

# Association Between Parental Cocaine Use and Sudden Infant Death Syndrome: A Systematic Review



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## Association Between Parental Cocaine Use and Sudden Infant Death Syndrome: A Systematic Review

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### ABSTRACT

**Introduction:** Sudden infant death syndrome (SIDS) is defined as the unexpected death of an infant under one year of age with no clear cause, typically occurring during sleep, and associated with various environmental risk factors. International recommendations for SIDS prevention include avoiding drug use, but the specific role of cocaine in increasing the risk of the syndrome is not well established. This is a systematic review of the literature on the association between parental cocaine use and the occurrence of SIDS. **Objective:** To conduct a systematic review of the literature on the association between parental cocaine use and the occurrence of SIDS. **Material and Methods:** The databases searched included PubMed/MEDLINE, Embase, Scopus, Web of Science, and LILACS, from their inception to December 2024. Study selection was conducted independently by two researchers, and disagreements were resolved by a third author. This review was registered in PROSPERO (CRD42024591448). **Results:** Eleven studies were included, all conducted in developed countries. A statistical analysis specifically correlating SIDS with cocaine use was available in seven studies, and in four of them, the results suggested an association between exposure and outcome. However, there were limitations related to the lack of data on the frequency, route, and intensity of drug use, with variation among studies in how this exposure was assessed. **Conclusion:** The studies analyzed in this systematic review suggest a possible association between cocaine use and the risk of SIDS. However, further research is needed to explore mechanisms related to maternal and paternal drug use during pregnancy and the postpartum period in order to establish a more accurate correlation with SIDS.

Keywords: Sudden Infant Death; Cocaine; Cocaine-Related Disorders; Systematic Review.

### RESUMO

**Introdução:** A síndrome da morte súbita do lactente (SMSL) é definida como a morte inesperada de um lactente menor de um ano por motivos inexplicados, geralmente durante o sono, possuindo diversos fatores de risco ambientais associados. As recomendações internacionais para prevenção da SMSL incluem evitar o uso de drogas, mas o papel específico da cocaína no risco da síndrome não está bem definido. Essa é uma revisão sistemática da literatura sobre a associação entre o uso parental de cocaína e a ocorrência de SMSL. **Objetivo:** Conduzir uma revisão sistemática da literatura sobre a associação entre uso parental de cocaína e ocorrência da SMSL. **Material e Métodos:** As bases de dados consultadas foram: Pubmed/MEDLINE, Embase, Scopus, Web of Science e LILACS, do período de origem da fonte até dezembro/2024. A seleção dos estudos foi realizada por dois pesquisadores de forma independente, e divergências foram definidas por um terceiro autor. Essa revisão foi registrada no PROSPERO (CRD42024591448). **Resultados:** Onze estudos foram incluídos, todos realizados em países desenvolvidos. Uma análise estatística correlacionando, especificamente, a SMSL com o uso de cocaína estava disponível em sete estudos, e, em quatro deles, os resultados sugeriram associação entre exposição e desfecho. No entanto, há limitações relacionadas a ausência de dados sobre frequência, via e intensidade do uso da droga, com variação entre os estudos na forma de avaliação dessa exposição. **Conclusão:** Os estudos analisados nesta revisão sistemática sugerem a possibilidade de associação entre o consumo de cocaína e o risco de SMSL. No entanto, são necessárias pesquisas que explorem mecanismos relacionados ao uso da droga na gestação e pós-parto, pela mãe e pelo pai, para estabelecer uma correlação mais precisa com a SMSL.

Palavras-chave: Morte Súbita do Lactente; Cocaína; Transtornos Relacionados ao Uso de Cocaína; Revisão Sistemática.



## INTRODUCTION

Sudden Infant Death Syndrome (SIDS) is defined as the unexpected death of an infant under one year of age, which remains unexplained even after a thorough investigation, including a complete autopsy, review of the circumstances surrounding the death, and clinical history.<sup>1</sup>

This phenomenon remains a significant contributor to infant mortality in the United States, representing the third leading cause of infant death, with an incidence of 0.539 deaths per 1,000 live births.<sup>2</sup> In Brazil, the epidemiology of SIDS is not well established, as there are no official statistics on its incidence.<sup>3</sup> A cohort study conducted in Passo Fundo, Rio Grande do Sul (RS) reported an incidence of 1.75 per 1,000 live births in 2003.<sup>4</sup> Similarly, a study from Pelotas (RS) found an incidence of 1.5 per 1,000 live births in 2004.<sup>5</sup>

SIDS is strongly associated with modifiable risk factors in the infant's sleep environment. These include bed-sharing—when the infant sleeps on the same surface (such as a bed, sofa, or armchair) as the caregiver—and the presence of loose objects in the crib, which may lead to accidental suffocation or thoracic compression.<sup>6</sup> In contrast, room-sharing—when the infant sleeps in the same room as the caregiver but on a separate surface—is considered a protective factor. Moreover, both prenatal and postnatal exposure to tobacco, alcohol, marijuana, opioids, and other illicit substances are recognized as detrimental to neonatal survival.<sup>6</sup>

Cocaine is a psychoactive substance that blocks dopamine reuptake, resulting in euphoria, increased blood pressure, tachycardia, and vasoconstriction, potentially leading to obstetric complications.<sup>7</sup> Due to its low molecular weight, cocaine easily crosses the placental barrier by simple diffusion, which has prompted numerous studies on the fetal consequences of maternal use. Evidence suggests several intrauterine effects, including increased fetal heart rate, ischemia with coronary vasospasm, and coagulation abnormalities, all of which elevate the risk of thrombosis. Congenital anomalies have also been reported, such as microcephaly, intrauterine growth restriction, central nervous system infarcts, cortical atrophy, urinary tract malformations, and neurological disorders.<sup>7</sup> In addition, cocaine use during pregnancy has been associated with fetal growth restriction and shorter gestational age, leading to newborns with low birth weight, reduced length, and smaller head circumference.<sup>8</sup>

Despite advances in the understanding of cocaine-related fetal effects, the association between cocaine use and SIDS remains poorly defined, with existing evidence being fragmented and inconclusive. Therefore, specific studies are warranted, particularly

those accounting for confounding factors such as the concurrent use of other substances. In light of these data gaps, the objective of this study is to conduct a systematic review of the literature on the association between parental cocaine use and the occurrence of SIDS.

## MATERIAL AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines<sup>9</sup> and was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42024591448.

To formulate the research question, the PECO strategy was adopted: Population (children up to two years of age), Exposure (parental cocaine use during the gestational and/or postnatal period in any form, dose or frequency), Comparison (absence of passive cocaine exposure during the gestational and/or postnatal period), and Outcome (occurrence of Sudden Infant Death Syndrome). The guiding research question was: "Is there an association between passive exposure to cocaine during the gestational or postnatal period and the risk of Sudden Infant Death Syndrome?"

The search was conducted independently by two researchers between September and December 2024, with no restrictions regarding publication date or language. The databases searched were ÷ PubMed/MEDLINE, Embase, Scopus, Web of Science, and LILACS. The search strategy applied was: ('cocaine' OR 'crack' OR 'coke' OR 'coca leaves' OR 'Cocaine-Related Disorders' OR 'Cocaine Smoking' OR 'Crack Smoking') AND ('sudden infant death' OR 'SIDS' OR 'cot death' OR 'crib death'). The search strategies used for each database are available in the Supplementary Material.

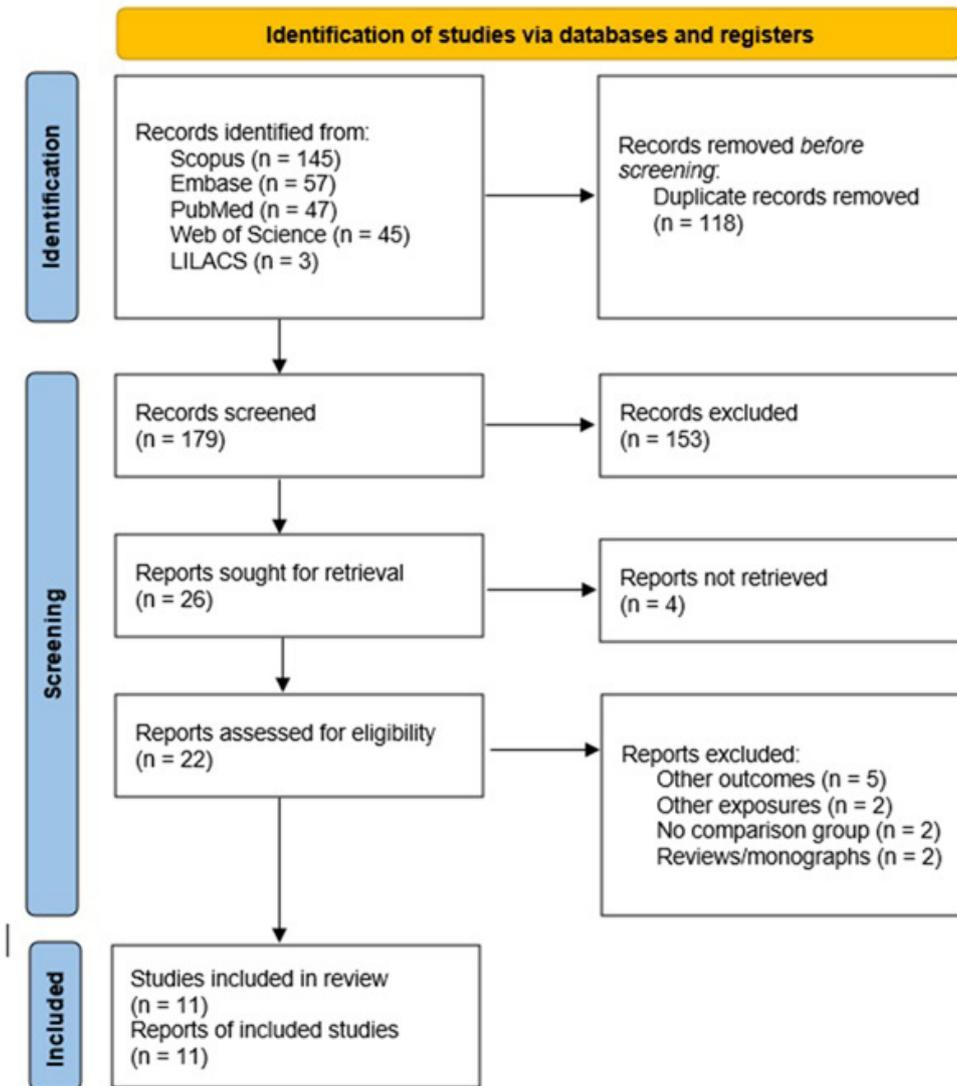
Study selection was independently and systematically performed by two researchers using Microsoft Excel®. Any disagreements were resolved by a third reviewer. Initially, titles and abstracts were screened, followed by full-text assessments in the second phase. The inclusion criteria were: (i) studies evaluating cocaine exposure, at any dose or route, during the gestational or postnatal period; (ii) studies assessing Sudden Infant Death Syndrome as an outcome; and (iii) case-control, cohort, or retrospective cross-sectional studies. The exclusion criteria were: (i) studies with exposures or outcomes different from those specified in the inclusion criteria; (ii) reviews, clinical protocols, and case reports; and (iii) studies published as book chapters, conference abstracts, letters to the editor, or editorials.

Figure 1 presents the flowchart detailing the study selection process for this review.

For the qualitative analysis, the following data were extracted from each study: authorship, year of publication, country where the study was conducted, study design, type of cocaine exposure, outcomes assessed, and main results and conclusions. The data collection process was also conducted by two independent researchers, who met at the end of this stage to resolve any potential discrepancies.

Risk of bias was assessed using the critical appraisal tools recommended by The Joanna Briggs Institute (JBI), applying the respective checklists for cohort, cross-sectional, and case-control studies.<sup>10</sup> The assessment criteria are described in detail in Supplementary Table 2. These risk of bias assessments were not used as exclusion criteria.

The decision regarding the performance of a meta-analysis comparing the exposure and control groups was based on the evaluation of the extracted



**Figure 1:** Flowchart of studies included in the systematic review.

data, particularly with respect to their heterogeneity. Due to the variability observed in exposure assessment methods, as well as in study designs, the authors chose not to perform this step.

## RESULTS

A total of 11 studies were included in this systematic review. Of these, only 2 (18.2%) were published within the last five years. Notably, almost all of the studies were conducted in the United States, with none analyzing data from developing countries. Table 1 summarizes the characteristics of these studies.

**Table 1:** Characteristics of the studies included in the systematic review.

Author, Year	Country, Language	Exposure	Outcome	N	Study Design	Statistical Analysis
Aoki, 1994 <sup>11</sup>	United States, English	Maternal history of cocaine abuse and/or positive urine toxicology in database records	SIDS confirmed by autopsy	78	Retrospective cohort	About 23% of infants who died from SIDS were exposed to cocaine. The risk of SIDS was significantly higher ( $p < 0.025$ ) among offspring of cocaine-using mothers.
	United States, English	Substance use including cocaine verified by prenatal and postnatal interviews and maternal urine testing postnatally	SIDS confirmed by autopsy	5	Prospective cohort	RR for SIDS among infants whose mothers used cocaine during pregnancy was 1.17 (95% CI: 0.13 - 10.43).
Claudet, 2022 <sup>13</sup>	France, English	Cocaine exposure identified by toxicological analysis post-mortem	SIDS diagnosed in national reference centers, cases with toxicological data included	398	Cross-sectional	Evidence of cocaine exposure found in 4 infants.
Durand, 1990 <sup>14</sup>	United States, English	Drug use interview with specialized obstetric and pediatric teams and urine tests of at-risk mothers and infants	SIDS confirmed by autopsy	18	Retrospective cohort	SIDS incidence was 6.76 times higher in offspring of drug-using mothers during pregnancy (85% cocaine users) vs control ( $p < 0.0002$ ). Cocaine-specific incidence not reported.
Habel, 1990 <sup>15</sup>	United States, English	Gestational cannabis exposure identified by birth records via maternal report	Cause of death defined by medical records	1350	Retrospective cohort	SIDS mortality rate was 6.5 per 1000 for drug-exposed infants vs 1.5 in general population. No difference for cocaine-only exposed infants.
Hauck, 2022 <sup>16</sup>	United States, English	Self-reported cocaine use during pregnancy	Cannabis use during pregnancy	195	Case-control	Adjusted odds ratio 4.65 for cocaine use (95% CI: 1.02–21.3).
Kandall, 1993 <sup>17</sup>	United States, English	Cocaine use during pregnancy assessed by chart review, maternal interview, and urine samples from mother and infant	SIDS confirmed by autopsy	1760	Retrospective cohort	SIDS incidence was 3 times higher among offspring of cocaine-using mothers compared to controls (incidence rate 3.32 [2.44–4.52]).
Klonoff-Cohen, 2001 <sup>18</sup>	United States, English	Parents interviewed about cocaine use from conception until child death	SIDS confirmed by autopsy	239	Case-control	Cocaine use analyzed with other recreational drugs. No association found between maternal drug use and SIDS during conception, pregnancy, or postnatal periods.
Ostrea, 1997 <sup>19</sup>	United States, English	Gestational cannabis exposure identified by meconium analysis	Cause of death defined by medical records	11	Retrospective cohort	SIDS incidence among cocaine-positive infants was 5.5 per 1000 live births (OR=1.9; 95% CI: 0.58–6.3).

Rosen, 1988 <sup>20</sup>	United States, English	Maternal report of cocaine use during prenatal care; confirmed in infants by urine testing	SIDS defined by autopsy report	4	Observational cohort	Of the 4 infants who died from SIDS, 3 were children of mothers using cocaine along with other substances.
Ward, 1990 <sup>21</sup>	United States, English	Gestational cocaine exposure based on maternal reports or positive urine tests in mother or infant	SIDS confirmed by autopsy	415	Retrospective cohort	SIDS incidence was 7.27 times higher for infants exposed to cocaine.

**Legend:** CI = confidence interval; OR = odds ratio; RR = relative risk; SIDS = sudden infant death syndrome

Among the studies included, the methods for assessing cocaine exposure varied, encompassing interviews, medical record reviews, and toxicological examinations. There was also variation in the timing of exposure, which could have occurred at conception, during pregnancy, or in the postnatal period. The data regarding frequency, dosage, and route of cocaine use were not reported in the studies analyzed. Only one study specifically evaluated paternal cocaine use.

Regarding the outcome of death due to SIDS, the studies primarily relied on autopsy reports or medical records. The number of SIDS-related deaths assessed in each study ranged from 4 to 1,760 cases. In total, the studies included in this systematic review evaluated 4,473 SIDS deaths.

A statistical analysis specifically correlating SIDS with cocaine use was available in seven of the eleven included studies. In four of these seven studies, the findings suggested an association between exposure and outcome. In the retrospective cohort study by Aoki (1994),<sup>11</sup> approximately 23% of infants who died from SIDS had been exposed to cocaine, and the risk of SIDS was significantly higher ( $p < 0.025$ ) among offspring of cocaine-using mothers. However, this association was attenuated after controlling for family ethnicity. In the case-control study by Hauck (2022),<sup>16</sup> an adjusted odds ratio (OR) of 4.65 for cocaine use was reported (confidence interval [CI] 95%: 1.02–21.3). The findings indicated that maternal cocaine use during pregnancy increased the risk of SIDS three- to fivefold, even after adjustment for sociodemographic variables. Similarly, the retrospective cohort study by Kandall (1993)<sup>17</sup> showed that the incidence of SIDS was three times higher among offspring of cocaine-using mothers compared with controls (incidence rate 3.32 [2.44–4.52]). Finally, the retrospective cohort study by Ward (1990)<sup>21</sup> demonstrated an increased incidence of SIDS among infants exposed to cocaine (relative risk [RR] 6.28; 95% CI: 4.04–11.6), although the authors also noted that social determinants may act as confounding factors in this association.

In the remaining three studies, although a potential trend toward association was observed, the confidence intervals did not support a definitive conclusion, or a risk analysis was not conducted. In the prospective cohort study by Bauchner (1988),<sup>12</sup> RR of SIDS among infants whose mothers used cocaine during pregnancy was 1.17 (95% CI: 0.13–10.43). Notably, the wide confidence interval and the authors’ observation suggest that the observed increase in risk may actually reflect health behaviors and sociodemographic factors within the sample. In the retrospective cohort study by Habel (1990),<sup>15</sup> the SIDS mortality rate was 6.5 per 1,000 among drug-exposed infants compared with 1.5 per 1,000 in the general population; however, the authors found no difference among infants exposed exclusively to cocaine. Finally, the retrospective cohort study by Ostrea (1997)<sup>19</sup> reported a SIDS incidence of 5.5 per 1,000 live births among cocaine-positive infants (OR = 1.9; 95% CI: 0.58–6.3). In addition to the wide confidence interval, this study focused on multiple causes of mortality among children exposed to drugs during the perinatal period and included only two cases of SIDS.

The risk of bias assessment for the studies included in this systematic review is presented in Table 2. Overall, the studies met most of the criteria associated with a lower risk of bias, according to the appraisal tools applied. However, control of confounding factors appeared to be an important limitation in the included cohort studies, as assessed by criteria 4 and 5 of the tool used.

**Table 2:** Critical appraisal checklist for cohort, cross-sectional, and case-control studies. The assessment criteria are described in detail in Supplementary Table 2.

<b>Cohort studies</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<b>11</b>
Aoki, 1994	NA	Y	Y	U	NA	Y	Y	Y	Y	NA	Y
Bauchner, 1988	Y	Y	Y	U	NA	Y	Y	Y	Y	NA	Y
Davidson, 1990	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y
Durand, 1990	Y	Y	Y	U	NA	Y	Y	N	N	NA	Y
Habel, 1990	Y	Y	Y	Y	NA	Y	Y	Y	Y	NA	Y
Kandall, 1993	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y
Ostrea Jr et al., 1997	Y	Y	U	N	U	Y	Y	Y	Y	NA	Y
Rosen; Johnson, 1988	N	Y	Y	Y	N	Y	Y	Y	Y	NA	N
Case-control studies	1	2	3	4	5	6	7	8	9	10	
Hauck; Blackstone, 2022	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
Klonoff-Cohen; Lam-Kruglick, 2001	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
Cross-sectional studies	1	2	3	4	5	6	7	8			
Claudet et al, 2021	Y	Y	Y	Y	Y	N	Y	N			

**Legend:** Y = Yes; N = No; U = Unclear; NA = Not applicable

## DISCUSSION

In this systematic review, eleven studies were identified that investigated the association between parental cocaine use during the perinatal period and the occurrence of SIDS. However, it is important to highlight the heterogeneity among studies regarding the methods of exposure assessment, as well as the predominance of older research conducted in developed countries. Among the studies that presented statistical analyses enabling inferences about the potential risk of SIDS associated with cocaine exposure, most reported suggestive evidence of such an association. Furthermore, the analysis showed that the majority of the included studies had a low risk of bias.

In Brazil, in 2019, the disability-adjusted life years (DALYs) attributable to cocaine abuse were the highest in South America, at 45 per 100,000 inhabitants.<sup>22</sup> Additionally, the Americas exhibit a higher burden of cocaine use disorders than the global average, primarily due to South America’s role as the world’s largest supplier of this drug. The high prevalence of cocaine use in the region may be linked to proximity to production sites and the low cost of cocaine derivatives, particularly crack and coca paste.<sup>22</sup> However, none of the studies included in this systematic review were conducted in Latin America; studies involving North American populations predominated. Therefore, it would be important for the association between cocaine use and the risk of SIDS to be evaluated more specifically in Brazil and South America.

When exploring the relationship between cocaine use during pregnancy and the occurrence of SIDS, in addition to the afore mentioned effects, placental and

fetal alterations must also be considered as potential contributors. Cocaine may act both as a biological agent and as a social/environmental factor. Biologically, it is well-established that cocaine crosses both the placental and blood-brain barriers and acts on the fetal brain as a stimulant by inhibiting the reuptake of dopamine, serotonin, and norepinephrine.<sup>23</sup> Furthermore, during the postnatal period, cocaine can reach the infant through breastfeeding or direct inhalation.<sup>6</sup> Studies have identified a fourfold increased risk of placental abruption among users compared to non-users<sup>23</sup> and robust evidence linking prenatal cocaine exposure to low birth weight.<sup>24</sup> However, most studies have not adequately controlled for confounding variables such as concomitant alcohol, tobacco, and/or other drug use.

From a social perspective, drug-seeking behaviors may also compromise the safety of the infant’s living environment, exposing the child to poverty and violence. Potential consequences include delayed neurodevelopment, behavioral disturbances, and an increased risk of accidents.<sup>6,25</sup> Health-related risk behaviors and sociodemographic factors associated with drug-using populations were frequently identified by the authors of the included studies as potential confounders for the SIDS outcome.

According to the American Academy of Pediatrics (AAP), impaired caregiving arises from the inability to maintain alertness or to awaken in emergency situations when under the influence of substances.<sup>6</sup> The AAP firmly advises against bed-sharing with infants due to the increased risk of suffocation, falls, or crushing injuries. Among parents who use drugs, the risk of adverse outcomes may be up to ten times higher compared to bed-sharing without additional risk factors.<sup>6</sup>

In the present review, variability in exposure—whether in terms of frequency, dosage, route of use, or timing—hinders the establishment of a reliable causal relationship. The findings reveal a paucity of data on this topic, particularly concerning standardized exposure assessment and the elimination of confounding factors, such as the use of other substances. Moreover, the social conditions of children born to cocaine users—characterized by neglect and resource scarcity—may represent the actual causes of adverse outcomes within this age group, complicating the analysis of exposure from a strictly pathophysiological perspective. Additionally, a significant limitation of this review is that all included studies were conducted in developed countries. Due to socioeconomic disparities, these findings are difficult to extrapolate to the realities of developing nations, such as Brazil.

Notably, 36% of the analyzed studies identified a direct and statistically significant association between exposure (isolated cocaine use) and the outcome (SIDS).<sup>11,14,16,17</sup> These four studies assessed exposure similarly, through drug use history and urine toxicology tests, but reported their findings qualitatively, focusing solely on the presence or absence of the substance. This raises the hypothesis that higher urinary cocaine concentrations may be quantitatively associated with an increased risk of SIDS. Moreover, this consistency reinforces the reliability of the method for exposure assessment, given the significant associations observed.

Despite these positive findings, two studies reported associations between exposure and outcome that did not reach statistical significance, while five other studies were unable to control for confounding exposures such as tobacco or other illicit drugs. It is also important to consider that many studies assessed exposure based on parental self-report, which raises the possibility that exposure may be underrepresented in the sample due to participants' reluctance to disclose drug use during the perinatal period. Moreover, exposure to drugs that are more socially accepted, such as licit substances, may be reported more frequently than exposure to illicit drugs.

The predominance of older studies on this topic, many of which were published more than 20 years ago, is also noteworthy. This raises additional concerns, as patterns of licit and illicit drug use vary across generations and cultural contexts, and findings from earlier studies may not accurately reflect current realities in terms of frequency of use, routes of administration, contaminants, production methods, and interactions with other substances.

Some of the included studies, in particular, presented additional concerns in the risk-of-bias assessment. The study by Durand (1990),<sup>14</sup> for example, does not clearly report the duration of participant follow-up, which may have resulted in unrecorded

outcomes within the cohort. Similarly, the study by Rosen and Johnson (1988)<sup>20</sup> does not address potential confounding factors in its sample, nor did it perform a statistical analysis of the results regarding the SIDS outcome. Finally, the only cross-sectional study included in this systematic review, conducted by Claudet et al. (2021),<sup>13</sup> did not report strategies to mitigate potential confounding factors and did not employ appropriate statistical analysis to allow robust conclusions regarding the association between cocaine use and the risk of SIDS.

Based on the evidence presented, it is possible to infer a relationship between cocaine use during pregnancy and SIDS. However, the scarcity of related studies, the challenges in eliminating confounding variables, the heterogeneity in exposure assessment, and the lack of research in developing or underdeveloped countries impede the formulation of a precise conclusion. Therefore, further studies addressing these gaps are warranted to refine the analysis of cocaine as a causal factor in the etiology of SIDS. Such research would also contribute to the development of targeted intervention policies, providing robust statistical evidence of the potential harms to infants and informing prevention efforts through public health campaigns, clinical care initiatives, and other strategies aimed at progressively reducing exposure and, consequently, the incidence of SIDS.

## CONCLUSION

In summary, while existing evidence suggests a potential association between prenatal cocaine exposure and an increased risk of sudden infant death syndrome (SIDS), significant methodological limitations—such as heterogeneous exposure assessments, uncontrolled confounding variables, and a lack of studies from low- and middle-income countries—undermine the ability to draw definitive conclusions. Future research with standardized methodologies and greater geographical diversity is essential to clarify the role of cocaine as a risk factor for SIDS and to guide effective public health interventions.

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