

In a study, only 18 out of 382 babies born less than 500g (4.7%) were discharged alive from the hospital. Most of the babies were treated in NICU for weeks, and spent much money. Only one of the 18 infants discharged alive was considered to have appropriate weight for gestational age, the other 17 were SGA. Of the 18 infants discharged from the hospital alive, there were 13 survivors, to live beyond 3 years of age; the other 5 died during the first year of life from disabilities. Four infants had no disabilities, 4 had one disability (one CP and 3 mental retardation [MR]), and 5 had multiple disabilities (3 CP and MR; one with CP, MR and blindness, and one with CP, MR, blindness and deafness).¹ As the possibility of survival is low and the possibility of having disability is high and the high rate of costs, the decision of active resuscitation and carrying on intensive care is difficult in case of these babies.^{6,7} It is pleasing that the neuromotor development of our patient is normal up to the 14th month; there is only one eye blindness. In the situation of chronic placental insufficiency and intrauterine stress, fetal maturation can be better and glucocorticoids, thyroid hormones, epidermal growth factors and cyclic AMP have positive effects on the lung maturation and production of surfactant. As the hyaline membrane disease (HMD) is commonly seen in male newborns, it is thought that androgens have negative effects on HMD's.⁸

In our patient, there was no explanation of having good maturity other than, stress factor as twins, and female born infant.

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References

1. Sauve RS, Robertson C, Etches P, Byrne PJ, Dayer-Zamora V. Before viability: A geographical based outcome study of infants weighing 500 grams or less at birth. *Pediatrics* 1998; 101: 438.
2. Papageorgiou A, Bardin CL. The Extremely-Low-Birth-Weight Infant. In: Avery GB, Fletcher MA, MacDonald MG, editors. *Neonatology: Pathophysiology and Management of the Newborn*. 5th ed. Philadelphia (PA): J. B. Lippincott Company; 1999. p. 445-472.
3. O'Shea TM, Klinepeter KL, Goldstein DJ, Jackson BW, Dillard RG. Survival and developmental disability in infants with birth weights of 501 to 800 grams, born between 1979 and 1994. *Pediatrics* 1997; 100: 982-986.
4. Walker M, Hull A. Preterm Labor and Birth. In: Taeusch HW, Ballard RA, editors. *Avery's Diseases of The Newborn*. 7th ed. Philadelphia (PA): WB Saunders company; 1998. p. 144-152.
5. Behrman RE, Shiono PH. Neonatal risk factors. In: Fanaroff AA, Martin RJ, editors. *Neonatal-perinatal medicine/Diseases of the fetus and infant*. 6th ed. New York (NY): Mosby; 1997. p. 1-12.
6. Doron MW, Veness-Meehan KA, Margolis LH, Holoman EM, Stiles AD. Delivery room resuscitation decisions for extremely premature infants. *Pediatrics* 1998; 102: 574-582.
7. Campbell AGM. Ethical problems in neonatal care. In: Rennie JM, Robertson NRC, editors. *Textbook of Neonatology*. 3rd ed. New York (NY): Churchill Livingstone Publishers; 1999. p. 1345-1350.
8. Gross I. Respiratory Diseases. In: Oski FA, editor. *Principles and Practice of Pediatrics*. Philadelphia (PA): J. B. Lippincott Company; 1990. p. 329-349.

Neonatal systemic candidiasis. A 14-year review

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The case records of all neonates admitted to the Special Care Baby Unit (SCBU), Al-Wasl Hospital, Dubai, United Arab Emirates (UAE) in a period of 14 years from May 1987 to April 2001 were analyzed, a total of 9060 admissions, 102 were diagnosed to have systemic candidiasis (1.1%). The mean gestational age was 29.3 weeks and birth weight 1131g. Fifty-two percent were premature, less than 1000g and only 2% were full term infants. All had undergone either umbilical, or peripheral vein catheterization and had received broad spectrum antibiotics except 2 with congenital candidiasis. Lethargy persistent pulmonary infiltrates, recurrent apnea, gastric intolerance and abdominal distension were the common clinical features. Persistent thrombocytopenia sustained more than 3 days was the most common finding in the peripheral smear. Two patients with congenital candidiasis presented with severe leukocytosis [white blood cells (WBC) count >25000/mm³] without thrombocytopenia. Urine and blood were the most common site for isolation of candida. Twelve percent of death were attributed to candida. Amphotericin B was used in all babies and in 7 cases, 5 flucytosine was added. Five infants had transient rise of blood urea nitrogen >30mg/dL or serum creatinine level >1mg/dL or both.

This study is a retrospective analysis of culture-verified cases of neonates systemic candidiasis. The records were evaluated for gestational age, sex, birth weight, indwelling catheters, days on antibiotics at the onset of symptoms, treatment details and outcome. The clinical data were collected on

standardized form and entered in to the database for analysis. Systemic candidiasis was defined as growth of candida species isolated from one or more normally sterile body fluids (blood, cerebro-spinal fluid, urine, peritoneal fluid) in the presence of clinical signs of infection. Systemic candidiasis was considered contributory to mortality if death occurred within 3 days of a positive culture from sterile body fluids. Specimen were collected and processed according to standard microbiologic techniques. Presumptive identification of *candida albicans* was carried out on germ tube test. Germ tube negative isolates were grouped as *candida spp.* All babies receiving amphotericin B or 5 flucytosine or both were monitored for renal and hematological toxicity. **Table 1** shows characteristics of neonates with systemic candidiasis. No significant difference was found in infants infected with *candida albicans* and *candida spp* regarding birth weight, gestational age and age at diagnosis and risk factors. Before diagnosis there was no difference between groups in their need for ventilatory support, parenteral nutrition and broad spectrum antibiotic treatment. There was a significant drop of platelet counts ($<50000/\text{mm}^3$) despite broad spectrum antibiotic coverage before the diagnosis of all acquired cases of systemic candidiasis. Most common clinical presentation were lethargy, and involvement of respiratory symptoms.

Ninety-eight percent were premature or had low

birth weight or both. The highest number of cases were seen in infants weighing less than 1000gm (52%). Seventeen cases received dexamethasone (5-day course) as a treatment for chronic lung disease. All patients had peripheral or umbilical catheterization (venous or arterial) or central line insertion and 33 (22%) were on total parenteral nutrition. Abdominal or renal ultrasonography was performed for all infants with confirmed systemic candidiasis; 2 had increased renal medullary echogenicity detected. Brain ultrasonography was normal in all infants. Echocardiography was performed for 53 infants with cardiac murmur or positive blood culture; only one infant had intracardiac vegetation on the atrial septum. Ophthalmoscopic evaluation was normal in all except one with endophthalmitis. All patients were treated with amphotericin B intravenously with initial dose of 0.25-0.5mg/kg and increased to 1mg/kg/day. The cumulative dose of amphotericin B ranged from 20-30mg/kg (median 26mg/kg). Seven infants with candida meningitis also received oral 5 flucytosine in dosage ranging from 75-100mg/kg/day. Five infants had transient nephrotoxicity manifested by blood urea nitrogen levels $>30\text{mg/dL}$ or a serum creatinine level $>1\text{mg/dl}$ or both, which fell to the normal range when daily dose of amphotericin was decreased to 0.75mg/kg. Thirteen (12.7%) of 102 infants died; 7 of these patients had definite meningitis and one had endophthalmitis. No difference was observed in mortality pattern for *candida albicans* and *candida spp.*

Systemic candidiasis is a serious problem particularly in very low birth infants and mortality up to 54% has been reported.¹ Incidence of disseminated candidal infections in neonates correlates with improved survival of very low birth weight infants. Possible reasons for this association include the compromised host defenses, colonization of gastro-intestinal tracts, frequent broad spectrum antibiotics and corticosteroid therapy and multiple invasive procedures. It was of interest to perform this study in a SCBU. To our knowledge, it has not been previously undertaken. In our study, the incidence was one per 1000 live births. Consistent with many reports blood and urine was the most common sites of candidal growth. Meningitis was diagnosed only in 7 cases, although Marisol et al² reported frequent occurrence of meningitis (25%). Possible reason could be early suspicion of candida infection and initiation of antifungal therapy. The mean age of onset of candidiasis was 22.4 days (ranged from 1-30 days) which is consistent with most of the previous reports from different parts of the world. Although

Table 1 - Characteristics of neonates with systemic candidiasis.

Characteristic	n
Live birth	96612
SCBU admissions	9060
Total number of cases with candidiasis	102
Male to female	61:41
Inborn	80
Transported	22
Incidence/1000 live birth	1
Gestational age (weeks)	29.3 (24- 37)
Birth weight (gms)	1131 (580-3200)
Age of onset of candidiasis (days)	22 (1-30)
Mortality (inborn) (%)	8/80 (10)
Overall mortality (%)	13/102 (12.7)
SCBU - special care baby unit	

Narang et al³ report much earlier onset of candidiasis. The ratio of mean duration of antibiotics to mean age at onset was 0.55 while studies by Faix¹ 0.58 and Narang et al³ 0.82. The mean birth weight and gestational age was comparable with several studies.^{1,5} Most of our babies had non-specific clinical manifestation. Therefore, high index of suspicion for candidiasis in such ill neonates especially when clinical sepsis with thrombocytopenia sustained more than 3 days, fail to respond to broad spectrum antibiotics. Similar findings were reported by Benjamin et al.⁴ Adverse effects, such as nephrotoxicity and electrolyte imbalance can be diminished or reversed by decreasing the dose of amphotericin B to 0.75mg/kg/day and careful fluid management. Present study confirms the relative rarity of toxicity of amphotericin B in neonatal period.

It is concluded that systemic candidiasis is relatively common in this part of the world and empiric use of third generation cephalosporins and other broad spectrum antibiotics are associated with candidiasis in very low birth infants. This study also suggests that amphotericin B is a reasonably safe choice for empiric therapy in a newborn with birth weight of <1500g, and who is deteriorating despite usual empiric antibacterial treatment.

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References

1. Faix RG. Invasive neonatal candidiasis: comparison of albicans and Parapsilosis infection. *Pediatr Infect Dis J* 1992; 11: 88-93.
2. Marisol F, Edina HE, Daniel EN, Carol JB. Candida Meningitis in neonates: A 10 year Review. *Clin Infect Dis* 2000; 31: 458-463.
3. Narang A, Pankaj B, Agrawal P, Chakrabarti A, Kumar P. Epidemiology of systemic candidiasis in a tertiary care neonatal unit. *J Trop Pediatr* 1998; 44: 104-108.
4. Benjamin DK Jr, Ross K, McKinney RE Jr, Benjamin DK, Auten R, Fisher RG. When to suspect fungal infection in neonates: A clinical comparison of Candida albicans and Candida parapsilosis fungemia with coagulase-negative staphylococcal bacteremia. *Pediatrics* 2000; 106: 712-718.
5. Saxen H, Vixtanen M, Carlson Petal. Neonatal Candida Parapsilosis with high case fatality rate. *Pediatr Infect Dis J* 1995; 14: 776-781.

Neutropenia

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There is an increasing observation of clinical neutropenia in healthy Omani individual. According to the international range for neutrophil counts ($2.5 - 7.5 \times 10^9/L$), more than 60% of Omani are neutropenic. In Oman, a different range for the neutrophil count is being used. Although this range is lower than the international range, 36% of individuals still have a lower neutrophil counts. In this study it appears that a lower range ($0.5 - 4.4 \times 10^9/L$) is required to cover 95% of the normal Omani individual. Neutrophils are important in providing immunity against bacterial and fungal infections. They are also important in the removal of exogenous and endogenous debris. The neutrophil count ranges between 2.5 and $7.5 \times 10^9/L$. A circulating neutrophils count below $1.5 \times 10^9/L$ is usually abnormal, although lower counts may be normal for certain non-white genetic groups, in particular Blacks and Arabs. In these healthy individuals, there are relatively more cells in the marginating pool, and they are able to mount a normal response to infection. Patients with neutrophil counts less than $0.5 \times 10^9/L$ for whatever reason are at increased risk of infection.¹⁻⁵ In Oman, the range for neutrophil is $2.0 - 7.5 \times 10^9/L$, which is lower than the international level. Despite this lower value, some Omani still have even a lower values. According to these ranges, considerable numbers of healthy Omani individuals are considered as neutropenic.

The aims of this study are to find out the percentage of Omani healthy individuals considered as having neutropenia using the international reference range; to find out percentage of Omani healthy individuals considered as having neutropenia using the Oman reference range and to recalculate the reference range that will cover 95% of Omani population.

The study sample was selected from healthy blood donors. The following donors were excluded: individual with history of recent infection or on antibiotics course, individual with allergy or on anti-allergic medications, had a recent immunization, any bleeding tendency, any individual who had surgery or delivered over the last 6 months and those who received recent blood or blood product transfusion. In addition to these, any donors found to have abnormality in hemoglobin level, platelet, or total white blood cell