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Research Paper

Neonatal Abstinence Syndrome: Retrospective Descriptive Study Carried Out at the Toxicology Service of Bab El-Oued University Hospital between 2023 and 2025

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ABSTRACT

Background: Neonatal abstinence syndrome (NAS) comprises clinical manifestations resulting from the abrupt cessation of prenatal exposure to psychoactive substances. Although classically associated with opioids, increasing exposure to nonopioid substances has altered its epidemiological profile. Our goal is to characterize newborns referred for suspected NAS, identify the psychoactive substances involved, and evaluate the concordance between maternal history, neonatal clinical presentation, and toxicological findings.

Methods: We conducted a monocentric, retrospective descriptive study at the Toxicology Service of Bab El Oued University Hospital (Algiers) between January 2023 and December 2025. Newborns were included if they were investigated because of clinical signs, maternal history, or social risk factors. Data were collected from toxicology service registries, and urinary drug screening was performed in newborns and, when available, their mothers, using qualitative immunochromatographic assays.

Results: Seventy-five newborns were included, with a marked increase in annual cases over the study period. A male predominance was observed (sex ratio 1.70), and 50.7% were screened within the first 24 hours of life. Toxicological screening was positive in 60.0% of newborns. Pregabalin was the predominant substance, detected in 91.1% (41/45) of positive cases and as the sole agent in 64.4%. Polysubstance exposure occurred in 17.33% of cases, most commonly pregabalin combined with cocaine. Respiratory distress, tremors, hyperexcitability, and feeding difficulties were the most frequent clinical signs. In mother–newborn dyads with paired testing, toxicological findings contradicted or expanded maternal declarations in 57.1% (8/14) of cases.

Conclusion: Pregabalin was the substance most frequently detected among newborns investigated for suspected NAS in this Algerian cohort, suggesting a regional pattern that warrants confirmation in prospective, population-based studies.

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Introduction

Neonatal abstinence syndrome (NAS) comprises clinical manifestations resulting from the abrupt cessation of prenatal exposure to psychoactive substances. Although traditionally associated with in utero opioid exposure, NAS has also been reported following prenatal exposure to alcohol, benzodiazepines, nicotine, antidepressants, antipsychotics, and other psychoactive substances [1, 2]. Clinically, it is characterized by central nervous system hyperirritability, autonomic dysfunction, gastrointestinal disturbances, and, in severe cases, seizures [3].

The global incidence of NAS has increased substantially over the past two decades, representing an important public health concern. In the United States, the incidence increased from 4.6 to 6.7 cases per 1,000 in-hospital births between 2012 and 2016 [2, 4]. Similarly, Canada reported a 73% increase in NAS-related hospitalizations between 2010 and 2020 [5].

In Algeria, epidemiological data on NAS and the substances involved remain scarce. The present work aims to characterize the population of newborns investigated for suspected NAS at the Toxicology Service of Bab El Oued University Hospital, Algiers, to identify the psychoactive substances involved and to explore the relationship between toxicological findings and clinical presentation.

Materials and Methods

Study design and population

We conducted a monocentric retrospective descriptive study at the Toxicology Service of Bab El Oued University Hospital between January 1, 2023, and December 31, 2025. Newborns of both sexes were included if they met one or more of the following criteria:

- Presentation with clinical signs suggestive of NAS;
- Birth to a mother with a declared history of psychoactive substance use during pregnancy;
- Birth to a mother clinically or socially suspected of substance misuse;
- A physician-requested drug screen on the basis of specific risk factors (e.g., single motherhood, concerning social context), even without overt maternal history or clear neonatal symptoms.

Urinary drug screening was performed for a subset of mothers but was not systematic.

Because screening was triggered by clinical, historical, or social criteria rather than performed systematically in all newborns, the study population comprises newborns investigated for suspected NAS, not a population-based sample of confirmed NAS cases; the reported proportions should not be interpreted as reflecting the prevalence or incidence of NAS in the general neonatal population (see Limitations). Within this population, three levels of certainty were distinguished: newborns with a pediatrician-confirmed clinical diagnosis of NAS (with or without a documented Finnegan score), newborns with clinical signs suggestive of NAS without formal confirmation, and newborns investigated on the basis of maternal history or social risk factors alone, irrespective of toxicological results.

Data collection and processing

Data were extracted from the Toxicology service registers. The collected information included patient demographics, maternal history, clinical presentation, sample details, and toxicological analysis results. The data were compiled and analyzed via Microsoft Excel® (2019).

Toxicological testing was requested by referring clinicians, who contacted the toxicology service prior to sample submission on the basis of clinical suspicion (neonatal symptoms) or a maternal history of substance use. Because standardized withdrawal scoring (Finnegan score) and perinatal variables such as Apgar score are not routinely requested or recorded by referring clinicians at the time of sample submission, and because the number of requests increased markedly over the study period, these data were frequently missing from the toxicology service registries and could not be systematically retrieved retrospectively; this is reflected in the Limitations.

Toxicological analysis

Drug screening was performed using a qualitative immunochromatographic assay (DIAGNO-RAPIDE-DROGUES® test cup) that uses the following decision (cut-off) limits: pregabalin (2,000 ng/mL); tetrahydrocannabinol (THC) (50 ng/mL); cocaine (300 ng/mL); opiates (300 ng/mL); buprenorphine (10 ng/mL); tramadol (100 ng/mL); 3,4-methylenedioxymethamphetamine (MDMA) (500 ng/mL); benzodiazepines (300 ng/mL); barbiturates (300 ng/mL); and tricyclic antidepressants (1,000 ng/mL); results were interpreted qualitatively as positive or negative according to these limits. No confirmatory

analytical method (e.g., gas or liquid chromatography coupled with mass spectrometry) was performed.

Reported assay sensitivity and specificity were >98% and >90%, respectively. A cross-reactivity study (three replicates per panel, compounds tested at 100 µg/mL) found no cross-reactivity with more than 100 structurally or pharmacologically related compounds.

Results

Seventy-five newborns met the inclusion criteria. The annual number of newborns investigated for suspected NAS was 7 in 2023, 27 in 2024, and 41 in 2025.

Demographic distribution

Among the 75 cases, requests concerned 46 male and 27 female newborns, with sex unspecified in 2 cases, yielding a sex ratio (M:F) of 1.70.

Age of the newborns

At the time of toxicological testing, 38 newborns were aged ≤24 hours, 18 were aged 24–48 hours, and 16 were aged >48 hours.

Clinical presentation

Symptoms observed in newborns included respiratory distress (n=14), tremors (n=9), and hyperexcitability/agitation (n=8). Other common symptoms included feeding difficulties, abnormal movements, seizures, and hypertonia (5 cases each). The results are shown in Table 1.

Table 1. Symptoms of newborns investigated for NAS.

Symptom	n	%
Respiratory distress	14	18.7
Tremors	9	12.0
Hyperexcitability/agitation	8	10.7
Feeding difficulties	5	6.7
Abnormal movements	5	6.7
Seizures	5	6.7
Hypertonia	5	6.7
Hypotonia	4	5.3
Irritability	1	1.3
Vomiting	3	4.0
Apnea	2	2.7
Hypoglycemia	2	2.7
Apathy/lethargy	2	2.7
Somnolence	1	1.3
Incessant crying	1	1.3
Sleep disorders	1	1.3
Yawning	1	1.3
Asymptomatic	13	17.3
Insufficient clinical data	25	33.3

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Note: percentages in Table 1 are calculated using the total study population (n=75) as the denominator; because some newborns presented more than one symptom, the sum of individual symptom percentages exceeds the percentages of symptomatic newborns reported in the text.

Toxicological screening

Screening was motivated by two criteria:

The newborn's symptomatology

37 cases presented with specific clinical signs suggestive of NAS. Among these, the NAS was formally confirmed by the pediatrician in 12/75 patients (16.0%, 95% CI 9.4–25.9%); a Finnegan score was documented in only 5/37 symptomatic patients (13.5%, 95% CI 5.9–28.0%; scores: 4, 5, 7, 8, and 13). Given this low rate of formal confirmation, findings throughout this report should be understood as pertaining to newborns investigated for suspected NAS rather than confirmed NAS cases. For the other 25 symptomatic patients, the reported clinical signs prompted suspicion of NAS, although structured scoring was not documented.

The mothers' profiles

31 cases were screened due to a history of psychoactive substance use by the mother or due to specific social circumstances, even in the absence of obvious clinical signs in the newborn.

Toxicology results of the newborns

Toxicology screening was positive for one or more substances in 45 newborns and negative in 30 newborns. Among the positive cases, a single substance was detected in 33 newborns, with pregabalin (PGB) being the single agent in 29 of these cases. Polysubstance exposure (2–3 substances) was identified in 13 newborns: PGB + cocaine in 9 cases, followed by one case each of PGB with 3,4-methylenedioxymethamphetamine (MDMA), PGB with buprenorphine, and a combination of benzodiazepines with tricyclic antidepressants. One newborn tested positive for three substances: PGB, opiates, and tetrahydrocannabinol (THC). The results are shown in Table 2.

Toxicology results of mothers and their history

Maternal history was categorized as follows:

- Substance misuse: 53 cases

Table 2. Toxicology results in newborns investigated for NAS.

Category/Substance Pattern	n	% of Positive	% of Total
All cases investigated	**75**	—	**100.0**
Positive results	45	—	60.0
Negative results	30	—	40.0
Substances detected in positive cases (n=45):			
PGB	29	64.4	38.7
PGB + Cocaine	9	20.0	12.0
PGB + Buprenorphine	1	2.2	1.3
PGB + MDMA	1	2.2	1.3
Tricyclic antidepressants (TCA)	2	4.4	2.7
TCA + BZD	1	2.2	1.3
PGB, opiates, and tetrahydrocannabinol (THC)	1	2.2	1.3
Opiates	1	2.2	1.3
Any PGB (alone or combined)	41	91.1	54.7

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- Medical treatment/psychiatric history: 8 cases
- Suspected/Socioeconomic Risk Factors: 4 cases
- Unknown: 10 cases.

Among the 53 cases with a maternal history of substance misuse, specific substance data were available for 51 cases: PGB in 41/51, cannabis in 11/51, cocaine in 10/51, and heroin in 3/51. Polydrug use was documented in 29 mothers (56.9%), while 19 reported tobacco smoking and four reported alcohol consumption.

Mother–newborn dyads

Among the 14 mother–newborn dyads with paired toxicology tests, the results showed the following:

- 3/14 (21.4%, 95% CI 7.6–47.6%) of the mothers had a perfect match between their declaration and toxicology results.
- In 7/14 (50.0%, 95% CI 26.8–73.2%) of the cases, tests revealed additional substances not mentioned by the mother (under-declaration or partial truth).
- A total of 3/14 (21.4%, 95% CI 7.6–47.6%) were true negatives where the mother either reported no use or gave a vague history.

In one case, the mother declared specific substances that were not detected, while an undeclared substance was found (clear mismatch). The results are shown in Table 3.

Table 3. Concordance between maternal self-reports and toxicology results in 14 mother–newborn dyads.

Maternal Report	Mother's screening results	Newborn screening results	Matching degree
Pregabalin, cigarettes	PGB	PGB	Perfect match
Pregabalin, Subutex	PGB, BZD, BUP, THC	PGB, BUP	Underdeclaration
Pregabalin	PGB, COC, THC	PGB	Underdeclaration
None reported	Negative	Negative	True negative
Undetermined habits	PGB, THC, OPI	PGB	Underdeclaration
Pregabalin, heroin, cigarettes	PGB, THC, COC	PGB	Underdeclaration
Pregabalin, cigarettes	PGB	PGB	Perfect match
Substance user (unspecified)	PGB	PGB	Underdeclaration
Pregabalin, alcohol, cigarettes	THC	PGB	Mismatch
Substance user (unspecified)	PGB, THC	BZD, THC	Underdeclaration
Substance user (unspecified)	PGB, COC	BZD, TCA	Underdeclaration
Pregabalin, Cannabis	PGB	PGB	Perfect match
Suspicion of drug addiction	Negative	Negative	True negative
None reported	Negative	Negative	True negative

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Definitions used in Table 3: "Perfect match" = the substance(s) declared by the mother matched both her own toxicology screening result and the newborn's screening result; "Underdeclaration" = the mother's and/or the newborn's toxicology screening detected one or more substances taken by the mother that she had not declared; "True negative" = maternal report of no use, or a vague/unspecified history, together with a negative screening result in both mother and newborn; "Mismatch" = a discrepancy between the mother's own screening result and the newborn's screening result

Discussion

This work reveals a striking, near-sixfold rise in the annual number of newborns investigated for suspected NAS in our service between 2023 and 2025. In the

absence of data on the total number of live births, the number of newborns screened, and any changes in referral practices or testing availability over this period, this trend cannot be interpreted as a true increase in the incidence of NAS; it may instead reflect increased clinical awareness or referral. It nonetheless signals a growing clinical workload that warrants further prospective investigation.

According to the Algerian national neonatal guideline, newborns at risk of prenatal psychoactive substance exposure are identified on the basis of maternal history and clinical findings and monitored using validated scoring systems such as the Finnegan score [6]. Our findings must be interpreted within this framework of clinically triggered rather than universal screening.

Demographic distribution

The observed male predominance aligns with Knezovic et al. [7] (75.6% male) and Charles et al. [8] (ratio 1.09), though Unger et al. [9] found no sex difference but noted hypotheses centered on longer neurological maturation periods in male infants, potentially extending a window of vulnerability [8, 9].

Age of the newborn

Neonatal urine reflects maternal drug exposure during the days preceding delivery and may remain positive for 2–4 days, depending on the substance and timing of the last exposure [10]. More than half of the newborns (50.7%) were tested within the first 24 hours of life, with 24.0% tested at 24–48 hours and 21.3% after 48 hours, reflecting the variable onset of NAS symptoms.

Given its pharmacological similarity to gabapentin, which can produce withdrawal within 24 hours [11], our findings are compatible with the hypothesis that PGB may contribute to early-onset withdrawal signs, although the retrospective design, absence of exposure-timing and dosing data, and lack of neonatal drug concentrations preclude establishing causality. Early symptoms were observed even in newborns co-exposed to substances with later onset, such as buprenorphine (36–72 hours) or cocaine (2–3 days), which may suggest a contribution of PGB to the initial clinical presentation, though this remains a hypothesis rather than an established causal relationship, given that dose, timing of maternal exposure, and neonatal drug concentrations were not evaluated [3, 12]. PGB remained detectable in several newborns tested between 24 and 48 hours of life; and among those tested after 48 hours, positive results for PGB or tricyclic antidepressants (TCA) were also observed: these findings are consistent with the reported onset of withdrawal associated with TCA (24–48 hours) [3] and indicate that PGB can remain detectable more than 24 hours after birth; they do not, however, establish a temporal or causal relationship between PGB exposure and symptom onset.

Clinical presentation

17.3% of the newborns were asymptomatic (13/75, 95% CI 10.4–27.4%), while clinical data were insufficient for 33.3% (25/75, 95% CI 23.7–44.6%). Among symptomatic newborns, the clinical profile was consistent with the classic manifestations of NAS. Respiratory distress was the most frequent sign, followed by tremors, hyperexcitability, and feeding difficulties, reflecting the autonomic and central nervous system dysregulation characteristic of NAS [3, 13]. Respiratory distress was particularly frequent among pregabalin-positive newborns, consistent with previous reports of prenatal gabapentinoid exposure [14]. It was also observed in one newborn exposed to clomipramine, in agreement with reports describing respiratory complications following prenatal exposure to TCA [15]. As described by Kocherlakota, autonomic instability may impair respiratory function and muscle tone in newborns with NAS, while agitation and tremors are well-recognized manifestations of the syndrome [7]. Seizures occurred in 6.7% of our cases, consistent with the 2–11% prevalence reported in the literature [3] and reflecting the potential severity of NAS. Feeding difficulties were observed in 6.7% of positive cases, consistent with previous reports in infants prenatally exposed to psychoactive substances [16].

Toxicological screening

For newborns

The toxicology results represent the most striking finding of our study: PGB (alone or in combination with other substances) was present in 91.1% of positive cases (41/45, 95% CI 79.3–96.5%; see Table 2), which strongly contrasts with the global literature, where cannabis or opioids are typically the most documented substances in prenatal exposure studies [17].

The 40% rate of negative toxicological screening among investigated newborns illustrates the limitations of urine immunoassays. Delayed sampling, urine dilution, restricted analytical panels, and intermittent maternal drug use may all contribute to false-negative results [12, 13, 18].

Toxicology results of mothers and their history

Maternal substance use during pregnancy is not uncommon: a systematic review by Tavella et al.

reported that 12.28 % of pregnant women use illicit psychoactive substances during pregnancy [17]. In our cohort, among mothers with reported substance use data (n=51), PGB was the predominant substance (41 cases, 80.4%). This trend may reflect the increasing misuse and accessibility of PGB in Algeria [19]. The high prevalence of polydrug use (29 mothers, 56.9%) reflects frequent simultaneous exposure to multiple psychoactive substances, with important implications for both maternal health and neonatal outcomes. Tobacco smoking and alcohol consumption represent additional risk factors for NAS. As reported in the literature, polysubstance exposure, polypharmacy, and cigarette use are consistently associated with more severe neonatal abstinence manifestations [10].

Mother–newborn dyads

The analysis of 14 mother-newborn dyads revealed several matches and discrepancies:

- PGB was the substance most consistently detected in both mothers and newborns. In several dyads, newborns tested positive only for PGB despite maternal polysubstance use. This observation is consistent with its the documented placental transfer [20] but contrasts with previous reports describing frequent neonatal detection of substances such as cocaine, cannabis, and opiates following maternal exposure [21]. Several factors may explain these discrepancies, including differences in placental transfer, rapid neonatal elimination, low or intermittent maternal consumption, and the timing of urine collection. Furthermore, highly lipophilic compounds such as tetrahydrocannabinol preferentially accumulate in lipid-rich matrices, such as meconium, rather than in urine, potentially reducing neonatal urinary detection despite prenatal exposure [22]. One newborn was positive for both PGB and buprenorphine, while the mother was additionally positive for benzodiazepines and THC. This finding does not align with the findings of the study by Sampériz S et al., which reported positive screening for these substances in newborns when the mother was a user [21].

- One mother–newborn pair presented a mismatch, with maternal toxicology negative for PGB despite neonatal positivity, but considering its relatively short elimination half-life (approximately 6 hours), maternal discontinuation shortly before delivery could explain a negative maternal urine sample while fetal exposure remained detectable in the newborn [23].

Limitations

This work has several limitations. The retrospective, single-center design may limit the generalisability of the findings, as patient characteristics and substance availability may vary across Algeria. Because urinary toxicological screening was performed only in newborns referred on the basis of clinical findings, maternal history, or social risk factors, and maternal testing was not systematic, the study population is subject to substantial selection bias and cannot be used to estimate the prevalence or incidence of NAS in the general neonatal population. Clinical information was insufficient for a considerable proportion of newborns, and a standardized NAS assessment (Finnegan score) was documented in only 5/37 symptomatic newborns, so most included newborns represent suspected rather than confirmed NAS. Key perinatal and maternal variables (gestational age, birth weight, mode of delivery, Apgar scores, maternal medication use, neonatal outcomes, duration of hospitalization, and treatment received) are likewise not routinely requested by referring clinicians and were therefore not systematically available in the toxicology service registries; they could not be retrieved retrospectively and could not be analyzed. Toxicological analysis relied exclusively on qualitative immunochromatographic screening without confirmatory analytical testing. The mother–newborn dyad analysis was based on a small subsample (n=14), limiting the precision of concordance estimates. Finally, because the study did not assess dose, timing of maternal exposure, or neonatal drug concentrations, and lacked confirmatory testing, causal relationships between detected substances—particularly PGB—and neonatal clinical manifestations cannot be established from these data.

Conclusion

Accurate data on the prevalence of NAS in Algeria remain scarce, which limits the understanding of its full scope and hinders the development of tailored management strategies. It is therefore crucial to intensify research and data collection efforts to foster a better understanding and improved management of this syndrome.

Ethical Approval

This retrospective study was conducted using fully anonymized data extracted from the Toxicology Service records of Bab El Oued University Hospital. The study complied with the ethical principles of the Declaration of Helsinki. According to institutional and national regulations governing retrospective studies using anonymized routinely collected data, formal ethics committee approval was not required.

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Conflicts of Interest

The authors report there are no competing interests to declare.

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