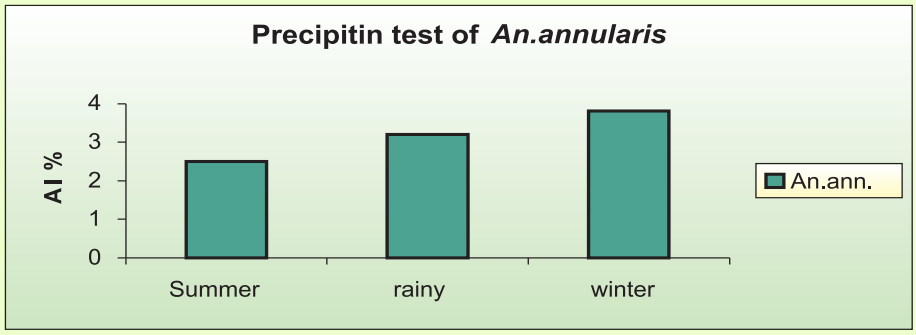
Fig. 8



Susceptibility Test

The susceptibility status of An.culicifacies B and C was done and it was observed that B and C both are resistant to DDT but they are susceptible to Deltamethrine 0.5%.

Though two sibling species reported in Anopheles annualris, the presence of species complex in Orissa is unknown. We have started the detection and identification of sibling species of An. annualris, which also plays an important role in malaria transmission. Molecular methods for identification of sibling species work initiated with standardization of D3 and ITS2 region

The data from two geographical areas have been generated and comared with the two ecotypes with regards to transmission and occurrence of malaria

11. A study on immunoregulation and genotyping for cytokine polymorphism in human cerebral malaria

Principal Investigator:
Dr.B.Ravindran
Co-Investigator: Dr A. K. Satapathy
Collaborators: Dr.Shobona Sharma, TIFR, Mumbai
Dr B.K.Das, SCB Medical College, Cuttack Starting date: January 2006
Closing date: December 2008
Funding: Extramural (ICMR PRC)

Objectives:

(1) To study B-cells responses (IgG and IgE) to malarial phospoproteins, Viz. PfPO, Pf2, Pf9 and MSP1, MSP3, AMA 1 and GPI in cerebral and/or in multiorgan dysfunction in human P.falciparum malaria.

(2) To quantify T-regulatory cells a) CD4+ CD25+ b) CD4+ CTLA 4+ in circulation in human cerebral malaria.

(3) 3) To type the following host gene polymorphism and to correlate predisposition to develop cerebral and/ or Multi-organ dysfunction in P.falciparum malaria: a) IL-10; b) TGF- â; c) TNF- á and d) IFN- γ

Work Progress:

One of the severe pathological manifestations of P.falciparum infection is the cerebral malaria and more crucially patients developing multiorgan dysfunction involving renal and hepatic dysfunction along with cerebral symptoms. However, only a subset of P.falciparum infected patients suffer from such clinical symptoms. The factors responsible for the precipitation of cerebral malaria amongst P.falciparum patients are not yet clearly identified. Several immune responses and host genetic polymorphism have been implicated in naturally acquired immunity and in cerebral malaria.

On Going Studies

Work Progress: Efforts are being made to collect samples from the following categories of malaria patients. (1) Clinically non-complicated P.falciparum cerebral malaria (NCM) (2) Cerebral malaria with renal or hepatic involvement-multiorgan dysfunction and (3) Endemic controls. About 130 blood samples of category (1) and (2) were collected at SCB Medical College, Cuttack. DNA were purified from the leukocytes and preserved. Isolated DNA will be used for typing genetic polymorphism of IL-10, TGF-â, TNF-á and IFN-γ. Sera were separated and preserved which will be used subsequently for quantification of antibodies responses to malarial phosphoproteins.

Principal Investigator:
Dr. Amarendra Mahapatra
Co- Investigators:
Dr. M.R. Ranjit, Mr. D.P. Hansda, Mr. H.S. Naik, Mr. B. Purohit & P.K. Jangid
Funding:
Extramural funding, NVBDCP (Initiated with Intramural grant)
Starting Date: March 2006
Closing date: February 2008

12. The effect of Choloroquine Chemo prophylaxis during pregnancy among the compliant and non - compliant mothers of Orissa.

Objectives:

1. To assess the frequency of malaria among the pregnant women and infants.
2. To assess the drug compliance pattern and impact of malarial chemoprophylaxis on pregnant mothers
3. To study the reasons of non-compliance and other best practices followed if any.

Work Progress:

The proposed study aims at to evaluate the efficacy of Choloroquine chemoprophylaxis in preventing or reducing malaria attack and consequently anaemia among the pregnant mothers. Besides this, the study will help us to calculate / quantify the malaria burden among the pregnant mothers and Infants at the community level, along with the community behaviour towards the disease-malaria. This can help us to plan better strategies for pregnant and infant care, and in turn to reduce the MMR, IMR, along with the proportion of Low Birth Weight Babies (LBW) in future.

Community Survey

Under the IMR mission Government of Orissa is supplying weekly 600mg of Choloroquine chemoprophylaxis, to all the pregnant mothers in the State, under the National Malaria Control Programme. The programme envisages covering all the pregnant women who are to be registered for immunization and ANC attendance at the Angan Wadi Center in the village. After first trimester of the pregnancy the AWC worker gives the chemoprophylaxis to all the pregnant women: since evidences reveal that chronic malaria infection is associated with anaemia in pregnancy, especially in primagravidae and indicate to take effective measures for prevention of malaria

and anaemia in pregnancy, especially in primagravidae. This in turn would significantly reduce anaemia and its deleterious effects on both the mother and the baby. This programme initiated in all districts since 2003 is yet to be evaluated. The study attempts to assess the compliance rate and thus compare the pregnancy outcomes of the compliant and non-compliant mothers.

Table –1 Distribution Hb% among the pregnant women

Anemia level	>11	Mild 9-11g/dl	Moderate 7-9g/dl	Sever < 7	Total No
No.	10	18	32	18	78

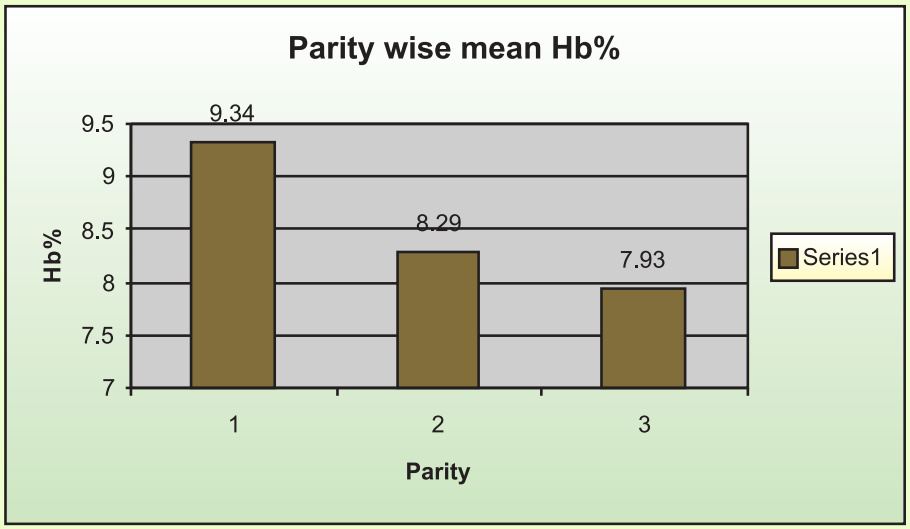
As per the study design a cohort of 500 pregnant women in their first trimester, will be prospectively followed up every three months, for their (i) Drug compliance, (ii) Fever History, (iii) parasite detection by both slide and from peripheral blood as well as cord & placental blood at time of delivery and ICT (iv) Hb status. The pregnancy out comes and fever history will be compared, with the cord & placental blood samples. The postpartum follow up of the study is extended to infants for 6 week to ascertain the transmission of infection. From mother by parasite detection from infant the Angan Wadi Worker's help is taken in this study.During this period a total 78 pregnant women were registered from 35 villages of Gania Block, in Nayagarh district. The preliminary results reveal association between parity and haemoglobin (Hb%) level. The mean Hb% among these subjects was 8.52% (Table-2) ; 10 of them were normal, 18 had severe anaemic and rest 50 had mild or moderate anaemic (Table-1). Out of 78 pregnant women 18 (23%) reported history of malaria. In the second follow-up 1 case out of 5 followed up reported malaria fever. Out of 78 pregnancies, 31 were in their 1st Parity. The rest 47 Pregnancies have reported a bad obstetrics history (BOH-10=21%) of last pregnancies; they are as follows: Still birth-2, Abortion- 4 and Infant died due to Malaria with in One year- 2 cases. In another 2 cases death occurred in the 4th and 7th day but the reasons of cause of death could not be ascertained.

Focus Group Discussion in Community in progress

Table-2 Epidemiological Detaild of all subjects:

Parity / Number	1st	2nd	3rd +	TOTAL
No.of Preg. Women	31	31	16	78
Malaria History	4	6	8	18 (23%)
Hb%	9.34%	8.29%	7.93%	8.52%

Fig. 1 Parity wise distribution of Haemoglobin level



Principal Investigator :
Dr. M.R. Ranjit
Co-Investigator :
Dr G.P.Chhotray, Dr. A.S.Acharya
Starting date : August 2006
Closing date : August 2009
Funding :
Extramural (Applied to NVBDCP)

13. Molecular analysis of drug resistance genes and prediction of treatment outcome in P falciparum infections in Orissa.

Objectives:

(i) To observe the frequency of the genotypes of PfCRT / PfMDR1 and DHFR-DHPS associated with Chloroquine and Pyremethamine-Sulphadoxine resistance in natural P.falciparum parasite populations of Orissa.

(ii) To study the origin and spread of resistant alleles through the parasite population in this region.

Background:

The EDPT chemotherapy is the most practical approach for control of this disease. According to the National Drug Policy, adopted in the state for control of malaria, Chloroquine is the first line and S-P is the second line of treatment of preference. But widespread development of resistance to the first line of drug (CQ) might be the cause of high incidence of malaria attributed deaths in the state, which needs continuous monitoring / surveillance to assess it's efficacy and develop a strategy to prevent it's spread. The WHO has outlined three ways of measuring drug efficacy; (i) The clinical responses of patients to drug treatment; (ii) the sensitivity of parasites to drugs in-vitro or (iii) accepted molecular markers as complementary tools for monitoring drug resistance. Though the first two methods are specific and quite sensitive, yet these are time consuming and sometimes raise ethical issues for its application. However, correlation of specific mutations in the genes that encode targets of the antifolate drugs and drug resistance, such as DHPS (targeted by Sulpha drugs) and DHFR (targeted by

DHFR inhibitors), are well established; and certain mutations in the P.falciparum Chloroquine transporter gene (PfCRT) and the P.falciparum multi-drug resistance gene analog (PfMDR1) has been observed to be associated with the development of resistance to Chloroquine in different studies including our own study conducted during 2002 – 03. However the frequency and distribution of CQ and S-P drug resistance markers has not been known. The proposed study aims at (i) generating a base line data on the frequency and distribution of CQ and S-P resistance markers in different physiographical regions of the state and (ii) predicting the origin and spread of these genotypes through P.falciparum populations in this particular region of the country. This information will serve as a public health tool to develop a rational drug policy and combat spread of drug resistance.

Work Progress

The project proposal has been prepared and submitted to NVBDCP for funding. However the work has been initiated with intramural funds. A total 131 blood samples positive for P.falciparum have been analysed. The genomic DNA of P.falciparum was isolated by standard protocol and point mutations in DHFR & DHPS genes responsible for SP drug resistance were analysed by PCR-RFLP technique. Of the total samples 32 were found to harbour single mutations (either N 51I, C 59R or S108N/T) in DHFR, 38 were having double mutations (51+59: 11, 59+108:17 and 108+51: 10) and 19 had triple mutations (51+59+108). In case of DHPS 16 samples were found to have single mutation (either A437G or K/L540E) none of the samples have double mutations. The study indicates that P.falciparum isolates harbouring SP drug resistant gene are prevalent in the state. However, the study is in progress to analyse other codons of DHFR (A50V, I164L) and DHPS (S/A436F, A581G, A613S/T) to know the level of resistance, its distribution & evolution.

14. A randomised clinical trial with Chloroquine and alternate drug regimens to study the comparative efficacy, in treatment of uncomplicated P.falciparum malaria in two endemic districts of Orissa

Principal Investigator:
Anna S Kerketta
Co-I nvestigators:
M R Ranjit, P K Jangid
Collaborators- 1.
Trupti Rekha Swain,
Pharmacology Department
SCB Medical College, Cuttack.
2. Dr S K Mishra- -IGH, Rourkela.
Starting period: March 2006
Closing period: February 2008
Duration: 2 years
Funding: Extramural

Objectives:

1. To study the comparative efficacy of four antimalarial drug regimens in treatment of uncomplicated P. falciparum malaria.
2. To differentiate the recrudescence and re-infection by using molecular marker.
3. To relate CQ failure with its plasma concentration.

Work progress

The study has been applied for extramural funding and initiated intramurally. The site selection work has been initiated in 8 villages of three high malaria endemic blocks. Daspalla of district Nayagarh, Kamakshya Nagar of district Dhenkanal &

Narsinghpur of district Cuttack were visited with the aim to assess the incidence of fever cases in a defined territory during this season examined. This aims to assess the treatment seeking behaviour of the fever cases and to assess the prevalence of P.falciparum mono infection since it is the pre-requisite for the study. The door-to-door household survey was made to collect information on fever cases daily for consequevtive 5 days in the same popyulation group to record the incidence. Blood slide was collected from each of the fever cases examined under mcirocscope for malaria parasite to confirm the occurrence of malaria. The malaria data was alsoobtained from their local health centre/ PHC to accertain the prevelance of malaria in that area. A total of 7996 populations covered under the survey. Out of this, occurrence of fever was recorded 298(3.7%). All the cases were examined clinically. The result shows 5 - 6% P.f prevalence of malaria in that region.

Mono infection with P.f was obtained in proporsonately small no of fever cases encountered in Nayagarh and Cuttack districts. After accessing the individual requirement as per inclusion criteria the anti-malarial regimen will be randomly allocated. The Blood slides will be examined subsequent to the therapy and while keeping close observation for safety signs as per the protocol. The study in on going.

Principal Investigator:
Dr.B.B.Pal,
Co-Investigators:
Dr.G.P.Chhotray,
H.K.Khuntia, S.K.Samal
Funding: Intra-mural
Starting date: September- 2005
Closing date: August-2006

15. Epidemiological characterization of bacterial entropathogens among the children suffering from acute diarrhoea-A hospital based study.

Objectives:

1. To isolate and identify the various bacterial enteropathogens like E. coli, Salmonella, Shigella, Vibrio cholerae from inpatient diarrhoea patients of paediatric age groups (<14yrs) from capital hospital, Bhubaneswar and Sishu Bhavan of Cuttack.
2. To type the various bacterial enteropathogens by specific antisera and to study their antibiogram.
3. Detection of toxic genes of pathogenic E. coli and Vibrio cholerae by PCR assay.

During this period from September-05 to March-06, 179 rectal swabs were collected and bacteriologically analyzed. Among the bacterial enteropathogens isolated E. coli were 83(82.2%), Vibrio cholerae O1 16 (15.9%), O139 serogroups 0%, Salmonella 0%, Shigella 2(1.98%). Among the Vibrio cholerae O1 strains Inaba serotype were 7 and Ogawa sero types were 9. This is the first report of Vibrio cholerae O1 Inaba serotype, isolated from the children suffering from acute diarrhoea patients. Besides this the same serotype along with some Ogawa serotype were also isolated from the different outbreak areas of Orissa in different time periods. This shows that this new serotype were widespread in thin region.

Three hundred and eighty-nine rectal swabs were also collected during the study period from adult diarrhoea patients from ID hospital, Puri. The predominant

enteropathogens isolated were E. coli- 158 (68.7%), followed by V. cholerae-60 (26.1%) and Shigella spp.- 6 (3.9%) respectively. Among the Shigella isolates, most of them were S. flexneri type-6 (4) followed by S. boydii (1) and S. dysenteriae type-1 (1). Among the 60 V. cholerae isolates; V. cholerae O1 Ogawa were 23 (10%), Inaba were 35 (15.2%) and V. cholerae O139 serogroups were 2 only. The Shigella isolates were showing sensitive to ciprofloxacin, norfloxacin, gentamicin, chloramplenicol and ampicillin; whereas resistant to tetracycline, streptomycin, nalidixic acid, co-trimoxazole, neomycin and furazolidone. All the Vibrio cholerae Ogawa and Inaba isolates were uniformly sensitive to ampicillin, ciprofloxacin, norfloxacin, tetracycline, gentamycin, and chloramphenicol. The resistant profile of Ogawa and Inaba serotype were FrNaN and FrNa respectively. The Inaba serotype was isolated from a cluster of cases of diarrhoea patients of Gaudabadasahi, Puri town during the month of August 2005. Then subsequently these Inaba serotype were also isolated from other districts like Bhubaneswar(Khurda) and Chasapada (Dhenkanal) from September to October 2005 respectively causing localized outbreaks including some isolates from other areas of Puri districts also.

PCR assay of V. cholerae:

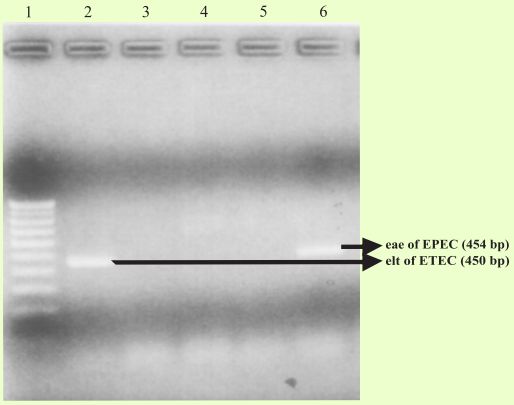
A multiplex PCR assay was conducted on some representative strains of Vibrio cholerae of Ogawa and Inaba for the detection of tcpA and ctx A gene. The multiplex PCR assay revealed that both the strains were ctx A and tcp A gene positive showing biotype El Tor.

Simultaneously the Inaba sero types were showing dominance over Ogawa serotype and they were wide spread in the coastal districts also. This shows that the future outbreak might be due to Inaba serotype. But this was not true while the cholera outbreak in Cuttack town during 2006 was due to V. cholerae O1 Ogawa. The predominance of Inaba serotype over Ogawa was observed during 2005. Where as the outbreak during March 2006 was due to Vibrio cholerae of Ogawa biotype El Tor. This shows that the Ogawa serotype has again remerged as a predominant serotype, which may cause the future outbreak of cholera in this region.

PCR assay of E. coli:

Fifty strains of E. coli were subjected to PCR assay for the detection of eae gene of EPEC and elt gene of ETEC strains. The PCR analysis revealed that 2.7% and 2% were positive for EPEC and ETEC strains respectively. Isolation of other pathogenic E. coli like EAggEC, EHEC including EPEC and ETEC from about 210 DNA isolates will be characterized by PCR assay. Further serogrouping and antibiogram of the pathogenic E. coli will be done.

Fig.1 **Lane 1: 100 bp Ladder, 2: Positive, ETEC (elt), 3-5: negative, ETEC and EPEC, 6: EPEC (eae).**



Principal Investigator :
Dr. Anna S. Kerketta
Co-Investigators :
Mr.P.K.Jangid, Dr.A.S.Acharya
Collaborator :
Director of Census Operation, Orissa.
Funding: Extramural
Starting date: January 2003
Closing Date: December 2006

16. A 6-year's Prospective study of the risks of death by cause from tobacco and alcohol use among 2million Indian men and women, a multicentric study.

Objectives:

1. To study all cause mortality and cause specific mortality (Tuberculosis, cancer, vascular disease, asthma, chronic obstructive pulmonary disease, and other causes) by age, gender and socioeconomic group in relation to tobacco and alcohol use among 2 million Indian adults surveyed for their tobacco and drinking patterns in 1998.
2. To study to what extent does tobacco smoking increases the risk of death from tuberculosis, vascular diseases, cancers and respiratory diseases in India.
3. To study what are the differences in patterns of tobacco and tobacco attributable mortality by socio-economic class, age and gender, and across various region (rural, urban, south, north) and find out the links to indoor air pollution and other potential confounders/effect modifiers.
4. To study to what extent do the alcohol use and amount drunk per week increase or decrease cause specific death rates from vascular disease, cancers, tuberculosis and unintentional and intentional injuries

Background:

The study envisages the following activities 1. Training and retraining of the SRS supervisors on Verbal Autopsy methodology 2.Resampling of 10% of VA of SRS supervisors 3. Assigning of cause of death as per ICD-10. Orissa SRS covers 36.7 million people; spread over 405 units and having 51 supervisors to carry out survey on vital statistics every half yearly.

Work Progress

The training of the supervisors of DCO Orissa was conducted, on Verbal autopsy methodology after which for first time the VA was implemented in SRS, during 2nd

HYS and 2003 1st HYS.A total of 2780 deaths were recorded from all age groups during these surveys. Refresher's training was imparted to the SRS supervisors especially on the use of newer modified manual, use of single page VA form and symptom list .In the Special Survey of death (SSD) covering period of 2001-2003 (except the HYS mentioned earlier). VA has been undertaken on a total of 7000 deaths. These form have been sent back to the physicians from SCB Medical college, Cuttack who had received training on assigning cause of death (coding) in October 2004 and refreshers training was conducted by RMRC in June 2005.The web based assignment of cause of death has been initiated and so far around 5000 deaths have been coded. It will be analysed centrally by CGHR and RGI of India. Resampling of 10% death event was conducted for both the 2nd HYS and 2003 1st HYS as a quality control measure.

17. Epidemiology of viral hepatitis in tribal populations of Orissa, Madhya Pradesh/ Chhatisgarh and Jharkhand, India – a multicentric study

Principal Investigator :
Dr. S. K. Kar
Co-Investigators:
Dr. B. Dwibedi,
Dr. A. S. Acharya,
Dr. B. V. Babu, and
Dr. A. Mohapatra
Collaborator :
Dr. S. P. Singh
(Asso. Prof. SCB. Medical College, Cuttack)
Funding : Extramural (ICMR tribal Task force)
Starting Date : March 2006
Closing date : February 2009

Objectives:

1. To determine the prevalence of antibodies to hepatitis A and hepatitis E viruses (HAV and HEV)
2. To determine the prevalence of hepatitis B, C and delta viruses (HBV, HCV and HDV)
3. To assess the risk factors for transmission of hepatitis viruses
4. To determine the circulating genotypes of HBV and HCV and prevalence of pre-core and basal core promoter mutants of HBV

Work Progress:

Funding received in March 2006 from ICMR. Clearance of Institutional Committee and permission from Department of Tribal development, Govt. of Orissa has been obtained for under taking the proposed research activity.

Clinical Examination of Hepatitis patients in field

Sampling and Study population:

Since the prevalence data for this region on hepatitis infection is available, taking the prevalence of 10% a sample size of 2500 has been estimated and this will be distributed proportionately among the different primitive tribes of the study area.

Mayurbhanj, the highest tribal populated districts of Orissa has been selected as the study area. There are seven (7) primitive tribes identified in this district are (1) Lodha/saora (2) Lodha (3) Kharia/Hill (4) Kharia, (5) Mankidi and (6) Mankidia & (7) Juanga.the distribution partern of primitive tribe settlements in various blocks of the district are mapped for earch of the 7 tribes. Samples are drawn representing the each

tribe and their settlement distribution. The population under different ITDAs has been identified in the first phase and administrative preparation started. District collector Mayurbhanj and Project Director ITDA Mayurbhanj were consulted regarding execution of the project and field level staff of the tribal agencies were contacted. Meetings organised with District welfare officer, special officers Lodha and Kharia, the community leaders of Lodha community as a part of motivation and awareness activity. IEC activities at village level were started in 2 villages in habited by Lodha tribe. Investigators meeting held for coordinating the activities among different centres and standardisation of laboratory and chemical reagents to be used to maintain uniformity, training in techniques was imparted to various new recruits of teams on ELISA for serology using around 100 sera standardisation of tests done. The study is ongoing.

Poster presentation by students during SAC Meeting in RMRC.