MedCrave
Step into the World of Research

Journal of Pediatrics and Neonatal Care

Oral Nystatin: An Effective Prophylaxis for Fungal Infection in Preterm Babies in a Tertiary Level Hospital

Abstract

Introduction: Candida is a common cause of oral mucous membrane and skin infections in newborn infants and an important cause of neonatal morbidity and mortality.

Methods: This Quasi experimental study was carried out in NCU, Department of Paediatrics, Sir Salimullah Medical College Mitford Hospital, Dhaka, over a period of 16months, to find out the efficacy of oral Nystatin in reducing colonization of fungus and fungaemia in preterm babies admitted in NCU. One hundred sixty consecutive preterm babies admitted in NCU within 72 hours of birth fulfilling the inclusion criteria were enrolled. Every alternate baby was taken as case and another was taken as control and the first one selected by lottery. Case group received oral Nystatin prophylaxis 1lacs unit 6 hourly for five days and control group given usual NCU care without antifungal prophylaxis. Babies were examined daily. Swab from oral mucous membrane was collected for gram staining, wet film preparation for direct microscopy and culture for fungus and blood culture for fungus and bacteria.

Results: The mean age of enrolled babies was 23.9±19.3 hours in case and 19.3±17.8 hours in control groups. Both the groups were similar regarding GA, sex, mode of delivery, anthropometry, duration of antibiotics uses, and mean hospital stay. Gram staining, wet film preparation with 20% KOH for direct microscopic examination and culture of oral swab and blood culture of cases & controls at baseline and follow up revealed no Candida or any other fungus. However, Gram staining of oral swab revealed Gram positive cocci both in case and control groups at base line and at follow up which was not significant. Both oral swab culture and Blood culture developed growth of various organisms without any fungus both in case and in controls at base line and at follow up, which was also not significant.

Conclusion & Recommendations: The present study revealed that Gram staining of oral swab, wet film preparation and culture of oral swab and blood at baseline and at follow up, 5 days after enrollment did not grow any fungus in both cases and controls. So Nystatin prophylaxis in the case was of no use in preventing oral colonization of fungus and fungaemia. For generalization of this hypothesis further multicenter study with a large sample size and longer duration of follow up is required.

Research Article

Volume 5 Issue 9 - 2016

Shafiqul Islam[1]*, Kamrul Ahsan Khan[2], Nazmun Nahar[3], Muzibur Rahman[4], ARM Lutful Kabir[5] and Sayeeda Afroza[6]

[1]*Department of Pediatrics, Central Police Hospital, Bangladesh*
[2]*Department of Neonatology, Sheikh Sayera Khatun Medical College, Bangladesh*
[3]*Department of Neonatology, MH Samorita Hospital & Medical College, Bangladesh*
[4]*Department of Neonatology, Institute of Child & Mother Health, Bangladesh*
[5]*Department of Pediatrics, Shahid Sohrawardy Medical College, Bangladesh*
[6]*Department of Pediatrics, Sir Salimullah Medical College, Bangladesh*

***Corresponding author:** Shafiqul Islam, Senior consultant Department of Pediatrics, Central Police Hospital, Dhaka, Bangladesh, Tel: 01711708500, Email: dr.shafiq98@gmail.com

Received: October 30, 2016 | **Published:** December 29, 2016

Introduction

Candida is a common cause of oral mucous membrane and skin infections in newborn infants. Disseminated candidiasis and Candidemia have become a frequent problem in neonatal intensive care unit [1]. *Candida* species are frequently encountered as part of the human commensal flora. Colonization by *Candida spp.* is the most important risk factor for development of Candidemia and IFI in premature infants [2]. In the immunocompromised host, fungi often invade skin, mucosa, tissues and bloodstream causing significant morbidity and mortality [3,4].

Skin colonization is common after 2 week of age. H_2 blockers, broad-spectrum cephalosporin, and delayed enteral feedings and altered gastrointestinal tract ecology facilitate colonization [1]. Pregnancy increases the rate of maternal vaginal colonization from <20% to >30% and maternal colonization rates at time of delivery correlate with the colonization rates of the newborns [1]. Other neonatal risk factors for invasive candidiasis include prematurity, VLBW, difficult birth, broad-spectrum antibiotic administration, abdominal surgery, prolong ventilator support, prolong intravenous catheterization, corticosteroid administration, the use of theophylline and parenteral therapy and gastrointestinal tract pathology [1, 5,6,7]. Health care workers (HCWs) play an important role in the transmission of yeasts. *Candida* species are frequently isolated from the hands of HCWs and can be transmitted from their hands to patients [4]. Although the etiology of neonatal fungal infection is multifactorial, LBW or extreme prematurity is an independent risk factor for invasive fungal infection (IFI), probably because of the degree of immunological immaturity. VLBW babies (<1500 g), are at greatest risk and the incidence rises with falling birth weight [8,9]. Approximately 10% of full-term infants become colonized

in the gastrointestinal and respiratory tract in the 1st 5 days of life; the colonization rate in infants weighing <1,500g approaches 30% [1]. The overall incidence of invasive fungal infection (IFI) varies in different studies and different countries. The estimated incidence of IFI is 1.6-10% in VLBW and 10 to 26% in ELBW neonates with a crude mortality of 30-75% [8-10].

In the recent years new opportunities for the diagnosis, treatment and prevention of fungal infections in preterm babies have become available in Bangladesh. Meta-analysis revealed that oral/topical non-absorbed prophylaxis significantly reduces the risk of invasive fungal infection (IFI) in VLBW infants. There is evidence of reduced incidence of fungaemia from 12% to 1.8% in all VLBW babies in NICU after introduction of oral Nystatin prophylaxis, and it has appeared effective, well tolerated, safer and cheaper, than Fluconazole.

In Bangladesh either oral Nystatin or systemic Fluconazole is commonly being used to treat oral thrush and to prevent fungaemia in newborns. However, the efficacy of the Nystatin has not yet been tested in Bangladeshi preterm babies. Data are scarce in this field. This prospective interventional study has been carried out to find the efficacy of oral Nystatin in reducing colonization of fungus and fungaemia in preterm LBW babies in NCU of Sir Salimullah Medical College & Mitford Hospital, Dhaka (Figure 1).

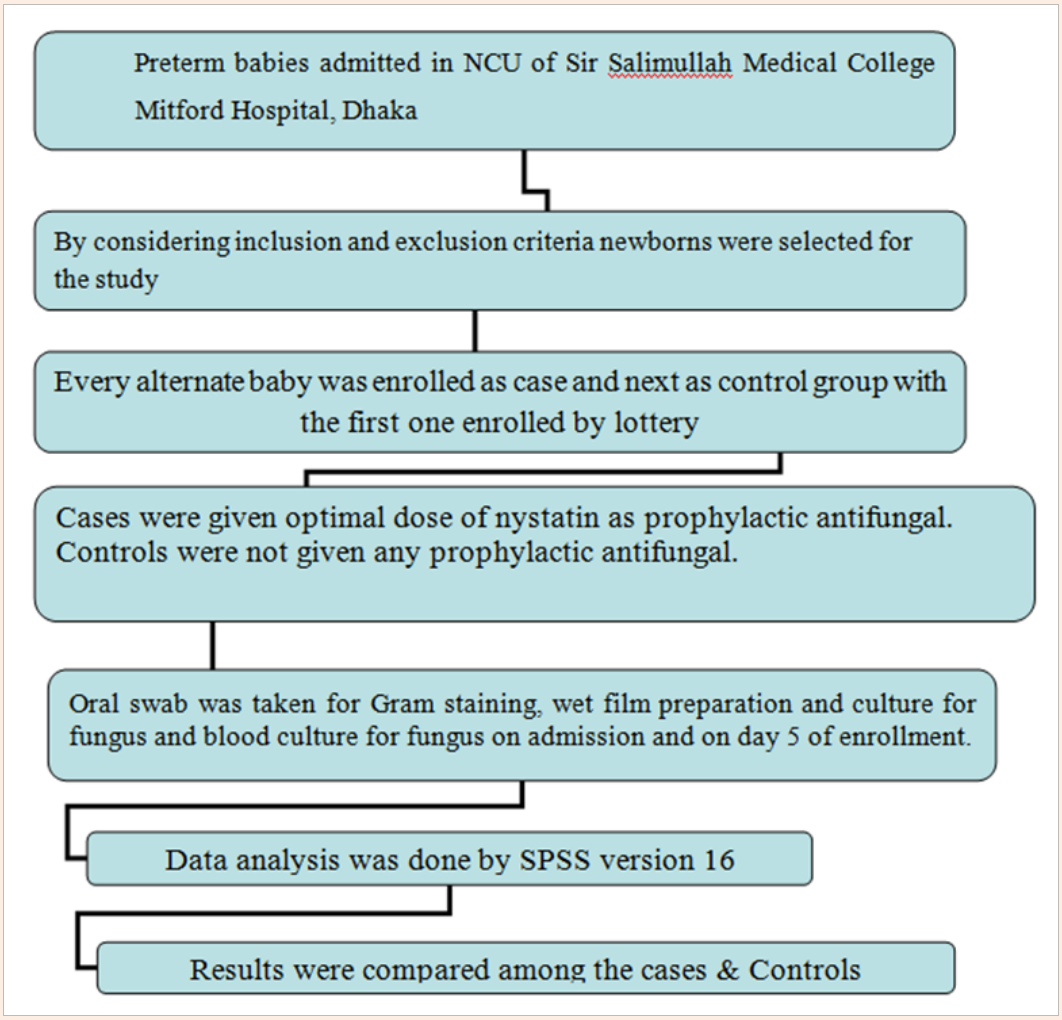

Figure 1: Preterm LBW babies in NCU of Sir Salimullah Medical College & Mitford Hospital, Dhaka.

Methodology

This Quasi experimental study has been carried out in the Neonatal Care Unit of the Department of Paediatrics of Sir Salimullah Medical College & Mitford Hospital, Dhaka from July 2010 to October 2011. Preterm and LBW babies admitted in the NCU of SSMH & MH fulfilling the inclusion criteria were eligible for enrollment. Total 160 babies have been enrolled by purposive method. Preterm and LBW babies admitted in NCU within 72 hours of birth having no oral thrush clinically, and parents or

legal attendants of whom has given voluntary informed consent has been enrolled. Newborns admitted after 72 hours of birth, or babies having oral thrush, congenital defects requiring surgical intervention, critically ill newborns having severe perinatal asphyxia, respiratory distress syndrome, septicemia, neonatal convulsion etc. has been excluded.

After enrollment every alternate baby was taken as case and another was taken as control. First case was taken by lottery. Both cases and controls had 80 babies in each group. Case was defined as preterm babies within 72 hours of birth admitted in NCU with clinically no oral thrush who were given prophylactic antifungal agent. Control was defined as preterm babies within 72 hours of birth admitted in NCU with clinically no oral thrush who were not given prophylactic antifungal agent. The optimal dose of Nystatin was 100,000 U in 1 ml 6-hourly. The oral cavity was coated with Nystatin suspension by instilling on the tongue drop by drop over 3 minutes. This was continued 6 hourly for 5 days [11]. Nystatin was given after feeding to the babies who were on enteral food. The babies who were on NG or parenteral feeding Nystatin was given to them 6 hourly without considering their time of feeding.

Detail information regarding gestation, birth weight, gender was recorded in a coded data collection sheet. Oral swab was taken soon after admission by a sterile swab supplied by microbiology lab of SSMC, and gram staining done to see the fungus and organism and direct microscopic examination was done with wet film preparation with 20% KOH (potassium hydroxide) solution to see the fungus (Yeast and Pseudohyphi). Culture of oral swab for fungus was done in Saboroids Agar or Blood agar media which was available in the lab and fungus identification was done by wet film preparation with KOH solution. The same procedure of oral swab gram stating and wet film preparation and culture of oral swab was repeated on day 5 after admission. Blood culture for fungus was done in each preterm baby admitted at NCU on day 1 and on day 5 after admission. Blood culture was done in Blood agar media or Saboroids agar media and subculture was done in Trypticase Soya broth. Identification of fungus was done by gram staining and direct microscopic examination with wet film preparation with 20% KOH solution. Both blood culture and oral swab culture for bacteria and fungus was done in the dept. of Microbiology of SSMC & Mitford Hospital.

Name of antibiotics used, their duration, and duration of hospital stay in days were also noted. The protocol of this study was approved by the 'Ethical Review Committee' of Sir Salimullah Medical College, Dhaka.

Data was analyzed by using a computer based statistical program SPSS (Statistical Package for Social Sciences) version 16. Quantitative data was expressed as mean (±SD) and qualitative data as frequency (%), and compared by student's t test and chi-square test respectively. Graphs and tables were constructed for easy visualization of the observation. 95% confidence interval was calculated and p value <0.05 was considered as significant.

Operational definition

Invasive neonatal fungaemia: was defined as a baby with (1) clinical signs of sepsis, for example, apnea, bradycardia, fever, hypothermia, tachycardia, tachypnea; and (2) a positive culture of a fungus from blood.

Preterm babies: Babies born before 37 completed weeks of gestation.

Low Birth Weight: Newborn babies having birth weight of <2500gms.

Results and Observations: To find out the efficacy of oral Nystatin in reducing the colonization and prevalence of fungaemia 160 preterm babies were studied. Eighty of them were in case group and 80 were in control group (Tables 1-5).

Table 1: Comparison of Baseline characteristics between cases (n=80) and controls (n=80).

Characteristics		Cases (80)	Controls (80)	p
Age group	Up to 24 hours	50(62.5%)	51(63.8%)	0.32
Frequency (%)	24-48 hours	21(26.3%)	25(31.3%)	
	48-72 hours	9(11.3%)	4(5.0%)	
Sex Frequency (%)	Male	49(61.3%)	45(56.3%)	0.521
	Female	31(38.8%)	35(43.8%)	
Mode of delivery	LUCS	38(47.5%)	31(38.7%)	0.635
	NVD	42(52.5%)	49(61.3%)	
Gestational age (weeks)	<28	4(5.0%)	0(0.0%)	0.088
	28 - <32	12(15.0%)	17(21.3%)	
	32 - <37	64(80.0%)	63(78.7%)	
	Mean (±SD)	33.16 (± 2.7)	33.2 (±2.4)	0.926
Supine length (cm)	Mean (±SD)	41.9(±4.3)	42.4(±4.2)	0.498
OFC(cm)	Mean (±SD)	30.3(±2.5)	30.4(±2.75)	0.964
Weight (Gm)	<999.9	3(3.8%)	1(1.3%)	0.18
	1000 - 1499.9	17(21.2%)	28(35.0%)	
	1500 - 2499.9	60(75.0%)	51(63.7%)	

Both the cases and control groups were comparable regarding age, sex, weight, supine length, OFC.

The mean age of enrolled babies was 23.9±19.3 hours in case and 19.3±17.8 hours in control groups respectively which was not statistically significant (p>0.05).

Table 2: Comparison of mean NCU stay and duration of antibiotics between cases (n=80) and controls (n=80).

Duration in days	Case	Control	P-value
NCU stay mean(±SD) Range	6.6(±4.6) 1-27	7.7 (±5.9) 1=27	0.179
Antibiotic use mean(±SD) Range	6.3(±3.8) 1-22	6.8 (±4.0) 1-20	0.398

Mean NCU stay and duration of antibiotics did not differ significantly between cases and controls (p>0.05).

Table 3: Comparison of use of antibiotics in cases (n=80) and controls (n=80).

Antibiotics used	Case Frequency (%)	Controls Frequency (%)	P-value
Ampicillin	71(88.8%)	72(90.0%)	0.798
Gentamicin	71(88.8%)	72(90.0%)	0.798
Ceftazidime	35(43.8%)	31(38.8%)	0.614
Amikacin	35(43.8%)	31(38.8%)	0.521
Meropenem	8(10.0%)	7(8.8%)	0.786
Ciprofloxacin	7(8.8%)	10(12.5%)	0.442
Metronidazole	11(13.8%)	9(11.3%)	0.633

Similar types of antibiotics were used in both the groups (p>0.05).

Table 4: Comparison of Gram staining findings of oral swab, culture of oral swab and blood culture at enrollment between cases (n=80) and controls (n=80).

Organism/Fungus	Case (80) Frequency (%)	Control (80) Frequency (%)	p-value
Gram staining of oral swab			
Fungus	0(0.0%)	0(0.0%)	
Gram positive cocci	15(18.8%)	12(15.0%)	0.807
Oral swab culture for fungus			
Fungus	0.00%	0.00%	-
CONS	3(3.8%)	1(1.3%)	
E coli	1(1.3%)	1(1.3%)	
Staph aureus	1(1.3%)	0(0.0%)	
Total	5(6.4%)	2(2.5%)	0.5
Blood culture for fungus			
Fungus	0.00%	0.00%	-
Acinatobacter	2(2.5%)	1(1.3%)	
Citarobacter	1(1.3%)	0(0.0%)	
CoNS	2(2.5%)	10(12.5%)	
E coli	1(1.3%)	2(2.5%)	
Pseudomonas	2(2.5%)	2(2.5%)	
Serratia	1(1.3%)	2(2.5%)	
Staph aureus	1(1.3%)	0(0.0%)	
Staph. epidermidis	1(1.3%)	0(0.0%)	
Total	11(13.8%)	17(21.3%)	0. 294

Table 5: Comparison of Gram staining findings and culture of oral swab and blood culture for fungus on day 5 between cases (n=48) and controls (n=50).

Organism/Fungus	Case (48)# Frequency (%)	Control (50)# Frequency (%)	*p*-value
Gram staining of oral swab			
Fungus	0(0.0%)	0(0.0%)	-
Gram positive cocci	6(7.6%)	7(8.8%)	0.952
Oral swab culture for fungus			
Fungus	0.00%	0.00%	-
Acinatobacter	0(0.0%)	1(2.0%)	
CONS	1(2.1%)	0(0.0%)	
E coli	1(2.1%)	0(0.0%)	
Staph aureus	1(2.1%)	0(0.0%)	
Total	3(6.3%)	1(2.0%)	0.403
Blood culture at follow up			
Fungus	0.00%	0.00%	-
CoNS	1(2.1%)	0(0.0%)	
E coli	3(6.2%)	1(2.0%)	
Pseudomonas	0(0.0%)	2(4.0%)	
Total	4(8.3%)	3(6.0%)	0.699

Gram staining revealed no fungus either in case or in control group. Similarly oral swab culture and blood culture for fungus revealed no fungal growth. Organism grown in both the groups were also not significant statistically.

Gram staining, oral swab culture and blood culture revealed no fungus either in cases or in control group. Presence of different organisms in both groups at follow up was not statistically significant (p>0.05).

Some 2nd samples (oral swab for stating, culture and blood culture sample) in both cases (32) and controls (30) could not be collected due to death of babies from comorbidities like late onset sepsis, DIC, etc., left against medical advice due to financial constraints, discharge on request, referral of the critical babies to other hospital with NICU facilities.

Gram staining, oral swab culture and blood culture revealed no fungus either in cases or in control group. Presence of different organisms in both groups at follow up was not statistically significant (p>0.05).

Some 2nd samples (oral swab for stating, culture and blood culture sample) in both cases (32) and controls (30) could not be collected due to death of babies from comorbidities like late onset sepsis, DIC, etc., left against medical advice due to financial constraints, discharge on request, referral of the critical babies to other hospital with NICU facilities.

Citation: Islam S, Khan KA, Nahar N, Rahman M, Kabir ARLM, et al. (2016) Oral Nystatin: An Effective Prophylaxis for Fungal Infection in Preterm Babies in a Tertiary Level Hospital. J Pediatr Neonatal Care 5(9): 00226. DOI: 10.15406/jpnc.2016.05.00226

Discussion

To find out the efficacy of oral Nystatin in reducing the colonization and prevalence of fungaemia in preterm LBW babies, total 160 babies were studied. Eighty of them were in case group and another 80 were in control group.

The study included preterm LBW babies because these babies are more prone to develop IFI. The case and control groups were similar in terms of age, sex and anthropometry. The mean (±SD) age of the babies of case and control groups were 23.9(±19.3) and 19.3(±17.8) hours respectively, which was not significant. Both the groups were comparable regarding gestational age, sex, anthropometric measurements.

The present study found that 52.5% babies in case and 61.3% babies in control groups were born by vaginal delivery. Different studies identified vaginal delivery as one of the risk factor for fungal colonization. These could not be verified in our study as no fungus has grown in this study and the mode of delivery in both case and control groups were comparable. Cochrane Database stated that both cohort and case control studies have identified vaginal birth as one of the risk factors for superficial fungal infection (SFI). Mahieu et al. [12] described that maternal vaginal candidiasis, birth weight below 1000 g, and vaginal delivery were associated with *Candida* colonization. Study by Mendiratta et al. [13] and Shetty et al. [14] also found vaginal colonization of mothers as a significant risk factors for colonization of babies. These also could not be validated in this study [15,16].

The mean duration of antibiotics was 6.3 days in case group and 6.8 days in control groups respectively. Duration of antibiotics is one of the risk factors for the development of SFI and IFI. Many studies identified, broad spectrum antibiotic administration as a neonatal risk factor for invasive candidiasis [1,3,5,7]. Longer duration of antibiotic treatment was identified as risk factors for SFI in cohort and case control studies [17]. In a retrospective review found that treatment with third-generation Cephalosporins subsequently developed Candidemia [18].

The present study found that in Gram staining of oral swab at baseline revealed Gram positive cocci in 15(18.8%) patients in case and 12(15.0%) patients in control and at follow up revealed Gram positive cocci in 6 (12.5%) patients in cases and 7(14.0%) patients in controls. Oral swab culture at baseline developed growth of various organisms in 5(6.4%) patients in cases and 2 (2.5%) patients in control group. Oral swab culture at follow up on day5 developed growth of various organisms in 3(6.3%) patients in cases and 1(2.0%) patient in control group. The slight reduction in the number of organisms at follow up in Gram staining and culture of oral swab in both case and control group may be due to administration of antibiotics during NCU stay.

Blood culture at baseline developed growth of various organisms in 11(13.8%) babies in cases and 17(21.3%) babies in controls. Blood culture at follow up developed growth of various organisms in 4(8.3%) babies in cases and 3(6.0%) babies in control group. The organisms were *acinatobacter*, *citarobacter*, CoNS, *E coli*, *pseudomonas*, *serratia* and *staph aureus* and *epidermidis*. The reduction of number of organisms at follows up in blood culture in both case and control group may be due to administration of several antibiotics during NCU treatment. Our findings are supported by Benjamin et al [16].

Gram staining and culture of oral swab and culture of blood at baseline and at follow up revealed no fungus in cases or in control group. The findings of the present study are not consistent with findings of others [1,3,8,9]. They stated that disseminated candidiasis and Candidemia have become a frequent problem in NICU because the early NICU course and VLBW favors the colonization and proliferation of fungi. Our patients were admitted in NCU within 72 hours of birth. Weisse & Aronoff [1] stated that *Candida* skin colonization is common after 2 weeks of age [1]. This may be one of the causes why we did not find any fungus in Gram staining or culture of oral swab and blood culture, as all samples have been collected within 8 days of birth.

The calculated sample size of the study was 105 cases and 105 controls. But due to financial and time constraints, data has been collected from 80 cases and 80 controls. Again 2nd sample could not be collected in all those babies due to death, LAMA, DOR, urgent referral to other hospital. For this reason second sample of oral swab and blood culture could only be collected in 48 babies in cases and 50 babies in control. These factors might also be another reason of not getting any fungal growth in cases and controls. More over the 2nd samples were taken 5 days after admission i.e. on day 8 post natal age, which might be another reason of not getting any fungal growth on 2nd samples. In some literatures it has been seen that the age of onset of disseminated fungal infection among NICU babies has a wide range, with the mean onset of infection ranges from 15 to 33 days of age [19]. SFI occurs from the 2nd wk. of life [18]. Candida skin colonization is common after 2 wks of age in VLBW baby. Thrush may develop at 7-10 days of age [1]. Invasive fungal dermatitis developed at mean age of 9 days with a range of 6-14 days [19].

Conclusion and Recommendation

The present study found that preterm LBW babies admitted in NCU within 72 hours of birth did not develop any fungal colonization in oral cavity or fungaemia on admission and after 5 days of admission with or without oral Nystatin prophylaxis. So, oral Nystatin prophylaxis in the cases were of no use in preventing oral colonization of fungus and fungaemia, as there was no evidence of fungal colonization in oral swab or in blood culture among cases and controls. For generalization of this hypothesis further multicenter study with a large sample size and longer duration of follow up is required.

Limitations of the study

The present study has some limitations. The calculated sample size of the study was 105 cases and 105 controls, but due to time and financial constrains 80 babies were enrolled in each groups. Again 2nd sample could not be collected in all those babies due to death, LAMA, and DOR, referral of critical babies to hospital where NICU facilities are available. All the samples were collected within day 8 post natal age. Babies could not be followed up for a longer

time due to financial constraints of the care giver. Department of Microbiology of SSMC Mitford Hospital has resource constrain and were unable to do more than 160 samples for Gram staining and culture of oral swab and blood culture.

References

1. Weisse ME, Aronoff SC (2008) Candida. In: Kliegman RM, Behrman RE, Jenson HB and Stanton BF, (Eds.), Nelson Textbook of Paediatrics. (18th edn), Elsevier, India, pp. 1307-1310.
2. Manzoni P, Farina D, Galletto P, Leonessa M, Priolo C, et al. (2007) Type and number of sites colonized by fungi and risk of progression to invasive fungal infection in preterm neonates in neonatal intensive care unit. J Perinat Med 35(3): 220-226.
3. Kaufman D (2004) Fungal infection in the very low birth weight infant. Current Opinion in Infectious Diseases 17(3): 253-259.
4. Lunel FMV, Meis JF, Voss A (1999) Nosocomial fungal infections: Candidemia. Diagn Microbiol Infect Dis 34: 213-220.
5. O'Grady MJ, Dempsey EM (2008) Antifungal prophylaxis for the prevention of neonatal candidiasis. Acta paediatrica 97(4): 430-433.
6. Kaufman D, Fairchild KD (2004) Clinical microbiology of bacterial and fungal sepsis in very-low-birth weight infants. Clinical Microbiology Review 17(3): 638-680.
7. Ozturk MA, Gunes T, Koklu E, Cetin N, Kot N (2006) Oral Nystatin prophylaxis to prevent invasive candidiasis in Neonatal Intensive Care Unit. Mycoses 49(6): 484-492.
8. Howell A, Isaacs D, Halliday R (2009) Oral Nystatin prophylaxis and neonatal fungal infections. Arch Dis Child Fetal Neonatal Ed 94(6): 429-433.
9. Isaacs D (2008) Fungal prophylaxis in very low birth weight neonates: Nystatin, fluconazole or nothing? Curr Opin Infect Dis 21(3): 246-250.
10. Manzoni P, Monstert M, Agriesti G, Priolo C, Galletto P, et al. (2007) Neonatal fungal infections: the state of the art. J Chemother 19(2): 42-45.
11. McIntosh N, Stenson B (2008) The Newborn. In: McIntosh N, Helms P, Smyth R, (Eds.), Forfar and Arneils's Text book of Pediatrics. (6th edn) Churchill Living stone, Eddinburgh, pp. 177-357.
12. Mahieu LM, Van GN, Wildemeersch D, Jansens H, Ieven M (2010) Number of sites of perinatal Candida colonization and neutropenia are associated with nosocomial candidemia in the neonatal intensive care unit patient. Pediatr Crit Care Med 11(2): 240-245.
13. Mendiratta DK, Rawat V, Thamke D, Chaturvedi P, Chhabra S et al. (2006) Candida colonization in preterm babies admitted to neonatal intensive care unit in the rural setting. Indian J Med Microbiol 24(4): 263-267.
14. Shetty SS, Harrison LH, Hajjeh RA, Taylor T, Mirza SA, et al. (2005) Determining risk factors for candidemia among newborn infants from population-based surveillance: Baltimore, Maryland. Pediatr Infect Dis J 24(7):601-604.
15. Austin NC, Darlow B (2013) Prophylactic oral antifungal agents to prevent systemic Candida infection in preterm infants. The Cochrane Database of Systematic Reviews (Protocol) 2012:3.
16. Benjamin DKJ, Ross K, McKinney REJ, Benjamin DK, Auten R, et al. (2000) When to suspect fungal infection in neonates: A clinical comparison of Candida albicans and Candida paraspilosis fungemia with coagulase-negative staphylococcal bacteremia. Pediatrics 106(4):712-718.
17. (2004) Americam Society of Microbiology, Clinical Microbiology Reviews 638-680.
18. Austin NC, Darlow B (2004) Prophylactic oral antifungal agents to prevent systemic Candida infection in preterm infants. Cochrane Database of Systematic Reviews 1: CD003478.
19. Ruan SY, Hsueh PR (2009) Invasive candidiasis: an overview from Taiwan. J Formos Med Assoc 108: 443-451.

Citation: Islam S, Khan KA, Nahar N, Rahman M, Kabir ARLM, et al. (2016) Oral Nystatin: An Effective Prophylaxis for Fungal Infection in Preterm Babies in a Tertiary Level Hospital. J Pediatr Neonatal Care 5(9): 00226. DOI: 10.15406/jpnc.2016.05.00226