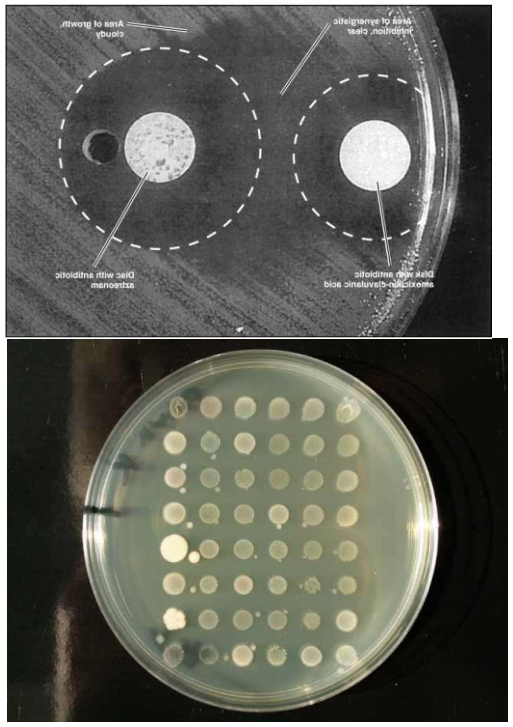
Conducting surveillance of antimicrobial resistance and residues in the hospital and community environment



Vishal Diwan

Associate professor

Public Health and Environment

R.D. Gardi Medical College, Ujjain, India

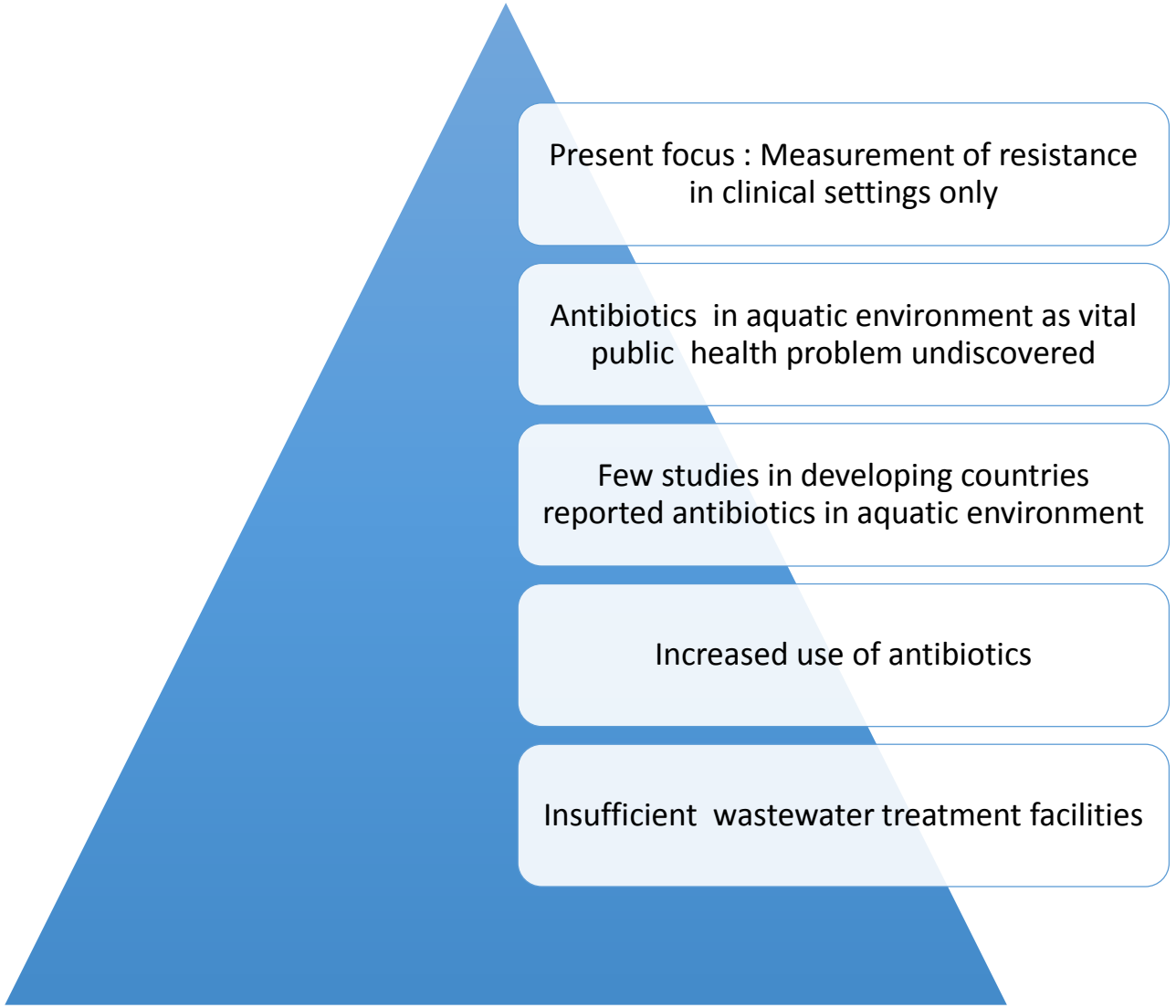
Researcher

Department of Public Health Sciences

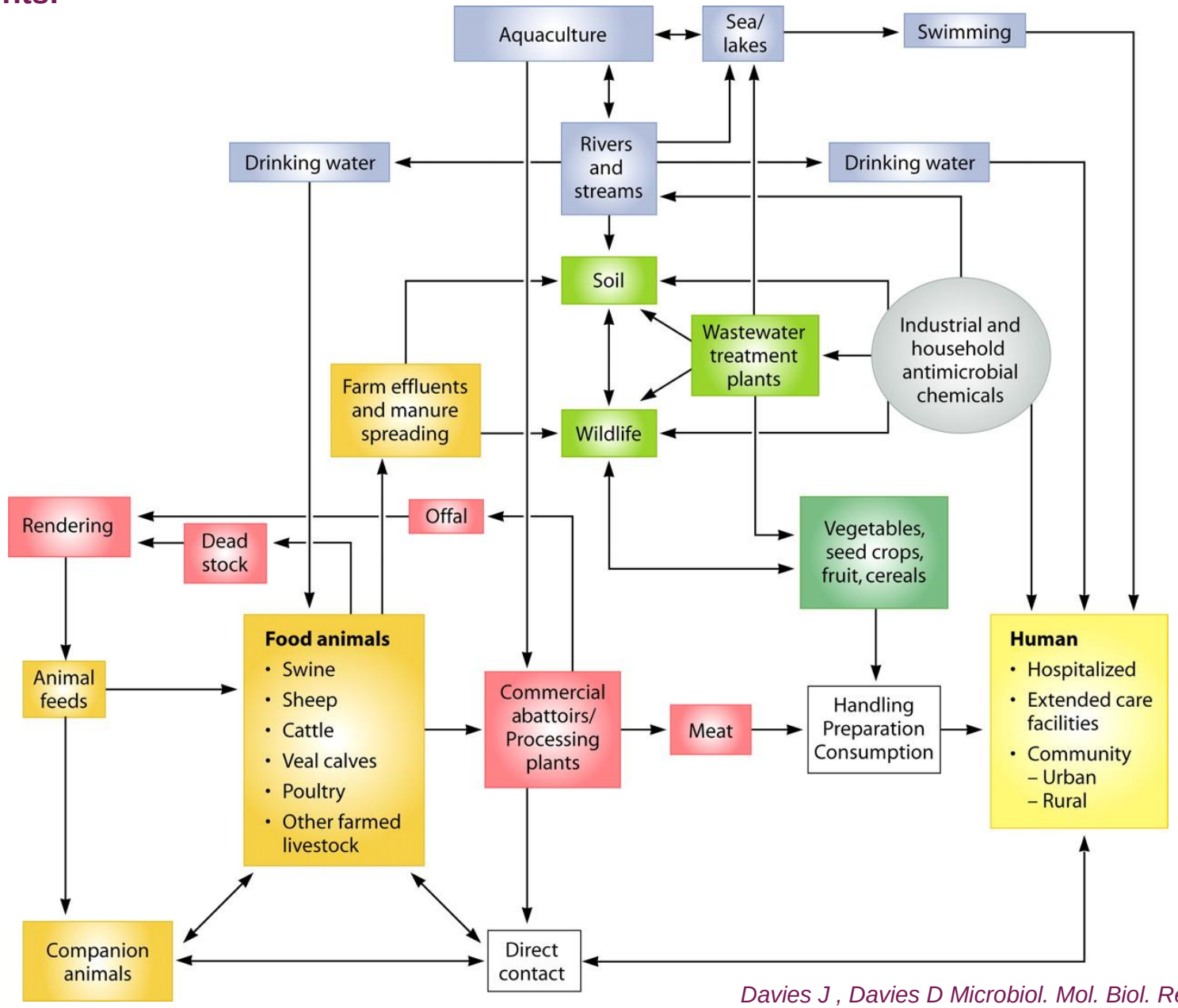
Karolinska Institutet, Sweden

vishaldiwan @hotmail.com

Relevance of Antibiotics and Environment studies



Dissemination of antibiotics and antibiotic resistance within agriculture, community, hospital, wastewater treatment, and associated environments.



Davies J , Davies D Microbiol. Mol. Biol. Rev. 2010;74:417-433

Scope of Present Presentation ……

- Community environment
- Hospital environment
- Water and waste water treatment plants
- River and Reservoir Environment

- Not Covered
  - Fish and Aquaculture
  - Poultry
  - Pharmaceutical Plants and related waste
  - Food and related Items

Environmental Surveillance of AMR depends on

- **Time**
  - Short term goals
  - Long term goals

Scale

- Pan India
- Few States
- Few districts

Available Resources

- data collection (Primary and Secondary)
- analysis cost
- result dissemination

Feasibility

Organization of Surveillance Activities

- Who will do it
- Part of ongoing initiative
- Vertical Programme
- Current capacity
- Required capacity Building (Laboratory, Analysis etc)
- Training, ethical issues etc
- Data Integration and Management

Selection of Antibiotics for residual analysis

- (i) the prescription pattern that area
- (ii) antibiotic residues found in the same setting in previous studies
- (iii) the degree of antibiotic metabolism by the human body
- (iv) environmental stability, and
- (v) the known and suspected environmental impact of an antibiotic

Selection of Antibiotics

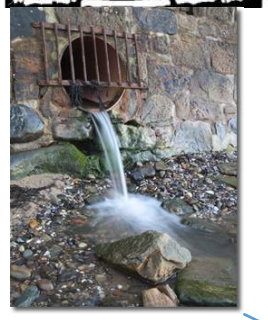
Antibiotics for AST Pattern

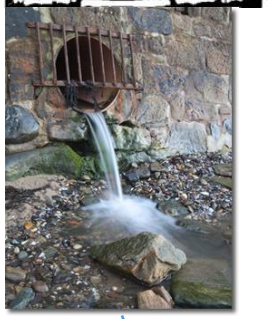
- Ampicillin, Cefotaxime, Ceftazidime, Cefepime, Imipenem, Meropenem, Ciprofloxacin, Nalidixic Acid, Gentamicin, Amikacin, Nitrofurantoin, Tetracycline, Sulphamethizole, Corimoxazole, colistin

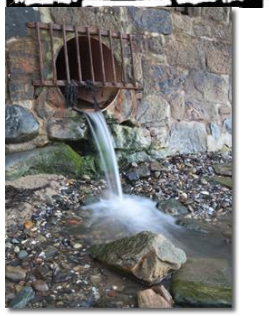
Antibiotics for Residual Testing

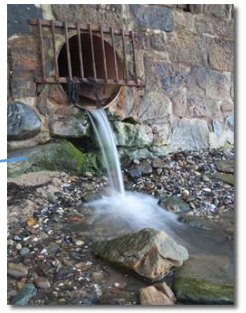
- Ciprofloxacin, Enrofloxacin, Erthromycin, Norfloxacin, Ofloxacin, Sulfamethoxozole, Trimethoprim, Metronidazole, Amoxicillin, Ampicillin, Total Residual Antibiotics as beta-lactam

Surveillance of Resistance and Residues in Hospital Environment









Untreated hospital effluent

Antibiotic residues , metabolites and antibiotic resistance bacteria

Table 5: Levels of monitored antibiotics (µg/l) in waters associated with a hospital in Ujjain, India using LC-MS/MS

Antibiotics	Site 1		Site 2		Site 3	
	Ground Water	Municipal Water	At 10:00	At 16:00	At 10:00	At 16:00
Amoxicillin	--	--	--	--	--	--
Ceftriaxone	--	--	--	--	--	--
Amikacin	--	--	--	--	--	--
Ofloxacin	--	--	--	4.5	5.6	7.5
Ciprofloxacin	--	--	2.2	218.3	67.3	236.6
Norfloxacin	--	--	--	6.4	29.6	22.8
Levofloxacin	--	--	--	5.0	6.8	8.8

-- = Below Detection Limit
Site 1 = Incoming safe water (received in hospital only once a day)
Site 2 = At the point of exit of inpatient wards of the hospital
Site 3 = 100 metres from the hospital in subsequent drains

Table 1. Concentration of antibiotic released/day/hospital (ng/L).

	CIP		LEV		OFL		NOR		FQ		MET		SUL		TOTAL	
	CS	GS	CS	GS	CS	GS	CS	GS	CS	GS	CS	GS	CS	GS	CS	GS
Summer	155.5	–	–	472	35	96	–	–	191	568	131	18	34	1174	355	1761
Rains	694	1239	66	88	90	85	40	225	891	1638	145	143	560	76	1596	1858
Winter	245	1836	578	1078	495	475	–	–	1318	3389	36	18	106	355	1460	3763
Total	1095	3076	644	1638	620	656	40	225	2400	5595	312	179	700	1605	3412	7381
Average (Total/3)	365	1025	214	546	206	218	13	75	800	1865	104	59.95	233	535	1137	2461

CIP: Ciprofloxacin, LEV: Levofloxacin, OFL: Ofloxacin, NOR: Norfloxacin, FQ: fluroquinolones, MET: Metronidazole, SUL: sulfamethoxazole,
CS: Continuous sampling, GS: Grab Sampling.

Surveillance of Resistance and Residues in Hospital associated waters

- Starting Point
  - Start with at least 10 Hospital with more than 100 beds
  - Scale up as per resources
- Sampling
  - Four Times in a year (to study seasonality)
  - Hospital waste water
  - Hospital incoming water
  - Continuous or Grab Sampling

  - Hospital Environment (OT, Labour room, surfaces)

- Indicator Bacteria
  - *E.coli*
  - *Klebsiella spp*

Analysis

- CFU
- Antibiotic Residues
- AST Patterns, ESBL
- Antibiotic resistance genes (optional)
- **Inpatient Hospital antibiotic use**

OPEN ACCESS Freely available online

PLOS ONE

Seasonal and Temporal Variation in Release of Antibiotics in Hospital Wastewater: Estimation Using Continuous and Grab Sampling

Vishal Diwan[1,2]*, Cecilia Stålsby Lundborg[1], Ashok J. Tamhankar[1,3]

1 Global Health (IHCAR), Department of Public Health Sciences, Karolinska Institutet, Tomtebodavägen, Stockholm, Sweden, **2** Department of Public Health & Environment, R.D. Gardi Medical College, Agar Road, Ujjain, India, **3** Indian Initiative for Management of Antibiotic Resistance (IIMAR), Department of Environmental Medicine, R.D. Gardi Medical College, Agar Road, Ujjain, India

Diwan *et al. BMC Public Health* 2010, **10**:414
http://www.biomedcentral.com/1471-2458/10/414

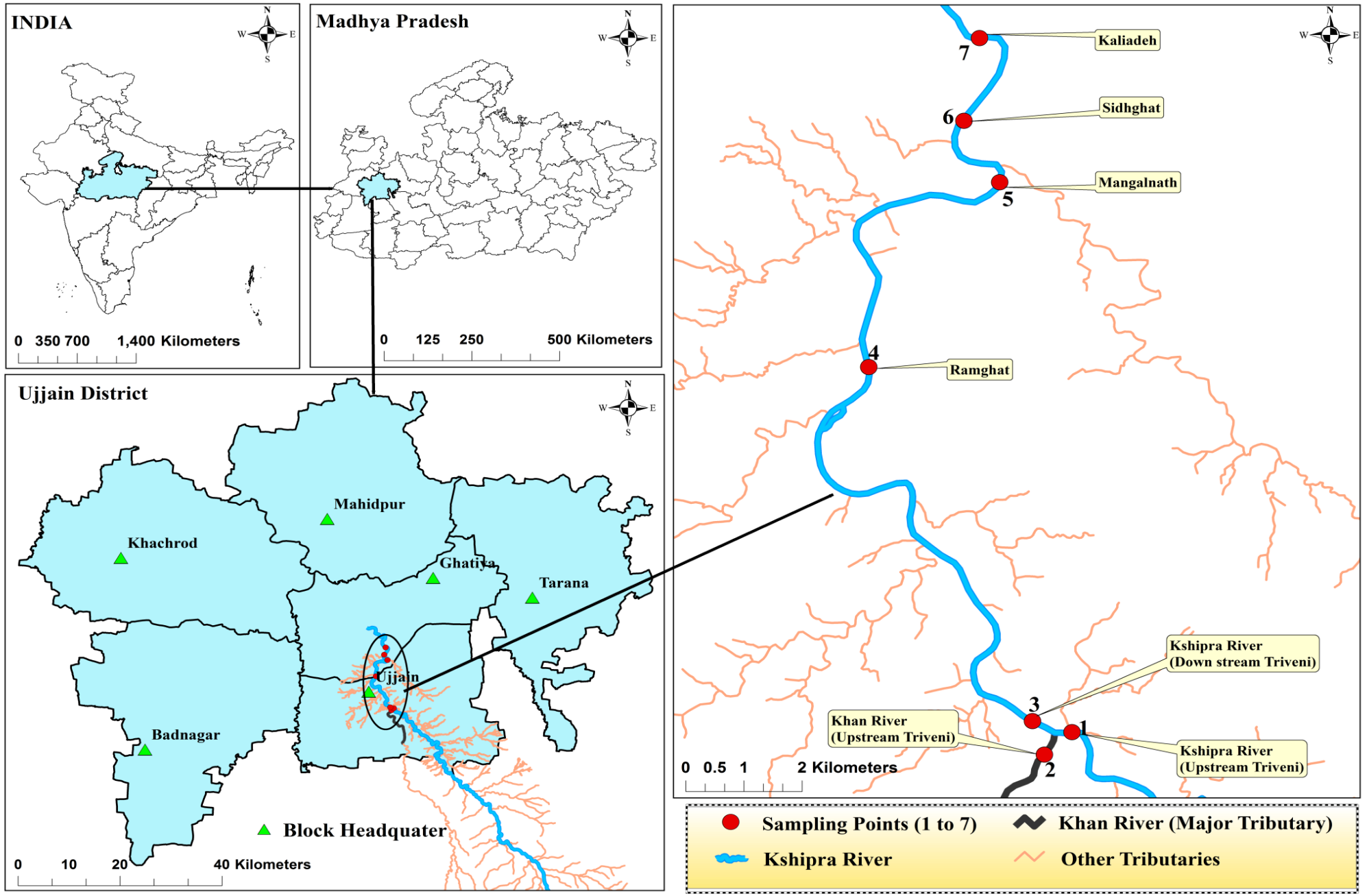
BMC Public Health

RESEARCH ARTICLE Open Access

Antibiotics and antibiotic-resistant bacteria in waters associated with a hospital in Ujjain, India

Vishal Diwan*[1,2], Ashok J Tamhankar[3,4], Rakesh K Khandal[5], Shanta Sen[5], Manjeet Aggarwal[5], Yogyata Marothi[6], Rama V Iyer[6], Karin Sundblad-Tonderski[7] and Cecilia Stålsby- Lundborg[1]

Surveillance of Resistance and Residues in River Environment


INDIA
0 350 700 1,400 Kilometers
Madhya Pradesh
0 125 250 500 Kilometers
Ujjain District
Mahidpur
Khachrod
Ghatiya
Tarana
Ujjain
Badnagar
Block Headquater
0 10 20 40 Kilometers
7
Kaliadeh
6
Sidhghat
5
Mangalnath
4
Ramghat
Kshipra River
(Down stream Triveni)
3
1
Khan River
(Upstream Triveni)
Kshipra River
(Upstream Triveni)
2
0 0.5 1 2 Kilometers
Sampling Points (1 to 7)
Khan River (Major Tributary)
Kshipra River
Other Tributaries

Antibiotic resistance and multidrug resistance patterns of *E. coli* isolated from river water samples in different seasons in Kshipra river in India

RIVER WATER SAMPLES					
	Summer n=70*	Rain n=80**	Autumn n=70***	Winter n=83****	p-value
Antibiotics	n(%)	n(%)	n(%)	n(%)	
Ampicillin	12 (17)	27 (33)	32 (45)	33 (39)	0.002
Cefotaxime	14 (20)	15 (18)	14 (20)	24 (28)	0.4
Imipenem	1 (1)	1 (1)	1 (1)	4 (4)	0.5
Meropenem	7 (10)	0 (0)	4 (5)	22 (26)	<0.0001
Ciprofloxacin	4 (5)	7 (8)	10 (14)	12 (14)	0.2
Nalidixic Acid	8 (11)	11 (13)	16 (22)	21 (25)	0.08
Amikacin	13 (15)	0 (0)	0 (0)	13 (15)	<0.0001
Sulphamethizole	5 (7)	11 (13)	12 (17)	7 (8)	0.2
ESBL	7 (8)	10 (11)	10 (12)	5 (6)	0.4
MDR	2 (2)	15 (17)	19 (24)	20 (23)	<0.0001

Antibiotic resistance and multidrug resistance patterns of *E. coli* isolated from river sediment samples in different seasons in Kshipra river in India

SEDIMENT SAMPLES				
	Rain n= 31*	Autumn n=27**	Winter n=39***	p-value
Antibiotics	n (%)	n (%)	n (%)	
Ampicillin	9 (29)	9 (33)	12 (30)	0.96
Cefotaxime	9 (29)	6 (22)	18 (46)	0.12
Imipenem	0 (0)	0 (0)	2 (5)	0.33
Meropenem	0 (0)	0 (0)	11 (28)	<0.0001
Ciprofloxacin	6 (19)	7 (25)	6 (15)	0.62
Nalidixic Acid	7 (22)	11 (40)	11 (28)	0.34
Amikacin	0 (0)	1 (3)	2 (5)	0.62
Sulphamethizole	5 (16)	7 (25)	7 (17)	0.65
Corimoxazole	6 (19)	8 (29)	7 (17)	0.55
MDR	9 (26)	10 (34)	10 (24)	0.67

Antibiotic resistance-coding genes present in the Escherichia coli isolates from river water in different seasons in Kshipra river in India

RIVER WATER					
	Autumn	Rain	Summer	Winter	p-value*
Antibiotic resistance genes	n(%)	n(%)	n(%)	n(%)	
CTX-M1[a]	9 (50)	10 (31)	8 (23)	8 (19)	0.09
CTX-M2[a]	0 (0)	0 (0)	0 (0)	0 (0)	-
CTX-M9[a]	0 (0)	0 (0)	0 (0)	0 (0)	-
qnrA.A[b]	0 (0)	0 (0)	0 (0)	0 (0)	-
qnrA.B[b]	0 (0)	0 (0)	(5)	0 (0)	0.2
qnrA.S[b]	2 (8)	6 (23)	2 (10)	7 (16)	0.5
Sul.1[c]	3 (13)	4 (12)	2 (5)	4 (12)	0.6
Sul.2[c]	5 (21)	6 (18)	4 (10)	4 (12)	0.6
NDM[d]	0 (0)	0 (0)	0 (0)	0 (0)	-
VIM[d]	0 (0)	0 (0)	0 (0)	0 (0)	-

Antibiotic resistance-coding genes present in the Escherichia coli isolates from river sediment in different seasons in Kshipra river in India

RIVER SEDIMENT				
	Autumn	Rain	Winter	p-value*
Antibiotic resistance genes	n(%)	n(%)	n(%)	
CTX-M1	2 (40)	5 (25)	7 (41)	0.6
CTX-M2	0 (0)	0 (0)	0 (0)	-
CTX-M9	0 (0)	0 (0)	0 (0)	-
QNR.A	0 (0)	0 (0)	0 (0)	-
QNR.B	0 (0)	0 (0)	0 (0)	-
QNR.S	2 (15)	0 (0)	4 (44)	0.3
Sul.1	3 (33)	1 (25)	2 (33)	0.9
Sul.2	3 (33)	1 (25)	4 (67)	0.5
NDM	0 (0)	0 (0)	0 (0)	-
VIM	0 (0)	0 (0)	0 (0)	-

Surveillance of Resistance and Residues in River Environment

- Starting Point
  - Major River River System
  - Reservoirs
  - Scale up as per resources

- Sampling
  - Four Times in a year (to study seasonality)
  - Surface water samples
  - Sediment samples
  - During Mass bathing Occasions
- Indicator Bacteria
  - *E.coli*
  - *Klebsiella spp*

Analysis

- CFU
- Basic Water quality and river flow
- Antibiotic Residues
- AST Patterns, ESBL
- Antibiotic resistance genes (optional)

International Journal of
Environmental Research and Public Health

MDPI

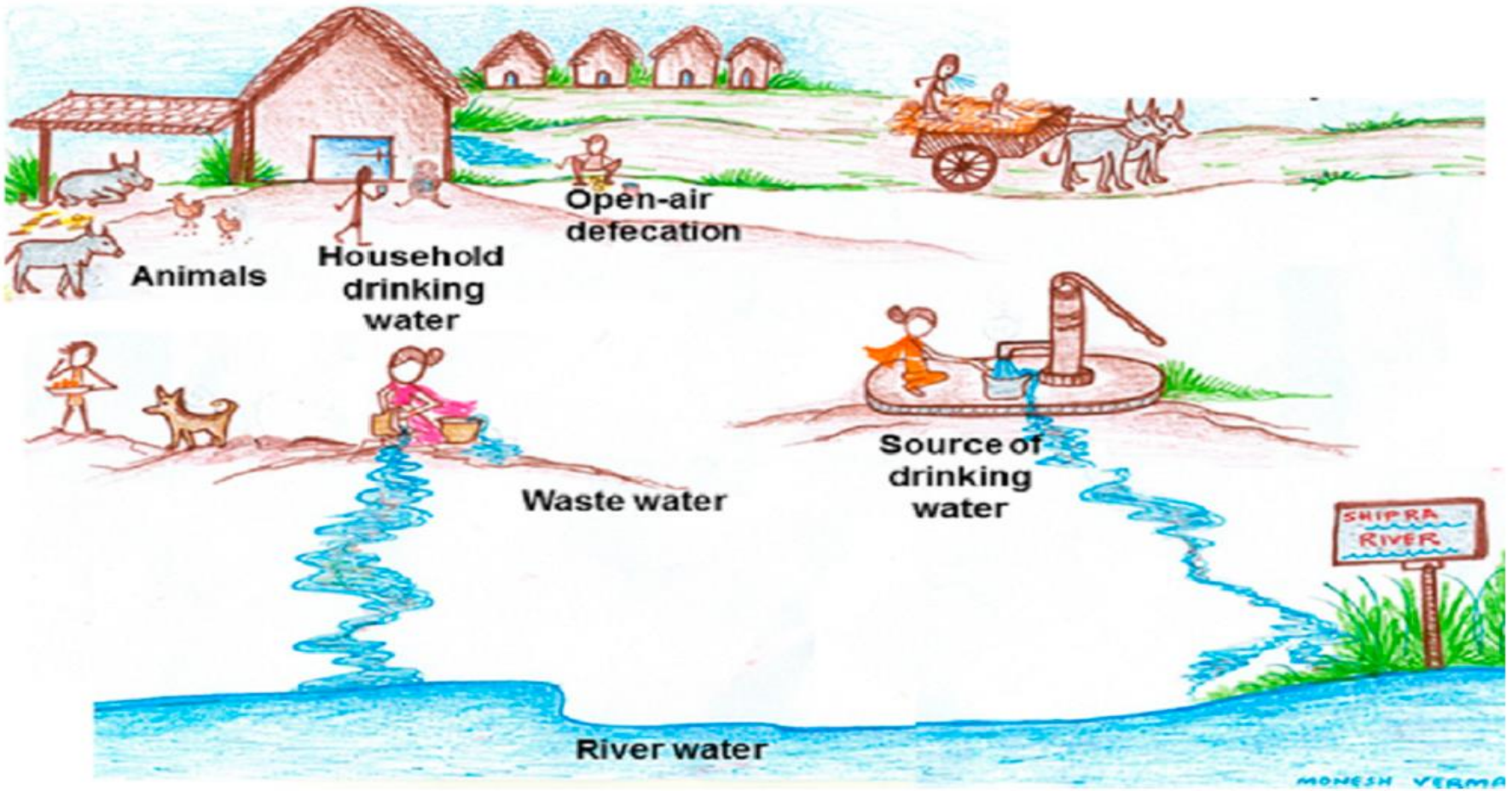
Concept Paper

A Three-Year Follow-Up Study of Antibiotic and Metal Residues, Antibiotic Resistance and Resistance Genes, Focusing on Kshipra—A River Associated with Holy Religious Mass-Bathing in India: Protocol Paper

Vishal Diwan [1,2,3,†,*], Manju Purohit [2,4,†], Salesh Chandran [2,5], Vivek Parashar [1], Harshada Shah [5], Vijay K. Mahadik [6], Cecilia Stålsby Lundborg [2,†] and Ashok J. Tamhankar [2,7,†]

1 Department of Public Health and Environment, R.D. Gardi Medical College, Ujjain 456006, India; vivekstream@yahoo.co.in
2 Department of Public Health Sciences, Global Health, Health Systems and Policy (HSP): Medicines focusing on antibiotics, Karolinska Institutet, Stockholm 17177, Sweden; manjuraj.purohit64@gmail.com (M.P.); saleshp@gmail.com (S.C.); cecilia.stalsby.lundborg@ki.se (C.S.L.); ejetee@gmail.com (A.J.T.)
3 International Centre for Health Research, Ujjain Charitable Trust Hospital and Research Centre, Ujjain 456001, India
4 Department of Pathology, R.D. Gardi Medical College, Ujjain 456006, India
5 Department of Microbiology, R.D. Gardi Medical College, Ujjain 456003, India; sharshada1955@yahoo.com
6 R.D. Gardi Medical College, Ujjain 456006, India; uctharc@sancharnet.in
7 Indian Initiative for Management of Antibiotic Resistance, Department of Environmental Medicine, R.D.

Surveillance of Resistance and Residues in Community



Antibiotic Resistance in Children Stool Samples and its Environment in Rural Ujjain

Antibiotic	% Resistance (*E.Coli*)				
	Human Stool	Animal Stool	Household Drinking Water	Source Drinking Water	Waste Water
Cefotaxime	51	14	21	35	30
Cefotaxime	50	13	22	35	31
Ampicillin	59	20	23	38	38
Nalidixic Acid	51	11	13	29	39
Ciprofloxacin	15	4	8	9	15
Imipenem	0	0	0	3	0
Meropenem	6	4	4	12	8
Sulphamethiazole	27	17	16	26	27

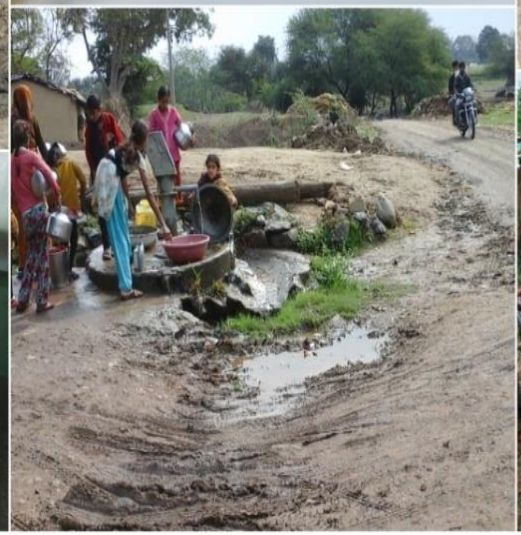
Surveillance of Resistance and Residues in Community

- Cohort of Household
  - Follow-up of all members of cohort
  - Health seeking behavior (common illness)
  - Drug information
  - **Sample Collection**
    - Human Stool
    - Drinking Water
    - Source Water
    - Waste Water
    - Animal Stool

One Health





Surveillance of Resistance and Residues in Community

- Scale
  - Start with 6 Household Cohorts in selected states
  - Three Urban and Three Rural Cohorts
  - Demographic Surveillance Site (DSS) can be ideal starting points

Follow up of Cohort (Short Term)

- Six Month Initially
- Sample collection two times

Follow up of Cohort (Long Term)

- Health seeking follow up every three month for one Month duration
- Sample collection three times in Year

- Indicator Bacteria

  E.coli

Analysis

- CFU, Basic Water quality parameters, AST
- Antibiotic Residues and Antibiotic Genes (can be optional)

Stålsby Lundborg et al. BMC Public Health (2015) 15:1321
DOI 10.1186/s12889-015-2632-2

BMC Public Health

STUDY PROTOCOL Open Access

Protocol: a 'One health' two year follow-up, mixed methods study on antibiotic resistance, focusing children under 5 and their environment in rural India

Cecilia Stålsby Lundborg[1*], Vishal Diwan[1,2,3], Ashish Pathak[1,4,5], Manju R. Purohit[1,6,7], Harshada Shah[8], Megha Sharma[1,9], Vijay K. Mahadik[10†] and Ashok J. Tamhankar[1,11†]

Surveillance of Resistance and Residues in wastewater treatment plants

- Starting Point
  - Start with at least 10 wastewater treatment plants
  - Sewage treatment plants
  - Waste water treatment plants (in hospitals)
  - Cooperation from hospital is must
  - Scale up as per resources
- Sampling
  - Four Times in a year (to study seasonality)
  - Incoming water waste water
  - Sludge
  - Treated water
  -
  - Continuous or Grab Sampling
- Indicator Bacteria
  - *E.coli*
  - *Klebsiella spp*

Analysis

- CFU
- Antibiotic Residues
- AST Patterns, ESBL
- Antibiotic resistance genes (optional)

Example of Integrated Surveillance- Setting Madhya Pradesh

- Urban and Rural Cohort in Ujjain
- Municipal wastewater treatment plants (Ujjain, Bhopal, Indore)
- Hospital wastewater treatment plants (Ujjain, Bhopal, Indore)
- Hospital waste water (Ujjain, Bhopal, Indore one hospital each)

Attention are also needed on ……

- Surveillance Biomedical waste management
- Collection and disposal of unused antibiotics in community
- Hospital hygiene and cleanliness surveillance
- Surveillance of antibiotic consumption from Pharmacy (with prescription without prescription)
  - Simulated client study
  - Prescription Audit at Pharmacy

Thanks for attention

vishaldiwan @hotmail.com