RESEARCH PAPER.

PREVALENCE, RISK FACTORS AND CLINICAL SIGNIFICANCE OF SILENT CHORIOAMNIONITIS CAUSED BY AEROBIC BACTERIA IN TERM DELIVERIES AT CASTLE STREET HOSPITAL FOR WOMEN: SRI LANKA

Niranga K K G[1], Karunarathne M[2], Pallemulla L[3]

[1] Castle Street Hospital for Women Ministry of Health Sri Lanka, [2] Consultant Immunologist, Ministry of Health Sri Lanka. [3] Consultant Obstetrician and Gynecologist, Ministry of Health Sri Lanka,

Corresponding Author: agnarin2@gmail.com

ABSTRACT

There are no typical clinical signs in silent chorioamnionitis. It is associated with adverse maternal and neonatal outcome and poor progression of labour. Subclinical chorioamnionitis is also more common in preterm gestations than term gestation and vaginal deliveries than caesarean sections. Descriptive cross-sectional study conducted in Castle Street Hospital for women. Term singleton pregnant mothers were included and preterm labour was excluded. Sample consisted of 154 participants. Antepartum and post-partum surveillances were conducted. amniotic fluid cultures with ABST patterns, perinatal neonatal and maternal outcomes were selected as outcome variables. Data was analysed by using SPSS version 25.0. According to the study mean age of the participants was 29.37 years (SD=5.30years). and the majority represented the 26-36 years age group. Half of the study sample consisted of primigravidae mothers. Occurrence of silent chorioamnionitis was significantly higher among primigravidae (OR=4.056:95%CI=1.270-12.952). Duration of labour exceeding more than 12 hours and performing multiple digital vaginal examinations (OR=3.929:95%CI=1.007-15.328) were identified as significant risk factors for silent chorioamnionitis. Maternal pyrexia (OR=21.000:95%CI=5.316-82.961) and surgical site infections were significantly associated with silent chorioamnionitis (OR=12.667:95%CI=2.570-62.427). Newborns who were admitted to SCBU due to early neonatal sepsis

(OR=16.875:95%CI=1.448-196.68) and who were unable to achieve an APGAR score of 7 at the 5th minute of their life (OR=4.571:95%CI=1.220-17.129) were significantly associated with maternal silent chorioamnionitis. According to the culture & ABST findings, *Staphylococcus aureus* and group B S*treptococci* were identified as causative organisms. Group B *streptococci* and *staph aureus* were identified as the causative microorganisms for silent chorioamnionitis. Management guidelines should be developed to reduce perinatal morbidities by implementing silent chorioamnionitis preventive strategies. To avoid prolonged labour, close monitoring strategies should be included to labour room management protocols and their implementations should be confirmed. Should identify the ability to use selected sensitive antibiotics as a prophylactic treatment method for risk pregnancies. Special attention should be paid on implementing necessary methods to minimize performing digital vaginal examinations during the intrapartum period.

Key words: Silent Chorioamnionitis, Antibiotic, Microorganisms

INTRODUCTION

Chorioamnionitis or intraamniotic infection is the infection of amniotic fluid, membranes, placenta and deciduas (1). It is typically due to ascending microorganisms in the setting of rupture of membranes. It can occur without membranes rupture also. There are several types of chorioamnionitis depending on the criteria used in diagnosis (1). Clinical chorioamnionitis; fever with two more clinical signs mentioned below are needed for the diagnosis can be mentioned as the most common type (2). Chorioamnionitis associated with no typical clinical signs, diagnosis by microbiologically or histologically would be categorized as silent chorioamnionitis. Positive culture of microbes from appropriately collected amniotic fluid or chorioamnion is called Microbiological chorioamnionitis. The histological chorioamnionitis can be described as, microscopic evidence of infection or inflammation on examination of the placenta or chorioamnionic specimens (3).

There are no typical clinical signs in silent chorioamnionitis. It is diagnosis by microbiologically or histologically as mentioned above. It is associated with poor maternal and neonatal outcome and poor progression of labour (4). Prevalence of silent chorioamnionitis varies according to method of diagnosis (either microbiologic or histologic), gestational age at deliver and route of delivery(5)(6). Silent chorioamnionitis is also more common in preterm gestations than term gestation and vaginal deliveries than caesarean sections (7).

Diagnosis of silent chorioamnionitis is achieved by microbiologically or histologically (3,8). Presence of positive culture of microbes from appropriately collected amniotic fluid or chorioamnion is essential for microbiological diagnosis(9). Histological diagnosis is fulfilled by microscopic evidence of infection or inflammation on examination of the placenta or chorioamnionic specimens (10). Many

aerobic and anaerobic microorganisms are cultured from amniotic fluid or swabs from amniochorion membranes (8,11). Most organisms are found in female genital tract suggesting ascending infection (12). Prevalence of microorganism varies according to the study. In some cases more than one organism was isolated suggesting polymicrobial infection (13).

Although definitive risk factors are available for clinical chorioamnionitis, few risk factors are found for silent chorioamnionitis in the literature. Nulliparity and prolonged labour can be identified as more common risk factors for silent chorioamnionitis (7,14). Silent chorioamnionitis is associated with adverse maternal and neonatal outcome and poor progression of labour with clinical chorioamnionitis (15). Maternal urogenital infections, congenital neonatal infections, premature rupture of membranes, premature deliveries and poor progression of labour culminating in emergency caesarean sections are common adverse perinatal outcomes which can be observed with silent chorioamnionitis(16).

Symptomatic chorioamnionitis is an area which was extensively studied by many researchers but only very few research studies are available on the silent chorioamnionitis at term deliveries. There are minimum data published in Sri Lanka related to silent chorioamnionitis and its clinical associations. So, it is a timely need to conduct research on silent chorioamnionitis at term deliveries to find out its prevalence, risk factors, responsible microorganisms with their sensitivity patterns and clinical significance in terms of adverse maternal and fetal outcomes.

Estimation of the prevalence of silent chorioamnionitis is a challengeable task in Sri Lanka. Because there is minimum information were published. However postnatal and neonatal infections are found in mothers who do not have clinical chorioamnionitis. Silent chorioamnionitis may be one reason for such maternal and fetal infections. Escherichia coli, Group B streptococci and Enterococcus faecalis are the mostly detected microorganisms in silent chorioamnionitis (17). Escherichia coli and Group B streptococci are the most common pathogens involved in early neonatal sepsis (18–20).

This study was targeted to determine the risk factors such as maternal medical illness, induction of labour and duration of labour etc. Those may be attributable to silent chorioamnionitis. If the associations are significant health care delivery system will be able to identify high risk mothers early to adopt preventive measures to avoid development of the silent chorioamnionitis and its complications. Relevant specimens can be sent for culture and ABST from high risk mothers to find out the causative agents and their sensitivity patterns early, as surveillance cultures. Also, we can closely observe mothers with risk factors and their babies. So, this data will be beneficial to both Obstetricians and Neonatologists.

Currently we observed treatment failures with traditional antibiotic combinations (IV C. Penicillin and IV Gentamycin) used in the neonatology unit (19,21). Blood cultures from neonates are difficult to obtain and sometimes antibiotics are started before obtaining specimens due to practical difficulties. Amniotic fluid cultures and swab cultures from the placental membranes will be good specimens to identify the pathogens and find out any changing patterns of antibiotic sensitivity (22). This data would be very useful to identify if there is any change

in sensitivity patterns of common pathogens responsible for chorioamnionitis, maternal and fetal infections {Merging Citations}.

There are few studies found on adverse maternal and neonatal outcomes of silent chorioamnionitis (16). Maternal urogenital infections, congenital newborn infections, premature rupture of membranes and preterm birth are some of them (25)(26). Mothers who were affected with silent chorioamnionitis and their babies were observed for one-month period following delivery for the development of complications.

Methods

Descriptive cross-sectional study was conducted in Castle Street Hospital for women. Term singleton pregnant mothers delivered vaginally (including instrumental deliveries) and by elective or emergency caesarean section were included for the study. Term pregnant women who received any antibiotics during past two weeks for any other infectious disease or following admission to ward, all pregnant women who were clinically diagnosed as chorioamnionitis, preterm labour, premature prelabour rupture of membranes, twin and multiple pregnancies were excluded. 152 participants were selected through systematic sampling method was applied for vaginal deliveries and caesarean sections in each ward for 3-month period. First pregnant mother was selected randomly and then every 3rd mother was selected till we get the pre-determined sample from each ward.

For vaginal deliveries swabs were obtained from space between amnion and chorion immediately after the delivery of placenta. Strict aseptic techniques were used during collection. Placentae were kept on sterile towel cotyledon facing down. Spaces between amnion and chorion were accessed after separating the amnion from chorion of placenta and samples were taken using sterile swabs.

During caesarean sections, amniotic fluid was collected to a sterile 10 ml syringe using a sterile needle before the administration of surgical prophylaxis and put it to a sterile container. Prophylactic parenteral antibiotics were given after clamping the cord. If membranes were intact, amniotic fluid was aspirated from bulging membrane once uterine incision was made. If membranes were ruptured prior to caesarean section, amniotic fluid was aspirated either from bulging membrane following uterine incision or from remaining pool under direct vision without damaging neonate. Strict aseptic techniques were used during collection.

Results

Age of the participants ranged from 18 years to 40 years. Mean age was 29.37 years (SD=5.30years). Majority of the study participants represented the 26-35 years age group (N=86 : 55.9%). All the study participants had completed their full term and the mean gestational age was 275.49 days (SD=6.63days). Higher percentage of participants were in their 40th week of gestational age. Half of the study participants were primigravidae mothers (N=70:50%). (Table 1)

Table 1: Distribution of age parity and gestational age of the participants

		Number(N)	Percentage (%)
Age			
	<20 years	7	4.5
	21-25 years	36	23.4
	26-30 years	48	31.2
	31-35 years	38	24.7
	>36 years	25	16.2
Gestational age			
	37 weeks	7	4.5
	38 weeks	46	29.9
	39 weeks	48	31.2
	40 weeks	53	34.4
Parity			
	1	77	50.0
	2	52	33.8
	3	17	11.0
	≥4	8	5.2
TOTAL		**154**	**100**

Although reported number of silent chorioamnionitis events was numerically high among mothers who delivered through normal vaginal deliveries, statistical calculations reveal that NVD is a protective factor for chorioamnionitis (OR=0.98:95%CI=0.367-2.654). But statistical evidence is not sufficient enough to conclude the concept as a significant protective factor. Numerically higher incidences of silent chorioamnionitis were recorded among the primigravidae mothers and there were statistical evidences to consider it as a significant risk factor for silent chorioamnionitis (OR=4.05:95%CI=1.270-12.952). (Table 2)

Table 2 : Association of silent chorioamnionitis with Mode of delivery

	Silent Chorioamnionitis		OR	95%CI
	Yes	**No**		
NVD	10	76	0.987	0.367-2.654
LSCS	8	60		
Primigravidae	14	63	4.056	1.270-12.952
Multigravida	4	73		
Total	**18**	**136**		

Table 3 : Association of silent chorioamnionitis with none modifiable clinical characteristics of the participants

	Silent Chorioamnionitis		OR	95%CI
	Yes	**No**		
HIP				
Yes	5	23	1.889	1.237-2.281
No	13	113		
PIH				
Yes	2	15	1.008	.211-4.822
No	16	121		
Past Section				
Yes	1	45	.119	.015-.992
No	17	91		
Rh-				
Yes	4	7	5.265	1.370-20.24
No	14	129		
Total	**18**	**136**		

HIP=Hyprglycaemia in pregnancy, PIH=Pregnancy induced Hypertension, RH- =Rhesus negative

Hyperglycaemia in pregnancy can be considered as significant risk factor for chorioamnionitis. Past history of LSCS can be demonstrated as a protector factor for silent chorioamnionitis. Diagnosis of PIH during the antenatal period is associated as a risk factor for silent chorioamnionitis. But adequate statistical evidence was not available to confirm this finding. Reported silent chorioamnionitis evidences among Rh (-) mothers was significantly high when compared to Rh (+) mothers. Being Rh (-) was the only significant risk factor identified among the non-modifiable clinical characteristics for occurrence silent chorioamnionitis. (Table 3)

Table 4: Association of silent chorioamnionitis with intrapartum clinical characteristics of the participants

	Silent Chorioamnionitis		OR	95%CI
	Yes	**No**		
Labour onset				
Induction	6	43	1.31	1.23-3.33
Spontaneous	4	33		
Augmentation with oxytocin				
Yes	5	27	1.81	0.48-6.83
No	5	49		
Vaginal Examination				
4 or more	6	21	3.92	1.01-15.32
3	4	55		
Duration of labour				
>12 hrs	10	31	-	-
<12hrs	0	45		
Total	**10**	**76**		

Induction of labour was identified as a significant risk factor for occurring silent chorioamnionitis. Equal incidences of silent chorioamnionitis were reported among mothers who were augmented with oxytocin and mothers who were not. Performing 4 or more digital vaginal examinations during induction of labour was identified as a significant risk factor for silent chorioamnionitis. Apart from them, all other reported silent chorioamnionitis incidences were confined to mothers who experienced more than 12 hours of labour.(Table 4)

Findings revealed that all the selected perinatal morbidities were significantly associated with silent chorioamnionitis (OR>1). Among them, all the babies delivered by meconium aspiration were reported to have mothers with silent chorioamnionitis.
(Table 5)

Table 5: Association of silent chorioamnionitis with perinatal outcome characteristics among participants

	Silent Chorioamnionitis		OR	95% CI
	Yes	**No**		
Maternal Pyrexia				
Yes	7	4	21.00	5.31-82.96
No	11	132		
Surgical site infection				
Yes	4	3	12.66	2.57-62.42
No	18	133		
Early neonatal sepsis				
Yes	2	1	16.87	1.45-196.68
No	16	135		
Meconium Aspiration				
Yes	2	-	-	-
No	16	136		
APGAR Score (5th Minute)				
<7	4	8	4.57	1.22-17.13
7	14	128		
Total	**18**	**136**		

Table 6: Antibiotic sensitivity of identified microorganisms

Micro organism	Sensitivity pattern
Group B streptococci	Ampicillin, penicillin, Erythromycin, Clindamycin, Cefotaxime
Staphylococcus aureus	clindamycin, Gentamycin, Cloxacillin, Fusidic acid
Group B streptococci	Ampicillin, penicillin, Erythromycin, Cefotaxime

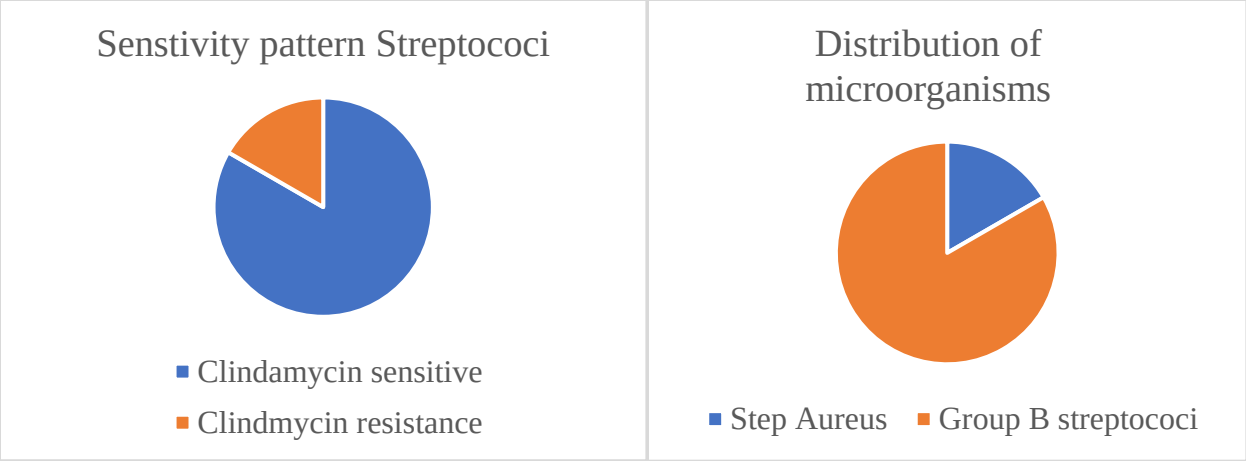

Figure 1: Microorganisms and sensitivity patterns

Among the 154 study participants, 18 participants were diagnosed of having silent chorioamnionitis with microorganisms (11.6%). According to the culture results two microorganisms were identified and they are group B streptococci and streptococci aureus. Majorities were positive for group B streptococci (N=15%). All the streptococcus aureus samples were sensitive for four antibiotics, namely Gentamycin, Clindamycin, Fusidic acid. All the group B streptococcus samples were sensitive for Ampicillin, penicillin, Erythromycin, Clindamycin, Cefotaxime antibiotics. Eight samples with group B *streptococci* were sensitive for clindamycin too. (Table 6: Figure 1)

Discussion

During this research 154 study participants were included into the study and prevalence of silent chorioamnionitis was 11.68% and was less when compared to the findings of other studies. The prevalence was 17.3% in the study conducted by Horvath et al in Hungaria (17). Present study findings also confirm the observation that "silent chorioamnionitis is more associated with vaginal deliveries" which was identified by Michela Torricelli et al, in previous studies (10). Although D.J Sherman had observed in his study that silent chorioamnionitis is expected from 26% of the term mothers who perform spontaneous vaginal deliveries (11). But prevalence of silent chorioamnionitis in mother who delivered vaginally in the present study was relatively less (Table 2). Nulliparity and prolonged duration of labour were associated with silent chorioamnionitis by Michela Torricelli et al in her study and present study confirmed it (10).

Maternal pyrexia and surgical site infections were more common in mothers who had silent chorioamnionitis. Study by Horvath et al found that maternal urogenital infections were common in mothers who had silent chorioamnionitis (17). Early neonatal sepsis and NICU admissions were more common in

babies who mothers diagnosed to have silent chorioamnionitis in the present study. But Michela Torricelli et al found that there were no above association (10). Horvath et al found the association between congenital and newborn infections and silent chorioamnionitis (17).

During a study done by Horvath et al for 16 years, 42 microorganisms which were responsible for silent chorioamnionitis were identified. But in the current study only two microorganisms were detected (17). Among those two organisms, group B *streptococci* was identified among the majority, which was the prominent microorganism detected in the study done by Horvath et al (17). With further studies it was revealed that group B *streptococci* infections were more common among preterm deliveries. As only full-term pregnancies were considered for the present study, it is not possible to arrive at a comparative conclusion regarding this incidence. On the other hand gram negative bacteria species such as *E.coli* were not detected in the current study although they were more detected in early studies.

There are three identified risk factors for chorioamnionitis in present study. Hyperglycemia in pregnancy is one of the risk factors which can be addressed in antenatal period as well as the pre pregnancy periods. So early identification of risk pregnancies for hyperglycemia in pregnancy would be helpful to prevent chorioamnionitis in delivery. The delivery of the confirmed pregnancies can be planned according to the curative and preventive management of chorioamnionitis. Regular clinic visits and blood pressure monitoring can be implemented in well-organized manner among pregnancies who was detected pregnancy induced hypertension. Early admission for the delivery and planning early termination of the pregnancy are practical options o prevent chorioamnionitis.

Application of antibiotic prophylaxis as a prevention strategy of chorioamnionitis should be study in details. The spectrum of the antibiotics and their cost effectiveness should be thoroughly evaluated before introduction to pregnant mothers. It is necessary to develop some clear guidelines regarding prophylaxis antibiotic usage as preventive strategy for chorioamnionitis. Avoiding unnecessary induction will reduce the incidence of chorioamnionitis. During the intrapartum period the adherence of existing monitoring protocols should be emphasized. Early detection of prolong intrapartum periods and early decision making to complete the child birth process will lead to reduction of chorioamnionitis. The frequency of vaginal examinations should be limited. Adequate supervisions should be done and protocol adherence should be promoted among the labour room staff regarding the digital vaginal examinations during labour.

Post-partum clinical morbidity surveillance activities should be implemented among all post-partum mothers to detect any adverse incidence following delivery. This should not be targeted to detect chorioamnionitis only, for the other perinatal morbidities also.

High prevalence of perinatal morbidities is identical as a huge health care burden at

present. Because further elongation of the child birth process which was prepared by pre-pregnancy planning and providing uninterrupted 40 weeks antenatal care is considered as an additional unexpected cost to the health care delivery system.

According to the present study findings being a Rh (-) mother is identified as a non-modifiable significant risk factor for chorioamnionitis. When the factors related to intrapartum period is considered, prolonged labour and multiple vaginal examinations are recognized as significant risk factors. When Rh (-) mothers are considered, they can be subjected to EM/LSCS with 12 hours of labour duration considering lack of progress. Attention should be paid on developing rational and relevant guidelines for these implications.

Digital vaginal examination is considered as a best procedural technique which can be used to monitor progress of labour. On the other hand, when duration of labour is prolonged number of performed Digital vaginal examination increases instinctively. When these two factors are combined together, risk of developing chorioamnionitis is further increased. Therefore, it is acceptable to consider the findings of the current study while revising the existing labour room management guidelines.

On the other hand, chorioamnionitis shows a contributory association which with labour induction. Labour induction is a cost-effective obstetric management strategy and observing a term completed mother for spontaneous on set of labour without induction may lead to severe obstetric complications than chorioamnionitis. Therefore, it is not possible to practice a risk factor eradication strategy. Minimization of undue prolongation of labour duration in labour induced mothers should be done.

Septic conditions are the cause of 4.4% of reported maternal deaths in Sri Lanka (27). Maternal mobility ratio is a predominant health care indicator which reflects the situation of health care services in the country. Therefore, prevention of chorioamnionitis can also be identified as a maternal death prevention strategy.

When risk factors identified in the present study are considered collectively, it is noted that chorioamnionitis is positively associated with induction of complicated mothers at full term, prolong duration of labour and normal Vaginal delivery. Depending on these findings a logic can be created that EL/LSCS is a better option than induction. When only risk irradiation of chorioamnionitis is considered this logic does not appear unacceptable. But when other medico-surgical complications and resource utilization associated with LSCS are considered it is difficult to identify LSCS as a more cost-effective intervention.

Conclusions

Occurrence of silent chorioamnionitis was significantly higher among primigravidae and hyperglycemia in pregnancy among the study participants. Induction of labour, duration of labour exceedingly more than 12 hours and performing multiple digital vaginal examinations were identified as significant risk factors for silent chorioamnionitis. Maternal perinatal outcome morbidities such as maternal pyrexia and surgical site infections wounds significantly associated with silent chorioamnionitis.

New borns who were admitted to SCBU, who were unable to achieve an APGAR score of 7^{th} at the 5^{th} minute of their life and who were diagnosed with early neonatal sepsis were significantly associated with maternal silent chorioamnionitis.

Management guidelines should be developed to reduce perinatal morbidities by implementing silent chorioamnionitis preventive strategies. Induction of labour if there are indications for early delivery only. Should identify the ability to use selected sensitive antibiotics as a prophylactic treatment method for risk pregnancies. Special attention should be paid on implementing necessary methods to minimize performing digital vaginal examinations during the intrapartum period. only necessary vaginal examinations, correct aseptic techniques. Postpartum surveillance of mothers and neonates who are at increased risk of silent chorioamnionitis for the development of complications.

REFERENCES

1. Alan Thevenet N Tita, Susan M Ramin VAB. Intraamniotic infection (chorioamnionitis). Up to Date.
2. Stotland NE, Caughey AB, Breed EM, Escobar GJ. Risk factors and obstetric complications associated with macrosomia. Int J Gynaecol Obstet. 2004 Dec;87(3):220–6.
3. Peng C, Chang J, Lin H. ScienceDirect Intrauterine inflammation , infection , or both (Triple I): A new concept for chorioamnionitis. Pediatr Neonatol [Internet]. 2018;59(3):231–7. Available from: https://doi.org/10.1016/j.pedneo.2017.09.001
4. Alexander JM, McIntire DM, Leveno KJ. Chorioamnionitis and the prognosis for term infants. Obstet Gynecol [Internet]. 1999;94(2):274–8. Available from: http://www.sciencedirect.com/science/article/pii/S0029784499002562
5. Romero R, Chaemsaithong P, Korzeniewski SJ, Kusanovic JP, Docheva N, Martinez-Varea A, et al. Clinical chorioamnionitis at term III: how well do clinical criteria perform in the identification of proven intra-amniotic infection? J Perinat Med [Internet]. 2016 Jan;44(1):23–32. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25918914
6. Romero R, Miranda J, Kusanovic JP, Chaiworapongsa T, Chaemsaithong P, Martinez A, et al. Clinical chorioamnionitis at term I:

microbiology of the amniotic cavity using cultivation and molecular techniques. J Perinat Med. 2015 Jan;43(1):19–36.

7. Garite TJ, Freeman RK. Chorioamnionitis in the preterm gestation. Obstet Gynecol [Internet]. 1982 May;59(5):539—545. Available from: http://europepmc.org/abstract/MED/7070724

8. Tita ATN, Andrews WW. Diagnosis and management of clinical chorioamnionitis. Clin Perinatol. 2010 Jun;37(2):339–54.

9. Hollander D. Diagnosis of Chorioamnionitis. Clin Obstet Gynecol [Internet]. 1986;29(4). Available from: https://journals.lww.com/clinicalobgyn/Fulltext/1986/12000/Diagnosis_of_Chorioamnionitis.8.aspx

10. Torricelli M, Voltolini C, Conti N, Vellucci FL, Orlandini C, Bocchi C, et al. Histologic chorioamnionitis at term: implications for the progress of labor and neonatal wellbeing. J Matern \& Neonatal Med [Internet]. 2013;26(2):188–92. Available from: https://doi.org/10.3109/14767058.2012.722724

11. Sherman DJ, Tovbin J, Lazarovich T, Avrech O, Reif R, Hoffmann S, et al. Chorioamnionitis caused by gram-negative bacteria as an etiologic factor in preterm birth. Eur J Clin Microbiol Infect Dis. 1997 Jun;16(6):417–23.

12. Romero R, Chaemsaithong P, Korzeniewski SJ, Tarca AL, Bhatti G, Xu Z, et al. Clinical chorioamnionitis at term II: the intra-amniotic inflammatory response. J Perinat Med. 2016 Jan;44(1):5–22.

13. Rouse DJ, Landon M, Leveno KJ, Leindecker S, Varner MW, Caritis SN, et al. The Maternal-Fetal Medicine Units cesarean registry: chorioamnionitis at term and its duration-relationship to outcomes. Am J Obstet Gynecol. 2004 Jul;191(1):211–6.

14. Buhimschi IA, Buhimschi CS. Chapter 19 - Chorioamnionitis and Its Effects on the Fetus/Neonate: Emerging Issues and Controversies. In: Ohls RK, Maheshwari A, editors. Hematology, Immunology and Infectious Disease: Neonatology Questions and Controversies (Second Edition) [Internet]. Second Edi. Philadelphia: W.B. Saunders; 2012. p. 317–34. Available from: http://www.sciencedirect.com/science/article/pii/B9781437726626000195

15. Miyazaki K, Furuhashi M, Matsuo K, Minami K, Yoshida K, Kuno N, et al. Impact of subclinical chorioamnionitis on maternal and neonatal outcomes. Acta Obstet Gynecol Scand. 2007;86:191–7.

16. Lau J, Magee F, Qiu Z, Houbé J, Dadelszen P Von, Lee SK. Chorioamnionitis with a fetal inflammatory response is associated with higher neonatal mortality, morbidity, and resource use than chorioamnionitis displaying a maternal inflammatory response only. Am J Obstet Gynecol [Internet]. 2005;193(3):708–13. Available from: http://www.sciencedirect.com/science/article/pii/S0002937805000955

17. Horvath B, Lakatos F, Tóth C, Bödecs

T, Bódis J. Silent chorioamnionitis and associated pregnancy outcomes: A review of clinical data gathered over a 16-year period. J Perinat Med. 2014;42:1–7.

18. Hameed C, Tejani N, Verma UL, Archbald F. Silent chorioamnionitis as a cause of preterm labor refractory to tocolytic therapy. Am J Obstet Gynecol. 1984 Aug;149(7):726–30.

19. Stoll BJ, Hansen NI, Sánchez PJ, Faix RG, Poindexter BB, Van Meurs KP, et al. Early Onset Neonatal Sepsis: The Burden of Group B Streptococcal and E. coli Disease Continues. Pediatrics. 2011;127(5):817–26.

20. Terrone DA, Rinehart BK, Einstein MH, Britt LB, Martin JN, Perry KG. Neonatal sepsis and death caused by resistant Escherichia coli: Possible consequences of extended maternal ampicillin administration. Am J Obstet Gynecol [Internet]. 1999;180(6):1345–8. Available from: http://www.sciencedirect.com/science/article/pii/S0002937899700177

21. Ziogos E, Tsiodras S, Matalliotakis I, Giamarellou H, Kanellakopoulou K. Ampicillin/sulbactam versus cefuroxime as antimicrobial prophylaxis for cesarean delivery: a randomized study. BMC Infect Dis [Internet]. 2010;10(1):341. Available from: http://www.biomedcentral.com/1471-2334/10/341

22. Simhan HN, Canavan TP. Preterm premature rupture of membranes: diagnosis, evaluation and management strategies. BJOG. 2005 Mar;112 Suppl:32–7.

23. Hillier S, Martius J, Krohn M, Kiviat N, Holmes KK, A. Eschenbach D. A Case–Control Study of Chorioamnionic Infection and Histologic Chorioamnionitis in Prematurity. N Engl J Med. 1988;319:972–8.

24. Glasgow TS, Young PC, Wallin J, Kwok C, Stoddard G, Firth S, et al. Association of Intrapartum Antibiotic Exposure and Late-Onset Serious Bacterial Infections in Infants. Pediatrics [Internet]. 2005;116(3):696–702. Available from: https://pediatrics.aappublications.org/content/116/3/696

25. Yancey MK, Duff P, Kubilis P, Clark P, Frentzen BH. Risk factors for neonatal sepsis. Obstet Gynecol. 1996;87(2):188–94.

26. Young G. Multistakeholder regional collaboratives have been key drivers of public reporting, but now faces challenges. Heal Aff. 2012;31(3):578-584.

27. Ministry of Health Sri Lanka. Dissemination of 2015 Data on Maternal death analysis. 2015;

