21.8 to 80.2)	–
CDT mean (SD)	**47.0** (13.8)	**40.3** (9.4)	<0.001
%CDT median (range)	**1.47** (0.83 to 2.47)	**1.52** (0.96 to 3.60)	–
%CDT mean (SD)	**1.48** (0.25)	**1.53** (0.24)	<0.001
GGT U/l median (range)	**11.4** (1.2 to 163.2)	**16.2** (5.4 to 814.8)	–
GGT U/l mean (SD)	**13.8** (9.7)	**22.5** (35.4)	<0.001
GGT-CDT median (range)	**2.45** (0.34 to 4.67)	**2.77** (1.66 to 5.89)	–
GGT-CDT mean (SD)	**2.47** (0.44)	**2.84** (0.49)	<0.001
MCV fl median (range)	**86** (57 to 133)	**85** (60 to 106)	–
MCV fl mean (SD)	**86** (5)	**85** (5)	0.067

Data are presented as medians and complete range of values and means including standard deviation (SD). Statistical analysis was performed by the Mann–Whitney U-test.

Table 3. Estimated Prevalence Rates of Harmful Alcohol Consumption Based on Biomarkers in Pregnant and Non-pregnant Women

Biomarker	Cutoff [Ref]	Sens (%)	Spec (%)	Pregnant (all) n = 2,182 % (95% CI)	Non-pregnant n = 743 % (95% CI)	p
%CDT	≥1.79 [2]	[a]	96.4	11.9 (10.5 to 13.2)	11.4 (9.2 to 13.7)	0.75
GGT U/l	≥40 [1]	33.0	96.4	2.1 (1.5 to 2.7)	8.1 (7.0 to 9.2)	<0.001
GGT-CDT	≥3.80 [1]	33.5	98.0	0.5 (0.2 to 0.7)	3.8 (2.4 to 5.1)	<0.001
One or more elevated biomarker	%CDT: ≥ 1.79 GGT: ≥ 40 GGT-CDT: ≥ 3.80	–	–	**13.8 (12.4** to **15.2)**	**18.6 (15.8** to **21.4)**	0.002

[a]Sensitivity was reported in dependence of birth of a child with (39.5%) or without FAS (4.2%). Rows 2-4 present cutoffs, sensitivity, and specificity, respectively, together with corresponding publication that were used for calculation of prevalence rates (%) that are shown as an estimate with 95% confidence interval. Statistical analysis was performed by the chi-squared test. [1] Niemelä and colleagues (2016a), [2] Niemelä and colleagues (2016b).

Table 4. Observed Constellations of One or More Elevated Biomarkers for Both Pregnant and Non-pregnant Women

Constellation	Pregnant n = 2,182 [n (% of all elevated)]	Non-pregnant n = 743 [n (% of all elevated)]
Isolated %CDT (≥1.79%)	**256 (85.0)**	76 (55.0)
Isolated GGT (≥40 U/l)	35 (11.6)	34 (24.6)
Isolated GGT-CDT (≥3.80)	0 (–)	0 (–)
GGT + GGT-CDT elevated	7 (2.4)	19 (13.8)
%CDT + GGT-CDT elevated	0 (–)	2 (1.5)
%CDT + GGT + GGT-CDT elevated	3 (1.0)	7 (5.1)
Sum of cases	301 (100.0)	138 (100.0)
Prevalence of elevated measurements (95% CI)	**13.8 (12.4–15.2)**	**18.6 (15.8–21.4)**

trimester as well as the non-pregnant women showed comparable levels of %CDT (medians: 1.56% vs. 1.55% vs. 1.52%) as shown in Fig. 2. To further evaluate the observed increase in %CDT from the first to second trimesters, analysis of absolute CDT revealed significantly higher values in pregnant women compared with controls (mean: 47.0 vs. 40.3 mg/l; $p < 0.001$, U-test; Table 2). Subanalysis in context to the 3 trimesters confirmed the known increase in absolute CDT during pregnancy (means: 40.7 vs. 54.9, $p < 0.001$; 54.9 vs. 62.2, $p < 0.001$; U-test) in dependence of gestational age (Fig. 3) as already published by Bakhireva et al (2012). GGT values were significantly lower in pregnant vs. non-pregnant women (mean: 13.8 vs. 22.5 U/l, $p < 0.001$, U-test; Table 2). Subanalysis concerning trimesters revealed a significant decrease from the first to second trimesters (mean: 15.9 vs. 10.5, $p < 0.001$, U-test) with comparable values between second and third trimesters (mean: 10.5 vs. 10.5, $p = 0.87$, U-test; Fig. 4). Similar pattern was observed for GGT-CDT between pregnant and non-pregnant women (mean: 2.47 vs. 2.84, $p < 0.001$, U-test; Table 2). GGT-CDT among the 3 trimesters demonstrated an almost identical pattern with significant reduction between first and second trimesters (mean: 2.55 vs. 2.35, $p < 0.001$, U-test; Fig. 5).

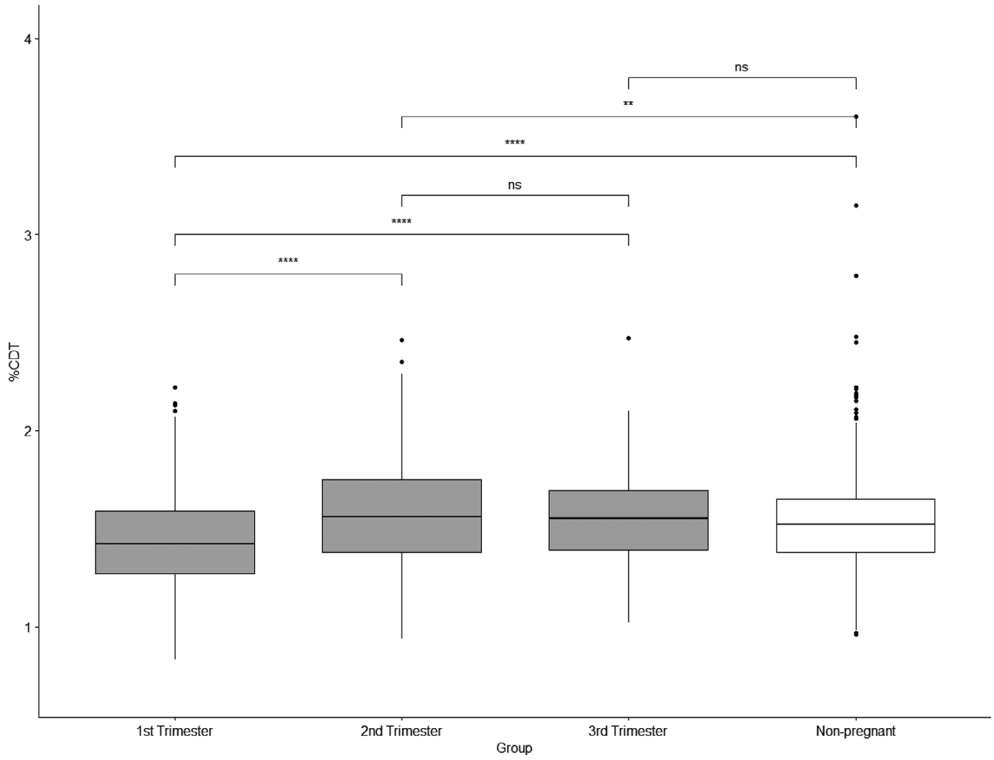

Fig. 2. %CDT in pregnant (gray boxes) and non-pregnant (white box) women. Data show a significant increase in %CDT from the first trimester to the second trimester. Second and third trimesters as well as non-pregnant women showed comparable levels of %CDT values. Significant and nonsignificant differences are marked as ****($p < 0.001$), **($p = 0.01$), and n.s., respectively (Mann–Whitney *U*-test). Data are shown as box plots (25th-75th range + median), and whiskers showing the last data point in ± 1.5 *Interquartile range. Outliers are shown by dots.

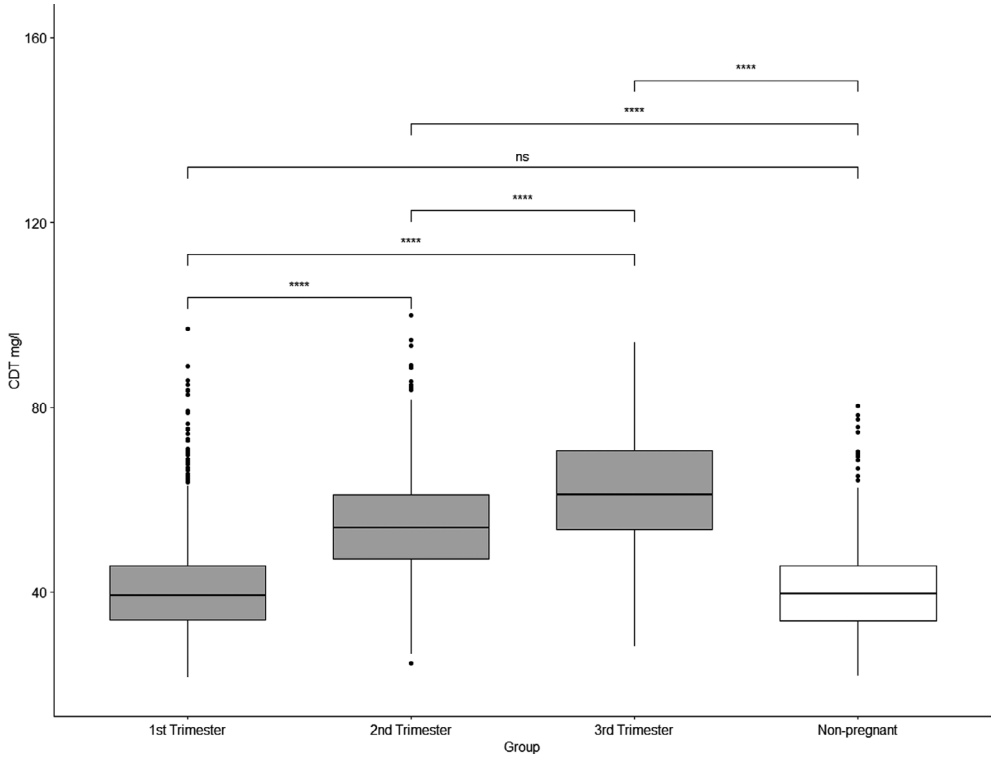

Fig. 3. Absolute CDT concentration (mg/l) in pregnant (gray boxes) and non-pregnant women (white box) in context to gestational age. Data show a significant increase in absolute CDT by trimester; data are shown as box plots as outlined in legend of Figure 2.

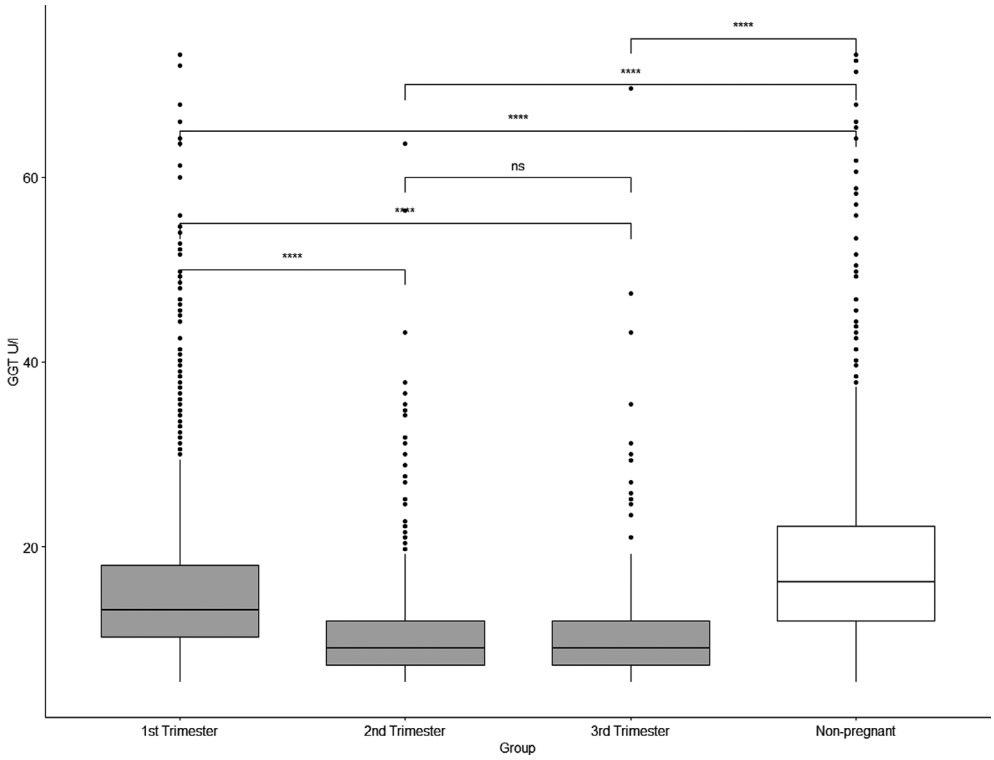

Fig. 4. GGT in pregnant (gray boxes) and non-pregnant (white box) women. Data show a significant decrease in GGT values from first trimester to second trimester as well as the significant difference between all trimesters and the non-pregnant women; data are shown as box plots as outlined in legend of Figure 2.

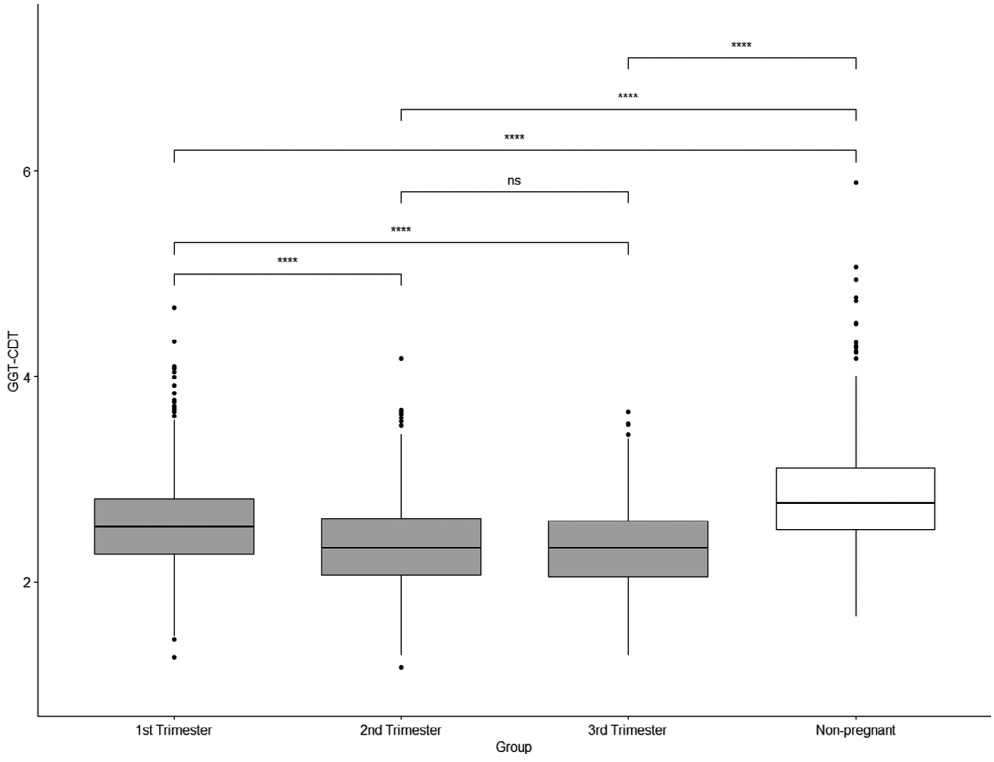

Fig. 5. GGT-CDT in pregnant (gray boxes) and non-pregnant (white box) women. GGT-CDT ratios show similar pattern as concentration of GGT alone (Fig. 4); data are shown as box plots as outlined in legend of Fig. 2.

Table 5. Estimated Prevalence Rates of Harmful Alcohol Consumption in Trimesters of Pregnancy

Biomarker	Cutoff	First trimester n = 1,356 % (95% CI)	Second trimester n = 551 % (95% CI)	Third trimester n = 275 % (95% CI)	p-values for comparison of means	
%CDT	≥1.79	7.2 (5.8 to 8.6)	20.9 (17.5 to 24.3)	17.1 (12.6 to 21.6)	1st vs. 2nd:	<0.001
					1st vs. 3rd:	<0.001
					2nd vs. 3rd:	1
GGT U/l	≥40	2.9 (2.0 to 3.8)	0.5 (0.0 to 1.1)	1.1 (0.0 to 2.3)	1st vs. 2nd:	<0.001
					1st vs. 3rd:	<0.001
					2nd vs. 3rd:	1
GGT-CDT	≥3.80	0.7 (0.3 to 1.1)	0.2 (0.0 to 0.6)	0.0 (–)	1st vs. 2nd:	<0.001
					1st vs. 3rd:	<0.001
					2nd vs. 3rd:	1

Prevalence rates (%) are shown with 95% confidence interval. p-values for comparison of means between the 3 trimesters were estimated using the Mann–Whitney U-test with the Bonferroni adjustment.

DISCUSSION

The aim of this study was to estimate the prevalence of harmful alcohol consumption in pregnancy using biomarkers. As shown in Table 3, estimated prevalence rates of harmful alcohol consumption differ significantly between the different biomarkers and the cutoffs used, resulting in a range of 0.5% and 11.9% for pregnant women and 3.8% and 11.4% for non-pregnant women. These findings are based on the different levels of sensitivity and specificity of each biomarker. Comparing different studies using different protocols, testing methods, and cutoffs, broad variations exist among prevalence rates of harmful alcohol consumption based on biomarkers reported in pregnant women. Using increased GGT values alone (>45 U/l), Howlett and colleagues (2020) identified 4.2% of pregnant women in early pregnancy with elevated measurements, whereas the analogous GGT-based rate of women in the first trimester in our cohort was lower [2.9% (95% CI: 2.0 to 3.8)] even a slightly lower cutoff (>40 U/l) was applied. Notably, using elevated %CDT as only biomarker, corresponding rates of 1.7 % and 7.2% for Howlett et al. and our study, respectively, were identified. This striking discrepancy between both rates in the same cohorts by using 2 different biomarkers linked to alcohol consumption reflects the problem of assessing alcohol consumption by laboratory biomarkers. The estimated prevalence rate of harmful alcohol consumption in pregnant women, defined by one or more elevated biomarkers, in our cohort, was 13.8% compared with 25.2% reported by Popova et al. who assessed alcohol consumption of any kind in pregnancy in Europe using questionnaires (Popova et al., 2017). This higher estimation of alcohol consumption by Popova et al. compared with our data is plausible since analyzed biomarkers (GGT, CDT, %CDT) are only increased in case of harmful alcohol consumption as outlined in introduction. These biomarkers are not able to identify women who drink only little amount of alcohol during pregnancy (Hietala et al., 2006). Comparing the estimated prevalence rate with recently published data about riskful drinking patterns in the general population in Germany, our result seems to fit well (13.8% vs. 19.7% (pregnant women vs. women in general, indicating a lower rate of harmful alcohol consumption in pregnancy) and 18.6% vs. 19.7% (non-pregnant women vs. women in general, showing a comparable level of harmful alcohol consumption in non-pregnant women)) Atzendorf and colleagues (2019). Using the most specific biomarker to detect harmful alcohol consumption in pregnancy according to the literature (GGT-CDT, cutoff: ≥3.8; Niemelä et al., 2016a), one would expect 83 cases of newborns in 2019 in Saxony-Anhalt (0.5% of 16,619 newborns in 2019), respectively, and 3,890 cases in Germany in 2019 (0.5% of 778,100 newborns in 2019) who have been exposed to harmful alcohol consumption during pregnancy. Interestingly, these estimates are in the range of reported numbers of 100 "FAS-like" malformations per year in average, published by the Malformation Monitoring Centre of Saxony-Anhalt (Rissman et al., 2014), and 2.930 cases calculated for whole Germany (95% CI: 1,720 to 4,500, Kraus et al. 2019). However, it should be noted that these corresponding numbers represent primarily an association only and do not provide any evidence of a causal linkage between our estimated prevalence rates and the numbers of "FAS-like" malformations. Firstly, FASD- and FAS-affected newborns, children, and adolescents show more symptoms than just "FAS-like" malformations. Secondly, the biomarkers used in our study identify only women with a certain amount of alcohol consumption that we termed "harmful." Other types of alcohol consumption, which might also lead to FASD- and FAS-affected newborns, remain undetected.

It is remarkable that 85.0% of all pregnant women with elevated biomarkers (as illustrated in Table 4) showed an isolated elevation of %CDT. This effect seems to be caused by the physiological increase in CDT in pregnancy (Bakhireva et al., 2012). Therefore, it has been recommended to report the relative amount of CDT in correspondence with total transferrin (%CDT) to avoid false high results of CDT (Kenan et al., 2011). However, our data suggest that there is a slightly increase in %CDT between the first and second trimesters and comparable concentrations of %CDT in the second and third trimesters. In addition to higher %CDT values in context to gestational age, the higher numbers of elevated %CDT measurements in second and third

trimesters in comparison with non-pregnant females strongly imply that not only absolute levels of CDT, but also values of %CDT, increase with gestational age as well. This phenomenon would cause falsely high prevalence rates of harmful alcohol consumption in pregnant women using a single cutoff for evaluation of all 3 trimesters. This finding implies the need for new evaluation of %CDT cutoffs in pregnancy in general since there are no trimester-specific reference intervals either. In case of GGT, trimester-specific reference intervals were published in 2008, showing slightly increased upper reference limits from 7th to 17th gestational weeks (34.8 U/l) than at higher gestational age (second/third trimester: 24.0 U/L and 25.8 U/L, respectively; Larsson et al., 2008), but all estimated upper reference limits were below the cutoff (40 U/l) used in this study. Taking a closer look at GGT and GGT-CDT, our data showed a significant decrease in means between the first trimester and the second trimester, while the difference between the second and third trimesters was significantly lower and even medically negligible. This finding is supported by a recent analysis of alcohol consumption in pregnant women from the United States (England et al., 2020). England et al. found a prevalence of current drinking (at least one drink in the last 30 days) in pregnant women of 19.6% in the first trimester with a significant decrease to 4.7% in second and third trimesters. Main strengths of this study are the high number of pregnant women and age-matched controls from the same area, sample processing in the same laboratory, prevalence estimation using cutoffs established with the same test kit as used in this study, and the usage of various alcohol-related biomarkers for monitoring harmful alcohol consumption. Furthermore, the fact that no consent of participants was needed reduces the rate of possible underreporting due to social stigmatization. Although the used biomarkers are widely available in routine laboratories, other biomarkers with better specificity and sensitivity (e.g., ethyl glucuronide) exist and might be more suitable for separating harmful from medically neglectable alcohol consumption.

CONCLUSION

This study revealed 2 main findings. Firstly, estimated prevalence rates differ greatly with respect to the biomarkers and cutoffs used. Secondly, the isolated measurement of CDT/%CDT might result in an overestimation of harmful alcohol consumption due to the physiological increase in CDT during pregnancy that seems to be insufficiently corrected using %CDT. Therefore, new studies focusing on trimester-specific reference limits and cutoffs for CDT and % CDT are needed.

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CONFLICTS OF INTEREST

None.

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