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## **The relationship between history of caesarean deliveries with placenta previa: A meta-analysis**

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**Abstract**--Placenta previa is known as one of the most feared adverse maternal and fetal-neonatal complications in obstetrics. It has been reported that history of caesarean deliveries was associated with increased risks of placenta praevia. This study aimed to investigate

the association between alcohol consumption during pregnancy with placenta previa and abruptio placenta. The PubMed databases were systematically reviewed, with the period of articles published between 2000 until 2022. Statistical analysis was carried out by Review Manager 5.3 (RevMan 5.3). The databases search yielded 228 studies and 14 of them matched eligibility criteria. The results of this meta-analysis suggest that. Mothers with history or previous of caesarean delivery had higher risk to develop placenta previa compared with mothers who had a normal or vaginal deliveries (Pooled OR= 2.08; 95%CI: 1.73–2.51). this result was statistically significant.

**Keywords**---placenta previa, caesarean deliveries, pregnant.

## **Introduction**

Placenta previa (PP) is characterized by the abnormal placenta overlying the endocervical os, and it is known as one of the most feared adverse maternal and fetal-neonatal complications in obstetrics (Fan et al., 2016; Silver, 2015). A study reported that the overall prevalence of placenta previa was approximately 5 per 1000 pregnancies by world region, however, there is also some evidence suggestive of regional variation (Cresswell et al., 2013).

Placenta previa have long been recognized as major obstetric complications that result in maternal and fetal mortality as well as morbidity. The effect of this bloody obstetric complications on perinatal health is multifactorial: blood loss, premature delivery, intrauterine growth restriction, the risk of perinatal asphyxia, the risk of sepsis, and hyperbilirubinemia (Giordano et al., 2010; Crane et al., 2000; Oyelese & Ananth, 2006; Rosenberg et al., 2011). Women with placenta previa are at an approximately 4-fold increased risk of second trimester vaginal bleeding (Silver, 2015).

The risk of placenta previa is also reported to be higher among women with previous uterine surgery, including cesarean section (Gurol-Urganci et al., 2011). The risk of placenta previa in a pregnancy after a CS delivery has been reported to be between 1.5 and 6 times higher than after a vaginal delivery. A meta-analysis of studies published before 2000 of previous CS as a risk factor for placenta previa found an overall odds ratio of 2.7 (Faiz & Ananth, 2003).

Previous studies on the relationship between caesarean section and the risks of placenta praevia and placental abruption in subsequent pregnancies had significant limitations. Many were conducted at tertiary care hospitals and there were relatively small number of births in these studies. Furthermore, many important confounding factors, such as maternal age, race, and parity as well as smoking and drinking during pregnancy have not been adequately adjusted (Q Yang et al., 2007). The purpose of this study was to examine the relationship between history of caesarean deliveries with placenta previa.

## **Methods**

This meta-analysis was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

### **Eligibility criteria**

Only observational, peer-reviewed English-language published studies were included, without restriction regarding date of publication and geographical location.

### **Inclusion Criteria**

We included studies eligible for inclusion in this meta-analysis if they reported an association between alcohol consumption with placenta previa and abruptio placenta, and also represent the general population of pregnant women. The study which used other than the English language were excluded. Furthermore, randomized intervention trials, experimental animal studies, reviews, meta-analyses, case reports, letters, commentaries, research protocols, and editorials were excluded.

### **Search strategy**

Studies by an electronic search of PubMed with search of articles published between 2000 until 2022 were detected. The following filters were used: "Placenta previa" [MeSH Terms] OR ("placenta" [All Fields] AND "previa" [All Fields] OR "placenta previa"[All Fields]) AND OR "placenta previa"[tw]. "Caesarean deliveries"[MeSH Terms] OR ("caesarean"[All Fields] AND "deliveries"[All Fields]) OR "caesarean deliveries"[All Fields]. In addition, reference lists of all included papers were searched for relevant studies not identified during the databases search.

### **Study selection**

Based on eligibility and exclusion criteria, the titles and abstracts were independently reviewed by researchers, and full texts of potentially relevant studies were obtained for further assessment. Disagreements between reviewers were resolved by consensus.

### **Data extraction**

Data extraction for eligible studies was conducted by authors independently, using a predesigned piloted extraction form. Data extraction for each study included: first author, year of publication, study location, study design, sample size, duration of the study, and results of the risk factors analyzed in aOR with 95% Confidence Intervals.

## Statistical Analysis

By utilizing Review Manager (REVMAN) 5, statistical analysis was performed to inspect the determinants of HG. Extracted data, including the hazard ratio and CI 95% were entered into REVMAN. The effect size was calculated as an adjusted odds ratio (aOR) with a confidence interval of 95% and a two-sided p-value less than 0.05, signifying a statistical significance difference between groups. The pooled odds ratio was utilized to estimate the association between risk factors and HG. The heterogeneity between studies was measured statistically by using the intuitive index (I<sup>2</sup>). An intuitive index is a total variation across studies that describe the percentage because of heterogeneity instead of the error of the sample (Deeks JJ, Higgins JPT, 2019; JPT, 2003). An I<sup>2</sup> value of more than 50% indicates a substantial heterogeneity level (JPT, 2003). Random effect analysis models are used if heterogeneity is detected by more than 50% (OM, 2018). Publication bias was assessed by funnel plot asymmetry test. The symmetrically distributed shape of funnel plots indicates no potential publication bias; otherwise, the asymmetrical shape of funnel plots signifies potential publication bias (Godavitarne et al., 2018).

## Results

A total of 228 studies were identified through a systematic search. After exclusions of the title or abstract of the paper, or of review articles, and not English-language papers, 25 full-text studies remained to be assessed. Out of these, 11 studies were excluded for reasons, resulting in 14 studies for inclusion in this meta-analysis. Figure 1 shows the Prisma flow diagram of the selection process.

### Characteristics of the included studies

A summary of the characteristics and findings of the included studies is presented in Table 1. The 14 included studies were published between 1995 and 2020. Two studies were conducted in Norway (Daltveit et al., 2008; Rasmussen et al., 2000), three in the USA (Lydon-Rochelle et al., 2001; Senkoro et al., 2017; Yang et al., 2009), three in Israel (Baumfeld et al., 2017; Rosenberg et al., 2011; Sheiner et al., 2001), two in Australia (Kennare et al., 2007; Olive et al., 2005), one in Uganda (Kiondo et al., 2008), one in Nigeria (Eniola et al., 2002), one in Croatia (Tuzović et al., 2003), and one in Ethiopia (Adere et al., 2020). Five were cohort and 4 were case-control designed studies. The total sample sizes of the studies included in this meta-analysis were 9,042,007 pregnant women.

### Association between history of caesaeran delivery with placenta previa

The results of meta-analyses for the association between history of caesarean delivery and plasenta previa among pregnant women are presented as a forest plot in Fig.1. Mothers who had history of caesarean delivery had higher risk to experience plasenta previa compared with mothers who had a normal or vaginal deliveries (Pooled OR= 2.08; 95%CI: 1.73–2.51). The results were statistically significant (p< 0.00001) and use random effects (I<sup>2</sup> statistic= 98%; p< 0.00001).

### **Publication Bias**

We assessed the funnel plot in analysis and overall, it did show any substantial asymmetry (Fig. 3), one study more inclined to the right side of the plot indicated that the result may over estimated.

### **Discussion**

This study investigated the association between history of caesarean delivery with placenta previa. Pregnant women with previous history of caesarean delivery had odd 2.08 increased risk of plasenta previa. Our results are in agreement with other recent studies. Previous meta-analysis suggested that there is a strong association between having a previous cesarean delivery, spontaneous or induced abortion, and the subsequent development of placenta previa. The risk increases with number of prior cesarean deliveries. Pregnant women with a history of cesarean delivery or abortion must be regarded as high risk for placenta previa (Ananth et al., 1997).

A few studies have investigated whether the effect of a previous caesarean delivery on the risk of placenta previa was modified by other risk factors. A meta-analysis study by Gurol-Urganci et al., (2011) stated that among women in England, cesarean section in the first delivery increased the risk of placenta previa in the subsequent delivery by 60%. There was no evidence that the effect of caesarean delivery on placenta previa rates varied among different groups of women or by the time between two pregnancies. The risks of placenta previa in the second pregnancy also increased by previous placenta previa, advanced maternal age and with birth intervals of less than one year or more than four year.

### **Strengths and limitations**

Our study, which included a large number of participants, giving it sufficient statistical power, aimed to address the relation between alcohol consumption with placenta previa and abruptio placenta. Although the present study should be evaluated with caution due to the potential bias and evidence of heterogeneity. Furthermore, the evaluation of the eligibility of the identified studies was based on predefined criteria and done independently by researchers, who examined in detail the quality of those studies. In addition, we did conduct a subgroup analysis which certainly helps the figuration of more significant factors regarding the association between history of caesaeran delivery with plasenta previa. Several limitations also need to be acknowledged. First of all, the number of primary studies included in this meta-analysis was still limited. Secondly, the literature search was carried out only over three databases, and the included studies were only in the English language, potentially missing relevant information.

### **Conclusion**

In conclusion, this meta-analysis shows that there are sufficient evidence based on the observational studies that history of caesarean delivery is significantly associated with an increased risk of placenta previa. Therefore, history of caesarean delivery can beconsidered as a predictor of placenta previa. Future

studies with more determinants of placenta previa, appropriate design, using pregnancy and birth data, preferably not self-reported, and examining various confounders and adjusting for them in multivariable models, will greatly contribute to the issue. Thus, we conclude that further research is needed to establish the risk factors of placenta previa. Future high-quality research may likely challenge these conclusions.

### Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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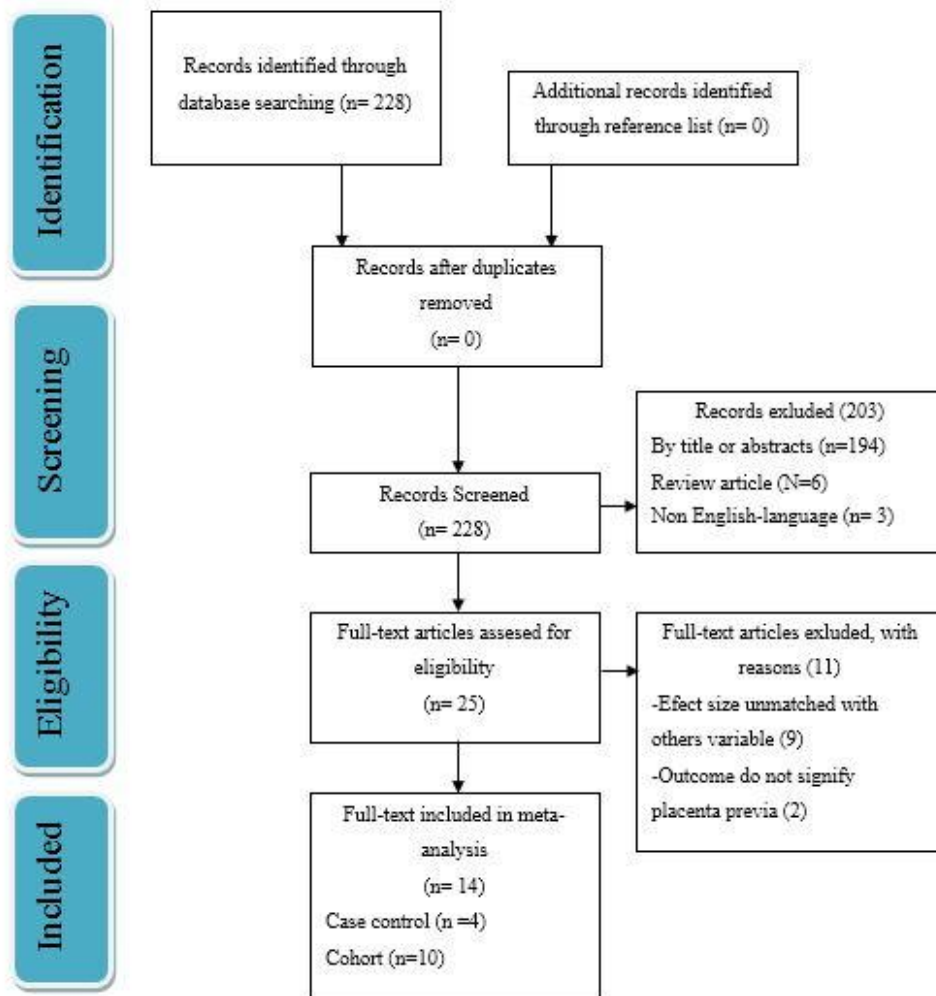


Fig. 1 PRISMA Flow Diagram



Table 1. Summary of the characteristic's studies included

No	Author (Year)	Study Design	Country	Sample Sizes	aOR extracted from articles
1.	Adere et al. (2020)	Case-control	Ethiopia	The woman medical records in Tikur Anbessa Specialized Referral and Gandhi Memorial Hospitals from September 2015 to January 2018, whereas the study population was all the delivery medical records with singleton pregnancies complicated with placenta praevia at Tikur Anbessa Specialized Referral and Gandhi Memorial Hospitals from September 2015 to January 2018 (cases= 303; control= 303).	2.7 (1.64-4.58)
2.	Baumfeld et al. (2017)	Cohort	Israel	In this retrospective study we collected data on all deliveries between January 1998 and December 2013 in the Soroka University Medical Center, a 1000-bed tertiary teaching hospital (n= 297,141).	1.18 (1.14-1.22)
3.	Dalveit et al. (2008)	Cohort	Norway	Births registered in the Medical Birth Registry of Norway between 1967 and 2003 (n= 880,309).	1.5 (1.3-1.8)
4.	Eniola et al. (2002)	Case-control	Nigeria	Cases= 136; control= 136.	4.7 (1.9-11.4)
5.	Kennare et al. (2007)	Cohort	South Australia	The South Australian perinatal data collection from 1998 to 2003, excluding late terminations of pregnancy (n= 36,038).	1.66 (1.30-2.11)
6.	Kiondo et al. (2008)	Case-control	Uganda	Between 15th November 2001 and 30th November 2002 (cases= 36; control= 180 women with normal delivery).	19.9 (6.4-61.7)
7.	Lydon-Rochelle et al. (2001)	Cohort	USA	The Washington State Birth Events Record Database (n = 96,975).	1.4 (1.1-1.6)
8.	Olive et al. (2005)	Cohort	Australia	NSW Department of Health de-identified, linked population databases: a perinatal database of all births in NSW	3.1 (2.0-4.7)

				and a database of all hospital separations in NSW (n= 375,790).	
9.	Rasmussen et al. (2000)	Cohort	Norway	The Medical Birth Registry of from 1967 through 1992 (n= 740,748).	1.32 (1.04–1.68)
10.	Rosenberg et al. (2011)	Cohort	Israel	The deliveries occurred between 1988 and 2009 at the Soroka University Medical Center (n= 185,476).	1.76 (1.48–2.09)
11.	Senkoro et al. (2016)	Cohort	USA	Maternally-linked data from Kilimanjaro Christian Medical Centre birth registry spanning 2000 to 2015 (n= 47,686).	9.68 (6.66–14.08)
12.	Sheiner et al. (2001)	Cohort	Israel	All singleton deliveries at our institution between 1990 and 1998 (n= 78,524).	1.8 (1.4-2.4)
13.	Tuzović et al. 2003	Case-control	Croatia	a total of 202 singleton pregnancies with placenta previa during a 10-year study period and 1,004 randomly selected simple singleton controls.	2.0 (1.17-3.44)
14.	Yang et al. 2009	Cohort	USA	a population-based, retrospective cohort study on the 1995 to 2000 U.S. national linked birth/infant mortality database provided by the National Center for Health Statistics, Centers for Disease Control and Prevention (n= 6,187,843).	1.79 (1.75-1.83)

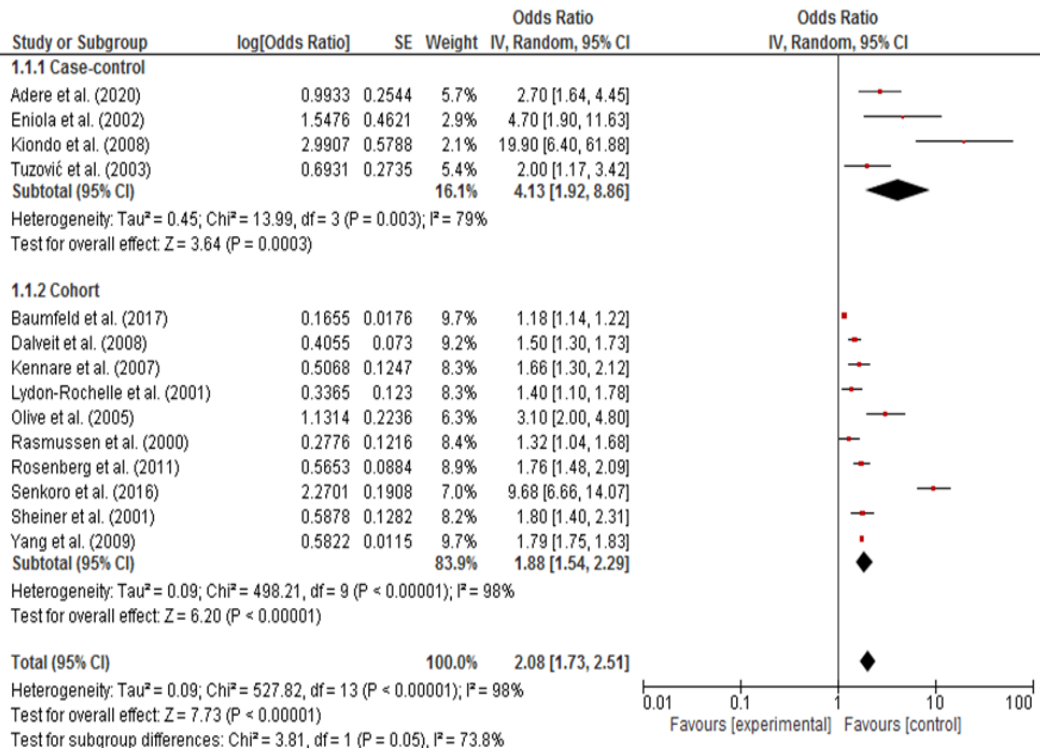


Fig. 1 Forest Plot

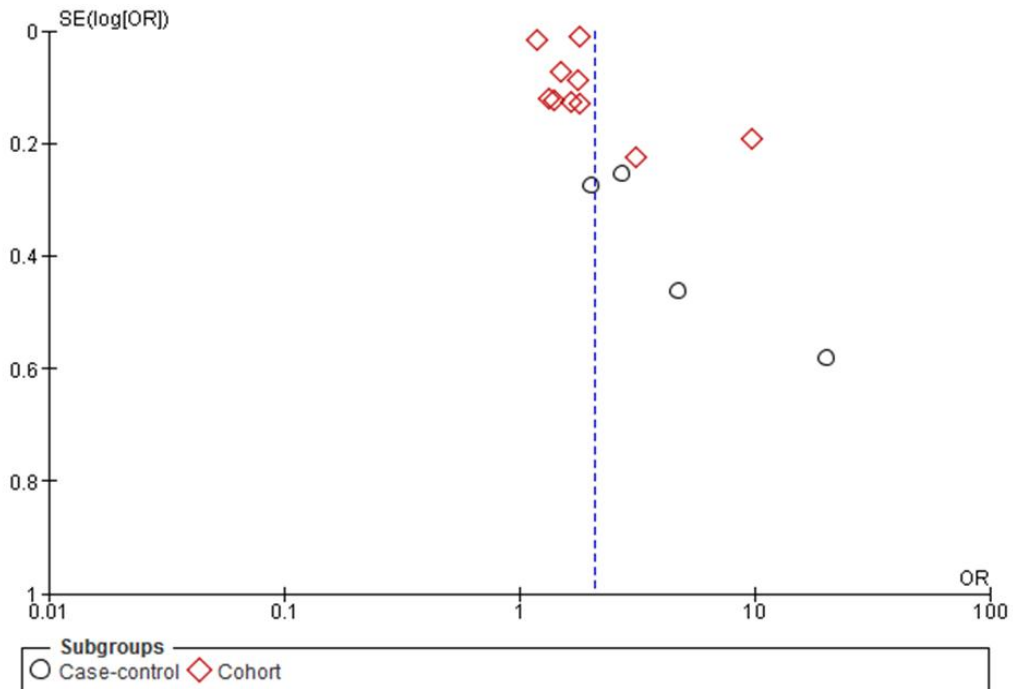


Fig. 2 Funnel Plot