

CANDIDAEMIA AND MORTALITY:

Is timely and appropriate antifungal drug treatment enough for survival of adult cases with candidaemia?

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Background

To evaluate the risk factors associated with mortality in patients with candidemia in context with *Candida* species and their susceptibilities, and mortality retrospectively.

Methods & Materials

All consecutive patients who developed candidemia at training and research hospital with an 800 beds were enrolled in this retrospective, observational, single center study during the period from June 2006 to December 2011.

Results

A total of 97 candidemia episodes were identified in 97 patients with an overall incidence of 4.19 episodes /10,000 admissions in adults during the study period. From 2006 to 2011, incident density rates were calculated as 2.38 (n: 5); 3.57 (n: 15); 5 (n: 21); 5.47 (n: 23); 4.04 (n: 17); 3.8 (n: 16) per 10,000 admissions in each year, respectively. Of 97 patients, 51 cases were male, mean age was 50.51±21.12; range of ages was between 15 and 90 years. *Candida* isolates of ICU patients composed of 76% (n: 74/97) of all isolates (*C.parapsilosis* (n: 24/39, 63%), *C.albicans* (n:21/32, 21%), and *C.tropicalis* (n:13/19, 68%), and others) followed by hematology ward (n:12, 12%), and surgery ward (n:9, 9%). Underlying conditions were recorded in 62 (63%) patients, and surgery was the most common predisposing factor in 55 cases (56%). Mean of APACHE II scores of the patients (n: 74) were 12.73±6.24. Central-line catheter (n: 82, 84%) and urinary catheter (n: 81, 83%) were most common recorded risk factors among cases. Crude 30-day mortality rates among patients with candidemia were 56% (55 of 97 cases). Urinary catheterization, immunosuppressive therapy, APACHE II score (≥ 16), hypoalbuminemia were found to be independent risk factors for fatal candidemia. Crude 30-day mortality rates among patients with candidemia were 56% (55 of 97 cases). Control blood culture controls drawn at 72-h of antifungal treatment were negative in 45 patients of 55 fatal cases and all surviving patients. CAS was recorded as empirical therapy in 18 of 42 survivor cases and 15 of 55 fatal cases (P= 0.109). Amphotericin B (AmB) was initiated empirically in 4 of 42 survivor cases and 10 of 55 fatal cases (P= 0.26). Switching to CAS from after 72-h of fluconazole treatment was in nine survivor patient and nine none-survivor patients. Switching to either CAS or voriconazole (VOR) did not achieve clinical response in two hemathological patients who were under either AmB or CAS treatment.

Table 1: Candida species and their antifungal susceptibilities of the patients with candidemia (n: 97)

Antifungal drugs	FCZ			ICZ			VCZ			5-FC			AmB		
	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)
<i>C.parapsilosis</i> (38, 39)	32 (85)	2 (5)	4 (10)	34 (90)	2 (5)	2 (5)	33 (86)	2 (6)	3 (8)	38 (100)	0 (0)	0 (0)	38 (100)	0 (0)	0 (0)
<i>C.albicans</i> (32, 32)	25 (78)	1 (6)	6 (16)	27 (84)	2 (6)	3 (10)	30 (90)	0 (0)	2 (10)	32 (100)	0 (0)	0 (0)	32 (100)	0 (0)	0 (0)
<i>C.tropicalis</i> (19, 19)	7 (37)	0 (0)	12 (63)	10 (53)	4 (21)	5 (26)	16 (84)	0 (0)	3 (16)	19 (100)	0 (0)	0 (0)	17 (89)	0 (0)	2 (10)
<i>C.glabrata</i> (5,5)	2 (40)	2 (40)	1 (20)	3 (60)	1 (20)	1 (20)	4 (80)	0 (0)	1 (20)	5 (100)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)
<i>C.krusei</i> (2, 2)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	2 (100)	1 (50)	0 (0)	1 (50)	1 (50)	1 (50)	0 (0)	2 (100)	0 (0)	0 (0)
<i>C.norvegensis</i> (1, 1)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)

FCZ: Fluconazole, ICZ: Itraconazole, VCZ: Voriconazole, 5-FC: 5-Flucytosine, AmB: Amphotericin B, S: Susceptible, I: Intermediate R: Resistant

Table 2: Distribution of categorized variables by survival group in the patients with candidemia (n: 97)

	Total (n,%)	Survivor (n:42) n (%)	Non-survivor (n:55) n (%)	Hazard Ratio (%95 CI)	P
Age	50.51±21.12	49.13±18.64	51.01±19.43		0.87
Male/Female	49/48	22/20	27/28		0.748
Interventions					
Central venous catheter	(82, 84)	37 (88)	45 (81)		0.572
Urinary catheter	(81, 83)	31 (73)	50 (90)	0,28 (0,08-0,88)	0,024
Total parenteral nutrition	(52, 53)	19 (45)	33 (60)		0.158
Surgery	(60, 61)	23 (54)	37 (71)		0.292
Transfusion	(53, 54)	23 (54)	30 (54)		0.983
Mechanic ventilation	(67, 69)	26 (61)	41 (74)		0.183
Broad-spectrum antibiotic use	(75, 77)	30 (71)	45 (81)		0.228
Underlying conditions					
Comorbid conditions	(74, 76)	31 (73)	43 (78)		0.638
Immunosuppressive therapy	(19, 19)	5 (11)	14 (25)	0,29 (0,09-0,9)	0,039
Neutropenia	(18, 18)	10 (23)	8 (14)		0.247
Diabetes mellitus	(17, 17)	6 (14)	11 (20)		0.460
Malignancy	(31, 31)	17 (40)	14 (25)		0.117
Hematological disorders	(15, 15)	6 (14)	9 (16)		0.779
Respiratory tract diseases	(16, 16)	10 (23)	6 (10)		0.105
Clinical Findings					
APACHE II score (≥ 16)	(35, 47)	9 (12)	26 (35)	0,3 (0,12-0,75)	0,011
Gastrointestinal bleeding	(12, 12)	8 (19)	4 (7)		0.545
Hypoxia	(49, 50)	17 (40)	32 (58)		0.103
Septic shock (n:16)	(16, 16)	6 (14)	10 (18)		0.607
Mucositis	(17, 17)	10 (23)	7 (12)		0.331
Diarrhea	(12, 12)	8 (19)	4 (7)		0.119

	Total (n,%)	Survivor (n:42) n (%)	Non-survivor (n:55) n (%)	Odds Ratio (%95 CI)	P
Laboratorial Findings					
CRP elevation	(83, 85)	38 (90)	45 (81)		0.26
Anemia	(68, 70)	26 (61)	42 (76)		0.124
Hypoalbuminemia	(65, 67)	21 (50)	44 (80)	4 (1,63-9,79)	0.002
Decreased creatinine clearance	(18, 18)	7 (16)	11 (20)		0.675
Thrombocytopenia	(27, 27)	13 (31)	14 (25)		0.55
ALT elevation	(25, 25)	11 (26)	14 (25)		0.935
AST elevation	(40, 41)	18 (42)	22 (40)		0.777
Microbiological Findings					
Concurrent bacteremia	(28, 28)	11 (26)	17 (30)		0.61
Candida growth in urine culture	(27, 27)	11 (26)	16 (29)		0.752
Candida growth in catheter culture	(9, 9)	3 (7)	6 (10)		0.728
Candida growth in peritoneal fluid	(6, 6)	3 (7)	3 (5)		0.733
Growth of <i>C.albicans</i> species	(32, 32)	13 (31)	19 (34)		0.419
Growth of non- <i>C.albicans</i> species	(65, 67)	31 (73)	34 (61)		0.277
Fluconazole resistance	(14, 14)	5 (11)	9 (16)		0.533
Fluconazole treatment	(50, 51)	20 (47)	30 (54)		0.499

Abbreviations: CRP: C reactive protein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CI: Confidence Interval

Conclusion

Adult cases with candidemia who are at risk factors associated with mortality are more likely to have poor prognosis inspite of appropriate and timely initiated antifungal drug. Empirical choice of antifungal drug should be tailored with respect to the severity of patients and local antifungal resistance status. Catheter removal should be evaluated by patient's benefits and harms. Severity of illness and underlying conditions of the patients are more likely to influence on treatment response rates and prognosis. Physicians should be take into consideration development of candidemia under voriconazole treatment due to increasing selection of voriconazole-resistant *Candida* species .