

# ANTIBIOGRAM AND MANAGEMENT OUTCOMES OF CULTURE POSITIVE PERITONITIS IN PATIENTS WITH END STAGE RENAL DISEASE ON CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

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**Abstract : Background:** Continuous ambulatory peritoneal dialysis (CAPD) is a widely used standard therapeutic modality for renal replacement therapy in End stage renal disease patients. Peritonitis is a common problem in patients undergoing CAPD and represents the most frequent cause of hospitalization, peritoneal catheter loss, frequent touch contamination, technique failure, discontinuation of CAPD, and mortality. AntibioGram is a profile of antimicrobial susceptibility of particular organism. **Aim and objectives:** With this background the present was undertaken to measure AntibioGram and management outcomes of culture positive peritonitis in patients of end stage renal disease on Continuous ambulatory peritoneal dialysis. **Materials and methods:** This was a hospital based retrospective observational study was carried out during the period of 2015-2017 worked on 40 patients in department of nephrology ward at Sri Venkateswara Institute of Medical Sciences Hospital, Tirupati. **Result:** E. coli was the most predominant pathogen isolated from peritoneal fluid samples. **Conclusion:** The present study findings suggest that gram negative bacterial infections are the predominant cause for peritonitis over gram positive bacterial infections related peritonitis. With effective antibiotic therapy, over two third of patient's recovered safe with gram positive and gram negative culture positive peritonitis.

**Key words:** Continuous ambulatory peritoneal dialysis, Peritonitis, End stage renal disease

### **Introduction:**

Peritonitis is a serious complication of peritoneal dialysis (PD) and hence responsible for poor outcome and high rates of PD failure resulting in death<sup>1-5</sup>. PD is an alternative mode of renal replacement treatment for the management of End stage renal disease (ESRD) patients<sup>6</sup>. Many risk factors are associated with PD related peritonitis which includes age, race, gender, body mass index, socioeconomic status and smoking<sup>4,7</sup>. Some of the infections originate in delivery system, with the consequence that staphylococcal infections have become less common and gram negative and polymicrobial infections have become proportionally more common<sup>8</sup>. The contamination of peritoneal cavity thus, can lead to infections, sepsis, and multisystem organ failure and if not treated in timely manner results in death<sup>9</sup>. To prevent PD associated infections, prophylactic administration of the antimicrobial agents before catheter placement, adequate patient training, exit site care and treatment for nasal carriage can be employed. Mupirocin ointment can reduce the risk of exit site infection by 46% but it cannot decrease the risk of peritonitis due to all organisms<sup>10</sup>. In a 3 year retrospective study conducted in 82 CAPD patients who developed increasing incidence of CAPD peritonitis reported that the *Streptococcus sp.* was the most common organism among the gram-positive peritonitis while *Pseudomonas sp.* was the most common organism in gram-negative peritonitis showing the higher incidence of gram negative peritonitis which might be due to inadequate hand washing. Poor hand washing might also pre-dispose the patient to contamination during the exchange procedure<sup>11</sup>. Despite some similarities, there were also some differences in microbiological profiles and outcomes of CAPD patients from those of other centres. The catheter loss rate was significantly, higher in Gram negative peritonitis, as compared to gram positive peritonitis. The incidence and outcome of mono microbial peritonitis in CAPD patients reported as gram positive peritonitis rate was found to be higher than the gram negative peritonitis with poor outcome<sup>12</sup>. The main outcomes of peritonitis was to switching from PD to hemodialysis and need of the hospitalization with no relationship between centre size and peritonitis rate as peritonitis was the cause of death in 2.6% of patients<sup>13</sup>. The frequency, predictors, treatment and clinical outcomes of PD associated polymicrobial peritonitis were found to be treated successfully using antibiotics alone without catheter removal in most cases, particularly in isolation of Gram positive organisms<sup>14</sup>.

### **Materials and methods:**

**Study design:** A retrospective analysis of culture positive peritonitis and its antibiogram with management outcomes in patients with ESRD on continuous ambulatory peritoneal dialysis programme was conducted during the period between January 2015 to December 2017 in the department of nephrology at Sri Venkateswara Institute of Medical Sciences, Tirupati. The age and gender of ESRD patients, the organism isolated and the antimicrobial susceptibility profiles were collected from the patients records using a standard data collection form. The data were entered into Microsoft Excel spread sheets for analysis. Of the total number of 130 patients, 40 patients experience peritonitis. Among the 40 patients, 59 episodes of peritonitis were observed.

Peritoneal dialysate (PD) fluid culture study was performed for the isolation of the microorganisms and antibiotic sensitivity was investigated.

### **PD fluid culture study:**

The patients' exchange bags containing effluent dialysate were submitted to the microbiology department for culture and sensitivity testing and were immediately processed. The bags which were not processed immediately were refrigerated at 4°C. From these exchange bags, 100 ml of fluid was withdrawn using a sterile needle and syringe under aseptic conditions. The fluid was centrifuged in sterile tubes at a rate of 3000 g for 15 min and supernatant was discarded, leaving 0.5 ml of deposit. In the centrifuged deposit, 10 ml of sterile distilled water was added and the mixture was shaken vigorously for 30 seconds. After vigorous shaking, the deposit was centrifuged at 3,000 g for 15 min and supernatant was discarded. A part of the deposit is inoculated onto blood agar (BA) and MacConkey agar at a temperature of 37°C for 24-48 h. Fungal culture was done on Sabouraud-Dextrose agar (SDA) with and without antibiotics (Chloramphenicol, Actidone) at 25°C and 37°C for 4 weeks. If turbidity is developed, the same was gram-stained and plated on appropriate media for isolation and identification of the microorganisms. Broths showing no growth were discarded after seven days of incubation<sup>15</sup>.

An antibiogram is an overall profile of antimicrobial susceptibility testing results of a specific microorganism.

**Classification of antimicrobial agents based on mechanism of action<sup>16</sup>.**

Group 1	Antibacterial agents	Examples
	1a. Inhibit cell wall synthesis	Penicillin, cephalosporins, vancomycin, glycopeptides, $\beta$ -lactamase inhibitors, carbapenems
	1b. Inhibit protein synthesis	Macrolides, Oxazolidinones, tetracyclines, chloramphenicol
	1c. Cause misreading of m-RNA affect permeability	Aminoglycosides
	1d. Cause leakage from cell membranes	Polymixin-B
	1e. Inhibit DNA gyrase	Quinolones
	1f. Interfere with intermediary metabolism	Sulphonamides
Group 2	Antifungal agents	Fluconazole, voriconazole, amphotericin-B

Group – 1: antibacterial agents, Group - 2: antifungal agents

**Antimicrobial susceptibility tests**

According to the standard operational procedures, antimicrobial susceptibility tests were done on Mueller-Hinton agar (Oxoid, Hampshire, England) using Kirby-Bauer disk diffusion method as per Clinical Laboratory Standards Institute (CLSI) guidelines 2012(17). Antibiotic sensitivity was carried out as per CLSI guidelines. All antibiotic discs and media used were obtained from Himedia laboratories PVT. LTD., Mumbai, India. The antimicrobial agents tested were: tetracycline, ampicillin, erythromycin, gentamicin, cefotaxime, cefazolin, clindamycin, chloramphenicol, ciprofloxacin, cotrimoxazole, ceftriaxone and linezolid, penicillin, vancomycin, amoxycillin, cefoperazone-sulbactam, imipenem, piperacillin-tazobactam, ceftazidime, netilmycin, polymyxin B, tigecycline. Antifungals used were amphotericin B, fluconazole, voriconazole.

Resistance data were interpreted according to CLSI guidelines 2012.

**Data analysis**

Continuous data was expressed as mean  $\pm$  standard deviation and categorical data was presented as percentages to compare the proportion of bacterial isolates between age, gender and comparison of antimicrobial resistance.

**Ethical considerations** Ethical approval was obtained from Institutional ethics committee of SVIMS university.

**Results :**

A total of 59 peritoneal fluid samples from 40 ESRD patients were analyzed for isolation and identification of organism and antimicrobial susceptibility testing. The age of the patients ranged from 18 years to 80 years, with mean age of  $54.8 \pm 16.29$  years. Out of 40 ESRD patients, 24 were male patients and 16 were female patients with male to female ratio of 3:2. The demographic characteristics of the patients are shown in Table 1.

Table1: Age and gender distribution of patients with suspected peritonitis:

S.NO:	Demographic details	Positive number of peritonitis (%)
1.	Age in years : < 20	3(7.5)
	21-40	2 (5)
	41-60	19 (47.5)
	61-80	16 (40)
2.	Gender: Male	24 (60)
	Female	16 (40)

Majority of the pathogens were isolated from males with isolation rate of 60% and females with isolation rate of 40%. The highest isolation rate was observed in the age group between 41 to 60 years (Table 1). The overall susceptibility profiles of bacterial isolates to various antimicrobial agents were shown in Table 2. High sensitivity rates to Group 2 (95 %), Group 1c (90.1 %) and Group 1b (84.2%) antimicrobial agents were documented. On the other hand, high degree of resistance rates to Group 1f (48.8%), Group 1a (28.4%), Group 1e (17.3%) antimicrobial agents were documented. Among gram negative organisms *Escherichia coli* (*E.coli*) with 11 episodes was the most predominant pathogen isolated from peritoneal fluid samples followed by *Klebsiella* with 9 episodes, *Pseudomonas* with 6 episodes, *Acinetobacter* with 5 episodes, Non fermentive gram negative bacilli (NFGNB) with 2 episodes and *Enterobacter* with 1 episode. Among gram positive organisms *Staphylococcus aureus* with 9 episodes was the most predominant pathogen isolated followed by *Staphylococcus epidermidis* with 3 episodes, Coagulase negative staphylococci (*CONS*) and Non hemolytic

streptococci with 2 episodes each, Staphylococcus hominis and Enterococci with 1 episode each. Among fungal organisms Candida albicans with 6 episodes was the predominant pathogen isolated followed by Aspergillus flavus with 1 episode of peritonitis as shown in (Table 3). Gram negative and Gram positive bacteria, and fungal isolates were responsible for 57.6%, 30.5% and 11.9% of peritonitis respectively.

Table 2. Showing the overall susceptibility profiles of bacterial isolates

Antimicrobial agents	T	Sensitivity(%)	Resistance(%)
Group 1a	271	194 (71.5)	77 (28.4)
Group 1b	70	59 (84.2)	11 (15.7)
Group 1c	81	73 (90.1)	8 (9.8)
Group 1d	6	5 (83.3)	1 (16.6)
Group 1e	52	43 (82.6)	9 (17.3)
Group 1f	43	22 (51.1)	21 (48.8)
Group 2	20	19 (95)	1 (5)

Group – 1: antibacterial agents 1a. Inhibit cell wall synthesis , 1b. Inhibit protein synthesis , 1c. Cause misreading of m-RNA affect permeability, 1d. Cause leakage from cell membranes , 1e. Inhibit DNA gyrase , 1f. Interfere with intermediary metabolism. Group - 2: antifungal agents

T – Total number of antimicrobial agents tested for isolation of organisms

R = Total number and percent of antimicrobial agents resistant to organisms

Table 3: Microorganism isolates from peritoneal fluid samples of patients with suspected peritonitis.

Isolated organism	Frequency	Percent(%)
<b>Gram positive</b>		
Staphylococcus aureus	9	<b>15.2</b>
Staphylococcus epidermidis	3	<b>5.1</b>
CONS	2	<b>3.4</b>
Non hemolytic streptococci	2	<b>3.4</b>
Staphylococcus hominis	1	<b>1.7</b>
Enterococci	1	<b>1.7</b>
<b>Gram negative</b>		
E coli	11	<b>18.6</b>
Klebsiella	9	<b>15.2</b>
Pseudomonas	6	<b>10.1</b>
Acinetobacter	5	<b>8.5</b>
NFGNB	2	<b>3.4</b>
Enterobacter	1	<b>1.7</b>
<b>Others</b>		
Candida albicans	6	<b>10.1</b>
Aspergillus flavus	1	<b>1.7</b>

Table 4: Antimicrobial susceptibility of Gram positive bacterial isolation from peritonitis patients.

Antimicrobial agent	S.A		S.E		CONS		NHS		ENT		SH	
	T	R (%)	T	R (%)	T	R (%)	T	R (%)	T	R (%)	T	R (%)
Group 1a	36	7 (19.4)	12	0	8	1(12.5)	8	3(37.5)	4	1(25)	3	0
Group 1b	36	1 (2.7)	12	2(16.6)	8	4(50)	8	0	4	2(50)	4	0
Group 1c	9	0	3	0	2	0	-	-	-	-	1	0
Group 1d	-	-	-	-	-	-	-	-	-	-	-	-
Group 1e	9	0	3	1(33.3)	2	0	2	0	1	0	1	0
Group 1f	9	4(44.4)	3	2(66.6)	2	1(50)	-	-	-	-	1	1(100)

Group – 1: antibacterial agents 1a. Inhibit cell wall synthesis , 1b. Inhibit protein synthesis , 1c. Cause misreading of m-RNA affect permeability, 1d. Cause leakage from cell membranes, 1e. Inhibit DNA gyrase , 1f. Interfere with intermediary metabolism

**S.A:** Staphylococcus aureus **S.E:** Staphylococcus epidermis **NHS :**Non-hemolytic streptococci **ENT:** Enterococci **SH :** Staphylococcus hominis

T – Total number of antimicrobial agents tested against organisms

R = Total number and percent of antimicrobial agents resistance to organisms

Table 5:Antimicrobial susceptibility of Gram negative bacterial isolation from peritonitis patients.

Antimicrobial agent	E.coli		Kleb		Pseudo		Acine		NFGB		Entero	
	T	R(%)	T	R(%)	T	R(%)	T	R(%)	T	R(%)	T	R(%)
Group 1a	66	28(42.4)	54	16(29.6)	30	1(3.3)	30	13(43.3)	12	2(16.6)	7	4(57.1)
Group 1b	-	-	-	-	-	-	-	-	-	-	-	-
Group 1c	22	4(18.1)	18	0	18	1(5.5)	10	3(30)	4	0	2	0
Group 1d	-	-	-	-	6	1(16.6)	-	-	-	-	-	-
Group 1e	11	5(45)	9	1(11.1)	6	0	5	1(20)	2	0	1	1(100)
Group 1f	11	8(72.7)	9	4(44.4)	-	-	6	1(16.6)	2	0	1	1(100)

Group – 1: antibacterial agents 1a. Inhibit cell wall synthesis, 1b. Inhibit protein synthesis, 1c. Cause misreading of m-RNA affect permeability, 1d. Cause leakage from cell membranes, 1e. Inhibit DNA gyrase, 1f. Interfere with intermediary metabolism

**E.coli :** Escherichia coli **Kleb :** Klebsiella **NFGB :** Non-fermentive bacilli

**Entero :** Enterobacter, **Acine:** Acinetobacter

T – Total number of antimicrobial agent tested against organisms

R = Total number and Percent of antimicrobial agents resistant to the organisms

Table 6: Antimicrobial susceptibility of fungal isolation from peritonitis patients.

Antifungal agent	Candida albicans		Aspergillus flavus	
	T	R(%)	T	R(%)
Group 2	18	1(16.6)	2	0

T – Total number of antimicrobial agent tested against organism

R = Total number and percent of antimicrobial agents resistant to organisms

#### Discussion:

The present study included 40 patients with culture positive peritonitis during the 3 years period. The peritonitis rate in the present center was observed as 0.52 episodes per patient – CAPD year, and is comparable to other leading centers who reported 0.63 episodes per patient year in Chennai study<sup>18</sup>, 0.6 peritonitis episode per patient year in Australian study<sup>19</sup> and 0.5 episodes per patient year in Saudi studies<sup>20</sup>

On year wise analysis the present study found 31.7% of overall gram positive infections, in that *Staphylococcus aureus* was 15.2%, *Staphylococcus epidermis* was 5.1%, Non hemolytic streptococci and CONS was 3.4% each, *Staphylococcus hominis* and Enterococci were 1.7% each found. In the present study overall 54.8% of gram negative infections were found, in that *E.coli* was 18.6%, *Klebsiella* was 15.2%, *Pseudomonas* was 10.1%, *Acinetobacter* was 8.5%, NFGNB was 3.4%, *Enterobacter* was 1.7% found. Overall fungal organisms included in our study was 11.7%, in that *Candida albicans* was 10.1%, *Aspergillus flavus* was 1.7%.

The overall analysis in the present study revealed that the most common causative gram negative organism was found as *E.coli* and *Staphylococcus aureus* in gram positive organism. Similar to the present study findings, the studies from other regions also showed predominance of *E.coli* in gram negative organism, *Staphylococcus aureus* in gram positive organism in Chennai study<sup>21</sup> and, *CONS* in gram positive, *E.coli* in gram negative in Lucknow<sup>12</sup> and Australian studies<sup>22</sup>. According to the present study findings the gram negative organisms have higher peritonitis rate when compared with gram positive bacterial pathogens. But in Australian studies gram positive pathogens have higher rate of peritonitis than gram negative organism<sup>19</sup>.

Based on our antibiogram pattern of Gram positive organism it showed 100% sensitivity to cephalosporins, tetracycline, linezolid, chloramphenicol, and 70-80% sensitivity to penicillin, macrolides, sulphonamides. Gram negative organism showed 100% sensitivity to carbapenems and 70-90% sensitivity to sulphonamides, betalactamase, quinolones, aminoglycosides, cephalosporins. Antimicrobial resistance in *E. coli* has increased worldwide and its susceptibility patterns show substantial geographic variation as well as differences in population and environment<sup>23</sup>. The result is consistent with the findings of previous studies<sup>24, 25</sup>. Hence we summarise that when the patient need to be treated without waiting for the antibiogram report, it may be safe to prescribe the group that have 100% sensitivity, preferably keeping in view of side effect profile cephalosporins, linezolid and imipenam are to be preferred.

In the present study patients with gram negative peritonitis, fungal peritonitis were significantly resulted in catheter removal, lower rates of resolution and transferred to hemodialysis. 46.6% of catheters are removed for candida and 33.3% for gram negative organisms. The mortality rate in the present study was low 5% during three years analysis as compared with other regions which revealed 14.63% in South India<sup>20</sup>, 15.27% in Saudi<sup>26</sup>, 5.7% in North India<sup>27</sup> and 2.6% in Australia<sup>28</sup>.

#### CONCLUSION:

The present study findings suggest that gram negative bacterial infections are the predominant cause for peritonitis over gram positive bacterial infections related peritonitis. With effective antibiotic therapy based on local antibiogram as per institute policy, over two third of patients recovered safe with gram positive and gram negative culture positive peritonitis. The present study results also re-strengthen the hand hygiene practices, adherence to aseptic procedures in PD as to prevent infection.

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