

Newborn outcomes exposure to crack cocaine during pregnancy: a critical review**Recém-nascidos expostos ao crack durante a gestação: uma revisão crítica**

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Tatiane Britto da Silveira

Doutora em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG

Instituição: Universidade Federal do Rio Grande - FURG

Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.

CEP: 96203-900

E-mail: taty.psico30@gmail.com

Marina dos Santos

Doutora em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG

Instituição: Universidade Federal do Rio Grande - FURG

Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.

CEP: 96203-900

E-mail: marina.wicks@gmail.com

Ronan Adler Tavella

Doutorando em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG

Instituição: Universidade Federal do Rio Grande - FURG

Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.

CEP: 96203-900

E-mail: ronan_tavella@hotmail.com

Rodrigo de Lima Brum

Mestrando em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG

Instituição: Universidade Federal do Rio Grande - FURG

Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.

CEP: 96203-900

E-mail: rodrigo.brum.93@gmail.com

Edariane Menestrino Garcia

Doutora em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG

Instituição: Universidade Federal do Rio Grande - FURG

Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.

CEP: 96203-900

E-mail: nanamenestrino@hotmail.com

Adriane Netto de Oliveira

Doutora em Enfermagem pela Universidade Federal de Santa Catarina

Instituição: Escola de Enfermagem, Universidade Federal do Rio Grande - FURG

Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.

CEP: 96203-900

E-mail: adrianenet@vetorial.net

Ana Luíza Muccillo-Baisch

Doutora em Sciences Biologique Et Médicales Biologie Santé pela Universidade de Bordeaux II

Instituição: Centro Regional de Estudos, Prevenção e Recuperação de Dependentes Químicos,
Universidade Federal do Rio Grande - FURG

Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.

CEP: 96203-900

E-mail: anabaisch@gmail.com

Flavio Manoel Rodrigues da Silva Júnior

Doutor em Ciências Fisiológicas pela Universidade Federal do Rio Grande - FURG

Instituição: Universidade Federal do Rio Grande - FURG

Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.

CEP: 96203-900

E-mail: f.m.r.silvajunior@gmail.com

ABSTRACT

Crack cocaine is a psychotropic and neurotoxic drug with high prevalence of consumption, considerate a public health problem and identified as risk factors to human health. Crack cocaine use among women in reproductive age increased in few year and the literature of the neonatal exposure to this substance during pregnancy are limited. Thus, this critical review discusses the major newborn outcomes reported in original studies, highlighting neurologic abnormalities and malformations outcomes. Sixteen studies were included in this review. The main physiological outcome found in newborn exposure to crack cocaine during gestation were lower birth weight; preterm birth; growth restricted infants; lower 5-minute Apgar scores; small for gestational age; and, small head circumference and congenital malformations. There were several negative neurologic and outcomes were reported on the literature. Moreover, there were still no consensus and the main criticism in this area is the limited studies available.

Keywords: Illicit drugs, gestation, neonate.

RESUMO

O crack é uma droga psicotrópica e neurotóxica, com alta prevalência de consumo, considerado um problema de saúde pública e tido como fator de risco para a saúde humana. O uso de crack entre mulheres em idade reprodutiva aumentou em poucos anos e a literatura sobre a exposição neonatal a essa substância durante a gravidez é limitada. Assim, esta revisão crítica discute os principais desfechos neonatais relatados em estudos originais, destacando como desfechos as anormalidades neurológicas e as malformações. Dezesesseis estudos foram incluídos nesta revisão. Os principais desfechos fisiológicos encontrados na exposição do recém-nascido ao crack durante a gestação foram menor peso ao nascer; nascimento prematuro; restrição de crescimento; menores escores de Apgar no 5º minuto; pequeno para a idade gestacional; menor circunferência da cabeça e malformações congênitas. Houve vários desfechos neurológicos negativos e os resultados foram relatados na literatura. Ainda assim, não houve consenso na literatura e as principais críticas nesta área são os limitados estudos disponíveis.

Palavras-chave: drogas ilícitas, gestação, recém-nascido.

1 INTRODUCTION

Drug abuse is one of the major social and public health problems in the world (UNODC, 2017). Cocaine is a product known since the beginning of history, considered a drug with great

potential dependence, and it is classified as a stimulant of the Central Nervous System (CNS) (Behnke, Eyler, Garvan, & Wobie, 2001). Cocaine can generate other drugs, such as crack cocaine, a cheap product, which can reach all social classes.

Crack cocaine is a smoked form and almost pure concentrate of cocaine. It is obtained by the conversion of hydrochloride form back into alkalized form. Crack cocaine may be a more dangerous form of cocaine (dos Santos et al., 2018). There are several psychotropic and neurotoxic effects of crack cocaine use, because of products generated from cocaine pyrolysis (Garcia et al., 2012). Indeed, crack cocaine use lead short-duration euphoria as a consequence of high bioavailability and metabolism.

The economic impact of crack addiction is not only due to the large number of cases, but to the high costs of detoxification, prolonged hospitalization, high morbidity and criminality (Guimarães, Dos Santos, Freitas, & Araujo, 2008). Crack cocaine consumption increased mainly after the 80's worldwide (Balbinot, Alves, Amaral Junior, & Araujo, 2011). According to the World Drug Report of 2017, presented by the United Nations Office on Drugs and Crime (UNODC, 2017), crack cocaine addiction is one of the public health problems in different countries and is identified as the twenty highest risk factors for human health.

The National Survey of Drug Use and Health, reported an increase of crack cocaine use among women and about 90% are in childbearing age (NSDUH, 2008). However, the exact prevalence of crack cocaine use during pregnancy is still not clear (Aghamohammadi & Zafari, 2016). The prevalence of illicit drug among pregnant women is approximately 5.2% at any time during pregnancy (NSDUH, 2008), which poses great risks to woman and infant health (Schempf, 2007).

The negative effects of crack cocaine use are well recognized. However, physiological changes during pregnancy increase crack cocaine effects, especially its cardiovascular toxicity (Botelho, Rocha, & Melo, 2013). In addition, chemical substances present in crack cocaine can cross the placental blood barrier and may affect intrauterine fetal development (Matos, Melo, Colombo, & Melo, 2011). The influences of this substance to newborn health are a concern (Aghamohammadi & Zafari, 2016). The literature identified newborn crack cocaine intoxicated as "crack babies" (Duailibi, L.B.; Ribeiro, M.; Laranjeira, 2008).

The literature about crack cocaine use during pregnancy and its effects in newborn are still controversial and restrict. Thus, the purpose of the study was evaluated, through a literature review, studies that reported neonatal outcomes exposure to crack cocaine during pregnancy.

2 MATERIAL AND METHODS

Search strategy

This study is a critical review of the literature on the topic of unfavorable outcomes in newborns from crack cocaine use during pregnancy. The research was carried out in august 2018, through the databases: Pubmed/Medline (Medical Literature Analysis and Retrieval System Online), Lilacs (*Literatura Latino-Americana e do Caribe em Ciências da Saúde*), Scielo (Scientific Electronic Library Online), Web of Science and Google Scholar.

The data search occurred from the descriptors: "*crack*", "*pregnant women*", "*child OR children OR newborn*", without date, country and language restrictions. The titles and abstracts were independently screened by two reviewers (RAT and MS). After consulting the databases and the application of the search strategies, duplicates between studies in different databases were identified. All pre-selected abstracts were read. In cases where the abstract reading was not sufficient, the full article was read to ensure its inclusion. After that, the integral reading of each study was performed, and the thematic analysis of content of the articles was carried out.

Inclusion and exclusion criteria

To be included in this review, studies must followed criteria adopted: studies addressing newborn outcomes from pregnant users of crack cocaine. Articles were excluded when they presented some of the following criteria: a) literature reviews, b) articles with socioeconomic outcomes, c) articles that did not provide the text in full or without a summary; d) articles that did not involve human beings; e) articles selected by the search system, but did not cover the outcome; and f) articles that addresses the outcomes of cocaine instead of crack in their results.

Data extraction and statistical analysis

Information was extracted from all eligible studies, including publication date, country, study design, sample size and newborn outcomes. In clinical trials studies were used only baseline data from the crack cocaine users.

3 RESULTS

A total of 188 titles were identified by searching the electronic databases, of which 172 were excluded during screening based on the inclusion and exclusion criteria (Figure 1).

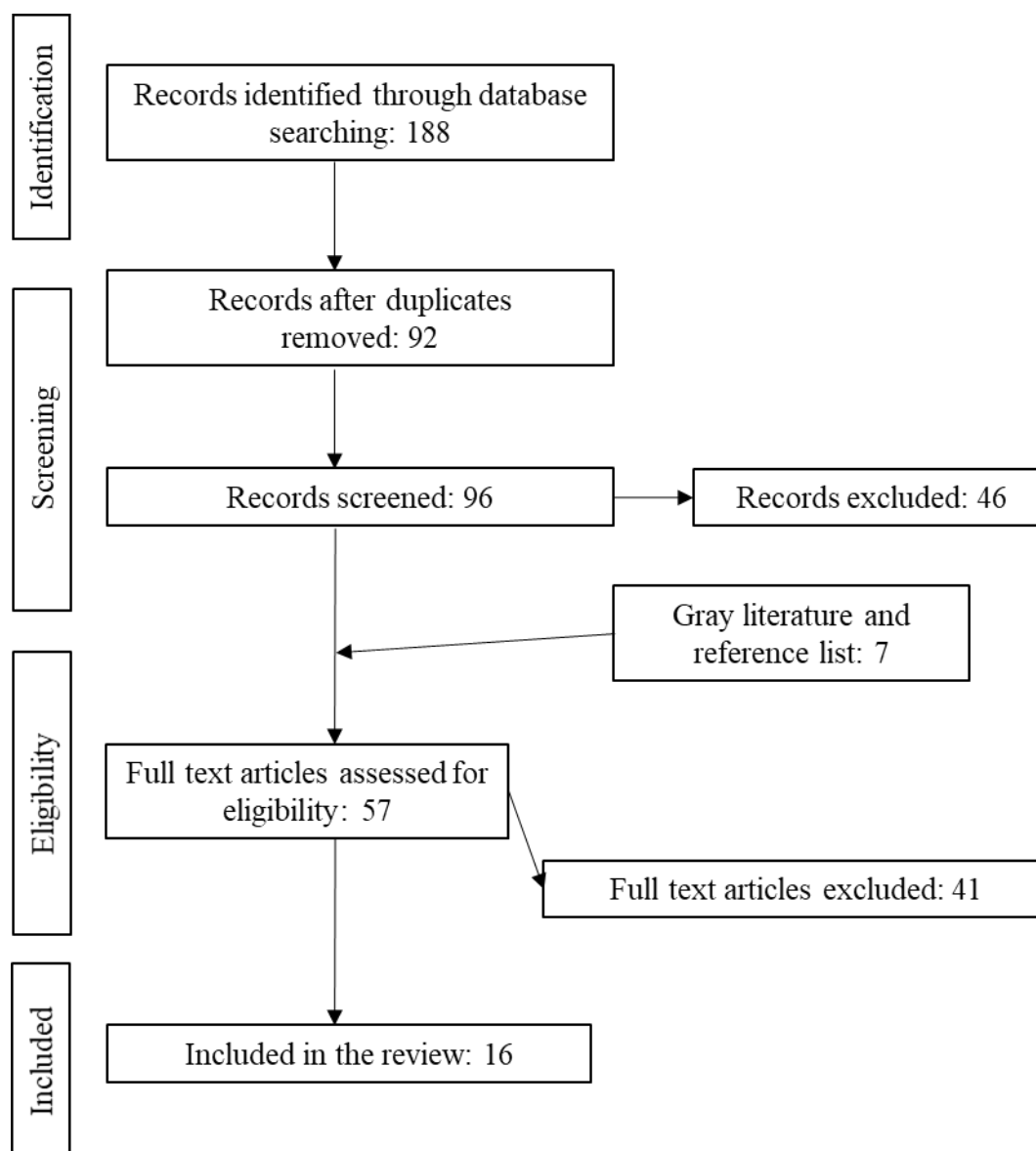


Figure 1. The flowchart of selected journal articles.

Thus, a total of 16 studies were included. The extracted data for each study are presented in table 1. The main birth outcomes found were: lower birth weight; preterm birth; growth restricted infants; lower 5-minute Apgar scores; small for gestational age; and, small head circumference. Regarded to neurologic outcomes, several behavior abnormalities were cited. While, just one study observe association with malformations (Xavier, Gomes, Ribeiro, Mota, & Alvarez, 2017).

Table 1. Characteristics of the ten included articles and significant newborn outcomes observed.

			Sample size	Neonatal repercussions	
				Birth Outcomes	Neurologic and malformations outcomes
Leblanc, 1987	EUA	Case-control	38	Low birth weight Preterm delivery Small for gestational age Small head circumference	Tremulousness Irritability Muscular rigidity
Cherukuri, 1987	EUA	Cohort	25	Low birth weight Preterm delivery Small head circumference	Abnormal neuromuscular symptoms
Cherukuri, 1988	EUA	Cohort	55	Lower birth weight Preterm delivery Small head circumference	Tremulousness Irritability Muscular rigidity
Bateman et al., 1993	EUA	Cohort	748	Lower birth weight Preterm delivery	Not verified
Eyler et al., 1994	EUA	Cohort	340	Congenital anomalies Placental abruption	Not verified
Sprauve et al., 1997	EUA	Cohort	483	Lower birth weight Preterm delivery Growth-restricted infants Lower 5-minute Apgar scores	No significant result
Eyler et al., 1998	EUA	Cohort	308	Preterm delivery	Not verified
Behnke et al., 2001	EUA	Cohort	272	Preterm delivery Lower birth weight Small head circumference Small for gestational age	Not verified
Fiocchi & Kingree., 2001	EUA	Cross-section	76	Low birth weight Preterm delivery	Not verified
Zavaschi et al., 2014	Brazil	Cross-section	12	Low birth weight Preterm delivery	Not verified
Reis & Loureiro, 2015	Brazil	Cross-section	14	Preterm delivery Small for gestational age	Exacerbated Moro reflex, Exacerbated/heightened hypoactivity irritability hypotonia weak sucking reflex lethargy Tremulousness
Mardini et al., 2016	Brazil	Cross-section	57	Lower birth weight High inflammatory state	Not verified
Aghamohammadi & Zafar, 2016	Iran	Control case	88	Low birth weight. Preterm delivery	Not verified
Madrini et al., 2017	Brazil	Cross-section	57	Lower birth weight	High lipid peroxidation
Xavier et al., 2017	Brazil	Qualitative research	15	Preterm delivery	Cleft palate and cleft lip Anomalies of mandible and ear microcephaly born without a lung malformation
Parcianello et al., 2017	Brazil	Cross-section	57	Low birth weight Lower 5-minute Apgar scores	High antioxidant action

4 DISCUSSION

The majority of studies reports assessment of alcohol, marijuana or cocaine use during pregnancy (Addis, Moretti, Ahmed Syed, Einarson, & Koren, 2001; Castro, Guilam, Sousa, & Marcondes, 2013; Frank, Augustyn, Knight, Pell, & Zuckerman, 2001; Gouin, Murphy, & Shah, 2011). In this critical review, it was availed studies that reported newborn outcomes exposure to crack cocaine during the pregnancy. Worldwide, crack cocaine use is a severe public health (UNODC, 2017), being one of the most prevalent form of the drug abused, mainly between EUA and Brazil (Rotta & Cunha, 2000). According to the literature, pregnant women among the lower economic classes used this drug, especially, due to the lower prices (Behnke, Eyler, Garvan, Wobie, & Context, 2017; Eyler, Behnke, Conlon, Woods, & Wobie, 1998).

The prevalence of intoxicated children by crack cocaine increased (dos Santos et al., 2018), because its metabolites cross the placenta and reach fetal tissues in high concentrations, which might affect child development (Zavaschi et al., 2014). The negative effect of crack cocaine do not depend on the dose, suggesting that any exposure levels increase the risk to newborn (White & Lambe, 2003). Indeed, crack cocaine effects in utero are very different for each newborn (Mardini et al., 2017; Parcianello et al., 2018) and the exposure impact may continue after birth, resulting in long-term effects on the child's organism (dos Santos et al., 2018; Jones, 2015).

The results show innumerable negative outcomes for newborn health. Concerning the common physiological outcomes, low birth weight (Aghamohammadi & Zafari, 2016; Bateman, Ng, Hansen, & Heagarty, 1993; Behnke et al., 2001; Bender et al., 1995; R Cherukuri, Minkoff, Feldman, A, & Glass, 1988; Radha Cherukuri, Howard, Parekh, Feldman, & Glass, 1987; Fiocchi & Kingree, 2001; Leblanc, 1987; Mardini et al., 2016, 2017; Parcianello et al., 2018; Sprauve, Lindsay Michael K., Herbert, & Graves, 1997; Zavaschi et al., 2014) preterm delivery (Aghamohammadi & Zafari, 2016; Bateman et al., 1993; Behnke et al., 2001; R Cherukuri et al., 1988; Radha Cherukuri et al., 1987; Eyler et al., 1998; Fiocchi & Kingree, 2001; Leblanc, 1987; Reis & Loureiro, 2015; Sprauve et al., 1997; Xavier et al., 2017) and small for gestational age (Behnke et al., 2001; Leblanc, 1987; Reis & Loureiro, 2015) were well establish risk between newborn exposure to crack cocaine during pregnancy (dos Santos et al., 2018). The low 5-minute Apgar score (Parcianello et al., 2018; Sprauve et al., 1997) and small head circumference (Behnke et al., 2001; R Cherukuri et al., 1988; Radha Cherukuri et al., 1987; Leblanc, 1987) were also reported as a risk to crack cocaine exposure.

The most common outcomes in children exposure to crack cocaine were preterm delivery, low birth weight, small for gestational age and small head circumference, when compared with the drug-free groups. These outcomes were possibly associated with nutrition problems during pregnancy, due to the gradual reduction in placental blood flow produced by vasoconstriction,

decreasing oxygen and nutrient transfer to the fetus (Aghamohammadi & Zafari, 2016) and complications in brain development (McCarthy, Kabir, Bhide, & Kosofsky, 2014; Nordstrom-Klee, Delaney-Black, Covington, Ager, & Sokol, 2002). Also, it is important that pregnant crack cocaine users usually present inadequate nutrition intake (Eide, Stevens, Schuetze, & Dombkowski, 2006; Fajemirokun-Odukeyi & Lindow, 2004).

It is important to highlight the fact that newborn of crack cocaine user mothers are private of breastfed, do not receiving benefits of breast milk, which get worse birth outcomes and may affect the health adult life (Xavier et al., 2017). Breast milk is an extremely complex and highly variable fluid to nourish infants and protect them from disease whilst their own immune system matures. The composition of human breast milk changes matching the infant's requirements (Fujita et al., 2012; Michaelsen, Skafte, Badsberg, & Merete, 1990). Therefore, the breast milk is vital for health development of newborn (Andreas, Kampmann, & Mehring Le-Doare, 2015).

Another important physiological newborn outcome reported were several congenital malformations such as, cleft palate and cleft lip, anomalies of mandible and ear, microcephaly, born without a lung and congenital malformation (Xavier et al., 2017). Regarding malformations outcomes, there were still no consensuses (Sprauve et al., 1997). In relation to neurologic outcomes, studies observed tremulousness; irritability, muscular rigidity (R Cherukuri et al., 1988; Leblanc, 1987) neuromuscular symptoms (Radha Cherukuri et al., 1987); abnormal receptive language and visual motor (Bender et al., 1995); exacerbated motor reflex, exacerbated/heightened hypoactivity, irritability hypotonia, weak sucking reflex, lethargy and tremors (Reis & Loureiro, 2015). It was observed high lipid peroxidation, representing the inflammatory response system exacerbated. Neurologic abnormalities are frequently reported in newborn of crack cocaine user mothers, although, biological mechanisms of these alterations are still unclear. It was suggest that crack cocaine acts on maternal and fetus central nervous system, inhibiting dopamine, noradrenaline and serotonin reuptake at the presynaptic terminals, and exacerbating their effects (Span, 2011). Additionally, the use of crack affects the monoamine neurotransmitter functions of the developing fetal brain (McCarthy et al., 2014). All these factors can generate inadequate neuronal functions development and potentiating neurological effects of newborn.

Also, newborn from crack cocaine user mothers frequently receive inadequate prenatal care (Sprauve et al., 1997) or abnegate the addiction on this moment, which make more difficult the identification of newborn at risk (Camargo & Martins, 2014). Indeed of physiological outcomes observed, series of psychological consequence on postnatal may affect the newborns, since their mothers, in general, do not form affective bonds, experience mothering and frequently abandoned their babies (Xavier et al., 2017; Yabuuti & Bernardy, 2014).

Crack cocaine use during pregnancy cause serious health outcomes and social consequences for newborn. Since, only a few pregnant women report drug use, the prevalence of treatment is low during pregnancy. Indeed, symptoms of crack cocaine addiction can be confused with the effects by other substances or with diseases (Rayburn, 2007). Thus, the number of newborns exposure to crack cocaine may be higher than the reported in the found literature. Although recent research has shown more robustly the impact of crack cocaine on neonatal health, this is a field of research that must be explored, since it has a multifactorial effect. Countries with a crack cocaine epidemic, such as Brazil, should prioritize actions to minimize the harm to these children, aiming at social equity

5 CONCLUSION

This review show the most common birth outcomes in newborn exposure to crack cocaine during pregnancy were preterm delivery, low birth weight, small for gestational age and small head circumference, highlighting neurologic abnormalities and malformations outcomes. There were several negative neurologic and malformations outcomes observed, however, there were still no consensus when compared newborn from drug-free mothers.

This research corroborates the need of further studies on the subject. Thus, future studies are needed to know how crack cocaine exposure during pregnancy may affect in long-term the development of these newborns, since, this population grows gradually. Besides that, it is need education as well as health professionals prepared to deal with this emerging demand.

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REFERENCES

- Addis, A., Moretti, M. E., Ahmed Syed, F., Einarson, T. R., & Koren, G. 2001. Fetal effects of cocaine: An updated meta-analysis. *Reproductive Toxicology*, 15(4), 341–369. [https://doi.org/10.1016/S0890-6238\(01\)00136-8](https://doi.org/10.1016/S0890-6238(01)00136-8)
- Aghamohammadi, A., & Zafari, M. 2016. Crack abuse during pregnancy: Maternal, fetal and neonatal complication. *Journal of Maternal-Fetal and Neonatal Medicine*, 29(5), 795–797. <https://doi.org/10.3109/14767058.2015.1018821>

- Andreas, N. J., Kampmann, B., & Mehring Le-Doare, K. 2015. Human breast milk: A review on its composition and bioactivity. *Early Human Development*, 91(11), 629–635. <https://doi.org/10.1016/j.earlhumdev.2015.08.013>
- Balbinot, A. D., Alves, S. G. L., Amaral Junior, F. A., & Araujo, R. B. 2011. Associação entre fissura e perfil antropométrico em dependentes de crack Relation between craving and anthropometric profile in crack dependents. *Jornal Brasileiro de Psiquiatria*, 60(3), 205–209.
- Bateman, D. A., Ng, S. K. C., Hansen, C. A., & Heagarty, M. C. 1993. The effects of intrauterine cocaine exposure in newborns. *American Journal of Public Health*, 83(2), 190–193. <https://doi.org/10.2105/AJPH.83.2.190>
- Behnke, M., Eyler, F. D., Garvan, C. W., & Wobie, K. 2001. The Search for Congenital Malformations in Newborns With Fetal Cocaine Exposure. *Pediatrics*, 107(5).
- Behnke, M., Eyler, F. D., Garvan, C. W., Wobie, K., & Context, A. 2017. The Search for Congenital Malformations in Newborns With Fetal Cocaine Exposure, 107(5).
- Bender, S. L., Word, C. O., DiClemente, R. J., Crittenden, M. R., Persaud, A. N., & Ponton, L. E. (1995). The Developmental Implications of Prenatal and/or Postnatal Crack Cocaine Exposure in Preschool Children: A Preliminary Report. *Developmental And Behavioral Pediatrics*, 16(6).
- Botelho, A. P. M., Rocha, R. da C., & Melo, V. H. 2013. Cocaine / crack use and dependence in pregnancy , delivery and puerperium. *FEMINA*, 41(1).
- Camargo, P. D. O., & Martins, M. de F. D. 2014. Os efeitos do crack na gestação e nos bebês nascidos de mães usuárias : Uma revisão bibliográfica. *Caderno Terapia Ocupacional*, 22, 161–169.
- Castro, A. P. de, Guilam, M. C. R., Sousa, E. S. S., & Marcondes, W. B. 2013. Violência na velhice: abordagens em periódicos nacionais indexados. *Ciência & Saúde Coletiva*, 18(5), 1283–1292. <https://doi.org/10.1590/S1413-81232013000500013>
- Cherukuri, R., Howard, M., Parekh, A., Feldman, J., & Glass, L. 1987. Alkaloidal cocaine (“crack”) in pregnancy: a prospective cohort study. *Developmental Pharmacology*, 2.
- Cherukuri, R., Minkoff, H., Feldman, J., A. P., & Glass, L. 1988. A cohort study of alkaloidal cocaine (“crack”) in pregnancy. *Obstetrics and Gynecology*, 72, 147–151.
- dos Santos, J. F., de Melo Bastos Cavalcante, C., Barbosa, F. T., Gitai, D. L. G., Duzzioni, M., Tilelli, C. Q., ... de Castro, O. W. 2018. Maternal, fetal and neonatal consequences associated with the use of crack cocaine during the gestational period: a systematic review and meta-analysis. *Archives of Gynecology and Obstetrics*, 298(3), 487–503. <https://doi.org/10.1007/s00404-018-4833-2>
- Duailibi, L.B.; Ribeiro, M.; Laranjeira, R. 2008. Profile of cocaine and crack users in Brazil Perfil dos usuários de cocaína e crack no Brasil. *Caderno de Saúde Pública*, 545–557. <https://doi.org/10.1590/S0102-311X>

- Eide, R. D., Stevens, A., Schuetze, P., & Dombkowsko, L. E. 2006. Cocaine-Using Mothers: The Role of Postnatal Cocaine Use and Maternal Depression. *Psychol Addict Behav*, 20(1), 1–10. <https://doi.org/10.1161/STROKEAHA.110.605600>.Five
- Eyler, F. D., Behnke, M., Conlon, M., Woods, N. S., & Wobie, K. 1998. Birth Outcome From a Prospective, Matched Study of Prenatal Crack/Cocaine Use : I . Interactive and Dose Effects on Health and Growth. *Pediatrics*, 101(2).
- Fajemirokun-Odudeyi, O., & Lindow, S. W. 2004. Obstetric implications of cocaine use in pregnancy: A literature review. *European Journal of Obstetrics Gynecology and Reproductive Biology*, 112(1), 2–8. <https://doi.org/10.1016/j.ejogrb.2003.08.005>
- Fiocchi, F. F., & Kingree, J. B. 2001. Treatment retention and birth outcomes of crack users enrolled in a substance abuse treatment program for pregnant women. *Journal of Substance Abuse Treatment*, 20(2), 137–142. [https://doi.org/10.1016/S0740-5472\(00\)00159-8](https://doi.org/10.1016/S0740-5472(00)00159-8)
- Frank, D. A., Augustyn, M., Knight, W. G., Pell, T., & Zuckerman, B. 2001. Growth, development and behavior in early childhood following prenatal cocaine exposure: A systematic review. *Journal of the American Medical Association*, 285(12), 1613–1625. <https://doi.org/10.1001/jama.285.12.1613>
- Fujita, M., Roth, E., Lo, Y. J., Hurst, C., Vollner, J., & Kendell, A. 2012. In poor families, mothers' milk is richer for daughters than sons: A test of Trivers-Willard hypothesis in agropastoral settlements in Northern Kenya. *American Journal of Physical Anthropology*, 149(1), 52–59. <https://doi.org/10.1002/ajpa.22092>
- Garcia, R. C. T., Dati, L. M. M., Fukuda, S., Torres, L. H. L., Moura, S., De carvalho, N. D., ... Marcourakis, T. 2012. Neurotoxicity of anhydroecgonine methyl ester, a crack cocaine pyrolysis product. *Toxicological Sciences*, 128(1), 223–234. <https://doi.org/10.1093/toxsci/kfs140>
- Gouin, K., Murphy, K., & Shah, P. S. 2011. Effects of cocaine use during pregnancy on low birthweight and preterm birth: Systematic review and metaanalyses. *American Journal of Obstetrics and Gynecology*, 204(4), 340.e1-340.e12. <https://doi.org/10.1016/j.ajog.2010.11.013>
- Guimarães, C. F., Dos Santos, D. V. V., Freitas, R. C. De, & Araujo, R. B. 2008. Perfil do usuário de crack e fatores relacionados à criminalidade em unidade de internação para desintoxicação no Hospital Psiquiátrico São Pedro de Porto Alegre (RS). *Revista de Psiquiatria RS*, 30(2), 101–108.
- Jones, W. 2015. Cocaine use and the breastfeeding mother. *Practising Midwife*, 18(1), 19–22.
- Leblanc. 1987. Effects of Intrauterine Exposure to Alkaloidal Cocaine ('Crack'). *Australian Journal of Dementia Care*, 141, 937–938.
- Mardini, V., Rohde, L. A., Ceresér, K. M., Gubert, C. M., da Silva, E. G., Xavier, F., ... Szobot, C. M. 2017. TBARS and BDNF levels in newborns exposed to crack/cocaine during pregnancy: A

comparative study. *Revista Brasileira de Psiquiatria*, 39(3), 263–266. <https://doi.org/10.1590/1516-4446-2016-2035>

Mardini, V., Rohde, L. A., Ceresér, K. M. M., Gubert, C. de M., Silva, E. G. da, Xavier, F., ... Szobot, C. M. 2016. IL-6 and IL-10 levels in the umbilical cord blood of newborns with a history of crack/cocaine exposure in utero: a comparative study. *Trends in Psychiatry and Psychotherapy*, 38(1), 40–49. <https://doi.org/10.1590/2237-6089-2015-0081>

Matos, J. C., Melo, S. R. De, Colombo, J. V. P., & Melo, S. R. 2011. Neurological Effects of Exposure to Prenatal Cocaine/Crack. *Arquivos Do MUDI*, 15, 8–16.

McCarthy, D. M., Kabir, Z. D., Bhide, P. G., & Kosofsky, B. E. 2014. Effects of prenatal exposure to cocaine on brain structure and function. *Progress in Brain Research* (1st ed., Vol. 211). Elsevier B.V. <https://doi.org/10.1016/B978-0-444-63425-2.00012-X>

Michaelsen, K. F., Skafté, L., Badsberg, J. H., & Merete, J. 1990. Variation in macronutrients in human bank milk: Influencing factors and Implications for human mil banking. *Journal of Pediatric Gastroenterology and Nutrition*, 11, 229–239.

Nordstrom-Klee, B., Delaney-Black, V., Covington, C., Ager, J., & Sokol, R. 2002. Growth from birth onwards of children prenatally exposed to drugs: A literature review. *Neurotoxicology and Teratology*, 24(4), 481–488. [https://doi.org/10.1016/S0892-0362\(02\)00232-5](https://doi.org/10.1016/S0892-0362(02)00232-5)

NSDUH. 2008. Substance Abuse and Mental Health Services Administration. Results from the 2007 National Survey on Drug Use and Health: National findings.

Parcianello, R. R., Mardini, V., Ceresér, K. M. M., Langleben, D. D., Xavier, F., Zavaschi, M. L. S., Szobot, C. M. 2018. Increased cocaine and amphetamine-regulated transcript cord blood levels in the newborns exposed to crack cocaine in utero. *Psychopharmacology*, 235(1), 215–222. <https://doi.org/10.1007/s00213-017-4759-6>

Rayburn, W. F. 2007. Maternal and Fetal Effects from Substance Use. *Clinical Perinatol*, 34, 559–571. <https://doi.org/10.1016/j.clp.2007.09.001>

Reis, F. T., & Loureiro, R. J. 2015. Repercussões Neonatais Decorrentes da Exposição ao Crack Durante a Gestação. *Revista Eletrônica de Saúde Mental Alcool e Drogas*, 11(4), 217–224. <https://doi.org/10.11606/issn.1806-6976.v11i4p217-224>

Rotta, N. T., & Cunha, G. B. 2000. Prenatal exposure to cocaine : review of the neurobehavioral effects. *Jornal de Pediatria*, 76(3), 179–184.

Schempf, A. H. 2007. Illicit Drug Use and Neonatal Outcomes : A Critical Review. *Obstetrical and Gynecological Survey*, 62(11), 749–757.

Span, S. differences in the effects of cocaine abuse across the life. 2011. span. Dow-Edwards, Dina, 100(3), 208–215. <https://doi.org/10.1016/j.physbeh.2009.12.017>.Sex

Sprauve, M. E., Lindsay Michael K., Herbert, S., & Graves, W. 1997. Adverse Perinatal Outcome in Parturients Who Use Crack Cocaine. *Obstetrics & Gynecology*, 89(5), 674–678. [https://doi.org/10.1016/S0029-7844\(97\)00078-1](https://doi.org/10.1016/S0029-7844(97)00078-1)

UNODC, C. U. N. O. on D. and. 2017. Estimating prevalence: Indirect methods for estimating the size of the drug problem. <https://doi.org/10.1163/15718085-12341263>

White, S. M., & Lambe, C. J. T. L. 2003. The pathophysiology of cocaine abuse. *Journal of Clinical Forensic Medicine*, 10, 27–39. [https://doi.org/10.1016/S1353-1131\(03\)00003-8](https://doi.org/10.1016/S1353-1131(03)00003-8)

Xavier, D. M., Gomes, G. C., Ribeiro, J. P., Mota, M. S., & Alvarez, S. Q. 2017. Use of crack in pregnancy: Repercussions for the newborn. *Investigacion y Educacion En Enfermeria*, 35(3), 260–267. <https://doi.org/10.17533/udea.iee.v35n3a02>

Yabuuti, P. L. K., & Bernardy, C. C. F. 2014. Perfil de gestantes usuárias de drogas atendidas em um centro de atenção psicossocial. *Revista Baiana Saúde Pública*, 38(2), 344–356. <https://doi.org/10.5327/Z0100-0233-2014380200009>

Zavaschi, M. L. S., Mardini, V., da Cunha, G. B., Martins-Costa, S. H. de A., Guarienti, F., Pianca, T. G., ... Szobot, C. M. (2014). Socio-demographic and clinical characteristics of pregnant and puerperal crackcocaine using women: Preliminary data. *Revista de Psiquiatria Clinica*, 41(5), 121–123. <https://doi.org/10.1590/0101-608300000000025>