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Review Article

Antimicrobial usage in pregnancy: Guidelines and challenges in India; A systematic review

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ABSTRACT

Antimicrobial policy in pregnancy is an important area of concern in the field of obstetrics and gynecology. The use of antibiotics and other antimicrobial agents during pregnancy can have significant effects on both the mother and the developing fetus. The objective of antimicrobial instituting policy in pregnancy is to prevent and treat infections while minimizing the risk of adverse outcomes. The guideline are based on a careful evaluation of the benefits and risks associated with the use of antimicrobial agents during pregnancy, as well as the potential impact on the development of antimicrobial resistance. This study provides a brief overview of the current antimicrobial policy in pregnancy, highlighting the importance of appropriate antibiotic selection, dosing, and duration of therapy. It also discusses the role of healthcare providers in implementing and monitoring antimicrobial policy in pregnancy, as well as the importance of patient education and informed choices for rational use of antimicrobial.

1. Introduction

Antimicrobial are frequently prescribed to treat bacterial and fungal infections. During pregnancy, the use of antibiotics may be necessary to treat some infections that could affect both the mother and the foetus. Antibiotic use during pregnancy has, however, been linked to significant hazards and challenges. When giving a pregnant lady antibiotics, there are a number of things to take into account. The potential effect of the medicine on foetal development is a crucial factor to consider while prescribing. While some antibiotics have been proven to be safe to take while pregnant, others may harm the foetus (Teratogenicity). Antimicrobial resistance (AMR) is a worldwide issue that is affecting public health. The indiscriminate use of antibiotics is the cause of rising prevalence. The need to weigh of AMR the potential hazards and advantages for both the mother and the foetus makes using antibiotics during pregnancy challenging.[1,2]

For the treatment of numerous infections during pregnancy, antibiotics are commonly administered. Antibiotic usage during pregnancy has, however, been linked to a number of undesirable outcomes, such as preterm birth, low birth weight, and congenital defects. Hence, the benefits and dangers of using antibiotics during pregnancy must be taken into account when developing antimicrobial policies. Nonetheless, doctors have been hesitant to recommend. Some antibiotics (such as tetracyclines) listed as human teratogens, others (such as gentamycin) had teratogenic effects in animal studies, and some could have hazardous effects after birth (e.g., streptomycin). The advancement of problems, intrauterine infections, and preterm labour may occur when essential antibiotic therapy for maternal infections is forgone.

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Tetracycline exposure during pregnancy has been cited as a reason to end pregnancies frequently in Hungary.[3,4]

According to reports, about 80% of all prescriptions taken during pregnancy are antibiotics, and roughly 20–25% of pregnant women will get one. Pregnant women are most frequently infected with upper respiratory tract infections (URIs), urinary tract infections (UTIs), and sexually transmitted infections (STIs), including pyelonephritis (URTIs). Untreated infections like UTIs or STIs are linked to severe foetal risk, including spontaneous abortion, preterm, and low birth weight. Using any medicine during pregnancy is a risk versus benefit decision. Randomized controlled trials rarely provide evidence on safety and efficacy because they are difficult to conduct on pregnant women and may be unethical. As a result, being pregnant is frequently a requirement for rejection from clinical trials.[5,6]

Pregnancy antibiotic exposure may have negative short- and long-term effects on newborn weight. A recent study found that prenatal exposure to antimicrobials caused the infant to have a birth weight that was about 138 g lower after accounting for a number of factors. Although specific antimicrobial class exposure was not established in the study, previous research has connected prenatal antimicrobial exposure to childhood obesity.[5–8]

Independent studies have examined the relationship between antenatal antibiotic use and the risk of atopic disease, such as atopic dermatitis and asthma, as well as neurologic disease, such as cerebral palsy and epilepsy. While some research show a relationship, others do not. One study found a link between prenatal antibiotic use and children at risk for asthma developing asthma by the age of three. Even less is known regarding the risk connected with drug use by trimester. When the mother used antibiotics in the second to third trimesters but not the first, there was a significant prenatal antibiotic risk associated with asthma and wheeze.[1,9,10]

2. Literature Survey/ The Larger Question

Before producing this paper, we typically examine several types of research articles on the impact of antibiotics on pregnancy in order to gather the data we need for this review. The most crucial details from these many study articles have been integrated into our review paper. The article "Antibiotics on in Pregnancy - A Prospective Cohort Study the Policy of Antibiotic Prescription" is the subject of our investigation. Its author is Anne M. Heikkila. Anne M. Heikkila provides a brief summary of these studies on the relationship between antibiotic use and pregnancy.

She demonstrated in the report that, 4055 pregnant women, who eventually gave birth to a live infant, participated in the study during a period from June 15, 1987 to June 14, 1988. The Central Statistics Office of Finland reports that during the same time period, there were 63,047 live births nationwide and 8536 live births in the specific district. Based on specific questionnaires that were completed by either the prescribing doctor or the nurse at the maternal health care facility or hospital, the data on antibiotic consumption was compiled. During the course of the pregnancy, information on the type of antibiotics prescribed, the indication,

dosage, length of treatment, the mode of administration, and the timing of the length of gestation were noted.[11]

At the woman's first visit to the maternity health centre between gestational weeks 8 and 16, the basic information regarding the mother's age and parity, as well as information on the use of antibiotics during the early weeks of pregnancy, were noted on the questionnaire. After the births, the questionnaires were gathered from the district's 10 hospitals. SAS computer programme was used to process the data. After gathering all of this information, it was determined that 2174 infections were diagnosed during pregnancy, resulting in the prescription of 23 different medicines.

The most often used antibiotics, accounting for 65.4% of all antibiotics, were penicillin, erythromycin, and pivmecillin. 72% of the infections that needed to be treated were vaginal candidiasis and infections of the respiratory or urinary system. Urinary tract infection, whether acute or recurrent, was the sole indication for pivmecillinam.Figure 1 While 54.0% of all acute cystitis cases were treated with pivmecillinam, 20.6% with nitrofurantoin, and 9.8% with cephalexin, it showed that pivmecillinam was the medicine of choice for treating cystitis.[11]

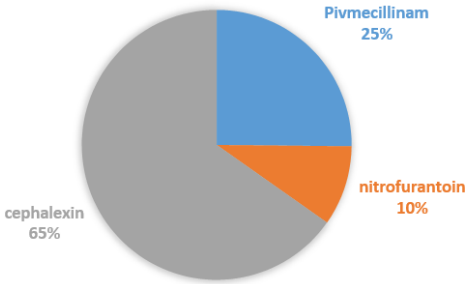

Fig. 1: Acute cystitis cases were treated with pivmecillinam, nitrofurantoin and cephalexin[11]

Nitrofurantoin, methenaminehippurate, and pivmecillinam were used to treat recurrent or chronic urinary tract infections in 43.5%, 26.1%, and 13.0% of cases, respectively. The second trimester, peaking at 16 weeks of gestation, had the highest prevalence of antibiotic use. From a different angle, the use of antibiotics was marginally more prevalent in the first half of pregnancy than in the second (52.5% vs. 47.5%). Oral administration was used 94.6% of the time. 4.6% of instances employed

the vaginal method of administration. In the majority of cases (75.4%), only metronidazole was administered vaginally. Cefoxitin, cefuroxime, and ceftazidime, which are only available in parenteral form, were administered intravenously.

Only two instances required intravenous penicillin administration. The typical treatment period for the most frequently prescribed antibiotics was 10 days. In the case of nitrofurantoin, a 7- day course of treatment seemed to be more typical than a 10-day course; 29.2% of nitrofurantoin treatments and 100% of methenamine hippurate treatments, which were clearly

prescribed for prevention in cases of chronic or recurrent cystitis, lasted longer than 14 days. The dosages were largely the same as those suggested for the general population who weren't pregnant. In a few instances, erythromycin and amoxicillin were taken at lower quantities while penicillin was supplied at higher amounts.[11]

We learn from Patricia A. Yu's article, "Safety of Antimicrobials during Pregnancy: A Systematic Analysis of Antimicrobials Considering for Treatment and Postexposure Prophylaxis of Plague," that there is additional research on this subject. This article demonstrates how the entire research process was separated into many segments and completed as a result. Generally speaking, some antimicrobial medication was chosen for this study. In this work, we demonstrate that amikacin, gentamicin, plazomicin, streptomycin, tobramycin, chloramphenicol, doxycycline, sulfadiazine, and trimethoprim/sulfamethoxazole are among the antibiotics that are being evaluated for the treatment and PEP of plague (TMP-SMX).

Despite the fact that some of these antimicrobials may not be now widely available in the United States, they were included due to their accessibility worldwide. Due to two previously published systematic evaluations on this family of antibiotics, fluoroquinolones also taken into consideration for the treatment of plague and PEP were not included in this review. After that, they gather the data. From the beginning of each database through February 2018, a CDC librarian searched CINAHL, Cochrane Library, Embase, Medline, and Scopus for English- language papers. The generic antimicrobial name was coupled with phrases related to pregnancy, foetal development, or new-borns in the search terms. They also keep up with the quality assessment, data synthesis, and eligibility criteria. After considering all of these, they come to the conclusion that a systematic review summarises data on the safety of 9 antimicrobials that are being investigated for treating plague and PEP during pregnancy and will inform CDC clinical guidelines for plague. Although data were usually sparse for all of the antimicrobials studied, unfavourable maternal, foetal, and neonatal outcomes were not consistently seen for the majority of them. Antimicrobials should be used to treat and prevent plague during pregnancy; the decision to employ one antibiotic over another may depend on these findings and the hazards associated with plague as stated in the systematic review of plague during pregnancy.[12]

According to our review, prolonged prenatal exposure to streptomycin may increase the risk of hearing and/or vestibular impairments in the mother and/or the foetus. Moreover, exposure to TMP-SMX during the first trimester seems to carry a possible risk of NTDs. Although exposure to doxycycline and chloramphenicol was linked to cardiovascular birth abnormalities in one study and spontaneous miscarriage in another, these relationships were based on small amounts of data from a single investigation and were not supported by other studies that were part of our review. Amikacin, gentamicin, tobramycin, and sulfadiazine use during pregnancy was not linked to poor outcomes for the mother, the foetus, or the newborn. The inability to identify uncommon connections, however, may be a result of the small number of prenatal exposures. Due to previous systematic assessments on the safety of fluoroquinolones, which would be taken into consideration for the treatment and Management of plague in pregnant women, they were excluded from our review. All three systematic reviews will be taken into account in the clinical guidelines for plague.

Numerous studies and case reports, the majority of which were for the treatment of tuberculosis (TB), and frequently involved prolonged streptomycin therapy in combination with other

medications throughout pregnancy, have reported a pattern of hearing and/or vestibular deficits in the mother and the newborn following exposure to streptomycin during pregnancy. The majority of the streptomycin related articles in our review were released before to 1970, a time when streptomycin was more frequently used in the United States. In combined investigations, the majority of pregnant women exposed to streptomycin (>60%) received treatment for 14 days. Due to the treatment's longitudinal character, the deficiencies found may also be connected to more pregnancies exposed to streptomycin beginning in the first trimester. The possible dangers of using streptomycin for treatment and PEP of plague during pregnancy may be minimal because it is anticipated that the course of treatment for these conditions will only last for around 14 days.

Amikacin, gentamicin, and tobramycin exposure during pregnancy did not result in any cases of nephrotoxicity or ototoxicity in either the mother or the foetus; however, there were few publications found and the treatment times were often shorter than those for streptomycin. Although no studies describing plazomicin exposure during pregnancy were found, nephrotoxicity has been described in clinical trials of non-pregnant adults, and the danger of ototoxicity cannot be completely ruled out based on the available information.[12]

The authors Flory T. Muanda, Odile Sheehy, and Anick Bérard's study "Use of antibiotics during pregnancy and risk of spontaneous abortion" is the next one we look at. We discovered some further information about the antibacterial effect on pregnancy while reading this paper. We can see from this report that the researchers done excellent research. They display a sound technique design in their article. The Research design, Data sources, Study population, Exposure, Covariates, Statistical analysis, and Ethics approval were all incorporated into the technique. They divided the people they were studying into two groups. Cases is one.

When they demonstrate that using diagnostic codes from the International Classification of Diseases, they were able to identify pregnancies with a diagnosis or procedure connected to spontaneous abortion before the 20th week of gestation. We only took into account females who had clinically proven spontaneous abortion. The spontaneous abortion's calendar date served as our definition of the index date. By deducting the gestational age from the date on the calendar of the spontaneous abortion, we were able to calculate the initial day of gestation for each case. We utilised an algorithm to estimate the gestational age when the data was missing from the database. Where they demonstrate that they matched 10 controls by gestational age and year of pregnancy for each case at the index date.

We selected this number of controls because, when the prevalence of exposure to the study drug is less than 15% among controls, the control case ratio must rise to 10 or higher in order to boost statistical power (as in our study). Such numbers have been utilised by Suissa and colleagues in numerous experiments with comparable circumstances. Based on a relative power table for nested case-control studies, we intended to find an odds ratio of 1:5, assuming a prevalence of exposure of 5% among controls, a fixed number of case-control sets, a control case ratio of 10, a relative power of 80%, and a type 1 error of 5%. In their case study, they discovered 182 369 pregnancies that satisfied the criteria for inclusion, 8702 (or 4.7% of them) of which resulted in a clinically diagnosed spontaneous abortion.Figure 2 In 1068 (12.3%) of the cases, the gestational age was determined based on ultrasound. Women who had spontaneous abortions were more likely to be older, live alone, have comorbid conditions, and have infections than the 87 020 matched controls. [13]

Usage of Antimicrobial Medication in Pregnancy and the Risk of Various Neonatal Outcomes: A Population Based Research by Anna Cantarutti provides us with further crucial study data. She and her team demonstrate yet another crucial study methodology. The research methodology was broken down into Setting, Study Cohort, Antibiotic Exposure, Outcomes, Maternal Covariates, Statistical Analysis, and Sensitivity and Subgroup Analyses in her work. This article's conclusion, which the author tries to convey, is that out of the 773,237 women who were a part

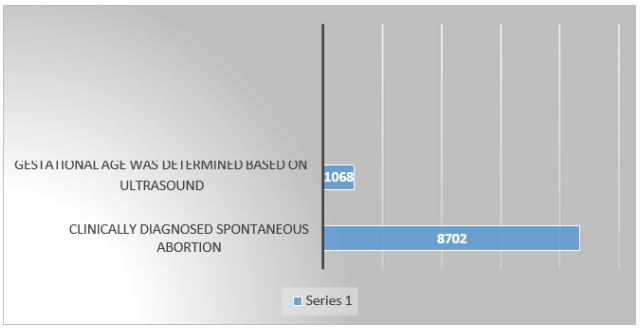

Fig. 2: 8702 (or 4.7% of them) of which resulted in a clinically diagnosed spontaneous abortion. In 1068 (12.3%) of the cases, the gestational age was determined based on ultrasound [13]

of the study cohort, 208,945 (27%) used antibiotics while pregnant. Of these, 132,024 (63%) were early users, while the remaining 76,921 (37%) were late users.Figure 3

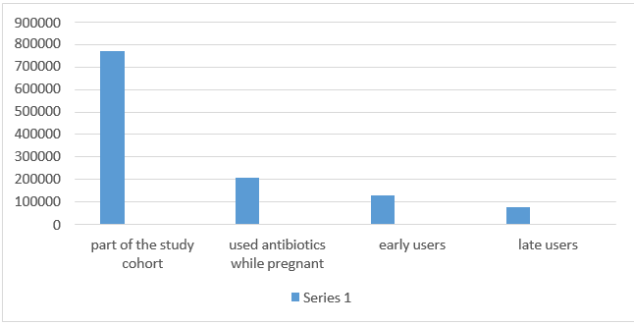

Fig. 3: Out of the 773,237 women who were a part of the study cohort, 208,945 (27%) used antibiotics while pregnant. Of these, 132,024 (63%) were early users, while the remaining 76,921 (37%) were late users [14]

There was no discernible difference between early and late users of antibiotics and the equivalent no users, with the exception of a higher incidence of antibiotic users among women with low education, unemployment, C-sections, and concurrent drug use. 31 061 preterm births (4%); low birth weights (4.4%); tiny for gestational age (7.3%); and low Apgar scores (0.4%) were all observed among the 773237 pregnancies. [14]

Even we also study more other research article such as "Bacterial profile and antimicrobial resistance patterns of common bacteria among pregnant women with bacteriuria in Ethiopia: a systematic review and meta-analysis" by Legese Chelkeba, et.al, "Antibiotic use amongst pregnant women in a public hospital in KwaZulu-Natal" by Sasha Naidoo, Varsha Bangalee and Frasia Oosthuizen, "Antibiotic knowledge, attitudes and reported practice during pregnancy and six months after birth: a follow-up study in Lao PDR" by Sengchanh Kounnavong, et.al, and after all these article study we conclude that proper antibiotic usage during pregnancy is vital to prevent and

treat infections while limiting the risk of undesirable effects. An effective antimicrobial policy in pregnancy must take appropriate antibiotic selection, dose, and therapy duration into account. Patient education and informed consent are crucial elements of successful treatment, and healthcare personnel play a crucial role in the implementation and oversight of antimicrobial policy. We can guarantee that pregnant women receive the greatest treatment while reducing the possibility of injury to themselves and their growing foetuses with ongoing focus and effort in this area. [15–18]

3. Discussion

Obstetrics and gynaecology must carefully weigh the importance of antimicrobial policy in pregnancy. The goal of this study was to investigate the state of antimicrobial policy in pregnancy while emphasising the significance of proper antibiotic selection, dose, and therapy duration. According to our research, using suitable antibiotics during pregnancy helps treat and prevent infections while lowering the risk of negative effects. The proper choice of antibiotics is one of the main concerns with antimicrobial policy during pregnancy. Pregnancy-related illnesses such chorioamnionitis, urinary tract infections, and group B streptococcal colonisation are frequently treated with antibiotics. Nonetheless, the potential dangers and advantages for the mother and the foetus must be taken into account while selecting an antibiotic.

For instance, some antibiotics, including tetracyclines and fluoroquinolones, are not advised during pregnancy due to the risk of teratogenicity and probable harm to the growth of the foetal bone and cartilage. The dosing and duration of medication are two additional crucial factors in antibacterial policy in pregnancy. To achieve adequate infection treatment while reducing the danger of side effects, the proper dosing and length of therapy must be carefully examined. Inadequate dose, on the other hand, may result in therapeutic failure and the emergence of antimicrobial resistance. As an illustration, continuous usage of antibiotics may raise the risk of preterm birth.

An important part of implementing and overseeing antimicrobial policy in pregnancy is played by healthcare professionals. To guarantee that a course of therapy is effective and that any side effects are quickly discovered and dealt with, adequate monitoring and follow-up are required. Patients must be informed of the risks and advantages of using antibiotics during pregnancy, therefore patient education and informed consent are also crucial elements of successful therapy. Another crucial factor in antimicrobial policy in pregnancy is the rising prevalence of antibiotic resistance. Antimicrobial resistance is a critical public health issue that can have negative effects on both the mother and the foetus in development. As a result, it's crucial to use antimicrobial drugs sparingly to reduce the chance of resistance emerging. [19,20]

4. Conclusion

In obstetrics and gynaecology, antimicrobial policy during pregnancy is a major topic of concern. Antibiotics and other antimicrobial substances should be carefully considered in light of the potential hazards and advantages to both the mother and the foetus that may result from their usage during pregnancy. Implementing an effective antibacterial policy in pregnancy requires careful consideration of the right choice, dosage, and length of therapy. Moreover, healthcare professionals are crucial in the implementation and oversight of antimicrobial policy, and informed patient consent and patient education are crucial elements of successful management. The significance of prudent antimicrobial usage in pregnancy is further highlighted by the rising prevalence of antibiotic resistance. The creation of evidence-based recommendations for the use of antimicrobial drugs during pregnancy, as well as methods to maximise their usage and reduce the risk of negative effects, should be the main topics of future research. We can guarantee that pregnant women receive the greatest treatment while reducing the possibility of injury to themselves and their growing foetuses with ongoing focus and effort in this area. [1,20]

5. Source of Funding

None.

6. Conflict of Interest

None.

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