

# Varicella Exposure in Neonatal Intensive Care Unit in a Low Resource Country: Successful Prophylaxis with Intravenous Immunoglobulins

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## ABSTRACT

**Background:** Varicella-zoster infection is a serious and potentially fatal disease, especially among newborns. Several studies have described postnatal varicella zoster exposure among neonates and reported on the efficacy of varicella-zoster immunoglobulins (VZIG) used as post-exposure prophylaxis. Unfortunately, VZIG is not available in Jordan. A limited number of studies have investigated the efficacy of intravenous immunoglobulins (IVIG) as an alternative preventive post-exposure to the varicella virus.

**Methods:** This retrospective descriptive study was conducted to review the outcomes of two separate incidents of varicella-zoster exposure and the prophylactic use of IVIG in the neonatal intensive care unit in Jordan.

**Results:** The sources of exposure in both incidents infected medical health workers. During the exposure, cohort measures were applied to neonates whose mothers did not receive immune prophylaxis against IVIG. Newborns were followed appropriately. Totally, 22 cases were identified representing two exposure incidents without a varicella-zoster infection.

**Conclusion:** The results indicated that IVIG was an effective prophylactic therapy for neonates post varicella virus exposure.

**Keywords:** Intravenous immunoglobulin, Neonate, Postnatal exposure, Prophylaxis, Varicella-zoster

## Introduction

Varicella-zoster infection is a serious and often fatal disease, especially among newborns (1). Hence, a varicella-zoster outbreak could yield tragic results (2). Several prior studies have reported postnatal varicella-zoster neonatal exposure (3-6). As well, the efficacy of varicella-zoster immunoglobulins (VZIG) used as post-exposure prophylaxis is well documented, especially among preterm neonates with a gestational age of lower than 28 weeks and weighing less than 1000 g at birth (7).

Unfortunately, VZIG is not available in Jordan. Alternatively, a limited number of studies have investigated the efficacy of intravenous immunoglobulins (IVIG) in preventing post-exposure varicella (8, 9). The varicella vaccine is

not a part of the national program in Jordan; thus, chickenpox is a common childhood disease. Furthermore, the proof of varicella immunity is not a requirement for health care workers. Consequently, affected adults are frequently observed in intensive care units in Jordan hospitals.

In this study, two incidents of varicella-zoster exposure were reported in neonatal intensive care unit (NICU) affiliated with Jordan University Hospital. The control measures used a type of post-exposure prophylaxis and the outcomes were also reported.

## Methods

This retrospective study included a review

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of medical charts and laboratory results. All neonates that received IVIG following postnatal exposure to varicella-zoster were included. The data in this retrospective study is part of the IVIG use among neonates. It was reviewed and approved by the Scientific Research of the University of Jordan and Institutional Review Board of Jordan University Hospital.

### Sampling

All premature neonates admitted to the neonatal unit at the time of both varicella exposure incidents who received IVIG therapy were included in this study.

### Setting

The NICU affiliated with Jordan University Hospital is a level three unit with a 30-bed capacity. Parents may stay in the unit and visit at any time; however, relatives and children are not allowed to enter the unit. There are three isolation rooms and four additional separate areas, each with a 6-8 bed capacity. A common entrance provides access to all areas; however, each area can be closed and separated from the other rooms in the unit.

### Description of varicella exposure incidents

The first varicella-zoster exposure occurred in 2012. A 26-year-old pediatric resident developed chickenpox during an NICU rotation. The resident exhibited mild symptoms two days prior to the appearance of a vesicular rash. Neonates were considered exposed if they stayed in NICU any time during the days the resident was ill.

In 2016, a 24-year-old neonatal nurse was diagnosed with chickenpox after working two days with an undiagnosed rash and mild systemic symptoms. Neonates in the unit from the start of her symptoms were considered exposed.

### Control measures

The isolation or cohorting of the exposed neonates from the new admissions was imposed. Staff with no prior exposure to varicella-zoster disease were not assigned to care for the new admissions. Further, the non-immune staff was encouraged to receive the varicella vaccine.

### Post-exposure prophylaxis

All preterm neonates were lower than 28 weeks or with a gestational age of  $\geq 28$  weeks and were born to mothers with an undocumented varicella immune status received IVIG (0.5 g/kg) over four hours, with administration initiated within 24 hours of identifying the index case. Two newborns included in this report received IVIG 5-7 days prior to the identification of the index case for the treatment of thrombocytopenia and isoimmune hemolytic anemia. These two neonates did not receive the second dose of IVIG.

### Statistical analysis

Means and standard deviations are provided for continuous variables, while frequencies and relative percentages are reported for categorical variables.

### Results

Totally, newborns with a mean gestational age of 31.3 weeks and a mean birth weight of 1676 g were included in the study. Of the neonates included in the study, 69% were male. The mean length of hospital stays in the NICU after exposure was 15.4 days. Demographic data are presented in Table 1. The neonates requiring hospitalization for  $<7$  days post-exposure were followed as outpatients. None of the newborns included in the study developed the disease, and there were no reported side effects of IVIG therapy.

**Table 1.** Demographic and clinical characteristics of varicella-zoster exposed neonates treated with IVIG

Character	(Mean $\pm$ SD)/Frequency
Gestational age	31.3 week $\pm$ 3.5
Birth weight	1676 g $\pm$ 609
Maternal age	28.1 years $\pm$ 3.9
C/S	17 (77%)
Male gender	9 (41%)
GA $< 28$ weeks	4 (18%)
GA $\geq 28$ and undocumented maternal immunity	18 (82%)
Length of hospital stay in post exposure	15.4 days $\pm$ 12

## Discussion

The definition of postnatal exposure is typically based on the identification of any contact between the newborn and the index case. The management of postnatal exposure to the varicella-zoster virus consists of isolation and post-exposure prophylaxis (7, 10, 11), with the type of intervention depending on several factors, mainly maternal serologic status, and gestational age (7).

All of the newborns admitted to NICU in Jordan University Hospital during both exposure incidents were considered exposed. All of these neonates were cohorted in separate areas and isolated from newly admitted patients for approximately 10 days after exposure or until discharge. Furthermore, specific areas were designated for newly admitted patients, and medical staff with a history of varicella-zoster disease were assigned to care for the new admissions.

Post-exposure prophylaxis primarily consists of the administration of varicella-zoster specific immunoglobulin (7, 9). Nonetheless, a limited number of studies have reported the use of acyclovir therapy (12) and intravenous immunoglobulins (8). Reportedly, post-exposure prophylaxis can prevent the disease or aids in mitigating disease severity (13).

The VZIG is recommended by the centers for disease control and prevention for the treatment of postnatal varicella-zoster exposure (7). Specifically, the administration of VZIG was indicated in premature neonates born with the gestational age of < 28 weeks, or newborns whose birth weight was < 1000 g, regardless of maternal immunity status. For those born with  $\geq$  28 weeks gestation, post-exposure prophylaxis was only indicated when maternal immunity could not be determined by serologic testing, prior varicella infection, or by documentation of prior vaccination (7). Due to the scarcity of existing literature on the use of IVIG (8), it is only considered as alternative prophylaxis if VZIG is unavailable (7). In the latter case, close monitoring for early signs of sickness in exposed neonates is mandatory for providing acyclovir treatment.

In this study, IVIG was used as an alternative to VZIG due to the unavailability of VZIG in Jordan. Accordingly, the VZIG eligibility criteria recommended by the CDC was applied and IVIG was administered to newborns that were below 28 weeks of gestational age and to a group of neonates with > 28 weeks for whom maternal

immunity could not be documented (7). The neonates who received IVIG did not develop varicella disease or experience any complications. This is a retrospective study with a small sample size. Larger prospective studies are needed to confirm the results.

## Conclusion

The IVIG appears to be a safe and effective alternative to VZIG for the prevention of post-exposure varicella among neonates. Nonetheless, due to the retrospective nature of the study, larger sample sizes are needed to confirm the results. Additionally, health care facilities in Jordan should require proof of varicella immunity among employees, especially those working with vulnerable hosts.

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## Conflicts of interests

The authors have no conflicts of interest to declare.

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