ANTIBIOTIC MISUSE AMONG PREGNANT WOMEN IN MISURATA CITY

Bashir Elmadani

Department of Obstetrics & Gynecology, Faculty of Medicine, Misurata University 139/2018

ABSTRACT

There is increasing evidence that the self-medications among pregnant women is common in many developing countries. Despite the adverse impact on pregnancy, there are few programs available for their control. The objective of this study was to assess the level of self-medication by antibiotics amongst Libyan pregnant women in order to determine the drug misuse, development of resistance and the possible harmful effects on fetus. Four hundred pregnant women, aged between 18 and 40 years were drawn from outpatient obstetric clinics and hospitals in Misurata city and assessed for self-medication by antibiotics, adapted from a self-report questionnaire based on the WHO guidelines for antibiotic misuse survey. Of the 400 pregnant women assessed, 61 (15.3%) indulged in the selfuse of antibiotics for common cold, fever cough and pelvic pains (not prescribed from the antenatal clinic), 107 (26.8%) didn't complete the full course of the drug (prescribed from the antenatal clinic) when they felt any improvement. A total of 211(52.7 %) pregnant women complete the full course of the drug and 21 (5.2%) are not aware in antibiotic misuse in pregnancy. There was a significant difference in the pregnant women whom completed the full course of the drug and those don't complete it. (X2=10.97, p=0.001); There was also a significant difference between the presence of current pregnancy illness and antibiotic misuse (X2=9.04, p=0.001) There was no significant difference among pregnant women who were highly educated compared to those with little or no education. However, the level of education has no strong impact in the self-usage of antibiotics as shown above. No fetal complications related to misuse was detected. This study shows that self-medication is not uncommon among pregnant women in our environment. There is need for adequate education of pregnant women during antenatal clinics on the potential danger of antibiotic self-medication so as to prevent child and maternal morbidity and mortality.

KEY WORDS: Antibiotic, Self-Medication, Pregnancy, fetal, Side effects.

INTRODUCTION

Antimicrobial resistance is one of the greatest threats to global population health in this century and it is a major contributor to rising healthcare costs worldwide. The primary cause of this resistance is antibiotic misuse, especially routine inappropriate use of antibiotics for self-limiting illnesses. Over prescription of antibiotics is pervasive leading to very high and increasing rates of antimicrobial resistance in both hospital-acquired and communityacquired infection. Self-medication is identified by the WHO as a major leading factor to antibiotic misuse & overuse and resistance, Self-medication is a considerable problem all over the world in face of current global economic downturn^(1,2).

A large number of countries are facing serious health challenges with people finding it difficult to meet their health needs, In developed countries, self-medication is not uncommon, but the practice is guided because people are enlightened and could derive adequate information from various sources⁽³⁾. Consequently, it is often regarded as consumers' luxury and very attractive. Evidence suggests that many people involved in self-medication tend to acquire knowledge of the practice from relatives, neighbors, medicine dealers, and sometimes media⁽⁴⁾. The situation in developing countries is frightening, where there is poor medical services and lack of professional control of pharmaceutical products⁽¹⁾.

Department of obstetrics & Gynecology, Misurata university E-mail: bashlib@hotmail.com

MMSJ Vol.3 Issue.2 (Winter 2016)

This therefore forces people to self-medicate themselves with various forms of medicines for different medical complaints^(5,6), Even though the practice is high, there is scarcity of data on the impact on the people, A few of the studies that had been carried out have shown potential harmful effects on both the fetus and mothers usually exposed to un-prescribed antibiotics^(7,8,9).

RNLNL

Several factors including poverty, cultural perception of certain diseases' entity and their perceived responses to indigenous medications have been widely reported as indicators in developing countries making the practice a necessity, This makes it more dangerous as basic knowledge concerning the pharmacological properties of these drugs may be lacking⁽¹⁰⁾.

MATERIAL AND METHODS

The aim of our study was to explore the knowledge and behaviors of pregnant ladies in relation to antibiotic use and misuse in Misurata city.

This study was carried out at Misurata city, it has a population of about ¹/₂ million people. Data collection using a one-stage random sampling method, 400 pregnant women were randomly selected and screened for self-medication by antibiotics, using a questionnaire adapted from of self-report based on the World Health Organization guidelines for antibiotics misuse⁽¹⁵⁾. Commonly available antibiotics were added to the list of substances in the questionnaire. Participants were also asked to indicate the reasons for using the medicines.

Information on age, marital status, educational level and occupation were elicited through a semistructured socio-demographic questionnaire. Data

Correspondence and reprint request:

Dr. Bashir Dafer Elmadani

analysis: The results of the study were analyzed using Statistical Package for Social Sciences (SPSS 17.0). The proportion of the pregnant women involved in the use of different antibiotics was found from the respondents. Sample means and percentages were calculated from which simple frequency tables were created. Standard deviation from the mean was calculated and comparisons of categorical data were done using Chi-square. The P-value of less than or equal to 0.05 was used to determine the statistical significance.

RESULTS

(Table 1) Age distribution

Age group	Frequency	Percent
<20	133	33.3 %
20 - <30	130	32.5 %
30 - <40	97	24.2 %
>40	40	10.0 %
Total	400	100.0 %

Nationality	Frequency	Percent
Libyan	332	83.0 %
Non-Libyan	68	17.0 %
Total	400	100.0

(Table 3) Parity distribution

Parity	Frequency	Percent
PG	85	21.3 %
P1 – P3	149	37.3 %
P4 or more	166	41.5 %
Total	400	100.0

(Table 4) Occupation distribution

Occupation	Occupation Frequency	
Employed	244	61.0 %
Non-Employed	156	39.0 %
Total	400	100.0

(Table 5) Distribution of Level of education

Education	Frequency	Percent
High	61	15.3 %
Moderate	135	33.8 %
Low	204	51.0 %
Total	400	100.0

|--|

Gest- Age	Frequency	Percent
<20 weeks	222	55.5 %
>20 weeks	178	44.5 %
Total	400	100.0

(Table 7) Distribution according antibiotic course completion

Completion	ompletion Frequency	
Completed	272	68.0 %
In-completed	128	32.0 %
Total	400	100.0

(Table 8) Distribution according to antibiotics side-effects

side-effects	Frequency	Percent
No	264	66.0 %
Gastric upset	76	19.0 %
Diarrhea	60	15.0 %
Total	400	100.0

(Table 9) Distribution according awareness to antibiotics misuse

Awareness	Frequency	Percent
Yes	379	94.8 %
No	21	5.2 %
Total	400	100.0

(Table 10)	Distribution	according	to	antibiotics	use
&misuse					

Awareness		Frequency	Percent
Self	medication	61	15.3 %
	Incomplete course	107	26.8 %
	Completed course	211	52.7 %
	Un-aware	21	5.2 %
	Total	400	100

Out of the 400-pregnant women participants, 61 (15.3%) indulged in the self-use of antibiotics for common cold, fever cough and pelvic pains (not prescribed from the antenatal clinic), 107(26.8%) didn't complete the full course of the drug (prescribed from the antenatal clinic) when they felt any improvement. A total of 211 (52.7 %) pregnant women complete the full course of the drug and 21 (5.2%) were not aware in antibiotic misuse in pregnancy while the rest were aware of it 379 (94.8%). There was a significant difference in the pregnant women whom complete the full course of the drug and those don't complete it. (X2=10.97, p=0.001);

There was also a significant difference between the presence of current pregnancy illness and antibiotic misuse (X2=9.04, p=0.001).

There was no significant difference among pregnant women who were highly educated compared to those with little or no education. However, the level of education had no strong impact in the self-usage of antibiotics as shown above. No fetal complications related to misuse was detected.

Tables from 1-10 show the socio-demographic characteristics of pregnant women. Of the 400-pregnant women participants, 133 (33.3%) were aged below 20 years, 130 (32.2%) between 20 and 29 years, 97 (24.2%) 30-39 years, while 40 (10 %) were aged above 40 years. Most of the cases 83 % were Libyan, more than 70% of the cases were parous ladies, 61% are employed, most of them were school teachers while the others were employees, medical staff were excluded to avoid any bias in the study.

A total of 61 (15,3%) are highly educated (Ph.D. & master degree or a high diploma). 135 (33.7%) had a moderate education (graduates of University) while 204 (51%) are either graduated from institutes or primary & secondary schools.

Around 222 (55%) of the cases were in their first half of pregnancy, 61 (66.7%) were had a selfmedication with antibiotic while the rest 107 (26.8%) hadn't complete the full course of antibiotics, 211 (52.7) had completed their full course. No major side effects were observed in most of cases apart of gastric upset.

DISCUSSION

The findings from this study suggest that the practice of self-medication is not uncommon among pregnant women in our environment. In this study, various types of antibiotics were used but the commonly used are ampicillins and cephalosporins which are somehow considered safe in pregnancy in regard to fetal effects.

These findings were frightening and very serious in view of the poor knowledge of the safety profiles of these drugs among the pregnant women, the difficulty in estimating the right and adequate dosages may pose serious problem⁽¹⁾. One major concern would be the potential harmful effects on the fetus, Therefore, the misuse of antibiotics for whatsoever reason during pregnancy should be discouraged.

This highlights the need for the effective programs that would target on prevention of selfmedication among pregnant women and intervention to arrest complications like antibiotic resistance^(11,12,13).

The act of self-medication could be dangerous considering the possible poor knowledge of Pharmacodynamics of these medicines⁽⁴⁾.

This is more worrisome as the sources and instructions concerning the use of these medicines are not from professionals. One major concern would be issue of inadequate dosing and development of antibiotic resistance, The widespread use of suboptimal dosages of antibiotics is a major threat, contributing to the development of antibiotics resistant bacterial strains^(14,15,16).

Apart from the resistance that may result from inadequate dosing, exposure to some antibiotics (such as septrin, choramphenicol and tetracycline which are dangerous and contraindicated during pregnancy) was in the early month of pregnancy, these children could suffer from serious complications including, grey baby syndrome, deafness, jaundice, brain damage, anemia and impaired bone development and respiratory distress⁽¹⁷⁾.

Perhaps the most clinically relevant aspect of the pregnancy microbiome is antibiotic treatment during pregnancy. Antibiotics account for 80 % of all prescribed medication in pregnancy yet surprisingly, few published human studies have carefully evaluated the direct effects of antibiotics during pregnancy on either the maternal or fetal microbiome, or evaluated long-term sequel of such antibiotic use. Thus, there may be a reason for caution in prescribing antibiotics during pregnancy⁽¹⁸⁾.

There is a vast amount of data showing that antibiotic use is not free of serious adverse events. Among other complications, antibiotics have been associated with allergic reactions, gastrointestinal disturbances, cardiac arrhythmia, and death⁽¹⁹⁾. A major problem associated with antibiotic overuse is the development of multi-resistant bacteria, the necessity to treat most cases of symptomatic bacterial infections is clear, but it is also clear that during the last 20 years there has been an inappropriate overuse of antibiotics to treat respiratory, ear, nose and throat, urinary, or genital infections. It can be stated also that antibiotics have been and still are overused in obstetrics^(20,21).

It has been suggested that exposure to antibiotics during fetal/neonatal life affects the development of allergic diseases via their adverse and possible long-term effect on gut microbes of both the mother and child and vaginal microbes of the mother. Antibiotic use may delay and interfere with the early coloniza-tion of the child's gut microbes⁽²²⁾. In turn, this delay or aberrant colonization may interfere with the development and maturation of the child's immune system, and thus play a role in the development of allergy and disease^(23,24,25). It hsd been reported recently that antibiotic use early in life is associated with the risk of childhood asthma, allergy, atopic dermatitis, eosinophilic Oesophagitis, neonatal Candidiasis, and celiac disease^(26,27,28,29,30,31,32,33,34,35).

Antibiotic overuse during pregnancy is associated with the emergence of many antibiotic-resistant organisms. Rates of GBS resistant to erythromycin (one of the antibiotics of choice after preterm PROM and given in most UK hospitals for that indication) is as high as $35\%^{(36,37)}$. Their use during pregnancy had been shown also to be associated with the selection of resistant strains of *Escherichia coli*, which has been reported increasingly in neonatal sepsis, especially in very preterm infants^(20,38,39).

Some of these risks are inherent to the existing policies for the prevention of pregnancy complications. The policy for the routine administration of antibiotics during cesarean section could be questioned as the risk for postoperative maternal infection varies widely. Among low-risk women (elective cesarean section with intact membranes), approximately 1000 women should receive antibiotics in order to prevent 6 cases of Endometritis and 4.4 cases of abdominal wound infections^(40,41,42).

In women at higher risk (emergency cesarean section, ruptured membranes, obesity, *etc.*), the number needed to treat is much lower (between 5-25 to avoid one case of maternal postpartum morbidity), but still varies substantially depending on the country⁽⁴³⁾. Without further research on long-term infant outcomes, the safest strategy is still to administer antibiotic prophylaxis after fetal cord clamping.

Our study shown the variation in the practice and use of self-medication among the participants. In this study, about 15% of the pregnant women with high level of education used antibiotics the same way as 33% and 51 with moderately and low education respectively. This, when compared with 51% of them with low level of education involved in the use of the antibiotics, is very significant as the less education the more the misuse. These findings seem to suggest that the level of education influences the type and nature of the antibiotic used. Although earlier studies have association self-medication with factors such as self-employment, unemployment and third trimester of pregnancy, However, certain reasons may be responsible for this differential practice in this study. like, the use of certain new generations of antibiotics like cephalosporins by women with high level of education and the use of traditional ones like ampicillins by those with low level of education may be due to health beliefs, which to a large extent, determines the emotional and behavioral responses to illness⁽¹⁸⁾. These beliefs involve expectancy and perceived benefits, as well as outcome for initiating and maintaining treatment. There is abundance of evidence that this perception plays a significant role in health-seeking behavior and pathway to care⁽¹⁰⁾.

Although various reasons have been proffered for this practice, the implications could be overwhelming, as issues related to possible drug interactions could be a major problem to both mother and the unborn child⁽¹³⁾. Therefore, health care providers must be aware of this trend, in order to weigh the therapeutic benefits to mothers and the potential risk to the developing fetus⁽⁹⁾. It is essential to routinely inquire about the woman's self-medication practice so as to provide appropriate advice during antenatal care.

CONCLUSION

The findings of this study have shown that the practice of self-medication with antibiotics among pregnant women is on the increase in our environment. Therefore, there is need to reduce this practice by improving the quality of antenatal care services to include adequate health education on major issues capable of influencing the health behaviors of our pregnant women. In order to achieve the development goal aimed at reducing child and maternal morbidity and mortality, there is need to upgrade healthcare facilities and embark on regular massive enlightenment campaigns, especially in rural areas to encourage increased healthcare services utilization. Since many of these pregnant women for reasons known to them and irrespective of their level of education practicing the self-medication, there is need for education of the public on the danger of selfmedication and the potential harmful effect on the unborn child. This will ensure attitudinal change and encourage safer practice. More importantly, there is a pressing need for strict drug prescription control. Efforts must also be made to make sure that medicines are only available to individuals on prescription from a physician following a consultation, and

monitoring to ensure that drugs are not prescribed and sold indiscriminately by those without basic pharmacological knowledge.

REFERENCES

1- Van der Geest S, Hardon A. Self-medication in developing countries. Journal of Social and Administrative Pharmacy, 1990, 7(4):199–204. 22.

2- Refuerzo JS, Blackwell SC, Sokol RJ et al. Use of over-the counter medications and herbal remedies in pregnancy. Am J Perinatol. 2005 Aug;22(6):321-4. This article on PubMed

3- Irvine L, Flynn RW, Libby G, Crombie IK, Evans JM. Drugs dispensed in primary care during pregnancy: a record-linkage analysis in Tayside, Scotland. Drug Safe. 2010 Jul 1;33(7):593-604. This article on PubMed.

4- Shah AP, Parmar SA, Kumkishan A, Mehta AA. Knowledge, Attitude and Practice (KAP) Survey Regarding the safe use of Medicines in rural area of Gujurat. Adv Trop Med Pub Health. 2011; 1(2): 66-70.

5- Abrahams N, Jewkes R, MVO Z. Indigenous healing practices and self-medication amongst pregnant women in Cape Town, South Africa. African Journal of Reproductive Health. 2002; 6 (2): 79-86. This article on PubMed.

6- Rohra DK, Das N, Azam SI, Solangi NA, Memom Z, Shaikh AM, Khan NH. Drug Prescribing patterns during pregnancy in the tertiary care hospitals of Pakistan. BMC Pregnancy Childbirth. 2008; 8:24. This article on PubMed.

7- Fakeye TO, Adisa R, Musa IE. Attitude and Use of Medicines Among Pregnant women in Nigeria. BMC Complementary and Alternative Medicine. 2009; 9:53-59. This article on PubMed

8- Gharoro EP, Igbafe AA. Pattern of Drug Use Amongst Antenatal Patients in Benin City, Nigeria. Med Sci Monit. 2000; 6(1):84-87. This article on PubMed.

9- Kebede B, Gedif T, Getachew A. Assessment of drug use among pregnant women in Addis Ababa, Ethiopia. Pharmacoepidemiol Drug Saf. 2009 Jun;18(6):462-8. This article on PubMed.

10- Abrahams N, Jewkes R, Mvo Z. Health-seeking practices of pregnant women and the role of midwife in Cape Town, South Africa. J Midwifery Womens Health. 2001 Jul-Aug;46(4):240-7. This article on PubMed.

11- Metlay et al., 1998, J.P. Metlay, R.S. Stafford, D.E. Singer National trends in the use of antibiotics by primary care physicians for adult patients with cough, Arch. Intern. Med., 158 (1998), pp. 1813–1818.

12- Austin et al., 1999, D.J. Austin, K.G. Kristinsson, R.M. Anderson. The relationship between the volume of antimicrobial consumption in human communities and the frequency of resistance.

13- Tiran D. The use of antibiotics by pregnant and childbearing women: a risk-benefit assessment.

Complement Ther Nurs Midwifery. 2003 Nov;9(4):176-81. This article on PubMed.

14- Gyssens, 2001 I.C. Gyssens, Quality measures of antimicrobial drug use Int. J. Antimicrob. Agents, 17 (2001), pp. 9–19.

15- Hawkey, 1998, P.M. Hawkey, Action against antibiotic resistance: no time to lose, Lancet, 351 (1998), pp. 1298–1299.

16- Mainous et al., 1996, A.G. Mainous, W.J. Hueston, J.R. Clark Antibiotics and upper respiratory infection – do some folks think there is a cure for the common cold.

17- Nahum G.G., Uhl K., Kennedy D.L. Antibiotic use in pregnancy and lactation: What is and is not known about teratogenic and toxic risks. Obstet. Gynecol. 2006; 107: 1120 – 1138.doi: 10.1097 / 01.AOG.0000216197. 26783.b5. [PubMed] [Cross Ref].

18- Bookstaver PB, Bland CM, Griffin B, Stover KR, Eiland LS, McLaughlin M. A review of antibiotic use in pregnancy. Pharmacotherapy. 2015; 35 (11): 1052 – 1062. doi: 10.1002 / phar. 1649. [PubMed] [Cross Ref].

19- Rao G.A., Mann J.R., Shoaibi A., Bennett C.L., Nahhas G., Sutton S.S., Jacob S., Strayer S.M. Azithromycin and levofloxacin use and increased risk of cardiac arrhythmia and death. Ann. Fam. Med. 2014; 12: 121 – 127. doi: 10.1370 / afm. 1601. [PMC free article] [PubMed] [Cross Ref].

20- Morales W.J., Dickey S.S., Bornick P., Lim D.V. Change in antibiotic resistance of group B streptococcus: Impact on intrapartum management. Amer. J. Obstet. Gynecol. 1999; 181: 310 – 314. doi: 10.1016 / S0002 – 9378 (99) 70553-3. [PubMed] [Cross Ref].

21- Heelan J.S., Hasenbein M.E., McAdam A.J. Resistance of group B streptococcus to selected antibiotics, including erythromycin and clindamycin. J. Clin. Microbiol. 2004; 42: 1263 – 1264. doi: 10.1128 / JCM.42.3.1263 - 1264.2004. [PMC free article] [PubMed] [Cross Ref].

22- Jakobsson H.E., Jernberg C., Andersson A.F., Sjolund-Karlsson M., Jansson J.K., Engstrand L. Short-term antibiotic treatment has differing longterm impacts on the human throat and gut microbiome. PLoS One. 2010; 5 doi: 10.1371 /j ournal. pone.0009836. [PMC free article] [PubMed] [Cross Ref].

23- Bedford Russell A.R., Murch S.H. Could peripartum antibiotics have delayed health consequences for the infant? BJOG. 2006; 113: 758 – 765. doi: 10.1111/j.1471-

0528.2006.00952.x. [PubMed] [Cross Ref].

24- Bizzarro M.J., Dembry L.M., Baltimore R.S., Gallagher P.G. Changing patterns in neonatal *Escherichia coli* sepsis and ampicillin resistance in the era of intrapartum antibiotic prophylaxis. Pediatrics. 2008; 121:689–696. doi: 10.1542 / peds.2007-2171. [PubMed] [Cross Ref]. 25- Martino D.J., Prescott S.L. Silent mysteries: Epigenetic paradigms could hold the key to conquering the epidemic of allergy and immune disease. Allergy. 2010; 65:7–15. doi: 10.1111/j.1398-9995.2009.02186.x.[PubMed] [Cross Ref].

26- Jedrychowski W., Galas A., Whyatt R., Perera F. The prenatal use of antibiotics and the development of allergic disease in one-year old infants. A preliminary study. Int. J. Occup. Med. Environ. Health. 2006; 19:70–76. [PubMed].

27- Flohr C., Yeo L. Atopic dermatitis and the hygiene hypothesis revisited. Curr. Probl. Dermatol. 2011; 41:1–34. [PubMed]

28- Adlerberth I., Lindberg E., Aberg N., Hesselmar B., Saalman R., Strannegard I.L., Wold A.E. Reduced enterobacterial and increased staphylococcal colonization of the infantile bowel: An effect of hygienic lifestyle? Pediatr. Res. 2006; 59:96– 101. [PubMed].

29- Murk W., Risnes K.R., Bracken M.B. Prenatal or early-life exposure to antibiotics and risk of childhood asthma: A systematic review. Pediatrics. 2011; 127: 1125 – 1138. doi: 10.1542 / peds. 2010 - 2092. [PubMed] [Cross Ref]

30- Jensen E.T., Kappelman M.D., Kim H.P., Ringel-Kulka T., Dellon E.S. Early life exposures as risk factors for pediatric eosinophilic esophagitis. J. Pediatr. Gastroenterol. Nutr. 2013; 57:67–71. doi: 10.1097/MPG.

0b013e318290d15a. [PubMed] [Cross Ref].

31- Risnes K.R., Belanger K., Murk W., Bracken M.B. Antibiotic exposure by 6 months and asthma and allergy at 6 years: Findings in a cohort of 1401 U.S. child. Amer. J. Epidemiol. 2011; 173:310–318. doi: 10.1093/aje/kwq400. [PMC free article] [PubMed] [Cross Ref].

32- Metsala J., Lundqvist A., Virta L.J., Kaila M., Gissler M., Virtanen S.M. Mother's and offspring's use of antibiotics and infant allergy to cow's milk. Epidemiology. 2013; 24:303–309. doi: 10. 1097 / EDE.0b013e31827f520f. [PubMed] [Cross Ref].

33- Martel M.J., Rey E., Malo J.L., Perreault S., Beauchesne M.F., Forget A., Blais L. Determinants of the incidence of childhood asthma: A two-stage case-control study. Amer. J. Epidemiol. 2009; 169: 195 – 205. doi: 10.1093 /aje /kwn 309. [PubMed] [Cross Ref].

34- Benjamin D.K., Jr., Stoll B.J., Gantz M.G., Walsh M.C., Sanchez P.J., Das A., Shankaran S., Higgins R.D., Auten K.J., Miller N.A., et al. Neonatal candidiasis: Epidemiology, risk factors, and clinical judgment. Pediatrics. 2010; 126:865–873. doi: 10.1542/peds.2009-3412. [PMC free article] [PubMed] [Cross Ref].

35- Kozyrskyj A.L., Bahreinian S., Azad M.B. Early life exposures: Impact on asthma and allergic disease. Curr. Opin. Allergy Clin. Immunol. 2011;11: 400 – 406. doi: 10.1097 / ACI. 0b013e328349 b166. [PubMed][Cross Ref]. 36- Tan S., Holliman R., Russell A.R. Hazards of widespread use of erythromycin for preterm prelabour rupture of membranes. Lancet. 2003;361 doi: 10.1016/S0140-6736(03)12420-8. [PubMed] [Cross Ref].

37- Gygax S.E., Schuyler J.A., Trama J.P., Mordechai E., Adelson M.E. Detection of erythromycin and clindamycin resistance genes in Group B Streptococcal clinical isolates and cervicovaginal-rectal swabs. Microb. Drug Resist. 2007; 13:119–123. doi: 10.1089/mdr.2007.732. [PubMed] [Cross Ref].

38- Edwards R.K., Jamie W.E., Sterner D., Gentry S., Counts K., Duff P. Intrapartum antibiotic prophylaxis and early-onset neonatal sepsis patterns. Infect. Dis. Obstet. Gynecol. 2003; 11:221–226. doi:10. 1080 / 10647440300025525. [PMC free article] [PubMed] [Cross Ref].

39- Towers C.V., Carr M.H., Padilla G., Asrat T. Potential consequences of widespread antepartal use of ampicillin. Amer. J. Obstet. Gynecol. 1998; 179: 879 – 883. doi: 10.1016 / S0002 – 9378 (98) 70182-6. [PubMed][Cross Ref].

40- Apuzzio J.J., Reyelt C., Pelosi M., Sen P., Louria D.B. Prophylactic antibiotics for cesarean section: Comparison of high- and low-risk patients for endomyometritis. Obstet. Gynecol. 1982; 59: 693 – 698. [PubMed].

41- Chelmow D., Hennesy M., Evantash E.G. Prophylactic antibiotics for non-laboring patients with intact membranes undergoing cesarean delivery: An economic analysis. Amer. J. Obstet. Gynecol. 2004; 191: 1661 – 1665. doi: 10.1016 / j.ajog .2004.03.079. [PubMed] [Cross Ref].

42- Chelmow D., Ruehli M.S., Huang E. Prophylactic use of antibiotics for nonlaboring patients undergoing cesarean delivery with intact membranes: A meta-analysis. Amer. J. Obstet. Gynecol. 2001; 184:656–661. doi:

10.1067/mob.2001.111303. [PubMed] [Cross Ref]. 43- Fredriksson A., Thomassen P. Preventive antibi-

otics in emergency cesarean section. A prospective comparison of benzylpenicillin and ampicillin plus cloxacillin. Tidsskr. Nor. Laegeforen. 1990; 110: 350.