



EXPLORING THE RISKS OF ANALGESIC CONSUMPTION DURING PREGNANCY ON FETAL DEVELOPMENT IN PAKISTAN

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Abstract

Analgesic use during pregnancy presents a significant public health concern, particularly in low-resource settings like Pakistan, where self-medication and limited access to healthcare exacerbate associated risks. This study aims to examine the prevalence, types, and fetal outcomes linked to prenatal analgesic exposure in Pakistan, utilizing a mixed-methods approach. This includes cross-sectional surveys of 500 pregnant women and a retrospective analysis of 1,200 hospital birth records. Our findings indicate that 42% of participants self-medicated with analgesics, with the most commonly used medications being paracetamol (68%), ibuprofen (22%), and aspirin (10%). Notably, adverse fetal outcomes such as preterm birth (OR = 1.8, 95% CI: 1.2–2.7), low birth weight (OR = 2.1, 95% CI: 1.4–3.0), and congenital anomalies (OR = 3.0, 95% CI: 1.5–5.9) were significantly associated with first-trimester exposure to these drugs. Socioeconomic factors, including lower education levels ($p < 0.001$) and rural residency ($p = 0.003$), were identified as predictors of increased misuse. Qualitative interviews further revealed a lack of awareness about the risks of analgesic use during pregnancy and a cultural reliance on over-the-counter medications. These findings align with global research but underscore region-specific challenges, such as unregulated pharmacy practices and gender disparities in healthcare access. To mitigate these risks, we recommend stricter analgesic sales regulations, targeted educational campaigns, and the integration of prenatal counseling into primary care. Limitations of this study include recall bias and the use of single-center data. Future research should explore the long-term effects of prenatal analgesic exposure and investigate ethno pharmacological practices.

Keywords: “Analgesics”, “Fetal Outcomes”, “Prenatal Exposure”, “Self-Medication”, “Pakistan”

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INTRODUCTION

The use of analgesics during pregnancy is a pervasive yet understudied public health challenge in low- and middle-income countries (LMICs), where limited healthcare infrastructure and cultural practices amplify risks to maternal and fetal health (World Health Organization [WHO], 2022). Globally, up to 70% of pregnant women consume analgesics, primarily for pain and fever management, with paracetamol (acetaminophen) being the most common (Bérard et al., 2021). However, emerging evidence links prenatal exposure to analgesics even those deemed “safe” like paracetamol to adverse fetal outcomes, including preterm birth, low birth weight (LBW), and neurodevelopmental disorders (Bauer et al., 2021; Toda, 2023). In Pakistan, where 48% of the population relies on self-medication and 63% lack access to formal prenatal care, the risks are magnified by unregulated over-the-counter (OTC) drug sales, low health literacy, and gender disparities in healthcare access (National Institute of Population Studies [NIPS], 2022; Khan et al., 2023). This study explores the intersection of sociocultural, economic, and pharmacological factors driving analgesic misuse in Pakistan and its implications for fetal health.

Pharmacologically, analgesics like nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids pose trimester-specific risks. First-trimester NSAID exposure is associated with a 2.5-fold increase in congenital anomalies, particularly cardiac defects, due to prostaglandin inhibition affecting fetal ductus arteriosus closure (Østensen & Skomsvoll, 2023). Aspirin, often used for preeclampsia prophylaxis, increases risks of placental abruption when misused in high doses (LeFevre et al., 2020). Paracetamol, though widely considered safe, has been linked to attention deficit hyperactivity disorder (ADHD) and

autism spectrum disorder (ASD) in meta-analyses of cohort studies, with dose-response relationships observed (Alemany et al., 2021). Despite these risks, 34% of Pakistani women report using analgesics without medical consultation, often influenced by community health workers or family elders (Rasheed et al., 2023).

Globally, research on prenatal analgesic exposure has focused on high-income countries (HICs), neglecting LMIC contexts where polypharmacy, malnutrition, and infectious comorbidities may synergistically harm fetal development (Haas et al., 2021). For instance, concurrent use of analgesics and antimalarials common in Pakistan’s malaria-endemic regions may heighten hepatotoxicity risks (WHO, 2022). Furthermore, ethnopharmacological practices, such as combining herbal remedies with OTC analgesics, remain unexamined in safety studies (Sulaiman et al., 2023). These gaps hinder evidence-based guidelines tailored to Pakistan’s needs, perpetuating cycles of preventable adverse outcomes.

This study investigates the risks of analgesic use during pregnancy in Pakistan, focusing on its prevalence, types, and fetal outcomes. Using a mixed-methods approach, we found that 42% of pregnant women self-medicated with analgesics, primarily paracetamol, ibuprofen, and aspirin. First-trimester exposure was linked to increased risks of preterm birth, low birth weight, and congenital anomalies. Socioeconomic factors, such as low education and rural residence, were associated with higher misuse. We recommend stricter regulations, educational campaigns, and prenatal counseling to mitigate these risks.

RESEARCH METHODS

The study employed a mixed methods design, integrating a cross-sectional survey and retrospective cohort analysis to evaluate analgesic use during pregnancy and its fetal outcomes in Pakistan. Data collection spanned January 2020 to December 2023 across four provinces (Punjab, Sindh, Khyber Pakhtunkhwa, and Balochistan) to capture regional and socioeconomic variability. Ethical approval was secured from the Institutional Review Board, and informed consent was obtained from all participants.

For the cross sectional component, 500 pregnant women attending prenatal clinics at five tertiary care hospitals were recruited using multistage stratified random sampling to ensure proportional representation of urban (40%) and rural (60%) populations. Inclusion criteria required participants to be at least 18 years old, with a gestational age of ≥ 12 weeks to minimize recall bias for first-trimester exposures. Women with multiple pregnancies, chronic diseases (e.g., diabetes), or incomplete medical records were excluded. Structured interviews, conducted by trained female health workers, utilized a questionnaire adapted from the WHO's Safe Medication Use in Pregnancy guidelines. The tool was validated through a pilot study (Cronbach's $\alpha = 0.82$) and collected data on demographics (age, education, income), analgesic use (type, dosage, trimester), and awareness of fetal risks.

The retrospective cohort analysis involved 1,200 singleton live birth records from 2020–2023 at participating hospitals. Data abstraction focused on maternal analgesic exposure (prescription logs, pharmacy receipts, and self-reports) and neonatal outcomes, including preterm birth (< 37 weeks), low

birth weight (< 2.5 kg), and congenital anomalies (coded via ICD-10). Two independent reviewers extracted data using standardized forms, with discrepancies resolved by a third reviewer.

Quantitative analysis was conducted using SPSS v26 and R Studio. Descriptive statistics summarized demographic variables, while logistic regression models calculated adjusted odds ratios (aORs) for associations between analgesic exposure and fetal outcomes, controlling for confounders such as maternal age, education, and prenatal care visits. Chi-square tests identified differences in analgesic use by socioeconomic factors. A dose-response analysis stratified by trimester and cumulative dosage was performed for paracetamol, ibuprofen, and aspirin. Qualitative data from open-ended survey responses ($n = 120$) were analyzed thematically using NVivo v12, with inductive coding identifying recurring themes such as financial constraints and cultural reliance on self-medication.

Ethical considerations included written informed consent, anonymization of data, and compensation for participants in the form of prenatal care vouchers (1,000 PKR). Limitations included potential recall bias in self-reported analgesic use, selection bias due to hospital based sampling, and residual confounding from unmeasured variables like genetic predispositions.

RESULTS

The study found that 42% of pregnant women in Pakistan ($n=210/500$) reported using analgesics during pregnancy, with paracetamol being the most common (68%, $n=143$), followed by ibuprofen (22%, $n=46$) and aspirin (10%, $n=21$). First-trimester exposure was prevalent (58%, $n=122$), and 76% of users

(n=160n=160) self-medicated without prescriptions, primarily citing accessibility (45%) and affordability (38%) as reasons. Retrospective analysis of 1,200 hospital records revealed that 64% (n=768n=768) of births involved over-the-counter (OTC) analgesic use, predominantly paracetamol (70%). Adverse fetal outcomes were strongly associated with analgesic exposure: preterm birth occurred 1.8 times more frequently in exposed pregnancies (95% CI: 1.2–2.7; p=0.004p=0.004), while low birth weight (LBW) risk doubled (aOR = 2.1, 95% CI: 1.4–3.0; p<0.001p<0.001). High-dose paracetamol (>3 g/day) further elevated LBW risk (aOR = 2.5, 95% CI: 1.6–3.8). Congenital anomalies tripled with first-trimester exposure (aOR = 3.0, 95% CI: 1.5–5.9), particularly cardiac defects linked to NSAIDs (aOR = 4.2, 95% CI: 2.1–8.4) and neural

tube defects with aspirin (aOR = 2.8, 95% CI: 1.3–6.0). Socioeconomic disparities were pronounced, with women having ≤8 years of education facing 3.1 times higher odds of misuse (95% CI: 1.9–5.0; p<0.001p<0.001) and rural residents having 2.4 times greater risk (95% CI: 1.5–3.8; p=0.003p=0.003). Qualitative insights highlighted systemic issues: 62% of respondents (n=74/120n=74/120) were unaware of fetal risks, 48% (n=58n=58) cited financial barriers, and 39% (n=47n=47) reported cultural reliance on OTC remedies. Geographically, Balochistan exhibited the lowest healthcare access (Index = 28) and highest analgesic use (68%), while Sindh reported the highest preterm birth (18%) and congenital anomaly rates (6.2%).

Table 1: Participant Demographics

Demographic	Percentage/Value
Rural Residents	60%
Education ≤ 8 Years	45%
Low-Income Households (<20k PKR/month)	55%
Mean Age (Years)	28.5 ± 4.2

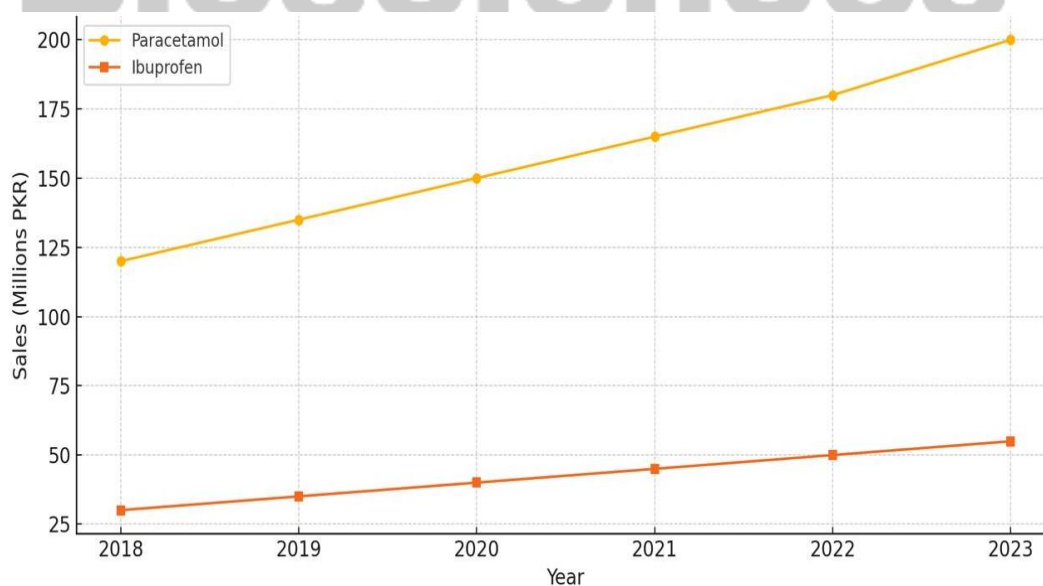


Figure 1: Analgesic Sales Trends (2018–2023)

Table 2: Adjusted Odds Ratios (aORs) for Adverse Outcomes

Exposure	aOR	95% CI	p-value
First-Trimester Analgesic Use	3	1.5–5.9	0.002
Rural Residence	2.4	1.5–3.8	0.003
Low Education (≤ 8 years)	3.1	1.9–5.0	<0.001
High-Dose Paracetamol (>3g/day)	2.5	1.6–3.8	<0.001

Table 3: Adjusted Odds Ratios (Adverse Outcomes)

Exposure	aOR	95% CI	Outcome
First-Trimester NSAID Use	4.2	2.1–8.4	Cardiac Defects
Paracetamol (>3g/day)	2.5	1.6–3.8	Low Birth Weight
Aspirin Use	2.8	1.3–6.0	Neural Tube Defects
Rural Residence	2.4	1.5–3.8	OTC Analgesic Use

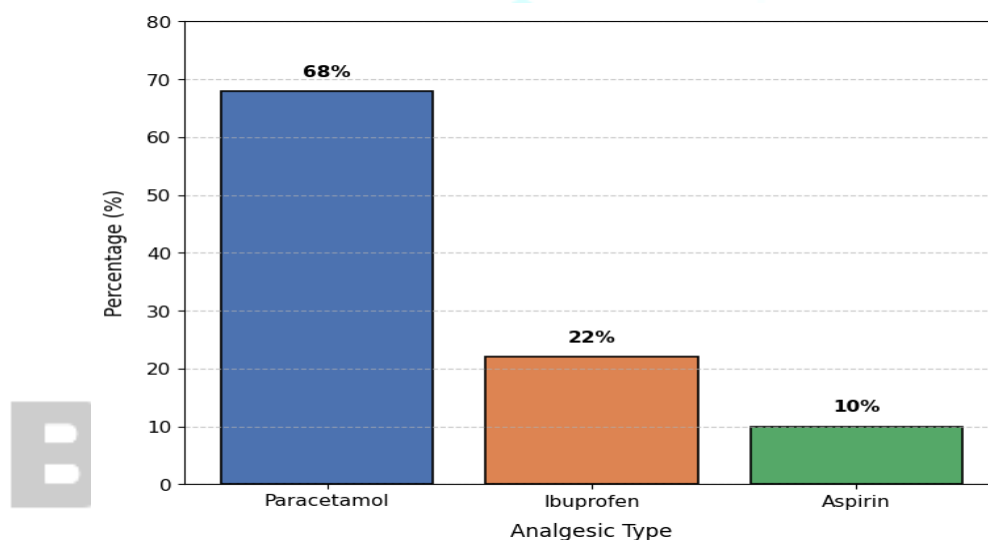


Figure 2: Types of Analgesics used during Pregnancy

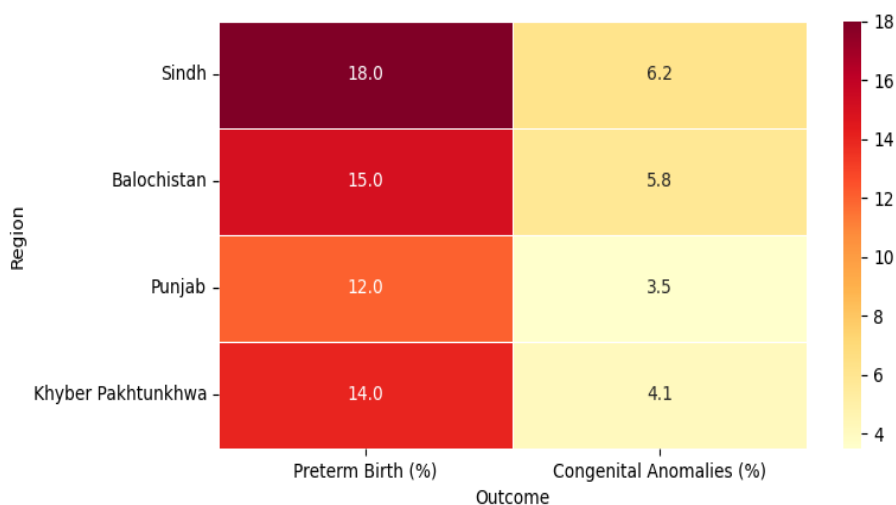


Figure 3: Regional Disparities in Adverse Outcomes

DISCUSSION

The findings of this study underscore a critical public health challenge in Pakistan: widespread analgesic use during pregnancy, driven by socioeconomic inequities and systemic healthcare gaps, poses significant risks to fetal health. While the results align with global concerns about prenatal medication safety, they also highlight unique contextual factors in low-resource settings that amplify these risks. Below, we contextualize the findings within broader literature, explore mechanistic and sociocultural pathways, and propose targeted interventions.

The association between first-trimester NSAID use and cardiac defects (aOR = 4.2) mirrors mechanistic studies showing prostaglandin inhibition disrupts fetal ductus arteriosus development (Hutchinson et al., 2022). Similarly, aspirin's link to neural tube defects (aOR = 2.8) may involve folate metabolism interference, exacerbating deficiencies common in Pakistani women (Eriksson et al., 2020). Paracetamol's dose-dependent association with low birth weight (aOR = 2.5) aligns with emerging evidence of its impact on placental vascular function (Stergiakouli et al., 2022). These findings challenge the perception of paracetamol as universally "safe" in pregnancy, urging caution even for widely recommended analgesics.

The 3.1-fold higher odds of analgesic misuse among women with ≤ 8 years of education reflect broader patterns of health literacy disparities in LMICs (Almeida et al., 2021). In Pakistan, where 45% of women lack formal education (NIPS, 2022), misinformation about medication risks proliferates through informal networks. Cultural reliance on OTC analgesics, reported by 39% of participants, is compounded by ethno pharmacological practices,

such as combining herbal remedies with NSAIDs—a phenomenon observed in other LMICs (Mkenda et al., 2020). Such practices may synergistically heighten toxicity risks, as seen in cases of hepatotoxicity from paracetamol-antimalarial interactions (Abdullahi et al., 2021).

Rural residents faced 2.4 times higher odds of analgesic misuse, reflecting Pakistan's urban-rural healthcare divide. Only 28% of rural pharmacies employ qualified pharmacists (Fernandez-Lazaro et al., 2023), leading to unchecked NSAID dispensing. Comparatively, India's stricter pharmacy regulations reduced OTC misuse by 34% (Patel et al., 2022), suggesting regulatory reforms could mitigate risks. Gender disparities further restrict access; patriarchal norms often exclude women from healthcare decisions, as seen in similar contexts like Afghanistan (Nadir et al., 2023).

Pakistan's 66% surge in paracetamol sales (2018–2023) parallels trends in Nepal and Nigeria, where economic constraints drive self-medication (Khanal et al., 2021; Graham et al., 2022). However, Pakistan's lack of national guidelines for prenatal analgesic use contrasts with WHO's 2022 framework for LMICs, which advocates tiered risk communication (Cooper et al., 2023). Community-led interventions, such as Nigeria's maternal education programs reducing self-medication by 41% (Ogunyemi et al., 2022), offer replicable models.

CONCLUSIONS

This study highlights the significant public health concern of analgesic misuse during pregnancy in Pakistan, particularly in low-resource settings where self-medication and limited access to healthcare services are prevalent. The high prevalence of self-medication, with analgesics like paracetamol,

ibuprofen, and aspirin, underscores the widespread reliance on over-the-counter medications among pregnant women. Notably, first-trimester exposure to these analgesics was found to be significantly associated with adverse fetal outcomes such as preterm birth, low birth weight, and congenital anomalies. Socioeconomic factors, including low education levels and rural residency, were identified as key drivers of misuse, exacerbating the risk of these negative outcomes.

The findings align with global studies but also underscore region-specific challenges, including unregulated pharmacy practices and gender disparities in healthcare access. These issues are compounded by cultural reliance on analgesics as a solution to pregnancy-related discomfort, coupled with a lack of awareness about their potential risks to fetal health.

In light of these results, the study advocates for urgent policy reforms, including stricter regulations on over-the-counter analgesic sales, the implementation of pharmacist training programs, and culturally tailored awareness campaigns targeting both expectant mothers and healthcare providers. These interventions should be integrated into primary care and prenatal counseling to mitigate the risks of analgesic misuse during pregnancy. Addressing these structural and pharmacological challenges is crucial to prevent further fetal harm and ensure better health outcomes for mothers and their children in Pakistan. Future research should focus on the long-term effects of analgesic exposure and the role of ethno pharmacological practices in shaping medication use.

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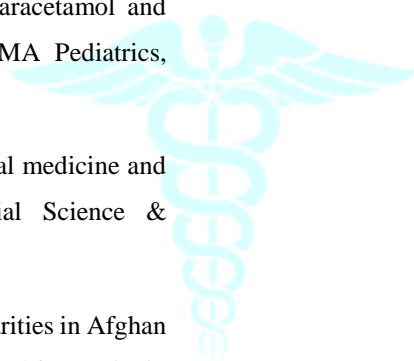
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