

Alcohol exposure prior to pregnancy—does hazardous consumption affect placenta- and inflammatory-mediated pregnancy outcomes? A Swedish population-based cohort study

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Abstract

Introduction: Alcohol consumption during pregnancy is related to severe birth complications such as low birthweight, preterm birth and birth defects. During the last decade, the Alcohol Use Disorders Identification Test (AUDIT) has been used as a screening tool in Swedish maternal healthcare units to identify hazardous, pre-pregnancy alcohol use. However, evaluation of the screening with AUDIT, as well as adverse maternal or neonatal outcomes, has not been assessed at a national level.

Material and methods: This was a population-based cohort study of 530458 births from 2013 to 2018 using demographic, reproductive and maternal health data from the Swedish Pregnancy Register. Self-reported alcohol consumption in the year before pregnancy, measured as AUDIT scores, was categorized into moderate (6–13 points) and high-risk (14–40 points) consumption, with low-risk (0–5 points) consumption as the reference group. Associations with pregnancy- and birth outcomes were explored with logistic regressions using generalized estimating equation models, adjusting for maternal and socioeconomic characteristics. Estimates are presented as adjusted odds ratios (aORs) with 95% confidence intervals (CIs).

Results: High-risk and moderate pre-pregnancy alcohol consumption was associated with preeclampsia, preterm birth and birth of an infant small for gestational age (SGA), but these associations were nonsignificant after adjustments. Prior moderate-risk (aOR 1.29, 95% CI 1.17–1.42) and high-risk consumption (aOR 1.62, 95% CI 1.17–2.25) increased the likelihood of intrapartum and neonatal infections.

Conclusions: Apart from identifying hazardous alcohol consumption prior to pregnancy and the offer of counseling, screening with the AUDIT in early pregnancy indicates a high risk of inflammatory-/placenta-mediated pregnancy and birth outcomes.

Abbreviations: ANOVA, analysis of variance; aOR, adjusted odds ratio; AUDIT, Alcohol Use Disorders Identification Test; CI, confidence interval; OR, odds ratio; SPR, Swedish Pregnancy Register.

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For most outcomes, AUDIT was not an independent contributor when adjusting for confounding factors. Hazardous alcohol use prior to pregnancy was independently linked to intrapartum and neonatal infections; conditions associated with morbidity and long-term sequelae. These associations may be explained by alcohol-induced changes in the maternal or fetal immune system in early pregnancy or persistent alcohol intake during pregnancy, or may depend on unidentified confounding factors.

KEYWORDS

alcohol drinking, placentation, pregnancy, prenatal care, preterm birth

1 | INTRODUCTION

For almost half a century, alcohol has been recognized as a teratogenic substance and its use during pregnancy increases the risk for adverse perinatal outcomes, such as fetal alcohol syndrome.¹ Heavy alcohol consumption during pregnancy has been associated with spontaneous abortion, low birthweight, preterm birth, birth defects and stillbirth.² A dose–response relation has been observed,^{3,4} but no lower threshold/safe period has been established for alcohol use. The recommendation from the World Health Organization and Swedish guidelines urge total abstinence from alcohol during pregnancy.^{2,5} Furthermore, it is urged to identify women with alcohol consumption early in pregnancy, so that counseling and treatment can be offered.²

Low to moderate alcohol consumption has anti-inflammatory effects, whereas high alcohol consumption is associated with elevated inflammatory marker levels and a suppressed immune system in non-pregnant subjects.⁶ In experimental studies, alcohol impacts placental morphology, leading to apoptosis of trophoblast cells. It also increases expression of oxidative stress markers and proinflammatory cytokines in the placenta.^{7,8} Higher levels of cytokines have been observed in infants with fetal alcohol syndrome and their mothers,^{9,10} potentially leading to an increased risk for severe infections in such infants.^{11,12} An increased inflammatory response and impaired placentation can lead to a wide range of adverse outcomes including spontaneous abortion, preeclampsia, placental abruption, intrauterine growth restriction and preterm birth.¹³ Moreover, pregnancy induces a major maternal immune system modulation and failures in this modulation are associated with a risk of adverse pregnancy outcomes.¹⁴ Studies on the effect of alcohol prior to pregnancy are scarce. However, a study of ethanol consumption before conception in mice demonstrated an increased risk of abnormal fetal development, including growth retardation,¹⁵ indicating that alcohol intake before pregnancy could influence birth outcomes.

Since 2012, maternity healthcare providers in Sweden have been recommended to use the Alcohol Use Disorders Identification Test (AUDIT) as a screening tool to identify hazardous/harmful alcohol consumption before and during pregnancy.^{16,17} The AUDIT questionnaire is completed by a midwife who interviews the pregnant woman at the first antenatal care visit regarding alcohol consumption for

Key message

Hazardous alcohol consumption before pregnancy, as based on the Alcohol Use Disorders Identification Test (AUDIT), is linked to a higher risk for intrapartum and neonatal infections. Therefore, AUDIT could serve as a screening tool for a wide range of adverse pregnancy outcomes.

the year prior to pregnancy. A score of six points or more is considered hazardous consumption and women will be recommended for an individual antenatal care program and/or medical assessment by a physician.²

There is a gap of knowledge regarding how consumption of alcohol prior to pregnancy affects the risk of adverse maternal and neonatal outcomes. Therefore, the aim of this study was to investigate whether hazardous alcohol consumption before pregnancy, based on AUDIT scores, was linked to placenta- and inflammatory-mediated pregnancy outcomes in a large population-based birth cohort. Another aim was evaluation of how well AUDIT served as a screening tool in identifying women at risk for adverse pregnancy and birth outcomes.

2 | MATERIAL AND METHODS

2.1 | Study population

This was a Swedish population register-based cohort study of births in 2013–2018 using demographic, reproductive and maternal health data from the Swedish Pregnancy Register (SPR). The SPR prospectively collects data on pregnancy and childbirth, from the first antenatal care visit in the first trimester to 8–16 weeks postpartum. Information in the register is collected from manually entered data by the midwife in antenatal care, and from electronic birth records, with predefined check boxes and diagnosis codes from the International Classification of Diseases (ICD-10).^{18,19} In 2018, SPR covered more than 98% of births for the included regions, resulting in a coverage of more than 91% of all births in Sweden.

For the purpose of this study, singleton births from 22 weeks of gestation were identified in the SPR ($n = 530458$) and analyzed based on AUDIT scores, pregnancy and birth outcomes. In all, 104349 women had more than one delivery during the study period, which was accounted for in analysis. Maternal characteristics included body mass index and smoking habits registered at the first antenatal visit, country of birth, and maternal age at delivery. Categorizations are shown in Table 1. Socioeconomic factors included: attained education (≤ 9 , 9–12 and >12 years), occupation (defined as employed, unemployed/on disability benefits, on parental leave, student, or other), and living condition (defined as cohabitant, one-person household, or other family situation). Pregnancy characteristics included parity (0, 1–3 or ≥ 4), pre-gestational medical conditions including hypertension, diabetes and ongoing or previous psychiatric disorders, recorded using check boxes (yes/no). For a small proportion of women, antenatal information was missing from the SPR. This could be due to the midwife not asking, not registering the information correctly, the woman not wanting to answer the question or the information not being retained in the register because the woman gave birth outside the region where she attended antenatal care.

2.2 | Exposures

The exposure was reported alcohol consumption in the year prior to pregnancy, defined as low-, moderate- or high-risk use, based on AUDIT scores. At the first antenatal visit, the antenatal care provider registers alcohol consumption in accordance with AUDIT. AUDIT is a questionnaire assessing alcohol consumption, drinking behaviors and alcohol-related problems. In Swedish guidelines,²⁰ 0–5 points is considered low-risk alcohol consumption, 6–13 moderate-risk, 14–17 high-risk and 18–40 very high-risk. Six points or more are considered hazardous consumption. Hazardous consumption (moderate and high-risk use) was analyzed with low-risk consumption as a reference group. Due to restricted numbers, high-risk and very high-risk groups were merged into one high-risk group in this study. Pregnancies with missing data from AUDIT were handled as a separate group called no AUDIT.

2.3 | Outcomes

Outcomes were divided, respectively, into pregnancy, labor and neonatal outcomes. Pregnancy outcomes included preeclampsia, placental abruption, stillbirth and preterm birth. Preeclampsia and placental abruption were identified by corresponding codes from ICD-10¹⁹ (Table S1). Preterm birth was defined as birth before 37 weeks. Very preterm birth was defined as birth before 32 weeks and moderate preterm as birth between 32 and 36 gestational weeks. Preterm birth was further divided into spontaneous (spontaneous onset of labor) and iatrogenic (induced labor or planned cesarean section) based on onset of labor as described in electronic

birth records. In Sweden, for the majority of women, expected date of delivery is based on a second trimester ultrasound.²¹

Labor and neonatal outcomes included maternal and neonatal infections, low Apgar score, and birth size. Infections were identified using ICD-10 codes (Table S1). Maternal infections were divided into intrapartum and postpartum infections. Neonatal infections were viral, bacterial, and parasitical (including infected umbilical stump), diagnosed before discharge from hospital after delivery. Low Apgar score was defined as below 7 at 5 min in born-alive and term-born infants. Birth size was defined as appropriate for gestational age (AGA), small for gestational age (SGA), or large for gestational age (LGA), based on birthweight. SGA was defined as below two standard deviations (SD) of expected birthweight for gestational age and sex, and LGA as two standard deviations above.²²

2.4 | Statistical analyses

Maternal background characteristics, based on data for all births, were described with absolute and relative frequencies, means with standard deviations, and by AUDIT group (ie low-, moderate-, high-risk or no AUDIT registered). Comparison between AUDIT groups with Pearson chi-square test and analysis of variance (ANOVA) were made and presented with *P*-values in Table 1.

Logistic regression analyses were used to estimate associations between moderate- and high-risk alcohol consumption during the year before pregnancy, as well as the group with no AUDIT recorded, adverse maternal and neonatal outcomes, with low-risk alcohol consumption as the reference group. Point estimates were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Associations between alcohol consumption and severity, as well as type of preterm birth were analyzed with multinomial regression, with term birth as the reference group. Ordinal regression was used for calculating associations with birth size categories, with AGA as the reference group. We used generalized estimating equations (GEE) in all analyses, since observations were not independent (women could have multiple births registered during the study period).

Directed acyclic graphs (DAG) were used to identify potential confounders (Figures S1–S4).²³ Age, parity, country of birth, living condition, smoking, and prior or ongoing psychiatric disorder were explanatory variables considered for all outcomes, and included as covariates to calculate adjusted ORs (aORs) with 95% CIs.

All statistical analyses were performed using IBM SPSS Statistics version 26.

2.5 | Ethics statement

The Regional Ethical Board at Uppsala approved the study on August 15, 2018 (Dnr 2018/287) with approved amendments 2018/287/1, 2019-04672, 2020-05731, and 2021-01146.

TABLE 1 Background characteristics of births 2013–2018 by AUDIT scores registered at first antenatal visit

	No. of births = 530458	%	AUDIT score 0–5 n = 391440	%	AUDIT score 6–13 n = 16764	%	AUDIT score ≥ 14 n = 1142	%	No AUDIT score n = 121112	%	P-value
Age (years), mean ± SD	30.95 ± 5.14										<0.01
<20	5859	1.1	3928	1.0	286	1.7	65	5.7	1580	1.3	
20–34	406370	76.6	299087	76.4	14172	84.5	939	82.2	92172	76.1	
≥35	118072	22.3	88341	22.6	2306	13.8	138	12.1	27287	22.5	
Data missing	157		84		-		-		73		
Body mass index (kg/m ²), mean ± SD	24.88 ± 4.75										0.24
<30	424259	80.0	328719	84.0	14192	84.7	944	82.7	80404	66.4	
≥30	67603	12.7	52982	13.5	2130	12.7	142	12.4	12349	10.2	
Data missing	38596	7.3	9739	2.5	442	2.6	56	4.9	28359	23.4	
Country of birth											<0.01
Nordic	349385	65.9	256205	65.5	14539	86.7	947	82.9	77694	64.2	
Other Europe	36343	6.9	28704	7.3	332	2.0	18	1.6	7289	6.0	
Non-Europe	89725	16.9	72057	18.4	699	4.2	64	5.6	16905	14.0	
Data missing	55005	10.4	34474	8.8	1194	7.1	113	9.9	19224	15.9	
Smoking (yes)	23700	4.5	17140	4.4	1785	10.6	351	30.7	4424	3.7	<0.01
Data missing	64410	12.1	24024	6.1	1028	6.1	88	7.7	39270	32.4	
Education, (years)											<0.01
≤9	38394	7.2	29652	7.6	963	5.7	225	19.7	7554	6.2	
9–12	227314	42.9	173006	44.2	6469	38.6	194	17.0	47645	39.3	
>12	167101	31.5	124536	31.8	6923	41.3	513	44.9	35129	29.0	
Data missing	97649	18.4	64246	16.4	2409	14.4	210	18.4	30784	25.4	
Occupation											<0.01
Employed	337246	63.6	251853	64.3	12797	76.3	563	49.3	72033	59.5	
Unemployed/ on disability benefits	27320	5.2	19656	5.0	1124	6.7	254	22.2	6286	5.2	
On parental leave	36518	6.9	28474	7.3	122	0.7	6	0.5	7916	6.5	
Student	51620	9.7	39278	10.0	1252	7.5	120	10.5	10970	9.1	
Other	22049	4.2	16926	4.3	232	1.4	78	6.8	4813	4.0	
Data missing	55705	10.5	35253	9.0	1237	7.4	121	10.6	19094	15.8	

(Continues)

TABLE 1 (Continued)

	No. of births = 530458	%	AUDIT score 0-5 n = 391440	%	AUDIT score 6-13 n = 16764	%	AUDIT score ≥ 14 n = 1142	%	No AUDIT score n = 121112	%	P-value
Living condition											
Cohabitant	463201	87.3	359446	91.8	14612	87.2	754	66.0	88389	73.0	<0.01
One-person household	10706	2.0	7810	2.0	536	3.2	132	11.6	2228	1.8	
Other family situation	23958	4.5	17717	4.5	1300	7.8	222	19.4	4719	3.9	
Data missing	32593	6.1	6467	1.7	316	1.9	34	3.0	25776	21.3	
Parity											
0	217523	41.0	159825	40.8	13722	81.9	972	85.1	43004	35.5	<0.01
1-3	282443	53.2	220998	56.5	2982	17.8	167	14.1	56296	48.1	
≥4	13423	2.5	10617	2.7	59	0.4	3	0.3	2744	2.3	
Data missing	17069	3.2	-	-	1	-	-	-	17068	14.1	
Pre-gestational disorders											
Hypertension	2479	0.5	1900	0.5	64	0.4	2	0.2	513	0.5	0.09
Diabetes	4198	0.8	2858	0.7	110	0.7	9	0.8	1221	1.1	<0.01
Psychiatric disorder	53429	11.8	38171	1.4	3452	23.7	517	53.4	11289	11.0	<0.01

Note: Continuous variables presented as mean ±SD. Comparison between groups with Pearson chi-square test and ANOVA including valid cases expressed in P-values. Abbreviations: AUDIT, Alcohol Use Disorders Identification Test; SD, standard deviation.

3 | RESULTS

Among 530458 births, 16764 women reported moderate-risk consumption of alcohol before pregnancy (3.2%) and 1142 reported high-risk consumption (0.2%). AUDIT was not recorded for 121 112 births (22.8%). Mean maternal age was 31 years and 66% were of Nordic origin. Smoking was more common in women with hazardous risk consumption. Low education and unemployment were associated with high-risk use. There was no difference between groups regarding hypertension but psychiatric disorders were more frequently observed among women in the moderate-risk alcohol use group and particularly in the high-risk group. Women with missing data for AUDIT were of similar background characteristics to the average for the cohort, but with more missing values on background characteristics (Table 1).

3.1 | Pregnancy outcomes

Figure 1 and Table S2 illustrate associations between alcohol consumption during the year before pregnancy and pregnancy outcomes. Compared with women with low-risk consumption, women with moderate-risk consumption had an increased likelihood of preeclampsia before adjustment for maternal and socioeconomic factors. However, after adjustment, a slightly reduced risk (aOR 0.88,

95% CI 0.80–0.96) of preeclampsia was observed among women with moderate-risk consumption. An association was seen between hazardous alcohol consumption and preterm birth, with 17% and 78% higher odds of preterm birth among women with moderate- and high-risk consumption, respectively. When separating preterm birth by severity (very and moderate preterm) and onset (iatrogenic or spontaneous), associations were observed with moderate preterm and preterm birth of spontaneous onset but not for iatrogenic onset or very preterm. After adjustment for maternal and socioeconomic factors, all associations for preterm birth became non-significant. Table S2 shows the data generating Figure 1, with number, OR and percentage of outcomes in each group including no AUDIT.

3.2 | Labor and neonatal outcomes

Figure 2 and Table S3 illustrate associations between alcohol consumption during the year before pregnancy along with labor and neonatal outcomes. Compared with women with low-risk consumption, women with either moderate- or high-risk consumption had higher risks for infections both during labor and in the neonatal period. After adjusting for the confounders (ie maternal age, parity, country of birth, living condition, smoking habits, history of psychiatric disorder), women with moderate- or high-risk consumption had 29% and 62% higher

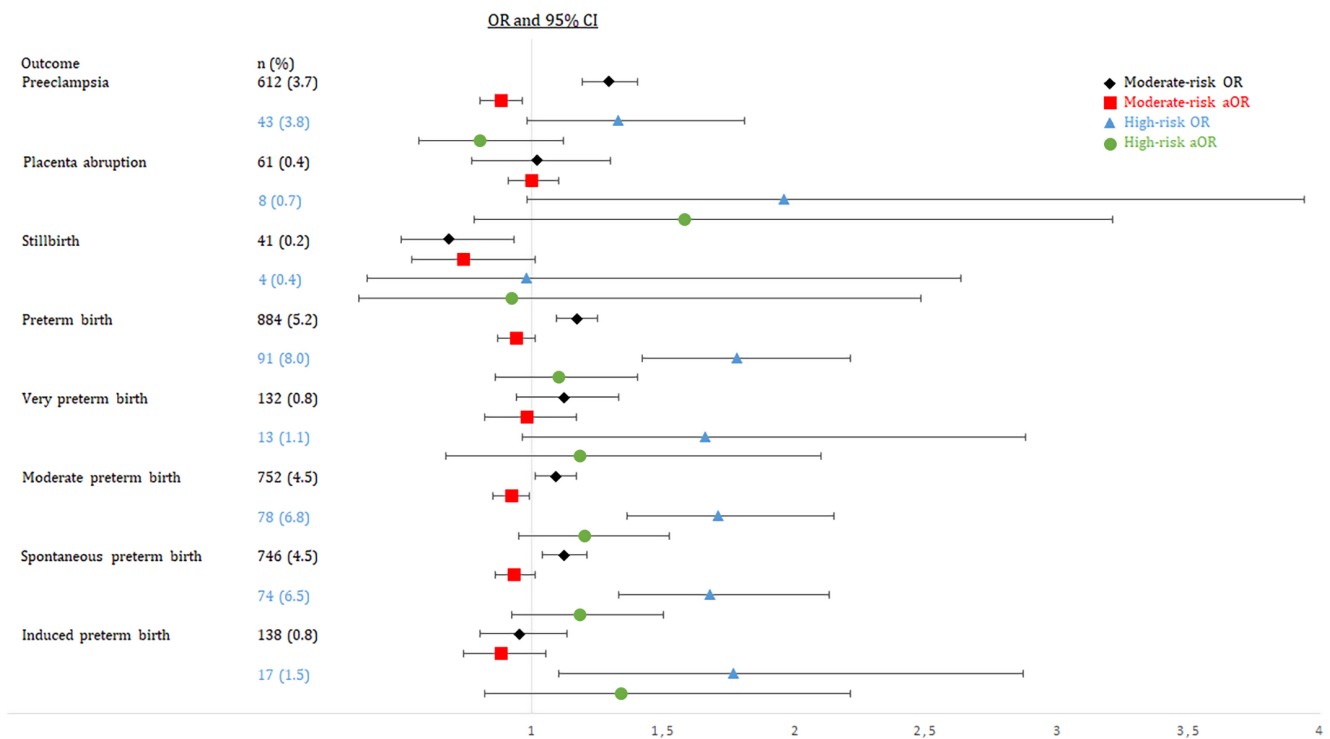


FIGURE 1 Forest plot showing odds ratios and adjusted odds ratios with 95% confidence intervals for pregnancy outcomes according to the AUDIT. ORs and 95% CIs were retrieved by means of logistic and multinomial regression using low-risk consumers as the reference group. Adjusted ORs with 95% CIs were retrieved by means of logistic and multinomial regression with adjustment for age, parity, country of birth, living condition, smoking, and prior or ongoing psychiatric disorder. AUDIT, Alcohol Use Disorders Identification Test; OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio; n, number of cases. Very preterm: (22+0)–(31+6) weeks + days of gestation. Moderate preterm: (32+0)–(36+6) weeks + days of gestation.

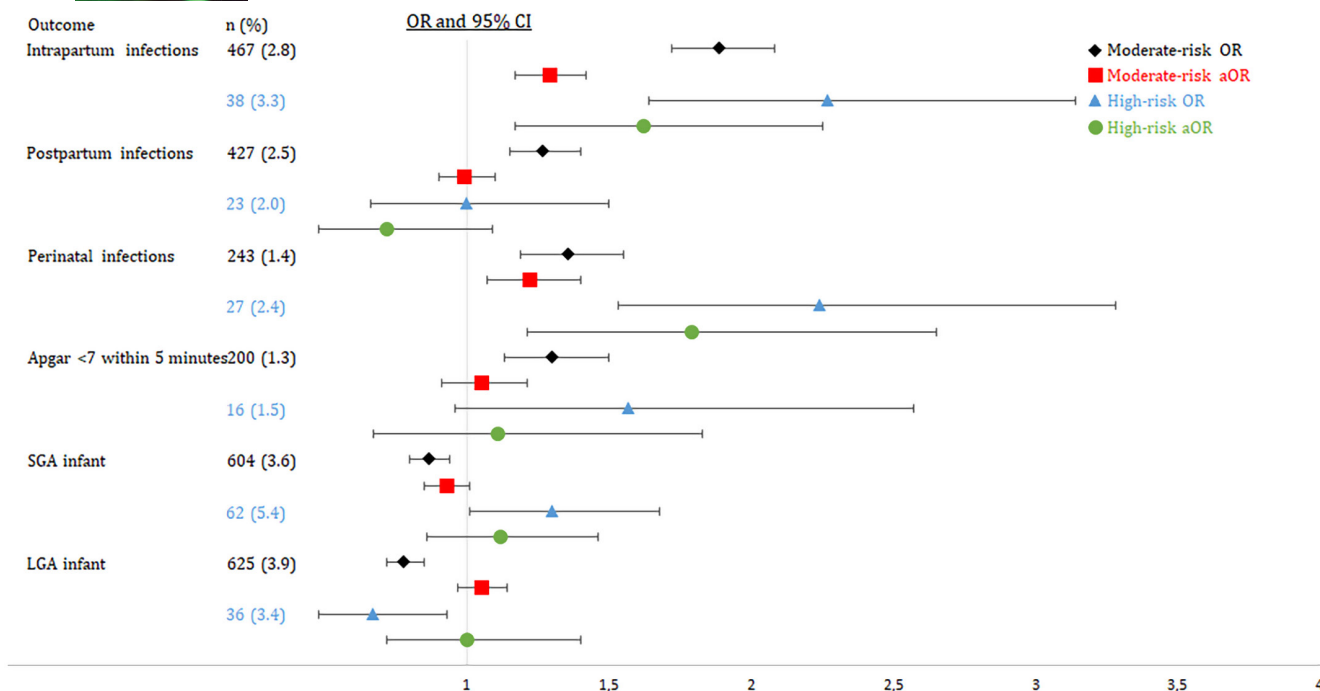


FIGURE 2 Forest plot showing odds ratios and adjusted odds ratios with 95% confidence intervals for labor and neonatal outcomes according to the AUDIT. ORs and 95% CIs were retrieved by means of logistic and multinomial regression using low-risk consumers as the reference group. Adjusted ORs with 95% CIs were retrieved by means of logistic and multinomial regression with adjustment for age, parity, country of birth, living condition, smoking, and prior or ongoing psychiatric disorder. AUDIT, Alcohol Use Disorders Identification Test; OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio; n, number of cases; SGA, small for gestational age; LGA, large for gestational age.

odds of intrapartum infection, respectively (aOR 1.29, 95% CI 1.17–1.42 and aOR 1.62, 95% CI 1.17–2.25). Neonatal infections had similarly increased odds for moderate-risk (aOR 1.22, 95% CI 1.07–1.40) and high-risk alcohol consumption (aOR 1.79, 95% CI 1.21–6.65). An Apgar score below 7 at 5 minutes was more common among women with high-risk consumption (OR 1.69, 95% CI 1.15–2.24), but after adjustment the difference disappeared. Moderate- and high-risk alcohol consumption prior to pregnancy was not an independent risk factor for birthing of an infant small or large for gestational age. Table S3 shows the results generating Figure 2, with number, OR and percentage of outcomes in each group including no AUDIT.

4 | DISCUSSION

We found that hazardous alcohol consumption before pregnancy was associated with infections in the mother and neonate. However, after accounting for maternal and socioeconomic factors, the association with preterm birth was non-significant. Yet, hazardous alcohol consumption prior to pregnancy remained linked to increased odds for maternal infections during delivery, as well as neonatal infections, in a dose-response pattern.

We recognize the strengths and limitations of this study. The SPR is a nationwide register covering more than 91% of births in Sweden and includes self-reported AUDIT scores, which would limit selection bias. Information on drinking habits was collected before

outcomes, controlling recall bias, which is important in studies of behavioral exposures and adverse birth outcomes. Furthermore, the SPR provided information pertaining to selected sociodemographic (eg age, parity, country of birth), economic (living condition etc.), behavioral (smoking) and medical factors (psychiatric disorder etc.). These were considered important confounders, identified using a theoretical framework and directed acyclic graphs, and were therefore possibly accounted for in analyses. A major limitation was lack of information on drinking patterns during pregnancy, which restricts interpretation for time of exposure and biological pathways. Thus, it cannot be ruled out that the results are affected by in utero alcohol exposure. Prior studies indicate that women with hazardous alcohol consumption during the year prior to pregnancy continue to drink until becoming aware of their pregnancy.²⁴ In a Norwegian population-based study, a periconceptional binge-drinking episode was reported by one of four women²⁵ and binge drinking within 4 weeks of conception was associated with increased risk for conduct problems in the offspring's childhood.²⁶ In our study, the AUDIT scores were based on self-reported drinking patterns prior to pregnancy and in more than a fifth of births, no AUDIT point was recorded. Women with missing AUDIT scores were similar to the main cohort in terms of baseline characteristics, but with more missing data in other background factors. The reasons for missing AUDIT scores could be due to administrative drop-out, omitting the question in maternal healthcare or not responding to the questionnaire. A higher proportion of preterm

birth was observed among women with no AUDIT score recorded. This could be explained by the fact that antenatal information is lost for women transferred to a secondary- or tertiary-level hospital, an example of administrative drop-out. This occurs when risk of preterm birth is diagnosed at a center without capacity for delivery of infants below a specific gestational age.

We believe that there is an underreporting of moderate- and high-risk consumption in our cohort, resulting in small numbers which restrict the precision of results and provide wide confidence intervals. Compared with prior reports, we found a much lower incidence (3.4%) of self-reported hazardous consumption prior to pregnancy, with 3.2% considered to have moderate-risk and 0.2% high-risk consumption. In a Swedish prospective study from 2003 with AUDIT scores anonymously collected at an antenatal clinic, 17.0% of women reported hazardous use of alcohol during the year preceding pregnancy.²⁷ In another Swedish study with a similar study design from 2021, 15.7% of women who chose to be anonymous reported hazardous alcohol use before pregnancy, but only 5.1% of those choosing not to be anonymous.²⁸ A slight decline in alcohol consumption, across all ages, has been observed in Sweden in the last decades²⁹ but alcohol consumption is a stigmatized subject, meaning that anonymously collected data are more reliable. How well AUDIT serves as a screening tool for alcohol consumption during pregnancy is uncertain. Skagerström et al.²⁴ reported from a Swedish multicenter study that a higher proportion of women with high-risk alcohol consumption in the year prior to pregnancy continued to consume alcohol, whereas moderate drinkers more frequently stopped drinking if planning a pregnancy. A Norwegian population-based study²⁵ showed that among planned pregnancies (78%), 1.5% reported continued heavy drinking during pregnancy and 39% reported light drinking.

We found increased rates and odds of infections in women with a moderate- or high-risk alcohol consumption prior to pregnancy when compared with low-risk consumption, indicating alcohol consumption is an independent risk factor for perinatal infections. High intake of alcohol suppresses the immune system, potentially leading to increased susceptibility to infections.⁶ In an observational study, women were interviewed about their alcohol drinking habits at four different occasions prior to and during pregnancy. Alcohol amount and drinking patterns both prior to and during pregnancy were associated with neonatal infections. After adjustments, excessive drinking (at least 7 drinks/week) in the second trimester increased the risk almost fourfold.³⁰ Other studies^{11,12} support the evidence that prenatal alcohol exposure leads to increased rates of neonatal infections. It is possible that the increased risks of infections are caused by a combination of hazardous alcohol intake prior to pregnancy and persistent drinking during pregnancy. The results support screening with AUDIT scores should be used and intervention for women with high scores is to be recommended. Although we have focused on inflammatory- and placenta-mediated disorders, multiple outcomes were investigated and not accounted for in our analysis, which increases the risk of a chance finding. The results and biological pathways need to be confirmed as well.

Since alcohol use has been related to surgical site infections, treatment using alcohol abstinence and cessation programs are an effective consideration to reduce postoperative complications.³¹

Infection and inflammatory changes during pregnancy are closely linked to preterm birth, with heavy alcohol consumption during pregnancy an established risk factor for preterm birth and low birth-weight.³ In our unadjusted analyses, there was an association between hazardous alcohol consumption and preterm birth. However, this association could be attributed to coexisting maternal and socioeconomic factors; the AUDIT score per se could not be regarded as an independent factor in preterm birth. Alcohol consumption is closely linked to demographic and socioeconomic factors, which is an important consideration when assessing birth outcomes. It should be noted that an absence of associations might reflect interventions during pregnancy for hazardous alcohol use found in antenatal screening. Our aim was to focus on placenta- and inflammatory-mediated pregnancy outcomes; therefore such outcomes should not be affected by counseling during pregnancy after placentation.

5 | CONCLUSION

Apart from identifying hazardous alcohol consumption prior to pregnancy and offering counseling, screening with the AUDIT in early pregnancy can reveal high risk inflammatory-/placenta-mediated pregnancy and birth outcomes. Hazardous alcohol use prior to pregnancy was independently linked to intrapartum and neonatal infections. Such conditions are associated with morbidity and long-term sequelae. Since the cohort is register-based and lacks information on alcohol exposure during pregnancy, it is not feasible to explain this association further. Possible explanations for such conditions might be alcohol-induced changes in the maternal or fetal immune system in early pregnancy, persistent alcohol intake during pregnancy or associated unidentified confounding factors.

AUTHOR CONTRIBUTIONS

JA, SH, and A-KW conceived the study. JA managed the data and performed the statistical analysis with technical input from SH. JA wrote the first draft. All authors contributed with critical input on analysis, interpretation of data, and the final article.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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