Editorial
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Ureaplasma urealyticum or *Ureaplasma parvum*: what's the difference?

Tae-Jung Sung, MD
Department of Pediatrics, Hallym University Kangnam Sacred Heart Hospital, Seoul, Korea

Recently, birth of premature babies and low birth weight babies has been increasing and survival rate of very low birth weight babies even under 500 g not to mention under 1,000 g is remarkably enhanced thanks to the development of neonatology. With the enhanced birth rate and survival rate, the issue of pediatrics majoring in neonatology is not increasing survival rate anymore but making them healthier babies. While treating premature babies in the field, it is found that some premature babies have better prognoses while others have poor prognoses.

As a part of efforts to identify the factors influencing prognoses of newborns, studies on prenatal infections are actively made. One of the hottest topics is *Ureaplasma* infection. Although it has been studied before, it has been perceived as 'sexually-transmitted disease' and has been studied in gynecology or urology. Recently, however, it is expanded to the field of complications of premature babies[1,2]. Additionally, studies have been actively performed since strain known as *Ureaplamsa urealyticum* was segmented to *Ureaplasma parvum* (UPA hereunder) and *Ureaplasma urealyticum* (UUR hereunder), which were further segmented to 14 serovars[2,3].

Past studies published before in Korea by Lim et al.[4] and by Chang et al.[5] were studies on overall prevalence before *Ureaplasma* colonization was segmented into two serovars. In this point, Eun et al.[6] is encouraging because it studied serovars of Korean premature babies.

However, it has limitations at the same time. Although it is meaningful that it tried to analyze premature babies according to serovar, it dealt with UUR only and the conclusion that there would be no difference between *Ureaplasma* serovars may be misleading. As authors mentioned before, *Ureaplasma* spp is segmented to two biovars such as UPA and UUR. Such two biovars can be segmented according to genome size, *16S rRNA* gene sequences, the 16S-23S rRNA intergenic region, enzyme polymorphisms, DNA-DNA hybridization, differential growth responses to manganese, and differences in the multiple banded antigen (*mba*) genes[2,3]. They are segmented to 14 serovars by polymerase chain reaction (PCR)-based methods based on the previously mentioned UPA (biovar 1, serovar 3, ATCC* 27815, NCTC** 11736), and UUA (biovar 2, serovar 8, ATCC* 27618, NCTC** 10177). According to characteristics of each serovar, serovar 1, 3, 6, and 14 fall under biovar 1, so to speak UPA, and rest of them fall under biovar 2, so to speak UUR. On the other hand strains that have not been clear in classification are more segmented and 5 more strains have been discovered[7] (Table 1).

Accordingly, authors should discuss the difference between UPA and UUR serovars first to claim that there was no difference in bronchopulmonary dysplasia (BPD) incidence in each servoar. It seems misleading that they say there was no difference according to BPD and serovars because their study had very limited subjects and approximately 1/3 had mixed serovars. Additionally, some investigators consider these mixed strains

Corresponding author: Tae-Jung Sung, MD
Department of Pediatrics, Hallym University Kangnam Sacred Heart Hospital, 1 Singil-ro, Yeongdeungpo-gu, Seoul 150-950, Korea
Tel: +82-2-829-5148
Fax: +82-2-829-4469
E-mail: neosung@hallym.or.kr

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as totally different serovars according to hybridization and wonder if studies investigating difference among serovars are meaningless[8]. Although it is one of major conclusions of Eun and et al.[6] that there is no difference between UUR serovars, the conclusion is not well established and it is better to get to a conclusion after experiments using UPA and UUR together.

Ureaplasma is known as a strain difficult to culture in the laboratory because it is very small such as 15–25 micrometer diameter and has no cell wall. This strain produces adenosine triphosphate through urea hydrolysis and dissolves urea into ammonia (NH3) and carbon gas. When culturing in the laboratory, infection is judged through pH change in liquid culture using such principle. But recently, as studies have shown that PCR method is more sensitive, PCR method is preferred to classical culture[1-3]. To make more explanations on culture and PCR method, authors perform tracheal aspiration and gastric aspiration at the same time to identify correlations with BPD. As tracheal aspiration samples show whether there is lower respiratory colonization, which means infection in most cases, and may judge infection of *Ureaplasma* spp regardless of skills of testers, it is the most preferred method. However, it has a drawback that sampling can be made in newborns only with intubation. A probable alternative is nasopharyngeal swab. It is easy to get samples and can be repeated many times, although some authors said that we cannot judge infection only with the result of this test showing upper respiratory colonization[1,2].

Interestingly, in Eun et al.[6] study, UUR serovar 9 is found to be the most common serovar, which was deal with Koreans. Whereas Sung et al.[9] studies on Caucasians and African-Americans found that serovar 11 was the most common. Such difference may imply difference between races, although it must be confirmed with further studies, because of small sample size of this study. In particular, as there have not been many studies regarding the difference between races, it will be an interesting field to perform a large-scale study including gene tests.

Many studies on relationship between *Ureaplasma* spp and complications of premature babies have been made recently and results are being published constantly. Among them, mechanism to make BPD by *Ureaplasma* spp. is considered as being made by activation of proinflammatory cytokines (tumor necrosis factor-α, interleukin [IL] 1β, IL-8) or blocking counterregulatory cytokines (IL-6, IL-10) rather than making direct damages on respiratory tract. There is a hypothesis that respiratory diseases and BPD of newborns are caused by phospholipase A2 created by other strains which coerces the creation of pulmonary surface activators. It is also know that infection in prenatal period stimulates infection consecutive infection of pulmonary alveoli, interferes the creation of pulmonary alveoli by directly or indirectly influencing respirator induced pulmonary damages, stimulates phagocytes composing cilliary disarray and clumping after composing colony on epithelial cells on respiratory tracts, and creates proinflammatory cytokine to cause BPD[1,10,11]. Such

Table 1. Overview of *Ureaplasma urealyticum* and *Ureaplasma parvum* genomes

Serovar	ATCC	GenBankaccession	PFGE size (kbp)	Genome size (bp)	Contigs	ORFs	Hypothetical proteins	% GC	Sequence coverage
1	27813	NZ_ABES00000000	760	753,674	8	604	212	25%	14.6X
3	27815	NC_010503	760	751,679	1	609	219	25%	10.2X
3	700970	NC_002162	Patient isolate	751,719	1	614	154	25%	-
6	27818	NZ_AAZQ00000000	760	772,971	5	619	221	25%	11.4X
14	33697	NZ_ABER00000000	760	749,965	7	594	199	25%	14.5X
2	27814	NZ_ABFL00000000	880	861,061	1	664	248	26%	10.7X
4	27816	NZ_AAYO00000000	910	835,413	4	654	206	26%	7.0X
5	27817	NZ_AAZR00000000	1140	884,046	18	677	252	26%	8.5X
7	27819	NZ_AAYP00000000	880	875,530	4	660	246	26%	8.3X
8	27618	NZ_AAYN00000000	890	874,381	1	673	232	26%	9.9X
9	33175	NZ_AAYQ00000000	950	947,165	10	711	244	26%	8.6X
10	33699	NC_011374	890	874,478	1	657	232	26%	12.1X
11	33695	NZ_AAZS00000000	840	876,474	6	644	236	27%	10.0X
12	33696	NZ_AAZT00000000	870	873,466	2	650	234	25%	9.0X
13	33698	NZ_ABEV00000000	900	846,596	5	655	234	25%	11.1X
2033	Unknown serovar	AJFX00000000	Patient isolate	804,560	16	646	190	26%	39.0X
2608	Unknown serovar	AJFY00000000	Patient isolate	856,546	14	667	258	26%	60.0X
4155	Unknown serovar	AJFZ00000000	Patient isolate	858,890	18	684	225	26%	73.0X
4318	Unknown serovar	AJGA00000000	Patient isolate	844,630	16	662	214	26%	52.0X

PFGE, pulsed-field Gel Electrophoresis; ORF, open-reading frame; GC, guanine-cytosine.

relationship with cytokines should be studied further in the future.

Conclusively, more studies are needed on the relationship between *Ureaplasam* and infection of newborns, in particular complications of premature babies including BPD. It is also needed to perform a large scale study on Korean newborns.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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