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AZITHROMYCIN'S ROLE IN PREVENTING ABORTIONS IN TOXOPLASMOSIS-POSITIVE PREGNANT WOMEN AT FAMILY HEALTH HOSPITAL, KOHAT

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ABSTRACT

Aim: To assess the effectiveness of azithromycin in preventing spontaneous abortion among pregnant women diagnosed with toxoplasmosis.

Methodology : This prospective observational study was conducted at the Department of Pharmacology, Islam Medical College Sialkot, Pakistan in the duration from September, 2023 to May, 2024, involving 88 pregnant women aged 18-40 years diagnosed with toxoplasmosis through serological testing. Participants, between 8 and 20 weeks of gestation, were divided into two treatment groups: Group A (Azithromycin) and Group B (Clindamycin). Exclusion criteria included a history of drug reactions to either medication and unwillingness to participate. Group A received oral Azithromycin (500 mg daily for three days, followed by 250 mg daily for four weeks), while Group B received oral Clindamycin (300 mg every six hours for four weeks). The primary outcome was spontaneous abortion before 20 weeks, and secondary outcomes included preterm birth, stillbirth, and congenital toxoplasmosis. Baseline demographic information and follow-ups every four weeks until delivery were recorded. Data were analyzed using SPSS version 22.0, with means, standard deviations, frequencies, and percentages calculated. Fisher's exact test compared treatment outcomes. The study was ethically approved, and informed consent was obtained from all participants.

Results: This study involved 88 pregnant women aged between 18-40 years with toxoplasmosis, divided into Group A (Azithromycin) and Group B (Clindamycin), each with 44 participants. The study evaluated primary outcomes of spontaneous abortion and secondary outcomes of preterm birth, stillbirth, and congenital toxoplasmosis. Participants were evenly distributed across age groups, with comparable health conditions, residential areas, socioeconomic statuses, and BMI categories between groups. Group A had a lower spontaneous abortion rate (4.55%) compared to Group B (9.09%),

although the difference was not statistically significant (p=1.000). Secondary outcomes also showed no significant differences. Despite the lack of statistical significance, the lower abortion rate in the Azithromycin group suggests a potential benefit, warranting further investigation.
Conclusion: The study's findings point to the possibility of using azithromycin rather than clindamycin to treat toxoplasmosis in pregnancy, as evidenced by the lower likelihood of spontaneous abortion in azithromycin treated group. Despite the lack of statistical significance, these results suggest that azithromycin could be an effective alternative.

Keywords: Azithromycin, spontaneous abortion, still birth, toxoplasmosis.

Introduction

A common infection that affects around one-third of the world's population is toxoplasmosis, which is brought on by the intracellular protozoan organism, *Toxoplasma gondii*.1 The majority of people whose immune systems remain intact either show no symptoms at all or have moderate symptoms. But there are serious hazards associated with the parasite, especially for pregnant women, as it can pass from mother to fetus through the placenta and cause congenital toxoplasmosis. Serious outcomes like stillbirth, miscarriage, or significant neurological and visual defects in the unborn child might arise from this transmission.2–4. Common ways to spread Toxoplasma gondii include eating or drinking contaminated animal products, water, and food items, as well as coming into contact with contaminated cat waste products.5. The parasite's capacity to infiltrate immune-privileged areas such as the liver, brain, and eyes highlights the severe consequences it may have on the developing fetus.6 The necessity of prompt detection and treatment during pregnancy is highlighted by the considerable increase in the risk of fetal transmission with gestational age.7

Pregnancy-related primary toxoplasmosis infection has substantial hazards for the fetus, with different outcomes possible depending on the gestational age at infection.8 According to estimates, the fetus will be exposed to 15% of the infection during the first trimester of pregnancy, 44% during the second, and 71% during the third.9 The liver, brain, and eyes are among the immune-privileged organs that Toxoplasma gondii targets when it crosses the placenta. Miscarriage and stillbirth are among the many unfavorable outcomes that may result from this, along with grave complications like as encephalitis, calcification of the intracerebral space, hydrocephalus, microcephaly, cognitive impairment, and thrombocytopenia.10 Even in cases where neonatal disease is asymptomatic at birth, there can be progressive damage, particularly to the central nervous system and eyes, highlighting the critical importance of managing toxoplasmosis in pregnancy to mitigate these serious risks.11

Azithromycin, a second-generation macrolide antibiotic, has emerged as a promising treatment option due to its favorable pharmacokinetic profile, including good transplacental transfer.12 It is widely used not only for treating infections such as sexually transmitted diseases and malaria but also for managing conditions like preterm pre-labor rupture of membranes (P-PROM) and providing prophylaxis during cesarean delivery. Importantly, azithromycin is categorized by the US FDA as pregnancy category B, indicating no evidence of risk in humans based on animal studies.13-14

While azithromycin's effectiveness in preventing spontaneous abortion specifically in toxoplasmosis-infected pregnancies requires further investigation, preliminary evidence supports its utility in reducing maternal-fetal transmission risks associated with this parasitic infection. The aim of this study is to explore the potential role of azithromycin, a second-generation macrolide antibiotic, in preventing spontaneous abortion among pregnant women infected with Toxoplasma gondii

Aim: To assess the effectiveness of azithromycin in preventing spontaneous abortion among pregnant women diagnosed with toxoplasmosis.

Materials and methods

Study design: This prospective observational study was conducted at the Department of Pharmacology, Islam Medical College Sialkot, Pakistan in the duration from September, 2023 to May, 2024**.**

Participants: The study involved 88 pregnant women aged 18-40 years, all diagnosed with toxoplasmosis through serological testing. These women, between 8 and 20 weeks of gestation, were categorized into two treatment groups i.e. Group A (Azithromycin) and Group B (Clindamycin). Exclusion criteria was any history of drug reaction to either azithromycin or clindamycin and unwilling to participate in the study. The group A participants received oral azithromycin (500 mg daily for three days, followed by 250 mg daily for four weeks), whereas the group B participants received oral clindamycin (300mg x 6 hourly daily for four weeks). The study monitored primary outcomes of spontaneous abortion before 20 weeks and secondary outcomes such as preterm birth, stillbirth, and congenital toxoplasmosis between both the treatment groups.

Data Collection

Baseline demographic information including age, medical history or comorbidities, residential area, socioeconomic status, BMI, parity and gestational age were recorded, with follow-ups every four weeks until delivery. The primary outcome was the incidence of spontaneous abortion before 20 weeks, while secondary outcomes included preterm birth, stillbirth, and congenital toxoplasmosis. Statistical analysis was conducted using SPSS version 22.0. The means and standard deviations of quantitative variables were calculated while the categorical data was expressed in frequencies and percentages. Meanwhile, the Fischer's exact test was used to compare the treatment outcomes between both the groups.

Ethical Considerations

The study was approved from the institute's ethical committee and informed consent was obtained from the patients before enrollment.

Results

The study included 88 participants having a mean age of 28 ±6.49 years, categorized in two treatment groups, Group A (Azithromycin) and Group B (Clindamycin), each consisting of 44 participants. In **Group A (Azithromycin)**, participants are evenly distributed across four age groups: 18-25 years (10 participants, 22.73%), 26-30 years (15 participants, 34.09%), 31-35 years (11 participants, 25%), and 36-40 years (8 participants, 18.18%). The mean ages range from 22.5 years in the youngest group to 38.8 years in the oldest. Across these groups, varying percentages of participants reported previous abortions (ranging from 25% to 60%), fetal deaths (10% to 50%), and multiparity (50% to 80%). Similarly, **Group B (Clindamycin)** shows a comparable distribution across age categories: 18-25 years (10 participants, 22.73%), 26-30 years (15 participants, 34.09%), 31-35 years (14 participants, 31.82%), and 36-40 years (5 participants, 11.36%). Mean ages also range from 22.5 years to 38.8 years. Reported percentages for previous abortions range from 20% to 60%, fetal deaths from 10% to 20%, and multiparity from 60% to 80%. The age-wise distribution of variables across both the treatment groups is denoted in the Table-1A.

Table-1A: Age-related distribution of demographic characteristics between both groups

Treatment group	Age Group (years)	Frequency N=88	Mean Age ± SD	Previous Abortions (%)	Fetal Death (%)	Multiparity (%)
Group A (Azithromycin) N=44	18-25	10 (22.73%)	22.5± 2.4	4 (40%)	1 (10%)	7 (70%)
	26-30	15 (34.09%)	28.2± 1.6	9 (60%)	3 (20%)	12 (80%)
	31-35	11 (25%)	33.1± 1.9	6 (54.55%)	2 18.18%)	8 (72.73%)
	36-40	8 (18.18%)	38.8± 1.2	2 (25%)	4 (50%)	4 (50%)
Group B (Clindamycin) N=44	18-25	10 (22.73%)	22.5± 2.4	4 (40%)	1 (10%)	7 (70%)
	26-30	15 (34.09%)	28.2± 1.6	9 (60%)	3 (20%)	12 (80%)
	31-35	14 (31.82%)	33.1± 1.9	7 (50%)	2 14.29%)	11 (78.57%)
	36-40	5 (11.36%)	38.8± 1.2	1 (20%)	1 (20%)	3 (60%)

Moreover, both groups show similar percentages for various health conditions. Hypertension affects 18.18% of Group A and 27.27% of Group B. Gestational diabetes is reported by 15.91% in Group A

and 18.18% in Group B. Hypothyroidism affects 9.09% in Group A and 13.64% in Group B. Depression is noted in 6.82% of Group A and 11.36% of Group B. Urban and rural residency rates are also comparable. Group A consists of 63.64% urban residents and 36.36% rural residents, while Group B has 54.55% urban and 45.45% rural residents. Satisfactory income versus low-income distribution is similar across both groups. Group A has 72.73% reporting satisfactory income and 27.27% with low income, whereas Group B reports 65.91% with satisfactory income and 34.09% with low income. Participants' distribution across BMI categories is evenly matched as well. In Group A, 59.09% fall into the normal weight range (18-24.9 kg/m²), 22.73% are overweight (25-30 kg/m²), 9.09% are obese (>30 kg/m²), and 9.09% are underweight (<18 kg/m²). Similarly, Group B shows 54.55% normal weight, 22.73% overweight, 11.36% obese, and 11.36% underweight. These findings illustrated in Table-1B, highlight the balanced distribution of demographic variables between the two treatment groups, which is crucial for ensuring comparability in analyzing outcomes between Azithromycin and Clindamycin treatments in the study.

Table-1B: Demographic Characteristics

Variables	Sub-group	Group A (Azithromycin) N=44	Group B (Clindamycin) N=44	Total (n=88)
Comorbidities	Hypertension	8 (18.18%)	12 (27.27%)	20 (22.73%)
	Gestational Diabetes	7 (15.91%)	8 (18.18%)	15 (17.05%)
	Hypothyroidism	4 (9.09%)	6 (13.64%)	10 (11.36%)
	Depression	3 (6.82%)	5 (11.36%)	8 (9.09%)
Area of Residence	Urban	28 (63.64%)	24 (54.55%)	52 (59.09%)
	Rural	16 (36.36%)	20 (45.45%)	36 (40.91%)
Socioeconomic Status	Satisfactory Income	32 (72.73%)	29 (65.91%)	61 (69.32%)
	Low Income	12 (27.27%)	15 (34.09%)	27 (30.68%)
BMI (kg/m²)	Normal Weight (18-24.9)	26 (59.09%)	24 (54.55%)	50 (56.82%)
	Overweight (25-30)	10 (22.73%)	10 (22.73%)	20 (22.73%)
	Obese (>30)	4 (9.09%)	5 (11.36%)	9 (10.23%)
	Underweight (<18)	4 (9.09%)	5 (11.36%)	9 (10.23%)

Figure-1: Overall distribution of Cases according to place of residence

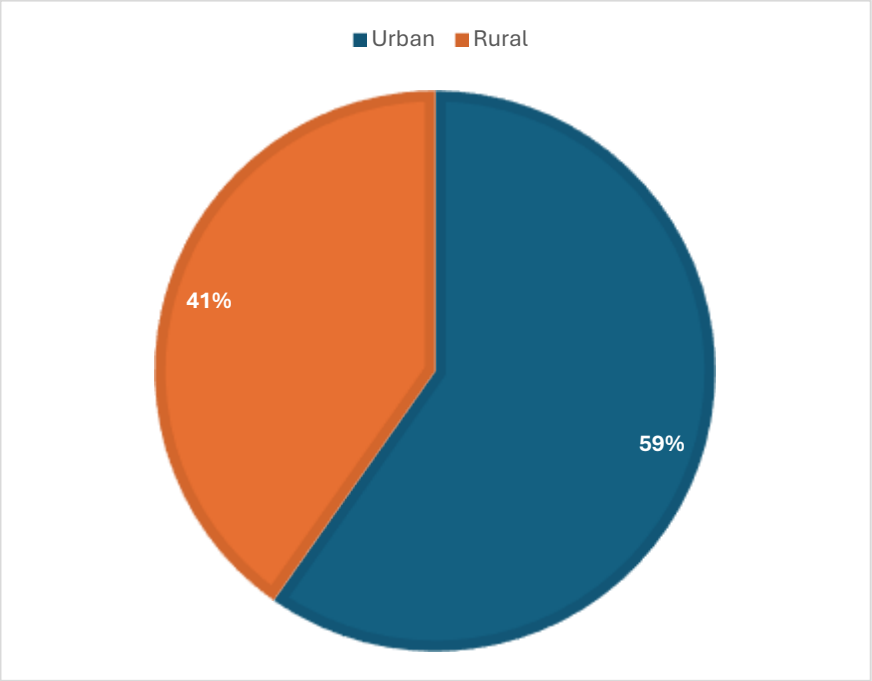
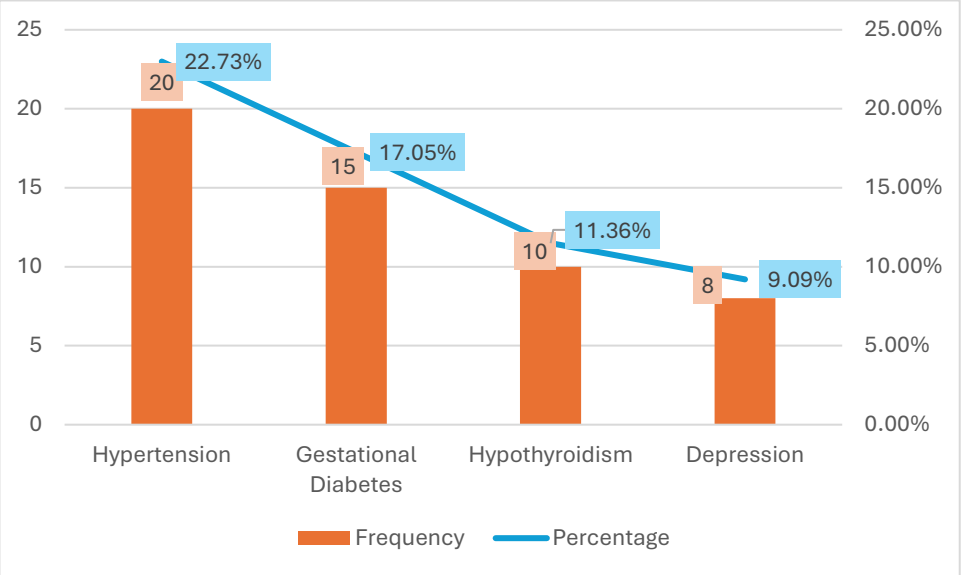


Figure-2: Overall trends of co-morbid conditions in the study group



The primary outcome of spontaneous abortion showed a notably lower rate in the Azithromycin group, with 4.55% compared to 9.09% in the Clindamycin group, resulting in an overall incidence of 6.82% across both groups, yet with a non-significant p-value of 1.000. Secondary outcomes including preterm birth (3.41%), stillbirth (2.27%), and congenital toxoplasmosis (5.68%) similarly exhibited no significant differences between the groups, all with p-values of 1.000. Although not statistically significant, the observation of a lower spontaneous abortion rate in the Azithromycin group warrants further investigation in larger studies to explore potential implications for maternal and fetal health outcomes under Azithromycin treatment compared to alternatives like Clindamycin.

Table-2: Pregnancy outcomes of the study group treated with azithromycin

Pregnancy Outcome(s)		**Group A (Azithromycin) N=44**	**Group B (Clindamycin) N=44**	**Total (n=88)**	**p-value**
Primary Outcome	Spontaneous Abortion	2 (4.55%)	4 (9.09%)	6 (6.82%)	1.000
Secondary Outcomes	Preterm Birth	1 (2.27%)	2 (4.55%)	3 (3.41%)	1.000
	Stillbirth	1 (2.27%)	1 (2.27%)	2 (2.27%)	1.000
	Congenital Toxoplasmosis	2 (4.55%)	3 (6.82%)	5 (5.68%)	1.000

Discussion

The study comparing pregnancy outcomes between Azithromycin and Clindamycin in toxoplasmosis treatment revealed intriguing findings that warrant discussion in the context of existing literature. In this study involving 88 participants (44 per group), the primary outcome of spontaneous abortion was notably lower in the Azithromycin group at 4.55% compared to 9.09% in the Clindamycin group, although the overall incidence across both groups was 6.82%, with a non-significant p-value of 1.000. Similarly, secondary outcomes including preterm birth (3.41%), stillbirth (2.27%), and congenital toxoplasmosis (5.68%) did not show statistically significant differences between the two treatment groups, all with p-values of 1.000.

Comparing these results with existing literature, previous studies have shown varying outcomes regarding the efficacy and safety of Azithromycin and Clindamycin in treating toxoplasmosis during pregnancy. Some studies like that of Castro-Filice et al.15 have suggested Azithromycin's potential benefit in reducing fetal complications such as spontaneous abortion and congenital toxoplasmosis due to its favorable pharmacokinetic properties and broad tissue penetration. Conversely, Clindamycin has been traditionally used and studied for its effectiveness in treating toxoplasmosis infections but may carry a different risk-benefit profile compared to Azithromycin.

The observed lower spontaneous abortion rate in the Azithromycin group somewhat mirrors with the findings of Nayeri et al. study suggesting its potential efficacy in reducing adverse pregnancy outcomes associated with toxoplasmosis.16 However, the lack of statistical significance in this study's results underscores the need for larger, randomized controlled trials to confirm these trends and establish definitive recommendations for clinical practice.

Moreover, the non-significant differences in secondary outcomes such as preterm birth, stillbirth, and congenital toxoplasmosis highlight the overall comparable safety profiles of both antibiotics in this context. These results offer insightful information, but they also highlight how difficult it is to manage toxoplasmosis during pregnancy, where it is crucial to weigh effectiveness against any dangers to the health of the fetus and mother.

In summary, although this study raises the possibility that azithromycin may be more successful than clindamycin in preventing spontaneous miscarriages in cases of toxoplasmosis treated during pregnancy, more thorough research is necessary to confirm these results and properly direct clinical decision-making. Larger sample numbers, longer follow-up times, and perhaps disease severity stratification should be taken into account in future research to improve the validity and practicality of the findings.

Conclusion

The study's findings point to the possibility of using azithromycin rather than clindamycin to treat toxoplasmosis in pregnancy, as evidenced by the lower likelihood of spontaneous abortion in azithromycin treated group. Despite the lack of statistical significance, these results suggest that azithromycin could be an effective alternative. More research is necessary to validate its safety and effectiveness in lowering the negative effects of toxoplasmosis on pregnancy outcomes.

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