

Pattern of Microbial Infections during the First 72 Hours of Neonate Life at Khafji General Hospital Neonatal Intensive Care Unit

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Abstract

Neonatal infection is an important cause of morbidity and mortality of neonates. The objective of this study is to evaluate the pattern of microbial infections during the first 72 hours of neonate life at *AlKhafji General Hospital Neonatal Intensive Care Unit*. This is a hospital-based retrospective study design in *AlKhafji General Hospital (KGH)* in *Khafji City*, Saudi Arabia. The data was collected from sensitivity reports and results of isolated cultures of random sample of 74 infected neonates admitted to NICU. Data was analyzed by SPSS program by descriptive statistics. Among the 74 significant culture positive cases, there were 54% male and 46% female neonates. The most common microorganism isolated from neonates in NICU was *Pseudomonas aeruginosa* (13.5%) followed by *E. coli* and *Enterobacter* (12.1%) and (9.5%) respectively. 18.9% of the isolated bacteria were sensitive to vancomycin including *Staphylococcus aureus*, *Staphylococcus hominis*, *Enterobacter*, *MRSA*, *Enterococi*, *C. diff* and *Listeria monocytogenes*. 12.2% of the isolated bacteria were sensitive to ampicillin including *Staphylococcus aureus*, *Acinetobacter*, *Enterobacter*, *Strep. pyogenes*, *Enterococi* and *Anaerobes*. 10.8% of the isolates were sensitive to imipenem including *Phenomena paucimobilis*, *Staphylococcus hominis*, *E. coli*, *Enterobacter*, *Staphylococcus sciuri* and *Pseudomonas aeruginosa*. Gram negative bacteria specifically *Pseudomonas aeruginosa* and *E. coli* are the most common causes of infection of neonates in NICU. Pathogens causing neonatal infections exhibit varying antibiotic sensitivity pattern. However, the most sensitivity recorded was for vancomycin. Additionally, the emerging multi drug resistant microorganism such as *Acinetobacter* in NICUs could be a health risk in future.

Keywords: Intensive Care Unit, Microbial Infections, Neonatal, Treatment

List of Abbreviations

C. diff: *Clostridium difficile*.

CDC: Center for Disease Control and prevention.

CoNS: *Cocciagulase-negative staphylococci*.

CVA catheter: Central Venous catheter.

E. coli: *Escherichia coli*.

HSV: *Herpes Simplex Virus*.

GBS: *Group B Streptococcus*.

GDS: *Group D Streptococcus*.

MRSA: *Methicillin-resistant Staphylococcus aureus*.

MSSA: *Methicillin-susceptible Staphylococcus aureus*.

NICU: *Neonatal Intensive Care Unit*.

VLBW: Very Low Birth Weight.

WHO: World Health Organization.

1. Introduction

Neonatal infection is an important cause of morbidity and mortality of neonates. Additionally, it is a major cause for prolonged admission among infants, particularly preterm

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infants and newborns with Very Low Birth Weight (VLBW)¹.

Neonates are highly prone to infections and if not diagnosed and treated quickly, may lead to fatality². Suspected infections including meningitis, pneumonia and sepsis account for an estimated 1.4 million neonatal deaths worldwide every year³. After the first week of life; infections are the main cause of neonatal mortality in many countries⁴. These infections can be acquired by the infant in different ways e.g. complications of treatment or other prenatal conditions and can be acquired in hospital (hospital-acquired or nosocomial infection) or at home (community acquired infection)⁴.

The survival rate of low birth weight and very low birth weight neonates in a Newborn Intensive Care Unit (NICU) has increased in recent years due to technological advancement, but the prolonged duration of admission and the number of invasive procedures may increase nosocomial infections⁵. Neonates' infections have a wide range of manifestations including osteomyelitis, arthritis, pneumonia, meningitis, septicemia and urinary tract infections⁶.

2. Rationale of the Study

To decrease mortality rate, it is necessary to treat neonatal infections rapidly by empirical use of suitable antimicrobial medications. The selection of empirical antimicrobial has always been based on the given data on type of microorganism and epidemiology of bacterial sensitivity patterns⁷.

The bacterial resistances to antibiotics become a major problem in most hospitals or health care facilities all over the world, particularly in developing countries due to inappropriate and random use of antibiotics. Center for Disease Control and prevention (CDC) reported that many types of bacteria become resistant to two or more classes of antibiotics in both large and small hospitals⁸.

Although many cases of infections occur in the first hours of the newborn life, however, no previous studies have been carried to evaluate the pattern of microorganism's infection of newborn in the first few hours of their life in Khafji- Saudi Arabia. The objective of the study is to evaluate the pattern of microbial infections during the first 72 hours of neonate life in Neonatal Intensive Care Unit.

Sepsis diagnosis depends mainly on the newborn's symptoms and the laboratory results. Several tests need to be conducted to try to determine the specific bacterium, virus or fungus that is causing the infection⁹.

According to the WHO "Infant mortality rate is about five million annually, 98% of which occurs in poor countries". Based on these data, early-onset sepsis is associated with acquisition of microorganisms from the mother¹⁰.

Hospital-acquired (nosocomial) infection is critical and often difficult to control in the Neonatal Intensive Care Unit (NICU)¹¹. Various NICUs acquire different types of pathogens¹² which is acquired during the first two to three days after hospitalization¹³. This type of infections increases the length of hospitalization and healthcare costs¹⁴.

In 2005, the WHO declares "more than 1.4 million people per year suffer from hospital acquired infections. Currently the incidence rate of hospital-acquired infections is approximately 25% in developing countries¹⁵."

Early onset sepsis often manifests with pneumonia and/or septicemia. There is a high risk of mortality. Sepsis at this early age is predominantly due to organisms acquired from the birth canal. Occasionally intrapartum haematogenous spread occurs such as listeria. Over 80% of cases are due to *Group B Streptococcus* (GBS) and Gram negative bacteria¹⁶. Neonatal sepsis arises when pathogenic microorganisms gain entry into the bloodstream causing devastating systemic infection. Risk factors of sepsis include: Underweight, long hospitalization, antibiotics consumption, storage of medical supply, along with using procedures such as: Parenteral nutrition with lipid emulsions, endotracheal tube, ventricular shunt, intravascular catheter^{17,18}.

Sepsis a cause of neonatal mortality encompasses various neonatal infections: septicemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infections. Superficial infections like conjunctivitis and oral thrush are not usually included under neonatal sepsis^{19,20}.

Among the pathogens causing hospital-acquired infections, *C. difficile* (12.1%) is the leading cause followed by *Staphylococcus aureus* (10.7%), *Klebsiella* (9.9%) and *Escherichia coli* (9.3%)²¹. Health care provider-associated infection via contaminated worker and fomite transmission has been well documented^{22,23}.

The clinical manifestations of neonatal sepsis vary considerably and are nonspecific, which makes the

diagnosis of early difficult, symptoms may include body temperature instability, unexplained jaundice, Apnea, tachypnea, dyspnea, flaring, retractions, grunting, or cyanosis^{24,25}.

Gram-negative bacteremia carries higher risks of severe sepsis, septic shock and death. Sundaram *et al.*,²⁶ Gram-negative Bacilli (GNB) are well-described causes of Healthcare-associated Infections (HAIs) among infants hospitalized in Neonatal Intensive Care Units (NICUs)²⁷.

3. Materials and Methods

Hospital based retrospective study design in *Khaffi General Hospital* (KGH) in *Khaffi City* Saudi Arabia.

Add IRB approval number.

The data was collected by analyzing sensitivity reports and results of isolated cultures of infected neonates admitted to NICU using data collection sheet (attached in the appendix) from October 2019 to March 2020. Random sample of 74 infected neonates admitted to NICU.

3.1 Inclusion Criteria

- Infected neonates in ICU in their first 72 hours of their life.
- Admitted to NICU in the period from June 2017 till June 2018.

3.2 Exclusion Criteria

- Neonates infected after the first 72 hours of their life.

3.3 Statistical Test

After data collection, all data coded and entered to excel spread sheet then transferred to SPSS program for statistical analysis. Descriptive statistics used for data analysis with calculation of frequency and percentage for categorical data and calculation of minimum, maximum and mean (SD) for continuous data and representing the results with figures.

4. Results

Among the 74 significant culture positive cases, there were 40 (54%) male and 34 (46%) female neonates. Table 1 gestational age of the included neonates ranged from 30 to 39 weeks with mean 35 weeks, birth weight of the

neonates included ranged from 1874 to 3890 gm with mean 2870 gm (Table 2).

Blood cultures accounted for (32.4%) of the total isolates, urine cultures accounted for 40.5% of the isolates and stool culture accounted for 10.8% of the isolates. Figure 1 shows the sources of culture among study subjects.

The most common microorganism isolated from neonates in NICU was *Pseudomonas aeruginosa* (13.5%) followed by *E. coli* and *Enterobacter* (12.1%) and (9.5%) respectively. Other microorganisms isolated were *Methicillin Resistant Staphylococcus aureus* (MRSA) (6.8%), *Staph. aureus* (5.4%) and *Neisseria meningitidis* (5.4%). Figure 4 show the details about microorganisms isolated from NICU.

The gram negative bacteria isolated from 37 (50%) of neonates; mainly *Pseudomonas aeruginosa* (13.5%) and *E. coli* (12.1%). The gram positive bacteria isolated from 30 (40.5%); mainly *Staphylococcus aureus* (5.4%). Figure 3 shows distribution of isolated bacteria according to gram stains affinity.

Table 3 shows the isolated microorganisms according to source of culture.

Pseudomonas aeruginosa isolated from blood (4.1%), urine (2.7%) and throat (2.7%). MRSA isolated from urine (5.4%), *Strep. pyogenes* isolated from urine (1.45) and blood (1.4%).

18.9% of the isolated bacteria were sensitive to vancomycin including *Staph aureus*, *Staphylococcus hominis*, *Enterobacter*, MRSA, *Enterococi*, *C. diff* and *Listeria monocytogenes*. 12.2% of the isolated bacteria were sensitive to ampicillin including *Staph. aureus*, *Acinetobacter*, *Enterobacter*, *Strep. pyogenes*, *Enterococi* and *Anaerobes*. 10.8% of the isolates were sensitive to imipenem including *Phingomonas paucimobilis*, *Staphylococcus hominis*, *E. coli*, *Enterobacter*, *Staphylococcus sciuri* and *Pseudomonase*. Table 4 shows sensitivity pattern of isolated microorganisms from positive culture from NICU.

Death rate among infected neonates was 12.2% (Table 5). Among them there were 77.8% females, the most causative agent of infection isolated was *Neisseria meningitidis* (22.2%) and *Pseudomonas aeurginosa* (22.2%). Their gestational age ranged from 30 to 35 weeks with mean 32-34 weeks and their birth weight ranged from 1894 to 2890 gm with mean 2491 gm Table 6.

Table 1. Distribution of study subjects according to gender

Variable	Categories	Frequency	Percentage
Sex	Male	40	54%
	Female	34	46%

Table 2. Distribution of study subjects according to birth weight and gestational age

Variable	Maximum	Minimum	Mean	Standard deviation
Birth weight (gm)	3890	1874	2870	514.7
Gestational age (weeks)	39	30	35	2.4

Table 3. Isolated microorganism according to source of culture

Microorganism	Wound swab	throat	urine	blood	CVA catheter	Eye discharge	Nasal discharge	Stool
<i>Acinetobacter</i>	0	0	0	0	1 (1.4%)	0	0	0
<i>Actinomyces</i>	0	0	1 (1.4%)	0	0	0	0	0
<i>Atypical</i>	0	0	1 (1.4%)	0	0	0	0	0
<i>C. diff</i>	0	0	1 (1.4%)	0	0	0	1 (1.4%)	1 (1.4%)
<i>Candida. albicans</i>	0	0	4 (5.4%)	0	0	0	0	0
<i>Candida. non. albicans</i>	0	0	1 (1.4%)	0	0	0	0	0
<i>Chlamydia trachomatis</i>	0	0	2 (2.7%)	0	0	1 (1.4%)	0	0
<i>E. coli</i>	0	0	1 (1.4%)	1 (1.4%)	0	0	0	4 (5.4%)
<i>Enterobacter</i>	0	0	3 (4.1%)	4 (5.4%)	0	0	0	0
<i>Enterococi</i>	0	0	0	3 (4.1%)	0	0	0	0
<i>HSV</i>	0	1 (1.4%)	0	0	0	0	0	0
<i>Listeria monocytogenes</i>	0	0	0	0	0	0	0	1 (1.4%)
<i>MRSA</i>	0	0	4 (5.4%)	1 (1.4%)	0	0	0	
<i>MSSA</i>	0	0	1 (1.4%)	1 (1.4%)	0	0	0	1 (1.4%)
3 (4.1%)	0	1 (1.4%)	0	0	0	1 (1.4%)	0	<i>N. meningitidis</i>
1 (1.4%)	0	0	0	0	0	0	0	<i>Sphingomonas paucimobilis</i>
3 (4.1%)	0	0	1 (1.4%)	1 (1.4%)	2 (2.7%)	2 (2.7%)	0	<i>Pseudomonas aeruginosa</i>
0	0	0	0	0	0	1 (1.4%)	0	<i>Staph. epidermis</i>
2 (2.7%)	0	0	1 (1.4%)	0	0	0	1 (1.4%)	<i>Staph. aureus</i>
1 (1.4%)	0	0	0	0	0	0	0	<i>Staphylococcus hominis</i>

5. Discussion

The immune system of the new born is usually unable to provide a robust defense against virulent pathogen faced in the postnatal environment. So, neonates are at high risk of developing invasive infection if exposed to pathogenic microorganisms especially premature neonates due to lack of protective maternal antibodies, underdeveloped innate immunity²⁸, Advanced medical technology, appropriate infection prevention, and proper patient counseling on the use of antibiotics determine the prevalence of newborns diseases, particularly those who depend on therapeutic interventions for survival^{29,30}.

The frequency of infection in NICUs varies from 8% to 10% in Europe and from 6% to 25% in the United States³¹. The present study conducted to evaluate the

0	0	0	0	0	0	3 (4.1%)	0	<i>Staphylococcus sciuri</i>
1 (1.4%)	0	0	0	0	0	0	0	<i>Staphylococcus capitis</i>
	0	0	1 (1.4%)	0	0	0	0	<i>Stenotrophomonas sp.</i>
1 (1.4%)	0	0	0	0	0	1 (1.4%)	0	<i>Strep. pyogenes</i>
0	0	0	1 (1.4%)	0	0	1 (1.4%)	0	<i>Strep. pneumoniae</i>

Table 4. Sensitivity pattern of isolated microorganisms from positive culture from NICU

Antibiotic	Frequency (percentage)	Sensitive microorganisms
Vancomycin	14 (18.9%)	<i>Staph. aureus, Staphylococcus hominis, Enterobacter, MRSA, Enterococi, C. diff and Listeria monocytogenes</i>
Gentamycin	5 (6.8%)	<i>Sphingomonas paucimobilis, Staph. aureus and Staphylococcus sciuri</i>
Amikacin	2 (2.7%)	<i>Streptococcus agalactiae</i>
Imipenem	8 (10.8%)	<i>Sphingomonas paucimobilis, Staphylococcus hominis, E. coli, Enterobacter, Staphylococcus sciuri and Pseudomonase</i>
Ceftriaxone	3 (4.1%)	<i>Acinetobacter, Strep. pneumoniae and Chlamydia trachomatis</i>
Ampicillin	9 (12.2%)	<i>Staph. aureus, Acinetobacter, Enterobacter, Strep. pyogenes, Enterococi and anaerobes</i>
Piperacillin	5 (6.8%)	<i>E. coli and Pseudomonas</i>
Amoxicillin/clavulanic acid	1 (1.4%)	<i>E. coli</i>
Fluconazole	3 (4.1%)	<i>Candida. Albicans and Candida non. albicans</i>
Pencillin	4 (5.4%)	<i>Strep. pyogenes and N. meningitidis</i>
Cefuroxime	3 (4.1%)	<i>Streptococcus agalactiae</i>
Piperacillin	2 (2.7%)	<i>Enterobacter, E. coli and Pseudomonas</i>
Cefotaxime	4 (5.4%)	<i>Staph. aureus and E. coli</i>
Ceftazidime	3 (4.1%)	<i>Pseudomonas</i>
Levofloxacin	2 (2.7%)	<i>Stenotrophomonas s.p and Strep. pneumonia</i>
Cefepime	2 (2.7%)	<i>Pseudomonase and E. coli</i>
Cefazoline	3 (4.1%)	<i>MRSA and MSSA</i>
Ceftaroline	3 (4.1%)	<i>MRSA</i>
Erythromycin	2 (2.7%)	<i>Chlamydia trachomatis</i>
Linezolid	1 (1.4%)	<i>Staph. aureus</i>
Clindamycin	2 (2.7%)	<i>Staph. epidermis and Strep. pyogenes</i>
Azithromycin	1 (1.4%)	<i>Atypical</i>
Acyclovir	1 (1.4%)	<i>HSV</i>
Metronidazole	1 (1.4%)	<i>C. diff</i>
Doxycycline	1 (1.4%)	<i>Chlamydia</i>
Pencillin G	1 (1.4%)	<i>N. meningitidis</i>
Pencillin VK	3 (4.1%)	<i>Actinomyces and N. meningitidis</i>
Dicloxacillin	1 (1.4%)	<i>Staph. aureus</i>

Table 5. Death rate in the study sample

	Categories	Frequency	Percentage
Occurrence of death	Yes	9	12.2%
	No	65	87.8%

Table 6. Details of died infected neonates in NICU (n = 9)

	Categories	Frequency	Percentage
Sex	Male	2	22.2%
	Female	7	77.8%
Type of micro organism	<i>Enterobacter</i>	1	11.1 %
	<i>Pseudomonas aeruginosa</i>	2	22.2%
	<i>Candida albicans</i>	1	11.1 %
	MRSA	1	11.1 %
	MSSA	1	11.1 %
	<i>E. coli</i>	2	22.2%
	<i>N. meningitidis</i>	2	22.2%
		Maximum	Minimum
Gestational age (weeks)	35	30	32.4 (0.4)
Birth weight (gm)	2890	1894	2491 (380.2)

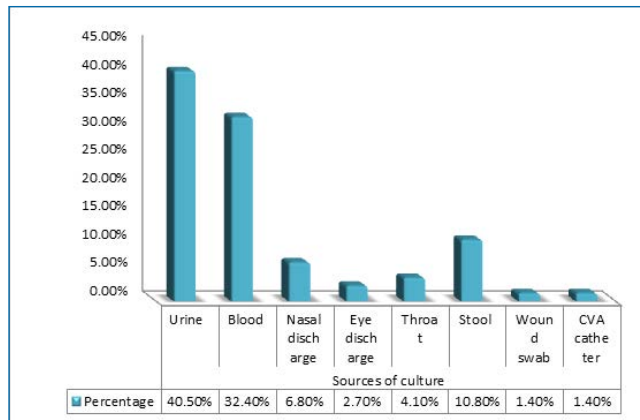


Figure 1. Sources of culture.

pattern of microbial infections during the first 72 hours of neonate life in Neonatal Intensive Care Unit.

According to the results, blood culture positivity rate in NICU cases is 32.4% which is lower than was found by I Roy *et al.*, and Kairavi. J. Desai, *et al.*,^{32,33}. To manage neonatal infection properly, it is urgent to study the bacteriological profile with their antibiotic sensitivity.

The infections in NICU in the current study were more prevalent in males than in females (54% vs. 46%). Similarly previous studies hypothesized that septicemia

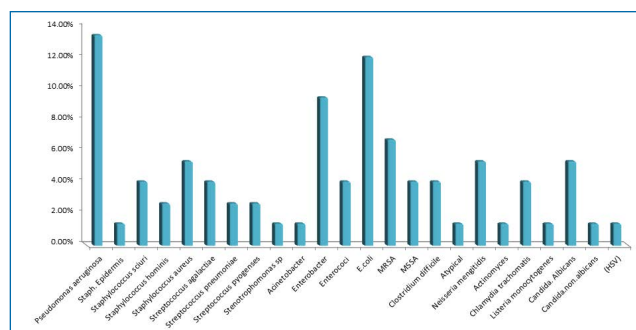


Figure 2. Distribution of microorganism isolates.

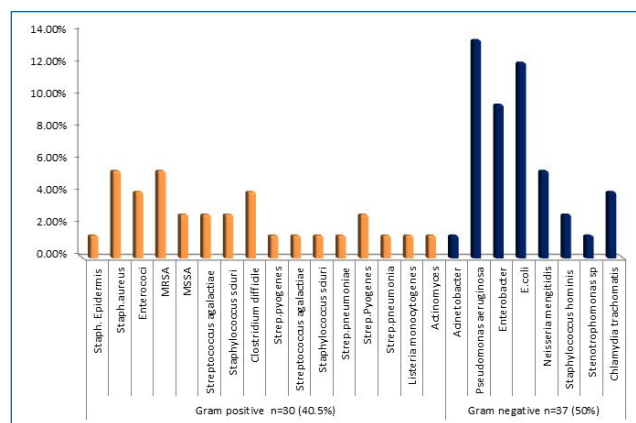


Figure 3. Distribution of isolated bacteria according to gram stain affinity.

was more in males than female neonates from 59%-82% because of factors which regulate gamma globulin on X chromosome³⁴.

The most common microorganism isolated from neonates in NICU was *Pseudomonas aeruginosa* (13.5%) followed by *E. coli* and *Enterobacter* (12.1%) and (9.5%) respectively. Other microorganisms isolated were *Methicillin Resistant Staphylococcus aureus* (MRSA) (6.8%), *Staph. aureus* (5.4%) and *Neisseria meningitidis* (5.4%).

In previous study by Jain *et al* showed that *Klebsiella spp.* and *S. aureus* are most common cause of early onset septicemia in NICU³⁵. In the present study, gram negative bacteria (50%) were the principle pathogen causing infection in the neonates especially *Pseudomonas aeruginosa* (13.5%) and *E. coli* (12.1%). A study by Roy I, Jain A *et al.*,^{32,36} showed similar results. Previous studies showed similar results indicated that gram-negative rods are the predominant microorganisms in NICU in Pakistan^{37,38}. This is in contrast to other studies showed that gram-positive cocci including *Staphylococcus aureus*, *Coagulase-negative staphylococci* and group B streptococci are the predominant agents^{39,40}.

The isolated bacteria included 5.4% *Staphylococcus aureus* which is lower than report of Narang A *et al.*, who reported 14.3% isolates of *Staphylococcus aureus*³⁶. A total of 40.5% gram positive organisms have been observed in the present study, which is higher than the results of I Roy *et al.*, who showed 28.57% gram positive organisms³². Amongst the gram positive organisms, *Staphylococcus aureus* was the predominant pathogen (5.4%). Vancomycin sensitivity was the higher among Gram negative bacterial isolates in the study (18.9%).

The major pathogenic species of *Candida* differ in their frequency, virulence and clinical associations. Recent surveys continue to support the long-established pattern of *C. albicans* as the most frequent cause of all forms of Candidiasis. *Candida parapsilosis* is increasingly being recognized as an important cause of invasive candidiasis in this population^{41,42}. *Candida* species have become important nosocomial pathogens in NICUs because the mechanisms of antifungal host defense that are poorly developed in neonates^{43,44} although *C. albicans* has been historically the most prominent species causing invasive fungal infections in premature infants, colonization and infection with non *C. albicans* spp. has also increased dramatically⁴⁵. In the present study, other than bacterial isolates, *Candida* species also isolated from neonates in NICU especially *Candida albicans* (5.4%) and non *Candida albicans* (1.4%). *Candida albicans* was susceptible to azoles, but some non *Candida albicans* spp. exhibited decreased susceptibility to these drugs.

Recent studies revealed high incidence of both *C. albicans* and non-*C. albicans* candida strains causing Vulvovaginitis among pregnant women in Beirut, Lebanon.

6. Conclusion and Recommendations

Gram negative bacteria specifically *Pseudomonas aeruginosa* and *E. coli* are the most common causes of infection of neonates in NICU. Pathogens causing neonatal infections exhibit varying antibiotic sensitivity pattern. However, the most sensitivity recorded was for vancomycin. It is therefore essential to monitor the epidemiology of neonatal infections and continuous surveillance for antibiotic susceptibility is needed to ensure proper empirical therapy. Additionally, the emerging multi

drug resistant microorganism such as *Acinetobacter* in NICUs could be a health risk in future.

The most commonly isolated bacteria in the present study can survive in the hospital environment therefore, strict infection control in neonatal units, rational use of antimicrobials, and protocols implementation are mandatory in the prevention of newborns infection.

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