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CASE REPORT *Volume 15 (Issue 1), 2026*

PAKISTAN JOURNAL OF MEDICINE & DENTISTRY

From Silence to Seizures: Benzodiazepine–Induced Neonatal Abstinence Syndrome in a Preterm Newborn— A rare Case from Darul Sehat Hospital

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ABSTRACT

This case report delves into the clinical presentation, examination and management of a neonate from Pakistan, diagnosed with Neonatal Abstinence Syndrome(NAS) at Darul Sehat. It's a withdrawal condition affecting infants with opioids or other Central Nervous System depressants in utero. The subject, born at 33 weeks via emergency C-section to a mother with history of opioid use, exhibited classical symptoms of NAS including high pitched cry, hyperirritability, seizures, tachypnea, tremors-within 24 hours postpartum. Thorough clinical evaluation supported by laboratory and imaging findings led to diagnosis of NAS secondary to maternal benzodiazepine abuse during pregnancy. A Finnegan Neonatal Abstinence Scoring System was used to monitor the severity of withdrawal symptoms and guide treatment. This case accentuates importance of early identification, standardized assessment protocols and multidisciplinary approach of NAS to improve short- and long-term outcomes. It also emphasizes the ongoing need for support systems for families affected by this disorder

Keywords: Abstinence Syndrome, Neonatal, Withdrawal, Passive Addiction

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How to cite: Fareed S, Taiba, Sidra Tul Muntaha, Amna, Alisha, Khatoon A, et al. From Silence To Seizures: Benzodiazepine-Induced Neonatal Abstinence Syndrome In A Preterm Newborn– A Rare Case From Darul Sehat Hospital. Pak J Med Dent. 2026 January ;15(1). Doi: https://doi.org/10.36283/ziun-pjmd15-1/032.

Received: Mon, August 18, 2025 **Accepted:** Fri, January 2, 2026 **Published:** Wed, January 14, 2026

INTRODUCTION

Neonatal abstinence syndrome refers to withdrawal symptoms in newborn of substance abuse mother[1] Every medicine taken during gestation can pass through the placenta and reach the fetus and amniotic fluid. These fetuses become drug dependent. When vaginal delivery occurs drug's transfer across the placenta stops, so signs of withdrawal are seen. These neonates are usually preterm[2]. For NAS affected babies statistical result show that mean birth weight was 3.141kg [3] .National Drug Use

Survey Pakistan 2022-24, on 26 October 2022, Islamabad revealed that 6%of the population from which 2.9% of the adult woman, making upto 6.7 million people using drugs apart from alcohol and nicotine [4]. NAS cases aren't filed due to inconsistent prenatal data and confined diagnostic methods. The sole aim of this paper is to stimulate discussion and awareness at intersection of neonatology, toxicology, psychiatry, and social medicine so that NAS cases be dealt with multidisciplinary approach

CASE PRESENTATION

A male neonate with a weight of 2.3 kg was delivered by way of emergency lower segment cesarean (EM-LSCS) at 33 weeks of gestation (8:46 PM,02-09-2023), at Darul Sehat Hospital, as the membranes had been ruptured for 18 hours, causing fetal distress as revealed by Cardiotocography (CTG). The Apgar scores were low, recorded as 5 at 1 minute and 6 at 5minutes. At birth, the infant was limp and exhibited no spontaneous cry or chest movements. The heart rate was at 128 bpm. Vigorous stimulation was performed. Efforts at oxygenation were used too. Two minutes after positive pressure ventilation, respiratory efforts were initiated. Subsequently, the newborn was shifted to the NICU. Bubble CPAP gave respiratory support.

Antenatal history revealed a 35-year-old G2P1+1 woman, a booked case with no history of gestational diabetes, pregnancy-induced hypertension, urinary tract infections, or other maternal infections. However, she wasn't on multivitamin supplementation. Her blood group was O+, and serology for hepatitis B and C was non-reactive. The infant presented with delayed cry, poor activity, and respiratory distress upon NICU admission. Initial examination showed a pink but hypotonic neonate with poor reflexes and a weak cry. The anterior and Posterior Fontanelle were open and flat. Vital signs showed 148bpm heart rate, 68 breaths per minute respiratory rate ,90/54 mmHg bp and SpO_2 of 92–93%. Anthropometry revealed a length of 42cm and an occipito-frontal circumference (OFC) of 34cm. Head-to-toe assessment showed subcostal and intercostal recessions, equal air entry in both lungs without added sounds, cardiovascular findings were normal, the abdomen was distended, soft but non-tender, and there was a micropenis with normally descended testes. Neurological evaluation showed poor Neonatal reflexes and reduced tone.

Table 1. Baseline investigations

Test	Results
Hb	15.3
Hct	44%
Tlc	8.3
Plt	202
CRP	0.9

PT/INR	16.2/1.1
APTT	35.1
Urea	10
BBG	A-ve
Creatinine	0.9
Na/K+	150/3.7
Cl/HCO3	0.67
PCT	113/25

Musculoskeletal exam revealed no polydactyly or syndactyly with a normal spine. Sepsis, Respiratory distress syndrome (RDS), and hypoxic-ischemic encephalopathy (HIE) were among the first differential diagnoses. Initial lab tests revealed 0.9 mg/dl CRP, 15.3 g/dl hemoglobin(hb), and an 8.3 × 10^9/L total leukocyte count with 85% neutrophils **Table 1**.

Chest X-ray demonstrated cardiomegaly, prompting further evaluation via echocardiography, which later revealed a subaortic ventricular septal defect (VSD) with left-to-right shunt, pulmonary hypertension, and mild tricuspid regurgitation **Figure 1.** The clinical course was complicated by hypotonia, and poor reflexes, and tachypnoea persisted, but no tachycardia, HR was 128bpm ↓ . Baby kept NPO with IV Fluids, Cefotaxime and Amikacin. Cyclical and involuntary movement episodes occurred, so Anticonvulsant therapy initiated with IV Phenytoin and then Levetiracetam. Considering persistent increased work of breathing, ABGs were done, revealed respiratory acidosis, then BCPAP was discontinued and mechanical ventilation was initiated

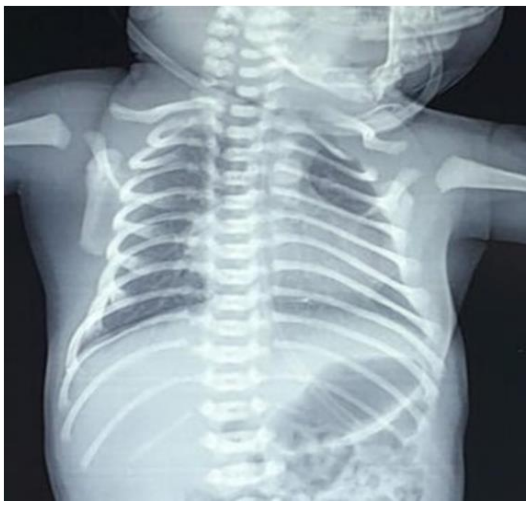

Figure 1: Chest Xray On First Day Of Admission

Figure 2. EEG confirmed continuous seizure activity. Toxicological evaluations were included. Labs revealed deranged PT/INR & low hb for which FFP's & PRBC'S were transfused. After the urine toxicology screen showed positive for benzodiazepine, confirmed the diagnosis, Neonatal Abstinence Syndrome (NAS). The counsellors uncovered a meaningful psychosocial background. The mother had Abusive marriage, handicapped first child and a history of prior abuse of Tablet Alprazolam and Inj. Nalbuphine for many years including current pregnancy. With regard to the poor prognosis that was given, the intensive care and counselling were just not enough. The family chose to take the infant to another facility against medical advice (LAMA).

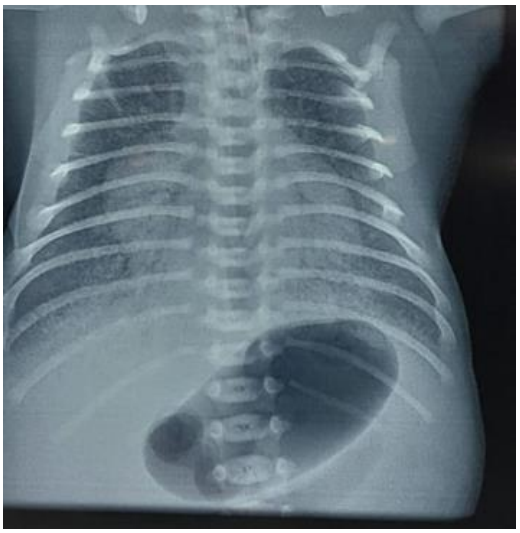

Figure 2 Chest X-ray: Post-Intubation

DISCUSSION

Our case report highlights a preterm male neonate born at 33 weeks via emergency C-section with respiratory distress, hypotonia, and poor neonatal reflexes, which was later diagnosed with Neonatal Abstinence Syndrome (NAS) secondary to in utero exposure to alprazolam (benzodiazepine) and nalbuphine (opioid analgesic). A population-based cohort study by[5] analyzed over 290,000 pregnancies and found that the risk of neonatal abstinence syndrome (NAS) increases significantly with long-term opioid use and third-trimester exposure, especially when combined with additional risk factors such as opioid misuse, use of psychotropic drugs, or smoking. Their findings support the idea that duration and timing of opioid exposure are key determinants of NAS severity, which aligns with our case where the mother had exposure to similar drugs throughout pregnancy. Our case exhibited signs of polysubstance-induced NAS, which is also seen in a study where prenatal exposure to both opioids and benzodiazepines significantly increased the risk of severe CNS withdrawal requiring pharmacologic treatment[6] .

A case reported that neonates with opioid withdrawal commonly present with poor feeding, irritability, tremors, hyperthermia, respiratory distress, and weight loss, a symptom pattern closely resembling with our case[7].Another case reported considerable variability in NAS management across NICUs in the U.S, with only 54.5% of centers having a written treatment protocol. The Finnegan scoring system was most commonly used (65%), and morphine was the preferred pharmacologic agent. In contrast, our case followed a structured approach, with treatment initiated based on clinical scoring and respiratory distress. Management was guided by institutional protocol, and the neonate responded well to supportive care and pharmacologic intervention, reflecting a more standardized and evidence-based approach compared to the variability described in their survey[8].Neurologic manifestations including feeding difficulty, tremors, seizure-like episodes, albeit with only 7.5% confirmed epileptic seizures [9]**.**Another case in 2021 also describes a constellation of feeding issues, irritability, weight loss, and autonomic disturbances, consistent with our neonate [i].Our case's presentation with respiratory distress, feeding difficulties, and CNS irritability aligns with patterns reported in the literature[10]. For example, A case in found higher rates of tachypnea and poor feeding among preterm NAS infants compared to term controls, observed that among term newborns, behaviors such as excessive sneezing, nasal stuffiness, tremors, and poor latch were present in over 10% of infants suspected of NAS, reinforcing that early respiratory and feeding difficulties are common[11]. In our case, the preterm infant similarly presented with respiratory distress and feeding issues, consistent with early NAS manifestations[12].Another study 2020 reported 262 NAS infants showed they were 34 times more likely to experience respiratory distress and 111 times more likely to have severe feeding difficulties compared to non-exposed infants. This aligns strongly with our neonate's combined respiratory and feeding challenges[13] .Similar to our case, where preterm NAS required respiratory intervention—the study 2021 surveyed 67 NICUs in the U.S./Canada caring for preterm infants (<34 weeks) with intrauterine opioid exposure. It found that preterm NAS infants often require respiratory support, frequently using morphine[2] .Another study 2020 further documented significant cardiorespiratory events in opioid -exposed neonates, necessitating respiratory support[14].A study in 2018 conducted a comprehensive review of 53 studies involving over 11,000 opioid-exposed mother-infant pairs and highlighted the substantial variability in the diagnosis and treatment of NAS. They emphasized that nonpharmacologic interventions such as rooming-in and breastfeeding were associated with decreased need for pharmacologic treatment and shorter hospital stays. In contrast, our patient was managed using a structured institutional protocol that included both pharmacologic treatment (morphine) and supportive care. Unlike the variability described by our case reflects a more standardized and proactive approach, particularly appropriate for a preterm infant with moderate to severe NAS symptoms. In conclusion, our case of a preterm neonate with in utero exposure to the above mentioned drugs, presented with severe NAS features.

The clinical course indicating the severity of withdrawal and possible combined neuro-respiratory depressive effects of the maternal drugs. Recommendations:

Early screening for maternal substance use should be integrated into routine antenatal care to allow timely identification and intervention. Neonatal intensive care units should be adequately prepared to manage complex withdrawal presentations in preterm neonates, particularly in cases involving multiple drug exposures. In addition, counselling and rehabilitation services for pregnant women with substance use should be prioritized to improve both maternal and neonatal outcomes

CONCLUSION

This case shows that even though NAS from benzodiazepines is uncommon, it can still happen and if you are not thinking about it, you might miss the diagnosis. That's why it is very important to ask mothers about their mental health, drug use, and personal history during pregnancy. Whenever a newborn presents with unexplained seizures, poor activity or other unusual signs you should always keep NAS in your differentials, especially if routine causes are not fitting the picture. Early identification of the problem and prompt management can improve the outcomes. This case also reminds us how important it is to include drug abuse screening in antenatal care so these problems can be prevented in the first place

FUNDING

None.

PATIENT'S CONSENT

Informed consent was taken from the Patient's Parents

CONFLICT OF INTEREST

None.

AUTHORS' CONTRIBUTION

All authors contributed equally as per ICMJE.

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