



Microbiology Newsletter

Sir Ganga Ram Hospital

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Fever – A diagnostic challenge

Fever remains a challenging clinical problem despite recent advances in diagnostic tools and techniques. Understanding the aetiologic factors of fever and incorporating thorough history taking and physical examination with relevant investigations can be rewarding.

CASE 1

A 42 years old male insurance agent, resident of Bajpur village near Nainital, presented with complaints of fever, retrosternal burning pain and throat pain for 3 weeks. Fever was high grade, continuous, associated with chills, headache, and night sweats. His oral intake was reduced in addition to weight loss of approximately 15 kg in last 10 months. There was no history of cough, chest pain, dyspnoea, haemoptysis, joint pains, rashes, dysuria or malaena. A history of fever, off and on, for last 10 months was associated with generalised weakness. There was no history of drug intake.

General examination done at admission did not reveal any abnormality except for tenderness in right hypochondrium and a palpable liver per abdomen. Routine hematological examination revealed mild leucopaenia with relative lymphocytosis of 60% although the total cell count of $6500/\text{mm}^3$ was within normal limits. Absolute lymphocyte count was $3900/\text{mcl}$ and ESR was 29 mm (1st hour by Westergren's method). Peripheral smear for malarial parasite, malarial antigen for *P. vivax* and *P. falciparum*, serological test for Epstein Barr virus, Widal test and HIV ELISA were negative. Urine examination, kidney and liver function tests, Chest X-Ray, and echocardiography were within normal limits. Mantoux test done was positive (13mm).

CT scan of thorax and abdomen done one month prior to present admission had revealed mild splenomegaly with a small hypodense lesion. In addition to earlier findings, it repeat now revealed periportal and peripancreatic lymph nodes with mild hepatomegaly. A small calcified lymph node at right pulmonary hilum with a nodular lesion in right middle lobe of lung was also seen on CT scan. Histopathology of the bone marrow revealed a granulomatous picture with focal areas of haemorrhage and necrosis but nucleic acid hybridization assay for tuberculosis (GenProbe) was negative.

CASE 2

In another similar case, a 30 years old male patient, an engineer by profession, presented to our medicine OPD with complaints of fever, cough with blood tinged sputum and loss of appetite for 10 days. Fever was high grade, intermittent and associated with chills. There was no history of burning micturition, pain abdomen, loose stools, joint pains, rashes or chest pain. Patient had a history of contact with a newly diagnosed patient of pulmonary tuberculosis (his wife) on ATT for past 1 month, and a history of travel to his native village in Andhra Pradesh where he has herds of cattle at his home.

General examination was primarily normal except for a slightly palpable liver. Patient was investigated on OPD basis. Routine

hematological and biochemical parameters were within normal limits except for a slightly raised ESR and mild lymphocytosis of 41%. CT scan of the thorax and ultrasound of the abdomen were within normal limits. Malarial antigen was negative for *P. vivax* and *P. falciparum*.

Microbiology investigations

In the first case, the blood culture was negative after 24 hours, but was flagged positive after 2.72 days of incubation by the BacT/Alert automated blood culture system. The Gram stain of positive BacT/ALERT broth revealed minute Gram negative coccobacilli which were identified as *Brucella melitensis* by Vitek-2 identification system. On checking with the patient, we found that the patient had liking for milk/ milk products as well as gardening, where cow dung was used as fertilizer.

Bone marrow culture also grew similar Gram negative coccobacilli after 3.3 days of incubation. Which was also identified as *Brucella melitensis*. The serum agglutination test (SAT) for *Brucella* antibodies by tube agglutination method was positive with a titre of 1:2560, which is highly significant.

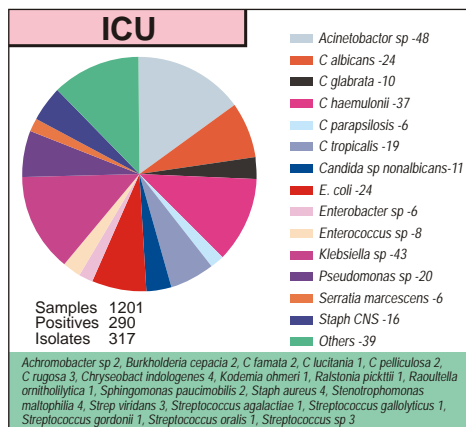
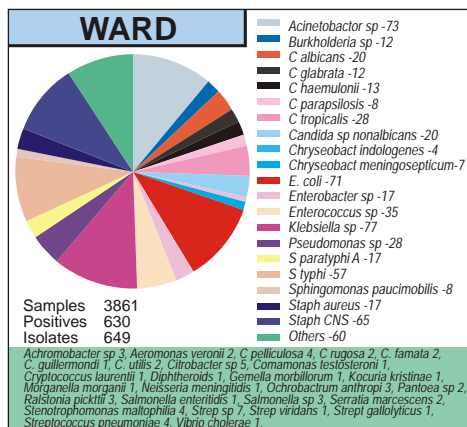
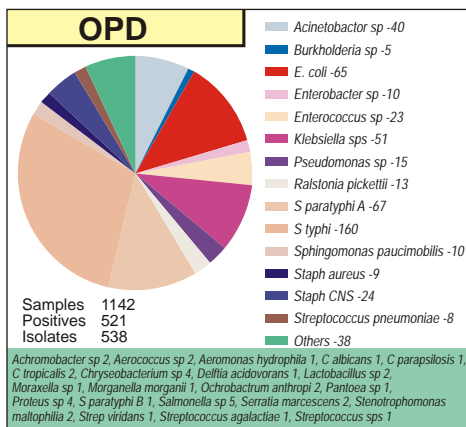


Growth of *Brucella melitensis* on blood agar after overnight incubation.

In the second case, two blood cultures similarly revealed minute Gram negative coccobacilli after 2.39 and 2.36 days of incubation by Bact/Alert, which were also identified as *Brucella melitensis* by the Vitek-2 identification system. The serum agglutination assay (SAT) for *Brucella* antibodies was positive in a titre of 1:5120.

Both patients were treated with Doxycycline 100mg BD and Inj. Streptomycin 0.75 gm/day and responded well to the therapy. Both became afebrile after a couple of days after start of therapy and were discharged in a stable condition.

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Percentage Resistance

OPD
WARD
ICU

GPC

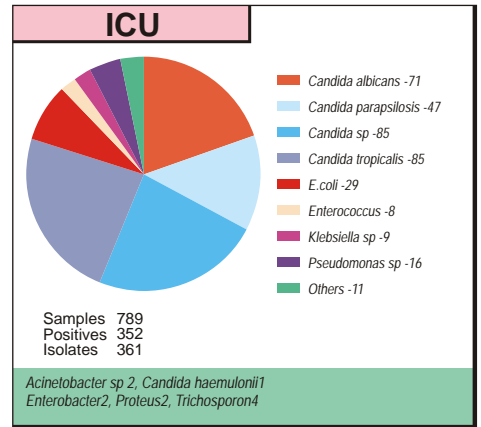
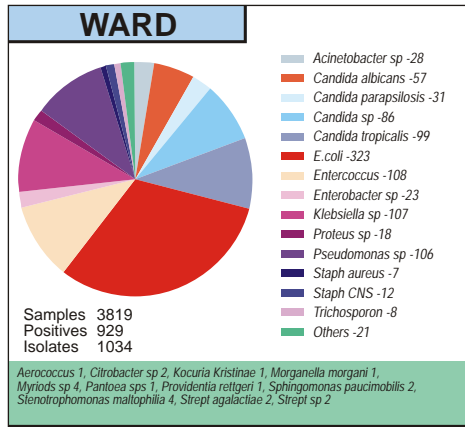
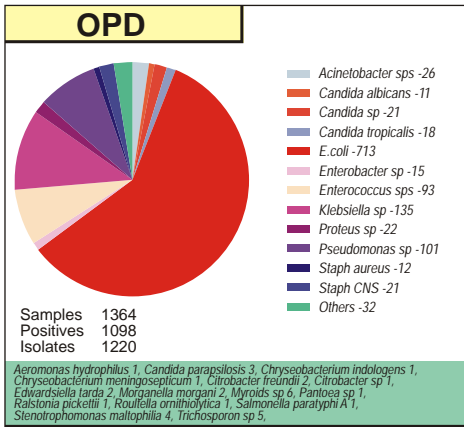
	No. of Isolates	Ampicillin	Penicillin	Oxacillin	Clindamycin	Gentamicin	HLAR Gentamicin	Vancomycin
<i>Staph aureus</i>	9	-	100	56	56	56	-	0
	17	-	100	33	33	20	-	0
	4	-	-	-	-	-	-	-
<i>Staph CNS</i>	24	-	100	50	50	75	-	0
	65	-	99	94	62	74	-	0
	16	-	100	92	82	89	-	0
<i>Enterococcus sp</i>	23	95	-	-	-	-	78	9*
	35	80	-	-	-	-	86	17**
	8	71	-	-	-	-	100	38***
<i>Strep. pneumoniae</i>	8	-	0	-	-	-	-	0
	4	-	-	-	-	-	-	-
	0	-	-	-	-	-	-	-

GRE (Glycopeptide Resistant Enterococci)
* 2 isolates ** 6 isolates *** 3 isolates

GNB

	No. of Isolates	Ampicillin	Ceftriaxone	Cefixime	Ceftazidime	Gentamicin	Nalidixic Acid	Amikacin	Ciprofloxacin	Co-trimoxazole	Chloramphenicol	Piperacillin+ Tazobactam	Cefepime+ Sulbactam	Imepemem	Colistin
<i>S. enterica</i> serotype Typhi	160	13	0	0	-	-	91	-	7	17	12	-	-	-	-
	57	12	0	0	-	-	85	-	6	21	12	-	-	-	-
	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>S. enterica</i> serotype Paratyphi A	67	0	0	0	-	-	98	-	2	0	0	-	-	-	-
	17	0	0	0	-	-	100	-	0	0	0	-	-	-	-
	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>E. coli</i>	65	88	70	-	-	41	-	5	82	-	-	20	10	2*	-
	71	99	81	-	-	70	-	10	96	-	-	25	24	8**	-
	24	96	90	-	-	58	-	8	92	-	-	33	33	0	-
<i>Klebsiella sp</i>	51	100	91	-	-	78	-	44	81	-	-	59	60	12***	-
	77	100	94	-	-	70	-	18	81	-	-	39	42	3 ^x	-
	43	97	97	-	-	88	-	57	94	-	-	67	79	3 ^{xx}	-
<i>Pseudomonas sp</i> [#]	15	-	-	-	58	58	-	58	67	-	-	17	70	67	0
	28	-	-	-	62	59	-	57	54	-	-	35	53	57	15
	20	-	-	-	87	79	-	73	77	-	-	38	73	71	9
<i>Acinetobacter sp</i>	40	100	100	-	100	83	-	83	100	90	-	100	85	97	3
	73	100	92	-	90	87	-	86	91	92	-	91	80	80	0
	48	100	100	-	100	100	-	91	100	100	-	98	94	91	2
<i>Burkholderia sp</i>	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	12	-	-	-	50	-	-	-	-	55	-	-	-	82	-
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Carbapenem resistant isolates (*Enterobacteriaceae*)
* 1 isolate ** 4 isolates *** 5 isolates ^{xx} 2 isolates ^{xx} 1 isolate
[#] *Pseudomonas* spp. Includes *P. aeruginosa*, *P. stutzeri*, *P. fluorescens* & *P. putida*



Percentage Resistance

OPD
WARD
ICU

GPC

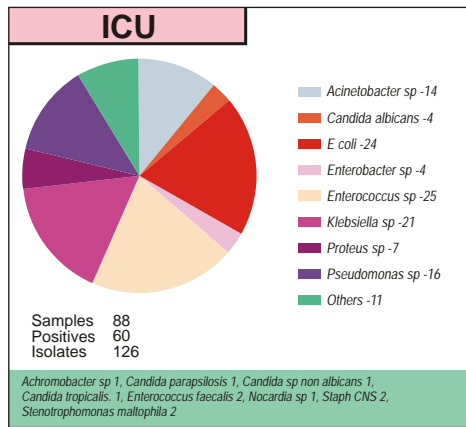
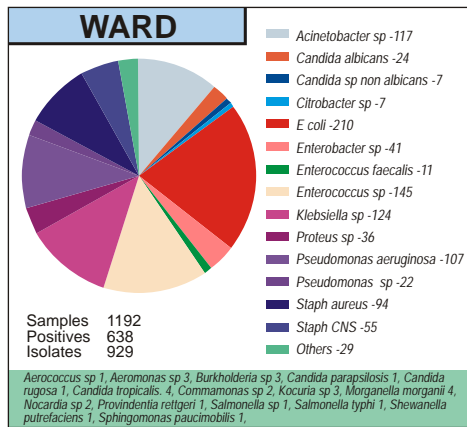
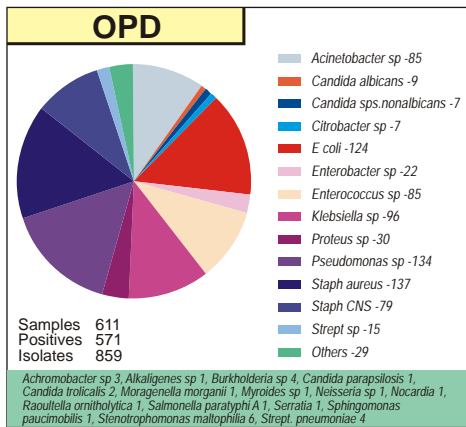
	No. of Isolates	Ampicillin	Penicillin	Oxacillin	Clindamycin	Gentamicin	Norfloracin	Nitrofurantoin	Vancomycin
<i>Staph aureus</i>	12	-	84	33	0	20	13	0	0
	7	-	100	0	0	0	66	0	0
	-	-	-	-	-	-	-	-	-
<i>Staph CNS</i>	21	-	90	75	33	61	100	0	0
	12	-	88	46	11	66	80	0	0
	-	-	-	-	-	-	-	-	-
<i>Enterococcus sp</i>	93	38	-	-	-	-	81	11	6*
	108	61	-	-	-	-	91	18	10**
	8	57	-	-	-	-	100	20	50***

GRE (Glycopeptide Resistant Enterococci)
* 5 isolates ** 10 isolates *** 3 isolates

GNB

	No of isolates	Ampicillin	Cefuroxime	Cefotaxime	Ceftazidime	Cefipime	Gentamicin	Netilmicin	Amikacin	Aztreonam	Nitrofurantoin	Nalidixic acid	Norfloracin	Ciprofloxacin	Co-trimoxazole	Cefoperazone+ Subactam	Piperacillin+ Tazobactam	Imipenem	Colistin
<i>E. coli</i>	713	89	73	82	-	66	55	35	16	71	18	91	82	82	77	19	32	1*	-
	323	96	79	81	-	71	67	47	26	81	24	94	88	87	78	37	52	1**	-
	29	100	92	81	-	72	75	55	36	72	31	95	95	82	82	36	54	0	-
<i>Enterobacter sp</i>	15	100	62	56	-	45	56	50	45	66	56	80	67	63	60	36	38	0	-
	23	86	72	62	-	55	56	50	20	33	43	56	50	53	70	33	36	0	-
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>Klebsiella sp</i>	135	97	79	74	-	76	61	49	30	74	56	80	76	75	80	40	49	4***	-
	107	99	85	83	-	78	65	53	37	85	61	80	72	78	80	42	63	0	-
	9	100	100	100	-	100	100	87	50	100	62	85	83	100	50	62	50	0	-
<i>Pseudomonas sp</i>	101	-	-	-	57	58	65	52	56	60	-	-	-	70	-	48	32	64	2
	106	-	-	-	70	67	82	76	76	56	-	-	-	86	-	63	47	55	9
	16	-	-	-	92	75	91	78	82	-	-	-	-	91	-	90	67	67	0
<i>Proteus sp</i>	22	35	41	11	-	5	24	21	5	14	100	60	17	21	41	0	0	0	-
	18	59	100	23	-	20	36	20	18	0	100	92	35	38	86	0	0	0	-
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>Acinetobacter sp</i>	26	-	-	77	82	82	76	71	86	80	64	50	80	93	94	56	63	25	10
	28	-	-	76	92	71	71	50	76	92	93	72	72	64	57	50	61	46	8
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Carbapenem resistant isolates (*Enterobacteriaceae*)
* 2 isolates ** 4 isolates *** 3 isolates



Percentage Resistance

OPD
WARD
ICU

GPC

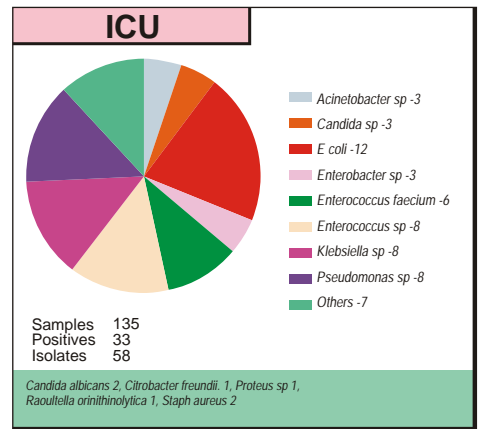
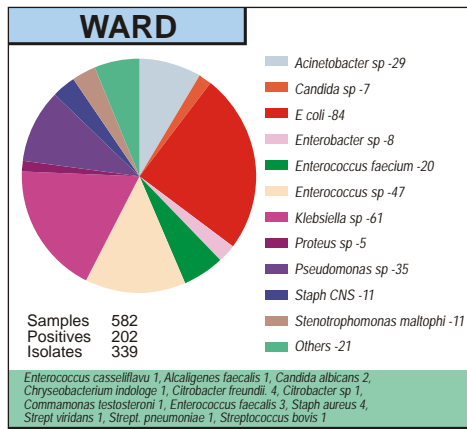
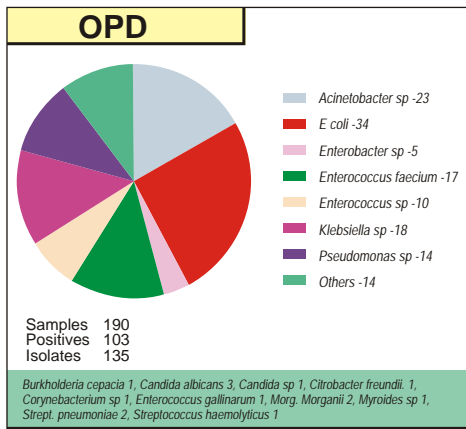
	No. of Isolates	Ampicillin	Penicillin	Oxacillin ^{##}	Gentamicin	Gentamicin [#] HLAR	Clindamycin	Erythromycin	Vancomycin
<i>Staph aureus</i>	137	-	89	28	29	-	14	46	0
	94	-	92	28	33	-	16	48	0
	?	-	-	-	-	-	-	-	-
<i>Staph CNS</i>	79	-	93	71	46	-	35	77	0
	55	-	90	67	50	-	42	81	0
	2	-	-	-	-	-	-	-	-
<i>Enterococcus faecalis</i>	11	11	-	-	-	89	-	-	9*
	11	9	-	-	-	73	-	-	0
	2	-	-	-	-	-	-	-	-
<i>Enterococcus faecium</i>	29	87	-	-	-	86	-	-	28**
	53	96	-	-	-	98	-	-	61***
	10	100	-	-	-	100	-	-	50 ^x
<i>Enterococcus species</i>	86	42	-	-	-	56	-	-	3 ^{xx}
	92	38	-	-	-	52	-	-	4 ^{xxx}
	15	71	-	-	-	86	-	-	0

GRE (Glycopeptide Resistant Enterococci)
* 1 isolate
** 8 isolates
*** 32 isolates
^x 5 isolates
^{xx} 3 isolates
^{xxx} 4 isolates
[#] HLAR: High Level Aminoglycoside Resistance
^{##} Oxacillin sensitivity can be extrapolated for all -lactams and -lactam-inhibitor combinations; and Vancomycin sensitivity for Teicoplanin

GNB

	No of isolates	Ampicillin	Cefuroxime	Cefotaxime	Ceftazidime	Gentamicin	Netilmicin	Amikacin	Ciprofloxacin	Ofloxacin	Co-trimoxazole	Co-amoxyclov	Cefoperazone+ Sulbactam	Piperacillin+ Tazobactam	Imipenem	Colistin
<i>E. coli</i>	124	97	89	87	-	70	41	23	89	95	80	80	27	44	2*	-
	210	96	85	83	-	69	58	28	89	89	82	100	37	52	2**	-
	24	100	84	83	-	74	72	44	100	81	74	100	53	61	4***	-
<i>Enterobacter sp</i>	22	100	80	47	-	53	44	19	63	33	67	66	22	25	0	-
	41	97	73	63	-	66	47	58	76	64	67	80	43	35	0	-
	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>Klebsiella sp</i>	96	98	81	83	-	63	47	26	48	67	75	73	49	56	6***	-
	124	98	78	78	-	63	49	16	80	60	72	80	45	52	0	-
	21	100	93	93	-	81	64	55	93	92	87	100	76	80	0	-
<i>Proteus sp</i>	30	87	58	62	-	53	52	39	71	65	79	29	3	4	0	-
	36	72	58	53	-	56	55	43	33	43	59	46	6	4	0	-
	7	86	57	57	-	57	40	57	100	40	80	0	0	0	0	-
<i>Acinetobacter sp</i>	85	-	-	-	-	88	80	56	78	88	81	-	69	79	74	1
	117	-	-	-	96	95	62	85	95	79	95	-	82	91	81	4
	14	-	-	-	100	93	84	86	80	80	92	-	90	91	83	11
<i>Pseudomonas aeruginosa</i>	122	-	-	-	39	49	39	37	53	49	-	-	35	17	26	1
	107	-	-	-	52	67	56	54	67	52	-	-	54	36	34	1
	13	-	-	-	67	85	75	86	100	75	-	-	68	36	66	0
<i>Pseudomonas sp</i>	5	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-
	22	-	-	-	55	54	67	46	0	87	?	-	38	36	45	13
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Carbapenem resistant isolates (Enterobacteriaceae)
* 4 isolates of *E. coli* ** 6 isolates of *Klebsiella* *** 4 isolates of *E. coli*



Percentage Resistance

OPD
WARD
ICU

GPC	No of isolates	Penicillin	Ampicillin	Oxacillin*	Gentamicin	Clindamycin	Erythromycin	Gentamicin 120*	Vancomycin
Staph aureus	-	-	-	-	-	-	-	-	-
	4	100	-	75	-	50	100	-	0
	2	-	-	-	-	-	-	-	-
Staph CNS	8	78	-	44	-	22	62	33	0
	11	100	-	55	67	42	-	-	0
	1	-	-	-	-	-	-	-	-
Enterococcus faecium	17	-	100	-	-	-	-	94	64*
	20	100	100	-	-	-	-	65	38**
	6	-	83	-	-	-	-	67	50***
Enterococcus sp	10	-	55	-	-	-	-	10	10#
	47	-	40	-	-	-	-	37	5##
	8	-	-	-	-	-	-	-	-

GRE (Glycopeptide Resistant Enterococci)

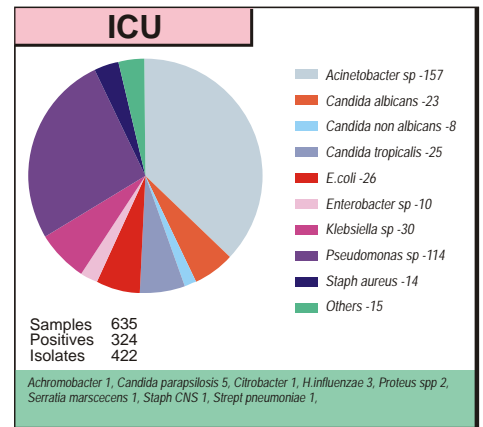
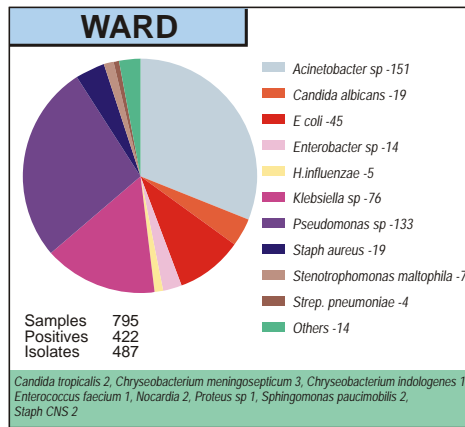
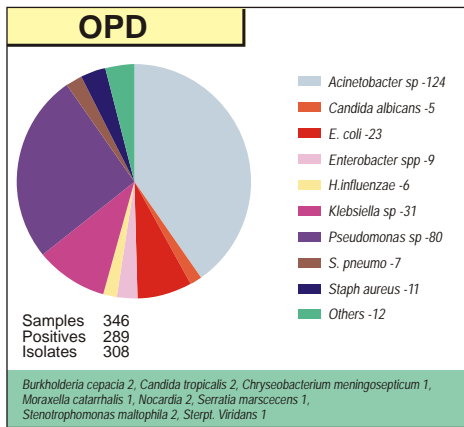
* 11 isolates ** 8 isolates *** 3 isolates # 1 isolate ## 2 isolates

x HLAR: High Level Aminoglycoside Resistance.

xx Oxacillin sensitivity can be extrapolated for all -lactams and -lactam-inhibitor combinations; and Vancomycin sensitivity for Teicoplanin.

GNB	No of isolates	Ampicillin	Cefturoxime	Ceftriaxone	Ceftazidime	Cefipime	Gentamicin	Amikacin	Ciprofloxacin	Ofloxacin	Co-trimoxazole	Co-amoxyclov	Cefoperazone+ Sulbactam	Piperacillin+ Tazobactam	Imipenem	Colistin
E. coli	34	93	80	72	-	75	51	14	87	84	75	100	25	40	0	-
	84	96	84	100	-	82	65	21	91	74	83	34	27	44	0	-
	12	100	100	100	-	100	83	25	100	100	77	100	36	50	8*	-
Enterobacter sp	5	100	100	33	-	60	60	0	-	40	50	100	20	25	0	-
	8	100	86	-	-	50	25	12	-	50	50	100	37	66	0	-
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Klebsiella sp	18	100	90	100	-	92	72	21	100	37	50	100	62	67	0	-
	61	100	82	85	-	76	60	23	75	62	68	81	52	51	2*	-
	8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pseudomonas sp	14	-	-	-	82	90	71	61	75	100	80	100	70	66	50	12
	35	-	-	-	71	45	61	57	86	53	100	-	66	50	45	12
	8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Acinetobacter sp	23	-	-	-	87	88	86	73	74	67	76	100	65	86	100	0
	29	-	-	-	88	92	85	75	84	62	64	-	72	58	56	0
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

*Only one isolate was Carbapenem resistant



Percentage Resistance

OPD
WARD
ICU

GPC	No. of Isolates	Penicillin	Oxacillin*	Clindamycin	Erythromycin	Gentamicin	Vancomycin
<i>Staph. aureus</i>	11	90	46	36	67	46	0
	19	100	68	56	84	77	0
	14	100	86	86	84	88	0
<i>Strept. pneumoniae</i>	1	-	-	-	-	-	-
	7	0	0	-	-	-	0
	4	-	-	-	-	-	-

* Oxacillin sensitivity can be extrapolated for all -lactams and -lactam-inhibitor combinations; and Vancomycin sensitivity for Teicoplanin.

GNB	No of isolates	Ampicillin	Cefuroxime	Cefotaxime	Ceftazidime	Ciprofloxacin	Ofloxacin	Co-trimoxazole	Gentamicin	Amikacin	Netilmicin	Cefeprozone+ Sulbactam	Piperacillin + tazobactam	Imipenem	Colistin
<i>E. coli</i>	23	91	76	76	-	83	75	64	45	8	19	41	48	0	-
	45	98	42	81	-	81	83	65	66	27	49	31	46	0	-
	26	100	96	96	-	94	91	70	76	42	75	60	59	0	-
<i>Klebsiella sp</i>	31	100	89	90	-	67	65	81	74	42	60	42	72	0	-
	11	100	84	93	-	91	74	78	76	58	71	60	75	0	-
	100	100	86	92	-	72	57	73	81	47	80	67	48	0	-
<i>Enterobacter sp</i>	8	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	12	100	83	56	-	-	-	-	100	13	33	25	25	0	-
	10	100	89	10	-	-	-	-	10	8	10	25	14	0	-
<i>Pseudomonas sp</i>	80	-	-	-	67	70	65	-	66	65	63	65	48	52*	1
	133	-	-	-	78	77	84	-	85	81	85	68	46	59**	14
	114	-	-	-	78	65	70	-	73	72	70	66	44	68***	8
<i>Acinetobacter sp</i>	124	100	95	96	96	97	90	86	85	95	76	74	96	85#	2
	151	100	98	98	93	98	92	97	95	97	91	86	96	77###	6
	157	100	100	100	94	99	97	100	99	98	88	98	100	79####	5

Carbapenem resistant isolates (*Enterobacteriaceae*)

* 41 isolates ** 78 isolates *** 77 isolates

106 isolates ### 117 isolates #### 124 isolates

PUBLICATIONS

- Raveendran R, Wattal C, Sharma A, Oberoi JK, Prasad KJ, Datta S. High level ciprofloxacin resistance in Salmonella enteric isolated from blood. Indian J Med Microbio, 2008; 26(1): 50-3
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DORIPENEM - the latest carbapenem

Doripenem is a semisynthetic carbapenem, having good activity against both gram-positive and gram-negative bacteria, and is stable against most beta-lactamases.

Mechanism of Action: It inhibits cell wall formation, facilitates bacterial cell lysis, and is bactericidal.

Dose: 500 mg IV every 8 hours (intravenously as an infusion).

Reconstitution requires 10 ml of sterile water for injection or normal saline. The reconstituted suspension is not meant for direct injection and further dilution is required for intravenous infusion. For a dose of 500 mg, the suspension is added to an infusion bag containing 100ml of normal saline and gently shaken till clear. The final infusion solution has a concentration of 4.5 mg/ml and should be infused over 1 hour.

Pharmacokinetics

- It is distributed into most body fluids and tissues, including bile, gallbladder, peritoneal exudate, retroperitoneal fluid, and urine.
- Low plasma protein binding (approximately 8.1%.)
- Excreted mainly unchanged in the urine (~70% excreted over 48 hours)
- Hepatic CYP enzymes are not involved in the metabolism of doripenem.
- Dose adjustments are required in patients with renal impairment.

Creatinine clearance	Dose adjustment
> 50 ml/min	No dose adjustment needed
30–50 ml/min	250 mg IV (over 1 hour) every 8 hours
10–30 ml/min	250 mg IV (over 1 hour) every 12 hours
< 10 ml/min	No recommendations due to insufficient data

Indications for use (as a single agent)

- Treatment of complicated urinary tract infection, including pyelonephritis, due to *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*
- Treatment of complicated intra-abdominal infections due to *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacteroides species*, *Streptococcus constellatus*, *Streptococcus intermedius* and *Peptostreptococcus species*
- Also being investigated for treating nosocomial pneumonia.

Contraindications / Adverse affects

- Hypersensitivity to any carbapenem /cephalosporin / penicillin / any beta-lactam
- Most common adverse reactions (approx. 5%) are headache, nausea, rash and phlebitis
- Associated with pseudomembranous colitis (~1%), nausea (0.2%), vulvomycotic infection (0.1%) and rash (0.1%) which may led to discontinuation of therapy
- Doripenem should be used cautiously in patients with a history of a seizure disorder
- Safe use during human pregnancy has not been established (Category B).

REFLECTIONS

It was wonderful to go through the 'new-look' SGRH microbiology newsletter. The addition of fungal isolate details and their susceptibility patterns coupled with prescription auditing of antifungals made interesting reading. Kudos to you and your team!

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Manipal Hospital, Bangalore

The Prescription auditing data could not be compiled due to HIS implementation

Fever - A diagnostic challenge

(contd. from page 1)



Growth of *Brucella melitensis* on chocolate agar after overnight incubation.

DISCUSSION

Brucellosis is an occupational zoonotic disease of worldwide distribution, endemic especially in countries of the Mediterranean basin, Arabian Gulf, Indian subcontinent, parts of Mexico, and Central and South America. World wide incidence of brucellosis varies from <0.01% to >200/100000 population.¹ Exact magnitude of the problem remains unknown due to the paucity of reports and difficulty in diagnosis. True incidence may be 25 times higher than the reported incidence due to misdiagnosis and under-reporting.¹ Brucellosis in India has been reported from almost all states.² Seroprevalence of 34% has been reported from Haryana in high risk persons³ and a seropositivity rate of 6.8% and 0.8% has been reported by Sen & Kadri in cases of PUO.^{4,5}

Brucella are minute Gram negative intracellular coccobacilli. Out of the 7 species, only 4 are known to cause human disease, with *Brucella melitensis* being the most virulent. Presence of rough or smooth lipopolysaccharide and the ability to replicate and persist in host cells correlates with the virulence of the disease in humans.⁶ Survival in tap water, dry and damp soil, liquid manure, faeces and slurry has been documented for a considerable time period depending upon environmental temperature.

Transmission to humans occurs through consumption of infected, unpasteurised animal-milk products, contact with infected animal parts, and through inhalation of infected aerosolised particles. Human to human transmission has been reported but is rare.⁷ Attack rate for laboratory acquired infection is 30-100%.⁸

Human brucellosis can vary from an acute febrile illness to an ill defined disease which can affect any organ. Malodorous perspiration is almost pathognomonic. Constitutional symptoms along with lymphadenopathy, hepatomegaly, splenomegaly are almost always seen. Complications as osteoarticular disease, CNS disorders, epididymo-orchitis, respiratory disorders, rashes and

cardiovascular disorders may be present. Relapses at a rate of 10% usually occur in the first year after infection.

The absolute diagnosis of brucellosis requires isolation of organism from blood or tissue cultures by Castaneda's method or Automated culture systems. Bone marrow cultures are considered the gold standard for the diagnosis, since the relatively high concentration of *Brucella* in reticuloendothelial system makes it easier to detect the organism. But because of the slow growth and difficulty in identification the sensitivity of cultures varies from 15-70% only.⁹ Diagnosis may thus rest upon serological techniques.

The classical Rose Bengal test may be used as a rapid screening test. Though the sensitivity reported is 99%, the specificity is low. For confirmation the Serum Agglutination test (SAT) or ELISA may be used.¹⁰ SAT measures the total agglutinating antibodies (IgM and IgG). Titres above 1:160 are considered diagnostic in non endemic areas. However a titre of 1:320, with a compatible clinical presentation is considered significant in endemic areas.¹¹

At our hospital, blood samples from 38 patients were received from January 2006 to March 2008, of which 3 were positive for *Brucella* antibodies by the SAT method with titres of 1:2560, 1:5120, and 1:640. Of these two cases were blood culture proven and one was serologically confirmed. Automated blood culture system appears to decrease the time to positivity considerably and Vitek identification system confirms the diagnosis.

Development of a specific PCR, though a recent advance, needs standardization and better understanding of clinical significance of the results.¹²

Treatment with Doxycycline 100mg for 6 weeks plus 1gm Streptomycin daily for 2-4 weeks is the accepted standard. Rifampicin 600-900mg for 6 weeks may however be substituted instead of Streptomycin.¹³ Complications may require prolonged therapy for at least 8 weeks.

The combination of potential exposure, consistent clinical features, a high degree of clinical suspicion, and raised levels of *Brucella* antibodies with or without positive cultures confirms the diagnosis of brucellosis.

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