

Neonatal Candidiasis

Alice Pong, MD (Rady Children's)



Neonatal Candidiasis

- ▶ Congenital Candidiasis
 - ▶ Congenital Cutaneous Candidiasis
 - ▶ Relatively uncommon in term neonates and generally benign
 - ▶ More severe in preterm infants (<27 weeks GA, <1000 g)



TABLE 1. Characteristics of Neonates With Congenital Cutaneous Candidiasis*

	<1000 g (n = 15)	1000–2500 g (n = 21)	>2500 g (n = 27)
Maternal factor			
IUD	7	1	0
Chorioamnionitis/funisitis	5	3	7
Presentation of rash			
First day of life	6	21	24
Days 1–2	4	0	1
Days 3–4	3	0	1
Days 5–6	2	0	1
White blood cell count			
Mean, range, n	17.8, 7.0–27.0, 4	31.1, 3.2–61.0, 9	33.1, 19.0–87.0, 14
Positive cultures for <i>Candida</i>			
Blood	7	2	0
Urine	5	5	2
Cerebrospinal fluid	4	0	1
Antifungal treatment			
Topical	1	8	22
Oral	1	4	18
Systemic antifungal agents	6	11	1
Outcome			
Survival	9	18	25
Death	6	3	1 ₁

* Based on references 2–37, which clearly described the presence of CCC and reported birth weight and outcome.

₁ An additional infant died at 2 hours of age with a diaphragmatic hernia.³⁷

Darmstadt GL et al, Congenital Cutaneous Candidiasis: Clinical Presentation, Pathogenesis, and Management Guidelines, Pediatrics 2000

Congenital Cutaneous Candidiasis

- ▶ Review of 2 large NICUs 2004-2015
- ▶ 0.1% NICU admissions, 0.6% infants <1000 g
- ▶ 90% in preterm infants (<37 weeks GA)



Table 1. Congenital Cutaneous Candidiasis: Maternal and Infant Characteristics

Characteristic	N = 21
Infant	
Gestational age, weeks	26 3/7 (23–40 4/7)
Birth weight, g	950 (640–3770)
Male	62% (13 of 21)
Vaginal delivery	81% (17 of 21)
Rupture of membranes	81% (17 of 21)
≥12 hours	38% (8 of 21)
≥2 days	24% (5 of 21)
Cerclage	10% (2 of 21)
Maternal	
Maternal age, y	25 (17–41)
Maternal race	
White	45% (9 of 20)
African American	55% (11 of 20)
Maternal antibiotics	90% (19 of 21)
Antenatal steroids	95% (19 of 20)
Maternal vaginosis during pregnancy	47% (8 of 17)
Histologic chorioamnionitis	100% (11 of 11)
Yeast identified on placental pathology	18% (2 of 11)

Values are presented as median (range).

Postnatal Neonatal Candidiasis

- ▶ Multicenter study (19 centers)
 - ▶ 1515 infants <1000 g enrolled
 - ▶ 137 developed candidiasis (positive sterile site culture)
- Most were vaginal delivery, <25 weeks GA, <750 g

TABLE 1 Demographic and Center Differences for Incidence of Candidiasis

Variable	Positive Sterile Culture for <i>Candida</i> , % (n/N)	Odds Ratio (95% CI) vs Reference Category	Unadjusted P
Mode of delivery			
Vaginal	14 (64/464)	2.14 (1.5–3.06)	<.0001
Cesarean delivery (reference)	7 (73/1051)	—	
Antenatal antibiotics			
1 = Yes	10 (96/941)	1.53 (1.04–2.25)	.0308
2 = No (reference)	7 (39/564)	—	
Race			
Black	10 (62/606)	1.24 (0.86–1.77)	.2531
Other	5 (3/62)	0.55 (0.17–1.8)	
White (reference)	8 (71/841)	—	
Gestational age, wk			
<25	19 (74/384)	11.7 (4.66–29.38)	<.0001
25–27	7 (58/881)	3.45 (1.37–8.71)	
≥28 (reference)	2 (5/250)	—	
Gestational age, wk			
22	25 (1/4)	38.67 (1.93–776.23)	<.0001
23	20 (17/85)	29 (3.77–222.79)	
24	19 (56/295)	27.18 (3.72–198.8)	
25	9 (31/334)	11.87 (1.6–87.94)	
26	5 (16/312)	6.27 (0.82–47.82)	
27	5 (11/235)	5.7 (0.73–44.67)	
28	3 (4/133)	3.6 (0.4–32.65)	
≥29 (reference)	1 (1/117)	—	
Birth weight, g			
<750	13 (88/680)	2.38 (1.65–3.44)	<.0001
750–1000 (reference)	6 (49/835)	—	
Birth weight, g			
≤500	7 (4/54)	1.4 (0.45–4.34)	<.0001
501–600	12 (21/182)	2.29 (1.17–4.46)	
601–700	17 (51/296)	3.65 (2.05–6.48)	
701–800	7 (23/324)	1.34 (0.7–2.56)	
801–900	6 (21/344)	1.14 (0.59–2.2)	
901–1000 (reference)	5 (17/315)	—	

Postnatal Neonatal Candidiasis

TABLE 4 Predictive Model of Invasive Candidiasis

Effect	Adjusted Odds Ratio (95% CI)	P
<i>Candida</i> -like dermatitis	3.22 (1.68–6.20)	.0005
Central catheter	1.85 (1.08–3.16)	.0242
Vaginal vs cesarean delivery	1.84 (1.25–2.70)	.0021
Enteral feeding	1.52 (1.01–2.28)	.0429
Lower gestational age, wk	1.29 (1.12–1.49)	.0005
Lowest glucose level (50 mg/dL) ^a	1.22 (0.99–1.49)	.0603
Lower platelet count (50 000) ^b	1.17 (1.06–1.28)	.0012
Antibiotic days	1.13 (1.05–1.22)	.0013

Predictors of invasive candidiasis include: presence of *Candida*-like dermatitis on examination, mode of delivery, presence of central catheter, enteral feeding, lowest glucose level in preceding 24 hours in increments of 50 mg/dL, antibiotic days in week before culture, platelet count in increments of 50 000, and gestational age in increments of weeks are shown.

^a Odds of invasive candidiasis increased with increasing blood glucose level.

^b Odds of invasive candidiasis increased with decreasing platelet count.

TABLE 2 Potentially Modifiable Risk Factors for Invasive Candidiasis at the Time of Culture

Effect	Adjusted Odds Ratio (95% CI)	P
Broadly acting antibiotics	1.98 (1.37–2.86)	.0003
Central catheter	1.94 (1.17–3.21)	.0098
Intravenous lipid emulsion	1.66 (0.98–2.81)	.0596
Endotracheal tube	1.58 (1.07–2.35)	.0226
Antenatal antibiotics	1.40 (0.97–2.03)	.0747

Risk factors included the presence of a central catheter, use of broadly acting antibiotics in the week before culture, use of intralipids, the presence of an endotracheal tube, and receipt of intrapartum antibiotics.

Benjamin DK et al, Neonatal Candidiasis: Epidemiology, Risk Factors, and Clinical Judgment, Pediatrics 2010

Treatment of Neonatal Candidiasis

- ▶ Amphotericin B deoxycholate vs. liposomal amphotericin
 - ▶ Limited concentration of liposomal amphotericin to kidneys
- ▶ Fluconazole
 - ▶ Good CNS penetration
 - ▶ *C. albicans*, *C. parapsilosis* usually susceptible
- ▶ Echinocandins (micafungin, caspofungin)
 - ▶ Agent of choice in adults and older children for invasive candidiasis
 - ▶ Agent with most data in infants is micafungin

Fluconazole prophylaxis

- 3 mg/kg every 3 days x 2 weeks, then 3 mg/kg every other day x 2 weeks, then 3 mg/kg daily x2 weeks
- Invasive infection occurred in 10 (20%) placebo, and none in fluconazole group

Kaufman D et al, FLUCONAZOLE PROPHYLAXIS AGAINST FUNGAL COLONIZATION AND INFECTION IN PRETERM INFANTS, NEJM 2001.

TABLE 2. EFFECTS OF FLUCONAZOLE PROPHYLAXIS ON FUNGAL COLONIZATION.*

EVIDENCE OF COLONIZATION	FLUCONAZOLE GROUP (N=50)	PLACEBO GROUP (N=50)	DIFFERENCE IN RISK (95% CI)	P VALUE
	no. of infants (%)			
≥1 site	11 (22)	30 (60)	0.38 (0.18 to 0.56)	0.002
≥2 sites	9 (18)	26 (52)	0.34 (0.14 to 0.52)	0.003
Any fungal species				
Skin	10 (20)	24 (48)	0.28 (0.07 to 0.47)	0.008
Stool	9 (18)	27 (54)	0.36 (0.16 to 0.54)	0.003
Nasopharynx	1 (2)	21 (42)	0.40 (0.21 to 0.57)	0.002
Umbilicus	2 (4)	6 (12)	0.08 (-0.08 to 0.24)	0.40
<i>Candida albicans</i>				
Any site	3 (6)	14 (28)	0.22 (0.03 to 0.40)	0.02
Skin	1 (2)	10 (20)	0.16 (-0.002 to 0.33)	0.05
Stool	3 (6)	13 (26)	0.20 (0.02 to 0.38)	0.03
Nasopharynx	0	11 (22)	0.22 (0.06 to 0.39)	0.005
Umbilicus	0	4 (8)	0.08 (-0.05 to 0.23)	0.31
<i>C. parapsilosis</i>				
Any site	8 (16)	14 (28)	0.14 (-0.08 to 0.31)	0.26
Skin	8 (16)	12 (24)	0.08 (-0.11 to 0.27)	0.47
Stool	5 (10)	10 (20)	0.10 (-0.08 to 0.28)	0.33
Nasopharynx	1 (2)	8 (16)	0.14 (-0.02 to 0.30)	0.09
Umbilicus	2 (4)	1 (2)	0.02 (-0.12 to 0.16)	0.89

*Data are for the infants with surveillance cultures that tested positive for fungal growth one or more times during the treatment period (mean [±SD], 5.2±1.4 weeks). CI denotes confidence interval.

References

- ▶ 1. Darmstadt GL et al, Congenital Cutaneous Candidiasis: Clinical Presentation, Pathogenesis, and Management Guidelines, Pediatrics 2000
- ▶ 2. Kaufman DA et al, Congenital Cutaneous Candidiasis: Prompt Systemic Treatment Is Associated With Improved Outcomes in Neonates, Clin Infect Dis 2017
- ▶ 3. Benjamin DK et al, Neonatal Candidiasis: Epidemiology, Risk Factors, and Clinical Judgment, Pediatrics 2010
- ▶ 4. Kaufman D et al, Fluconazole Prophylaxis Against Fungal Colonization and Infection in Preterm Infants, New Engl J Med, 2001