World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

# Non-steroidal anti-inflammatory drugs induced oligohydramnios in second trimester pregnancy: A case report

Sholen Acharya [1,*] and Deepak Rath [2]

[1] *Department of Reproductive Medicine and Surgery, Government Medical College, Thiruvananthapuram, Kerala, India.*
[2] *Department of Rheumatology, SUM Ultimate Medicare, Bhubaneswar, Odisha, India.*

World Journal of Advanced Research and Reviews, 2025, 25(02), 2693-2696

Publication history: Received on 08 January 2025; revised on 22 February 2025; accepted on 25 February 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.25.2.0542

## Abstract

We present a case of oligohydramnios induced by NSAID use (Etoricoxib and Diclofenac) in the second trimester. A 20-year-old primigravidae with an uncomplicated early trimester, was advised at 21 weeks to take Etoricoxib for five days due to knee bursitis after which she self-medicated with Diclofenac for a week. Due to complaints of reduced fetal movement, a scan was done at 23 weeks which revealed reduced liquor status. She was advised against NSAID use and followed up with a scan three weeks later which showed a reversal of oligohydramnios. While NSAIDs are discouraged in the third trimester, limited awareness exists regarding second-trimester risks, especially with self-medication. But our case emphasizes the need for strict monitoring while using NSAIDs even during the second trimester of pregnancy. This case is one of the earliest documented cases involving the adverse effect of Etoricoxib, a selective COX-2 inhibitor, on pregnancy and further study is required to look for long-term effects.

**Keywords:** NSAIDs; Oligohydramnios; Etoricoxib; Second Trimester; COX2 inhibitor

## 1. Introduction

Oligohydramnios, characterised by insufficient amniotic fluid surrounding the fetus, may lead to pregnancy complications such as fetal growth restriction, intra-uterine fetal demise or neonatal morbidity. Drugs like angiotensin-converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers and non-steroidal anti-inflammatory drugs (NSAIDs) pose a significant risk for the same. Among over-the-counter (OTC) medications in pregnancy NSAIDs are commonly used despite being categorised as FDA class D during third trimester (FDA class D drugs are associated with fetal risk and only used for life-threatening conditions when other safer alternatives are not available)[1].

Earlier it was recommended to avoid taking NSAIDs after 30 weeks of pregnancy but since Oct 2020, FDA released its recommendation against its usage even from 20 weeks of pregnancy based on certain studies reporting serious fetal effects like oligohydramnios and closure of ductus arteriosus[2]. Intake of NSAIDs between 20-30 weeks for a duration of more than 48 hours needs monitoring of liquor status, the only exception being low-dose aspirin (81 mg) used for pre-eclampsia prophylaxis[2].

As a result of limited awareness among the general public and many healthcare providers, fetotoxic drugs are often consumed during pregnancy[3]. This case involves the sequential use of multiple NSAIDs, including Etoricoxib and Diclofenac, during the second trimester, leading to the development of oligohydramnios.

* Corresponding author: Sholen Acharya

## 2. Case Presentation

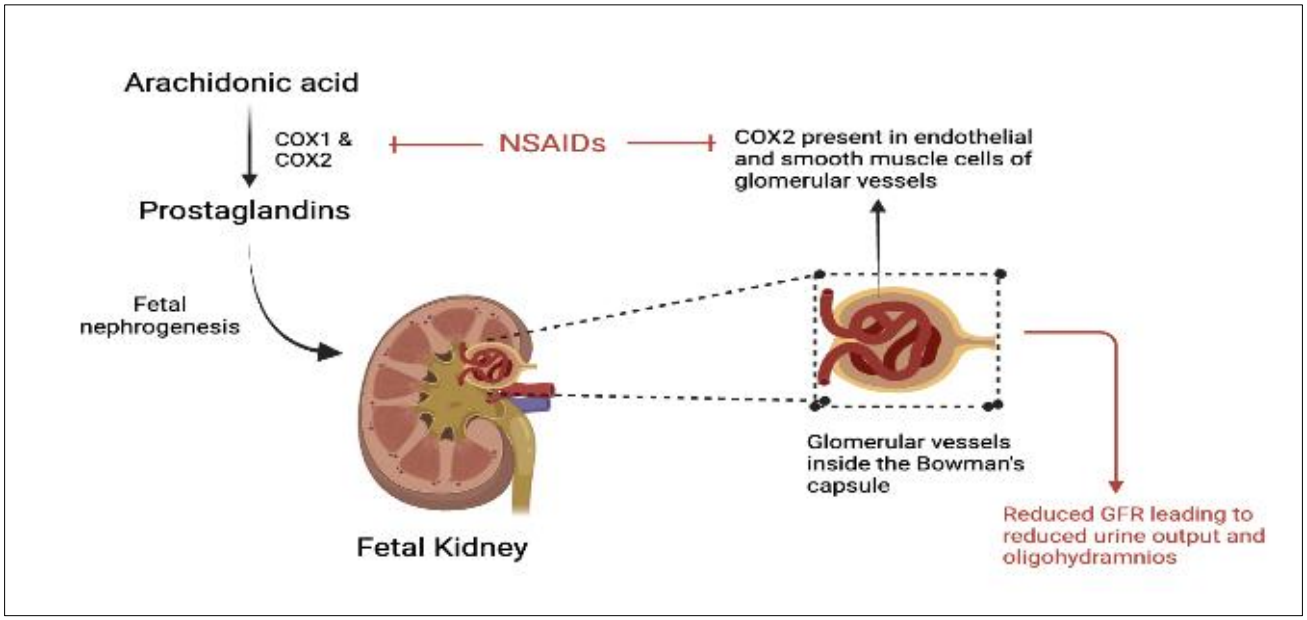
A 20-year-old primigravidae was referred to the maternal-fetal medicine department of the Child Development Centre and SAT hospital, Trivandrum, at 30 weeks of gestation for evaluation of previously diagnosed second-trimester oligohydramnios. She was married for 1 year, a non-consanguineous marriage with a history of spontaneous conception, and her pregnancy was unremarkable until the early second trimester. The combined first-trimester screening for aneuploidy performed at around 12 weeks showed low risk for trisomy 21, 18 and 13. A targeted fetal anomaly scan at 20 weeks showed no apparent congenital anomalies and the amniotic fluid volume was normal with a single deepest pocket (SDP) measuring 3.3cm.

Around 21 weeks gestation, she was hospitalized in the orthopaedics department for pain and swelling in her right knee, where she received a diagnosis of right knee bursitis (post-trauma). Managed with parenteral antibiotics and analgesics, she was discharged after three days with a prescription for Etoricoxib 90mg once daily for five days. Following completion of the Etoricoxib course, she self-medicated with Diclofenac 100mg once to twice daily for approximately one week, after which she noticed reduced fetal movements. At 23 weeks gestation, a scan revealed a significant reduction in amniotic fluid volume, with a single deepest pocket (SDP) measuring 2cm, and minimal distension of the urinary bladder. Other potential causes of oligohydramnios, such as renal anomalies, placental insufficiency, and premature rupture of membranes, were ruled out. Upon thorough history taking, she disclosed her NSAID intake for approximately two weeks, prompting advice to discontinue the medication.

Three weeks later, a follow-up scan at around 27 weeks gestation assessed liquor status and Doppler findings, revealing adequate amniotic fluid levels (AFI: 11.6cm, SDP: 3.7cm) and normal fetal Doppler studies. Fetal urinary bladder visualization showed normal distension with 3.5ml of urine, and fetal kidneys were observed normally. This improvement persisted, as evidenced by further normal findings in a 30-week scan indicating adequate amniotic fluid levels (SDP: 4.6cm) and normal Doppler findings.

## 3. Discussion

The main finding, in this case, is the development of fetal oligohydramnios at 23 weeks after the use of NSAIDs, Etoricoxib and Diclofenac taken sequentially over a duration of only 2 weeks. This drastic drop in Amniotic Fluid Index (AFI) with only 2 weeks of therapy cautions regarding its usage in 2nd trimester of pregnancy. Etoricoxib, a selective COX-2 inhibitor, is not FDA-approved yet used in many countries. There is no published literature regarding its adverse effect on pregnancy. However, another selective COX-2 inhibitor, Nimusilide, has been widely reported to cause oligohydramnios[4] and even anhydramnios[5].




Source: Author

**Figure 1** Mechanism of NSAIDs causing fetal oligohydramnios;

The mechanism which leads to oligohydramnios (Figure 1) is not fully understood. NSAIDs inhibit prostaglandin synthesis by blocking the action of cyclo-oxygenase enzyme (COX-1 and COX-2 are two isoforms). Fetal nephrogenesis requires the presence of prostaglandins, with various COX isoforms present in renal structures[6]. NSAID may directly influence nephrogenesis and cause irreversible damage[7]. Additionally, COX-2 is present in endothelial cells and smooth muscle cells of the glomerular vessels[6], therefore, selective COX-2 inhibitors significantly impair the renal blood flow and reduce the glomerular filtration rate affecting the urine output[8]. This reduction in urine output is corrected after stoppage of the medication as demonstrated in our case, and other cases[9] and this points towards a reversible pathology when timely intervened.

Most studies caution against the use of NSAIDs in the 3rd trimester[10], and there are few reports of adverse effects due to NSAID use in 2nd trimester of pregnancy[11]. Though the German Embryotox cohort study inferred that patients exposed to only 2nd trimester NSAID had a higher relative risk for oligohydramnios compared to combined 2nd and 3rd-trimester usage, the author attributed this outcome to the prolonged duration of treatment in the second trimester, where usage was not accompanied by established warnings as observed for the third trimester[12]. However, our case suggested that even brief NSAID exposure in 2nd trimester may lead to a significant reduction in amniotic fluid volume, which warrants further studies.

In previous reports, NSAIDs have commonly been used for indications such as tocolysis, treatment of feto-fetal transfusion syndrome and polyhydramnios, necessitating in-hospital management and regular monitoring. However, in our patient's case, NSAIDs were prescribed for symptom relief, and she continued taking them after discharge, a scenario that is often overlooked. The use of over-the-counter NSAIDs is typically not well-documented, especially when there are no prior warnings regarding their usage.

## 4. Conclusion

Use of NSAIDs in second-trimester pregnancy needs careful counselling and vigilant monitoring. Oligohydramnios induced by NSAIDs was observed at 23 weeks gestation, following just two weeks of usage, marking this case as one of the earliest instances reported. The earliest documented case occurred at 22 weeks gestation, following prolonged exposure to diclofenac [9]. Importantly, this is the only reported case involving the use of Etoricoxib. While Etoricoxib is not FDA-approved, caution must be exercised in regions where it is prescribed during pregnancy, and further study is needed to assess its long-term effects.

## Compliance with ethical standards

### *Acknowledgments*

We thank Dr Pio James J, Consultant Maternal-Fetal Medicine, SAT Hospital, Trivandrum, for his support and guidance; and sincere thanks to the patient and her family without whose consent this case could not have been reported.

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

### *Statement of ethical approval*

According to the guidance of IRC/IEC of Government Medical College, Thiruvananthapuram, ethical approval was not required for this case report. However , all necessary ethical considerations, including patient consent, were adhered to.

### *Statement of informed consent*

Informed consent was obtained from the patient to present her findings. The patient was explained that all due efforts would be made to conceal her identity.

## References

[1] R. A. Black and D. A. Hill, “Over-the-counter medications in pregnancy,” Am Fam Physician, vol. 67, no. 12, pp. 2517–2524, Jun. 2003.

[2] 2020 FDA Drug Safety Communication., "FDA recommends avoiding use of NSAIDs in pregnancy at 20 weeks or later because they can result in low amniotic fluid." [Online]. Available: https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommends-avoiding-use-nsaids-pregnancy-20-weeks-or-later-because-they-can-result-low-amniotic

[3] E. B. Schwarz, S. M. Parisi, S. M. Handler, G. Koren, G. Shevchik, and G. S. Fischer, "Counseling About Medication-Induced Birth Defects with Clinical Decision Support in Primary Care," Journal of Women's Health, vol. 22, no. 10, pp. 817–824, Oct. 2013, doi: 10.1089/jwh.2013.4262.

[4] V. D'Ambrosio et al., "Use of non-steroidal anti-inflammatory drugs in pregnancy and oligohydramnios: a review," The Journal of Maternal-Fetal & Neonatal Medicine, vol. 36, no. 2, p. 2253956, Dec. 2023, doi: 10.1080/14767058.2023.2253956.

[5] D. M. Paternoster, D. Snijders, F. Manganelli, A. Torrisi, and R. Bracciante, "Anhydramnios and maternal thrombocytopenia after prolonged use of nimesulide," European Journal of Obstetrics & Gynecology and Reproductive Biology, vol. 108, no. 1, pp. 97–98, May 2003, doi: 10.1016/S0301-2115(02)00343-3.

[6] M. Komhoff, H. J. Grone, T. Klein, H. W. Seyberth, and R. M. Nusing, "Localization of cyclooxygenase-1 and -2 in adult and fetal human kidney: implication for renal function," American Journal of Physiology-Renal Physiology, vol. 272, no. 4, pp. F460–F468, Apr. 1997, doi: 10.1152/ajprenal.1997.272.4.F460.

[7] F. Boubred, M. Vendemmia, P. Garcia-Meric, C. Buffat, V. Millet, and U. Simeoni, "Effects Of Maternally Administered Drugs On The Fetal And Neonatal Kidney:," Drug Safety, vol. 29, no. 5, pp. 397–419, 2006, doi: 10.2165/00002018-200629050-00004.

[8] A. Prévot, D. Mosig, S. Martini, and J.-P. Guignard, "Nimesulide, a Cyclooxygenase-2 Preferential Inhibitor, Impairs Renal Function in the Newborn Rabbit," Pediatr Res, vol. 55, no. 2, pp. 254–260, Feb. 2004, doi: 10.1203/01.PDR.0000100904.17064.47.

[9] S. Scherneck, F. L. Schöpa, M. Entezami, A. Kayser, C. Weber-Schoendorfer, and C. Schaefer, "Reversible oligohydramnios in the second trimester of pregnancy in two patients with long-term diclofenac exposure," Reproductive Toxicology, vol. 58, pp. 61–64, Dec. 2015, doi: 10.1016/j.reprotox.2015.08.002.

[10] R. Antonucci et al., "Use of Non-steroidal Anti-inflammatory Drugs in Pregnancy: Impact on the Fetus and Newborn," CDM, vol. 13, no. 4, pp. 474–490, Apr. 2012, doi: 10.2174/138920012800166607.

[11] K. Dathe, S. Hultzsch, L. W. Pritchard, and C. Schaefer, "Risk estimation of fetal adverse effects after short-term second trimester exposure to non-steroidal anti-inflammatory drugs: a literature review," Eur J Clin Pharmacol, vol. 75, no. 10, pp. 1347–1353, Oct. 2019, doi: 10.1007/s00228-019-02712-2.

[12] K. Dathe, J. Frank, S. Padberg, S. Hultzsch, E. Beck, and C. Schaefer, "Fetal adverse effects following NSAID or metamizole exposure in the 2nd and 3rd trimester: an evaluation of the German Embryotox cohort," BMC Pregnancy Childbirth, vol. 22, no. 1, p. 666, Aug. 2022, doi: 10.1186/s12884-022-04986-4.