IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

Open Access
Original Article

Relationship between Ureaplasma urealyticum Colonization and Bronchopulmonary Dysplasia in Very Low Birth Weight Premature Infants: A Prospective Cohort Study

Majid Mahallei[1], Mohmmad Bagher Hosseini[1], Heidar Esmaili[2], Gholam Reza Assadi[3]*

1. Pediatric Health Research Center of Tabriz, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
2. Department of Pathology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
3. Department of Pediatric, Tabriz Branch, Islamic Azad University, Tabriz, Iran

ABSTRACT

Background: Bronchopulmonary dysplasia (BPD) is the second prevalent lung disease and one of the care challenges of premature newborns. Different risk factors play an important role in the development of this disease. Therefore, the aim of the present study was to investigate the relationship between colonization with Ureaplasma urealyticum and BPD.

Methods: This prospective cohort study was conducted in 2017 in the neonatal intensive care unit of Alzahra Hospital in Tabriz, Iran. The samples included newborns weighing less than 1500 g with the gestational age of less than 32 weeks who required intubation within 72 h after birth. Following recording the initial information, the secretions within the trachea were aspirated and Ureaplasma urealyticum was detected in reference laboratory by polymerase chain reaction. Afterwards, we completed a follow-up of 28 days after birth for BPD.

Results: Our findings demonstrated that out of 82 infants, 21 cases (26.3%) were excluded from the study due to discharge from hospital or death before the age of 28 days. Among the rest (61 newborns), three cases (4.3%) were shown to have secretions infected with Ureaplasma and 33 cases (54.1%) suffered from BPD. All the three newborns infected with Ureaplasma had BPD. However, no significant relationship was observed between Ureaplasma infection and BPD (P=0.24).

According to the analysis of data, the most important factors contributing to BPD among the patients were the gestational age and birth weight. In other words, for one week increase in the age of pregnancy and for each 100 g increase in birth weight, the likelihood of BPD is reduced by 55% and 1%, respectively. In the present study, no relationship was found between Ureaplasma infection and BPD, which might be due to the low prevalence of this infection. Nonetheless, prematurity and low birth weight could be regarded as the two considerable risk factors for BPD.

Conclusion: In order to perfectly determine the role of bacterial colonization within the trachea in BPD, collecting and analyzing various samples for the existence of other bacteria are recommended.

Keywords: Bronchopulmonary dysplasia, Premature newborn, Ureaplasma urealyticum, Very low birth weight infant

Introduction

Bronchopulmonary dysplasia (BPD) or chronic lung disease is the most common chronic respiratory disorder in premature newborns, especially very low birth weight (VLBW) infants (less than 1500 g) (1-3). Furthermore, it is regarded as a major challenge of premature newborn care (4-6) The incidence of this disease has been reported as 11-57% and in the newborns of under 30 weeks has been reported up to 75% (4, 5, 7).

Despite the advancements over the past few decades in premature newborn care and survival, the number of deaths from BPD is still increasing (8-10) and the annual rate of death from this

* *Corresponding author*: Gholam Reza Assadi, Department of Pediatric, Tabriz Branch, Islamic Azad University, Tabriz, Iran. Tel: 09143312019; Email: ofoghahari@gmail.com

Please cite this paper as:
Mahallei M, Hosseini MB, Esmaili H, Assadi GR. Relationship between Ureaplasma urealyticum Colonization and Bronchopulmonary Dysplasia in Very Low Birth Weight Premature Infants: A Prospective Cohort Study. Iranian Journal of Neonatology. 2019 Dec: 10(4). DOI: 10.22038/ijn.2019.38304.1602

disease has been mentioned to be 10-15% (11). Furthermore, this disease causes long-term respiratory complications in childhood (12). The evidence indicates the effect of various factors on the occurrence of BPD (13, 14). Recently, great attention has been focused on the role of infection and inflammation before and after birth as a contributing factor in the etiology of this disease (15-17).

Ureaplasma urealyticum is one of the most important opportunistic pathogens in female genital system (18-20) and Ureaplasma species has been prevalently found in premature neonates (21). In the middle of 1970s, some researchers, after the isolation of Ureaplasma from the lung autopsy of premature newborns with pneumonia, mentioned the likelihood of the role of this organism in neonatal respiratory diseases (22). According to the literature, Ureaplasma infection in pregnant women is accompanied by an increase in amnionitis, the preterm rupture of amniotic sac, and preterm labor (5). On the other hand, newborns are highly prone to BPD. Therefore, Ureaplasma colonization can be considered as a contributing factor in this disease (8, 23, 24).

Investigations indicate that in newborns suffering from respiratory infection with Ureaplasma, the chance of affection with pneumonia is two folds higher, in comparison with the control infection-free group. Moreover, changes, including emphysema have been significantly greater two weeks after birth in the chest X-ray of such newborns (25). Furthermore, the need for hospitalizing newborns with Ureaplasma within the first year is higher than the control group (8, 16, 26).

The results indicate the likelihood of the onset of intra-uterine inflammatory response and lung trauma (27). Despite such evidence, the relationship between Ureaplasma and respiratory diseases is still disputable. Although in the previous studies 80% of newborns with Ureaplasma suffered from BPD, different results have been reported in this area (28). In fact, some investigations have found a significant relationship between developing Ureaplasma colonization and oxygen dependency at the age of 28 days after birth (29-31). However, other researchers did not find such relationship (24, 32).

Understanding the causes of a disease can assist in applying the suitable treatment strategies and reducing the death rate and contradictory results have been revealed in this regard. Subsequently, we attempted to conduct a study to investigate the relationship between Ureaplasma urealyticum colonization and the occurrence of BPD.

Methods

Study Design and Subjects

This prospective cohort study was conducted during March 2017-March 2018 in the neonatal intensive care unit (NICU) of Alzahra Obstetrics Hospital, Tabriz, Iran as a referral center in North-west of Iran and is the second largest university hospital in Tabriz. This hospital provides medical care for about 20,000 inpatients annually. The center serves four sub-branches of oncology, primatology, infertility, and urogynecology. The hospital has two NICUs with 50 beds and is recognized as the first service-providing center that uses the most advanced incubators.

The sample size was determined by census in 2017-2018 and sampling was conducted through convenience sampling method and all newborns meeting the inclusion criteria were selected. The inclusion criteria entailed being VLBW premature newborns, gestational age of less than 32 weeks, the lack of congenital diseases or complications, such as cardiac disease, intraventricular hemorrhage (IVH), and chromosomal anomalies, requiring intubation within 72 h after birth for any reason, including Intubation-Surfactant-Extubation (INSURE), and mechanical ventilation.

The exclusion criteria were neonatal mortality, hospital clearance of newborns to other center, and preterm discharge from the hospital before the age of 28 days or corrected 36 weeks pregnant that prevented the researcher from following-up the newborns, as well as the lack of consent from parents for sampling or pursuing the study. The research stages encompassed sampling, intubation process, taking sample from the pharyngeal secretions by GR by a neonatologist, and transfer to the laboratory. The laboratory tests were carried out by a pathologist.

The tools applied in this study included a researcher-made checklist for recording the demographic data and information about the developed disease according to the research aims. The questionnaire entailed questions regarding the information before and after birth. Some pieces of information including neonatal information in terms of age, gender, affection by a disease, the duration of oxygen therapy and mechanical ventilation, the duration of hospitalization, and Apgar score were collected from mother and medical records of newborn.

We used real-time polymerase chain reaction (PCR) to investigate the aspirated samples

regarding colonization with Ureaplasma urealyticum. The PCR method has the minimum false negative, in comparison to clinical laboratory cultures and can detect the microorganism when cultures are simultaneously negative (7). This method can discover positive cases 15% more than the culture method and 6% more than the conventional PCR (33).

The procedure for conducting the research was as follows: after receiving the confirmation from the Ethics Committee of Tabriz University of Medical Sciences and making the necessary arrangements, sampling was performed according to the inclusion criteria. Firstly, parental consents were received and in newborns that required intubation within 72 h after birth, the aspiration of endotracheal secretions was performed by a neonatologist as a researcher to identify endotracheal colonization with Ureaplasma in the respiratory tract.

In fact, after the tracheal intubation and before surfactant instillation, 1 ml of normal saline was instilled into the trachea tube under sterile circumstances using a 6fr catheter. Afterwards, 0.5-1 ml was aspirated by suction. Next, the fluid collected by the suction of trachea tube was emptied into the sterile tube and the sample was placed on ice, transferred to the laboratory, and preserved at a temperature of −20 degrees until PCR analysis.

The procedure was completed through BIORON RealLine Ureaplasma Urealyticum Fla-Format kit made in Germany and the extraction of DNA was implemented using Roche kit. Following obtaining the biopsies from endotracheal secretions, all newborns were followed-up until 28 days after birth and were evaluated by the research team (neonatologists) in terms of the occurrence of BPD and occurring diseases, namely retinopathy of prematurity (ROP) and necrotizing enterocolitis (NEC).

Data Analysis

The statistical analysis was conducted by the SPSS software version 22. The data were presented and analyzed using frequency (percentage) and mean ± standard deviation. Regarding the analysis of nominal and ordinal qualitative variables, Chi-square test and Fisher's exact test were applied. Moreover, the independent t-test and Mann-Whitney test were used to analyze the quantitative variables incase of abnormal data distribution. Furthermore, single-variable logistic regression test was used to assess the relationship of variables, such as age and birth weight with the occurrence of BPD. $P \leq 0.05$ was considered significant for all tests.

Results

In this study, among the 82 newborns with the inclusion criteria, 18 cases (22%) died prematurely and 3 cases (4.3%) were dispatched and excluded from the study. Finally, the information of 61 infants was included in the study. The mean and standard deviation of neonatal age and birth weight were 28.56 (1.95) years and 1100.66 (216.65) g, respectively. Moreover, 31 cases (50.8%) of the studied samples were female.

Over one-fourth of newborns (22 cases or 36.1%) scored less than five at the first-minute Apgar score, while the fifth-minute Apgar score in most cases (58 newborns or 95.1%) was more than 5. According to the data analysis, among the 61 newborns, only 3 cases (4.9%) were PCR-positive for Ureaplasma urealyticum. In addition, in most newborns (60 cases or 98.4%), continuous positive airway pressure was applied.

Furthermore, the results of studying the newborns at the age of 28 days indicated that 33 cases (54.1%) suffered from BPD and were dependent on oxygen therapy. In terms of ROP, sepsis, and NEC, 54 (88.5%), 58 (95.1%), and 59 (96.7%) newborns were not infected with such diseases, respectively.

According to the findings of the present study, there was a significant difference between the demographic characteristics, including age and weight of the group with Ureaplasma and the group without Ureaplasma. In fact, the mean of pregnancy age and birth weight in infants with Ureaplasma were 26 weeks and 868 grams, respectively. However, there was no significant difference between the two groups regarding gender, the occurrence of ROP, NEC, PDA, sepsis, and the preterm rupture of amniotic sac.

Although all the three neonates with Ureaplasma urealyticum colonization developed BPD, there was no relationship between the colonization of Ureaplasma urealyticum and BPD and the intensity was discovered. Furthermore, the data analysis demonstrated that there was no relationship between Ureaplasma urealyticum colonization and neonatal mortality (P=0.21) (Table 1).

The investigation of data indicated that most newborns weighed over 1000 g and did not develop BPD. In other words, the mean weight had a statistically significant difference between the two groups of with and without BPD. Moreover, most of the neonates without BPD aged ≥ 28

weeks and the mean age of two groups was revealed to have a significant difference.

In addition, the mean duration of receiving oxygen in infants with BPD was 48.95 days. In order to study the difference in the duration of receiving oxygen between the two groups of with and without BPD, t-test was applied. The results of this test showed that there was a significant difference between the two groups in terms of this variable (Table 2).

The single-variable regression analysis indicated that for each week increase in the age of pregnancy at birth, the likelihood of BPD occurrence reduced by 55% and for each 100 g elevation in birth weight, the likelihood of BPD diminished by 1% (Table 3).

Table 1. Information about VLBW infants in the two groups of with and without Ureaplasma urealyticum

Variable		With BPD Mean (SD)	Without BPD Mean (SD)	*P-value
Age of pregnancy (week)		26.33 (0.57)	28.67 (1.93)	0.03
Birth weight (g)		868.33 (32.53)	1111.67 (215.21)	< 0.001
Variable		With BPD N (%)	Without BPD N (%)	**P-value
Gender	Female	3 (4.9)	28 (45.9)	0.23
	Male	0	30 (49.2)	
Bronchopulmonary dysplasia	Has	3 (4.9)	30 (49.2)	0.24
	Does not have	0	28 (45.9)	
PROM	Has	13 (21.3)	45 (73.8)	0.54
	Does not have	1 (1.6)	2 (3.3)	
Sepsis	Has	0	3 (4.9)	1
	Does not have	3 (4.9)	55 (90.2)	
ROP	Has	1 (1.6)	6 (9.8)	0.31
	Does not have	2 (3.3)	52 (85.2)	
PDA	Has	0	7 (11.5)	1
	Does not have	3 (4.9)	51 (83.6)	
NEC	Has	0	2 (3.3)	1
	Does not have	3 (4.9)	56 (91.8)	
Intensity of disease	Mild	11 (33.3)	19 (57.6)	0.54
	Above average	2 (6.1)	1 (3)	

*Mann-Whitney test
**Fisher's exact test

Table 2. Comparing the information about VLBW infants between the two groups of with and without BPD

Variable		With Mean (SD)	Without Mean (SD)	*P-value
Age of pregnancy (week)		27.52 (1.41)	29.79 (1.79)	< 0.001
Birth weight (g)		990.45 (177.26)	1230.54 (186.35)	< 0.001
Duration of receiving oxygen		48.95 (18.44)	8.36 (6.06)	< 0.001
Variable		With N (%)	Without N (%)	**P-value
Gender	Female	16 (26.2)	14 (23)	0.9
	Male	17 (27.9)	14 (23)	
First-minute Apgar	Under 5	11 (18)	11 (18)	0.62
	5 and over	22 (36.1)	17 (27.9)	
Fifth-minute Apgar	Under 5	1 (1.6)	2 (3.3)	0.58
	5 and over	32 (52.5)	26 (42.6)	

*T-test
**Fisher's exact test

Discussion

In this prospective cohort study, the relationship between colonization with Ureaplasma urealyticum and BPD occurrence was investigated. According to our findings, only 4.9% of newborns were infected with Ureaplasma urealyticum and over half of the evaluated infants were affected by BPD.

The association between the presence of Ureaplasma urealyticum infection and BPD has been investigated by a large number of studies in

Table 3. Results of logistic regression for the effect of demographic characteristics on disease occurrence

Variable	OR (CI 95%)	P-value
Age of pregnancy at birth	0.453 (0.306 – 0.672)	< 0.001
Birth weight	0.994 (0.990 – 0.997)	< 0.001
Gender		
Male	Ref	0.906
Female	1.076 (0.388 – 2.91)	0.929
Receiving surfactant		
One dose	Ref	
Two dose	0.416 (0.687 – 7.697)	0.275
First-minute Apgar		
Under 5	Ref	
5 and over	0.773 (0.271 – 2.205)	0.63
Fifth-minute Apgar		
Under 5	Ref	
5 and over	0.406 (0.035 – 4.734)	0.472

the last twenty years and contradictory results have been achieved. The present study indicated that there is no relationship between Ureaplasma colonization and the occurrence of BPD. The latter result is in line with the studies performed by Courocli et al. (2000) (32) and Heggi et al. (2001) in Canada (15). In their studies, unlike our study that few cases were positive for Ureaplasma, 38% (66 individuals) had a positive culture. However, no relationship was discovered between Ureaplasma colonization and BPD (32).

On the other hand, the findings of the present study is not consistent with some other studies; for example, in the study completed by Colisee et al. (2006), they found a positive relationship between colonization with Ureaplasma and BPD. According to their study, among 139 newborns, 33 cases (24%) were positive for Ureaplasma urealyticum and 68 neonates (57%) suffered from BPD. These authors showed that there was a significant relationship between Ureaplasma colonization and BPD (8).

Furthermore, the present study is not in line with the study conducted by Payne et al. (1993) in Chicago. Their study included 93 newborns weighing less than 1200 g who received surfactant. Their findings revealed that 17 newborns (18%) had positive culture. According to the mentioned study, there was a significant relationship between the existence of Ureaplasma and BPD. They mentioned that infection with Ureaplasma increases the likelihood of BPD by 1.66% (34). In fact, the prevalence of colonization in a population may affect the results of a study. Therefore, one of the causes for inconsistency is the difference in the prevalence of Ureaplasma urealyticum in different societies.

Furthermore, most studies have been conducted prior to using surfactant and have obtained significant results. However, after using surfactant, the results of diverse studies were not in line with each another. One of the other causes of inconsistency can be the variation in the studied groups in terms of age and weight. The results of some studies on neonates weighing less than 1000 g indicated that the likelihood of BPD in infants with Ureaplasma rises by 2-3.8 times. On the other hand, in high-weight newborns, such a relationship has not been discovered. Consequently, it could be concluded that premature newborns are exposed to higher risk (8).

Contradictory results may also be due to different endotracheal biopsy methods and multiplicity of biopsies. Taking account of ethical considerations, our study was merely conducted on newborns requiring intubation, which can be regarded as a factor in selection bias. The method for the diagnosis of Ureaplasma urealyticum can be considered as another explanation for contradictions between the studies. In cases of using culture, the identification of a microorganism is based on living organisms and Ureaplasma urealyticum hardly grows on a culture medium. As a result, the identification of this organism is hardly achieved. According to the literature, 40% of results were false positive only for one sample (29, 35, 36).

Furthermore, the results have indicated that in the laboratory, surfactant can deactivate Ureaplasma. If the accuracy of this result is confirmed, further negative results may be reported following the administration of surfactant. However, this does not occur when PCR is applied because in this method even dead microorganisms are detectable. In fact, our sampling in all cases was before the administration of surfactant leading to the minimal effect of this factor in our study.

In the present study, approximately 54% of the newborns suffered from BPD, which is consistent with the study carried out by Colisee et al. (2006).

In their investigation, 57% of the samples suffered from BPD (8). However, our study is not aligned with the studies performed by Garland et al. (1996) (37) and Ollikainen et al. (2001) in which 39% and 43% of the newborns suffered from BPD, respectively (17). The difference in results may be due to the sample size.

According to the findings of the current study, with the reduction in age and birth weight, the risk of BPD augmented. In other words, for each week increase in the age of pregnancy at birth, the likelihood of BPD is reduced by 55%. Furthermore, for each 100 g elevation in birth weight, the chance of BPD is decreased by 1%.

One of the strength points of this study is the cohort design in order to determine the groups of exposure and non-exposure and follow-up the newborns until they got affected by the disease. Moreover, using the PCR method, which is superior to culture, is considered as another strength point. On the other hand, due to the ethical considerations, samples from the secretions of respiratory tract were obtained at a single stage, which can be regarded as the limitation of this study in identifying the infection. In addition, the low prevalence of this infection may have a potential role.

Using the information from medical records, which has been recorded by individuals other than the research team, may cause bias towards the information. Furthermore, taking samples from endotracheal secretions in neonates who required mechanical intubation and not investigating other newborns due to considering the problems of biopsy and ethical considerations were among the other weaknesses of this study.

In the present study, the prevalence of Ureaplasma in infants was negligible, while BPD was diagnosed in 33 cases (54%) and all the three newborns with Ureaplasma infection suffered from BPD. However, no relationship was observed between the occurrence of BPD and Ureaplasma urealyticum, which might be attributed to the low prevalence of this infection. Moreover, the findings of our investigation indicated that prematurity and low birth weight are related to BPD.

Ethical Considerations

This study is based on the research proposal approved by the Research Council Meeting of Tabriz University of Medical Sciences under the ethical code of IR.TBZMED.REC.1395.905. In addition, informed consents were received from the parents of newborns.

Conclusion

The result of this study support the need for further investigation of the role of Ureaplasma urealyticum in causing BPD in VLBW neonates. It is important to prevent prematurity and nosocomial infections to decrease the incidence of BPD. In order to perfectly determine the role of bacterial colonization within the trachea in BPD, it is recommended to collect and analyze various samples for the existence of other bacteria.

Acknowledgments

The present study was funded and supported by Tabriz University of Medical Sciences. The funders did not have any role in the study design, data collection, analysis, interpretation of data, or writing the manuscript.

Conflicts of interests

The authors of this study declare that they have no conflict of interests.

References

1. Carmichael SL, Kan P, Gould JB, Stevenson DK, Shaw GM, Lee HC. Maternal prepregnancy body mass index and risk of bronchopulmonary dysplasia. Pediatric. 2017; 82(1):8-13.
2. Inatomi T, Oue S, Ogihara T, Hira S, Hasegawa M, Yamaoka S, et al. Antenatal exposure to Ureaplasma species exacerbates bronchopulmonary dysplasia synergistically with subsequent prolonged mechanical ventilation in preterm infants. Pediatric. 2012; 71(3):267-73.
3. Lundstrøm K, Shaw N, Thomson MA. Chronic lung disease-cracking the condition in the 21st century. Neonatology. 2000; 78(3):233-68.
4. Day CL, Ryan RM. Bronchopulmonary dysplasia: old becomes New Again! Pediatr Res. 2016; 81(1-2):210-3.
5. Zheng XD, Li D, Yang DH, Xiang X, Mei H, Pu JR, et al. Association of Ureaplasma urealyticum colonization with development of bronchopulmonary dysplasia: a systemic review and meta-analysis. J Huazhong Univ Sci Technolog Med Sci. 2014; 34(2):265-9.
6. Soleimani F, Sharifi N, Rasti Borujeni F, Amiri M, Khazaiyan S. Nourodevelopmental follow-up in high-risk infants. Tehran Univ Med J. 2015; 72(11):733-41.
7. Rennie JM. Rennie & roberton's textbook of neonatology e-book. New York: Elsevier Health Sciences; 2012.
8. Colaizy TT, Morris CD, Lapidus J, Sklar RS, Pillers DA. Detection of ureaplasma DNA in endotracheal samples is associated with bronchopulmonary dysplasia after adjustment for multiple risk factors. Pediatric. 2007; 61(5 Pt 1):578-83.
9. Manktelow B, Draper E, Annamalai S, Field D. Factors affecting the incidence of chronic lung

disease of prematurity in 1987, 1992, and 1997. Arch Dis Child Fetal Neonatal Ed. 2001; 85(1):F33-5.
10. Ng G, da Silva O, Ohlsson A. Bronchodilators for the prevention and treatment of chronic lung disease in preterm infants. Cochrane Database Syst Rev. 2016; 12:CD003214.
11. Abbott MB, Vlasses CH. Nelson textbook of pediatrics. JAMA. 2011; 306(21):2387-8.
12. Davidson LM, Berkelhamer SK. bronchopulmonary dysplasia: chronic lung disease of infancy and long-term pulmonary outcomes. J Clin Med. 2017; 6(1):E4.
13. Jobe AH. The new bronchopulmonary dysplasia. Curr Opin Pediatr. 2011; 23(2):167-72.
14. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respir Crit Care Med. 2001; 163(7):1723-9.
15. Heggie AD, Bar-Shain D, Boxerbaum B, Fanaroff AA, O'riordan MA, Robertson JA. Identification and quantification of ureaplasmas colonizing the respiratory tract and assessment of their role in the development of chronic lung disease in preterm infants. Pediatr Infect Dis J. 2001; 20(9):854-9.
16. Northway Jr WH, Rosan RC, Porter DY. Pulmonary disease following respirator therapy of hyaline-membrane disease: bronchopulmonary dysplasia. N Engl J Med. 1967; 276(7):357-68.
17. Ollikainen J, Korppi M, Heiskanen-Kosma T, Heinonen K. Chronic lung disease of the newborn is not associated with Ureaplasma urealyticum. Pediatr Pulmonol. 2001; 32(4):303-7.
18. Najar Peerayeh S, Samimi R. Detection of ureaplasma urealyticum in clinical samples from infertile women by polymerase chain reaction. Iran J Pharmacol Ther. 2007; 6(1):23.
19. Viscardi RM. Ureaplasma species: role in diseases of prematurity. Clin Perinatol. 2010; 37(2):393-409.
20. Viscardi RM, Manimtim WM, Sun CC, Duffy L, Cassell GH. Lung pathology in premature infants with Ureaplasma urealyticum infection. Pediatr Dev Pathol. 2002; 5(2):141-50.
21. Viscardi RM, Hashmi N, Gross GW, Sun CC, Rodriguez A, Fairchild KD. Incidence of invasive ureaplasma in VLBW infants: relationship to severe intraventricular hemorrhage. J Perinatol. 2008; 28(11):759-65.
22. Waites K, Crouse D, Cassell GH. Therapeutic considerations for Ureaplasma urealyticum infections in neonates. Clin Infect Dis. 1993; 17(Suppl 1): S208-14.
23. Ollikainen J, Hiekkaniemi H, Korppi M, Sarkkinen H, Heinonen K. Ureaplasma urealyticum infection associated with acute respiratory insufficiency and death in premature infants. J Pediatr. 1993; 122(5 Pt 1):756-60.
24. Ollikainen J. Perinatal Ureaplasma urealyticum infection increases the need for hospital treatment during the first year of life in preterm infants. Pediatr Pulmonol. 2000; 30(5):402-5.
25. Crouse DT, Odrezin GT, Cutter GR, Reese JM, Hamrick WB, Waites KB, et al. Radiographic changes associated with tracheal isolation of Ureaplasma urealyticum from neonates. Clin Infect Dis. 1993; 17(Suppl 1):S122-30.
26. Gancia P, Delogu A, Pomero G. Ureaplasma and bronchopulmonary dysplasia. Early Hum Dev. 2014; 90:S39-41.
27. Castro-Alcaraz S, Greenberg EM, Bateman DA, Regan JA. Patterns of colonization with Ureaplasma urealyticum during neonatal intensive care unit hospitalizations of very low birth weight infants and the development of chronic lung disease. Pediatrics. 2002; 110(4):e45.
28. Benstein BD, Crouse DT, Shanklin DR, Ourth DD. Ureaplasma in lung. 2. Association with broncho-pulmonary dysplasia in premature newborns. Exp Mol Pathol. 2003; 75(2):171-7.
29. Da Silva O, Gregson D, Hammerberg O. Role of Ureaplasma urealyticum and Chlamydia trachomatis in development of bronchopulmonary dysplasia in very low birth weight infants. Pediatr Infect Dis J. 1997; 16(4):364-9.
30. Hannaford K, Todd DA, Jeffery H, John E, Blyth K, Gilbert GL. Role of Ureaplasma urealyticum in lung disease of prematurity. Arch Dis Child Fetal Neonatal Ed. 1999; 81(3):F162-7.
31. Pacifico L, Panero A, Roggini M, Rossi N, Bucci G, Chiesa C. Ureaplasma urealyticum and pulmonary outcome in a neonatal intensive care population. Pediatr Infect Dis J. 1997; 16(6):579-86.
32. Couroucli XI, Welty SE, Ramsay PL, Wearden ME, Fuentes-Garcia FJ, Ni J, et al. Detection of microorganisms in the tracheal aspirates of preterm infants by polymerase chain reaction: association of adenovirus infection with bronchopulmonary dysplasia. Pediatr Res. 2000; 47(2):225-32.
33. Gien J, Kinsella JP. Pathogenesis and treatment of bronchopulmonary dysplasia. Curr Opin Pediatr. 2011; 23(3):305-13.
34. Payne NR, Steinberg SS, Ackerman P, Chrenka BA, Sane SM, Anderson KT, et al. New prospective studies of the association of Ureaplasma urealyticum colonization and chronic lung disease. Clin Infect Dis. 1993; 17(Suppl 1):S117-21.
35. Abele-Horn M, Genzel-Boroviczeny O, Uhlig T, Zimmermann A, Peters J, Scholz M. Ureaplasma urealyticum colonization and bronchopulmonary dysplasia: a comparative prospective multicentre study. Eur J Pediatr. 1998; 157(12):1004-11.
36. Maksić H, Heljić S, Skokić F, Šumanović-Glamuzina D, Milošević V, Zlatanović A, et al. Predictors and incidence of hospitalization due to respiratory syncytial virus (RSV)-associated lower respiratory tract infection (LRTI) in non-prophylaxed moderate-to-late preterm infants in Bosnia and Herzegovina. Bosnian J Basic Med Sci. 2018; 18(3):279-88.
37. Garland SM, Bowman ED. Role of Ureaplasma urealyticum and Chlamydia trachomatis in lung disease in low birth weight infants. Pathology. 1996; 28(3):266-9.