

AN EMERGING INFECTION “SCRUB TYPHUS” – A DETAILED CLINICAL PROFILE AND COMPLICATIONS AMONG CHILDREN IN A TERTIARY HOSPITAL

AUTHORS -1. Vishnu Priya Ramasamy , 2. Tarun Jakkula 3. Swetha T Suresh ,4. P.Siva kumar

Post Graduate Students, Department of Paediatrics, Siddhartha Medical college, Vijayawada.

Corresponding Author : Dr.B.Suneetha asso. Professor , Paediatrics, SMC, Vijayawada. Mail: nitapaeds@gmail.com

ABSTRACT :

OBJECTIVES:

To study the clinical profile and complications of **Scrub typhus** in children.

METHODS:

This descriptive study conducted in Siddhartha Medical college, Vijayawada, among children less than 12 years for a period of one year (December 2020-November 2021). A total of 49 children who are serologically/clinically diagnosed cases of Scrub typhus.

RESULTS:

Scrub typhus mainly occurred in school going children with male predominance. Fever being the single most clinical presentation in most of the cases (95.9%) associated with pallor, hepatosplenomegaly. Co infection was documented in 14.2% cases with 85.7% cases showing increased morbidity and mortality. Mortality rate is more in infants.

CONCLUSIONS:

Among cases of Acute febrile illness, Scrub typhus accounts for 9.8% of cases. Main clinical features were persistent fever, hepatosplenomegaly, thrombocytopenia, anemia along with capillary leak signs like edema with or without eschar.

Infants are at high risk for complications and mortality.

KEYWORDS:

Scrub typhus, anemia, thrombocytopenia, hypotension.

INTRODUCTION:

Scrub typhus is an **Emerging infectious** disease that is caused by *Orientia tsutsugamushi* from chigger bite. It is common in Asia-Pacific countries especially in India^[1]. The disease is characterized by diverse clinical manifestations ranging from a mild, self-limiting state to variable severity like acute respiratory distress syndrome (ARDS), meningoencephalitis, low index of suspicion, and non-specificity of signs and symptoms^[2]. Scrub typhus and other rickettsial infections are **grossly under-diagnosed** in India because of their non-specific clinical presentation, low index of suspicion among clinicians, limited awareness about the disease and lack of diagnostic facilities^[3]. Hence a study is necessary to

improve the knowledge on various spectrum of clinical manifestations for early diagnosis and treatment. So that significant morbidity and mortality can be avoided in Children.

A cross sectional observational study was conducted, to study the clinical features and complications of pediatric scrub typhus. The aim of the study is to determine the clinical profile and risk factors in children presenting with scrub typhus and various clinical and laboratory clues to diagnose clinically , for the early diagnosis and treatment to prevent complications and mortality

AIMS AND OBJECTIVES:

PRIMARY OBJECTIVE:

1. To study the clinical profile of scrub typhus in children.
2. To study the complications of scrub typhus.

SECONDARY OBJECTIVE:

1. To find out the laboratory clues for early diagnosis.
2. Identify the risk factors for complications in scrub typhus infection.

METHODS AND METHODOLOGY:

- Study type: cross –sectional / observational/ institutional study.
- Place of study: department of pediatrics/old government general hospital,vijayawada affiliated to sidhartha medical college.
- Duration of the study: 1 year (december 2020 to november 2021)
- Sample unit: all children aged less than 12 years either positive scrub typhus
- Serology or clinically diagnosed scrub typhus cases(response to treatment).
- Sample size: 49 children meeting inclusion and exclusion criteria.
- Sampling technique: purposive sampling technique.

INCLUSION CRITERIA:

ALL CHILDREN OF AGE GROUP FROM BIRTH TO 12YEARS WITH

1. Positive scrub typhus serology
2. Clinically diagnosed cases where serology was not feasible(based on treatment response- Standard therapy of Doxycycline(oral or IV) 4-5mg/kg/day or Azithromycin(oral or IV) 5mg/kg/day.

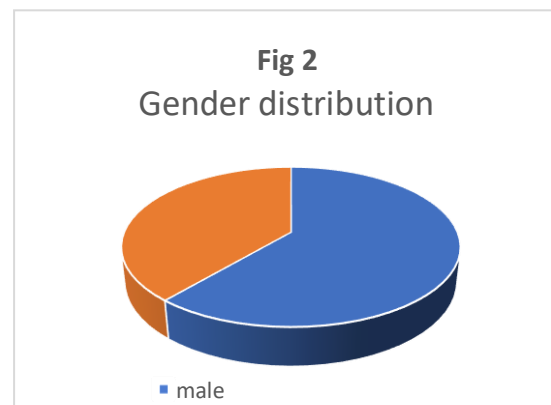
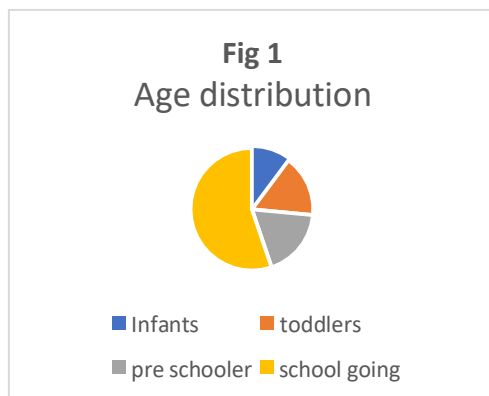
EXCLUSION CRITERIA:

Isolated other proven causes of acute febrile illnesses.

Serologically negative cases.

RESULTS

Totally **49 children** were diagnosed with Scrub typhus either serologically(**35**) or clinically(**14**). It comprised of about **9.8%** of cases with acute febrile illnesses. Scrub typhus affects mainly of **school going age group**(27(55%)) followed by preschool age group(9(18.4%)), toddlers(8(16.4%)) and infants(5(10.2%))^{Fig 1}. Affecting mainly boys(30(61.2%)) than girls(19(38.7%))^{Fig2}.



Clinical Presentation:

All 49 cases had a history of fever for a duration of <7days in 20(40%) cases, 7-14days in 22(45.8%) cases,>14days in 6(12.2%) cases. So most cases are presented with history of fever for 1 to 2weeks without diagnoses. Gastrointestinal symptoms were present in 25(51%) cases which includes vomiting(14(28.5%)),abdominal pain(10(20.4%)),loose stools 1(2%),abdominal distension(2(4%)) and jaundice(2(4%)) .

Clinical Features

Respiratory symptoms in 20(40.8%) cases which includes cough(11(22.4%)) and breathing difficulty (9(18.3%)).Central nervous system involvement in 15(30.6%) cases.Vascular leak symptoms like facial puffiness,hypotension in 4(8%) cases. Clinical signs includes altered sensorium in 5(10.2%) cases, tachypnea in 11(22.4%), tachycardia in 9(18.3%), hypotension and rash noted in 2(4%) cases, pallor in 35(71.4%) cases, icterus in 2(4%) cases, lymphadenopathy in 11(22.4%) cases, edema in 4(8%) cases. The most pathognomonic finding of scrub typhus, eschar is seen in 13(26.5%) cases. Hepatosplenomegaly was documented in 35(71.4%) cases.

Table 1: Clinical Profile: Symptoms and signs of Scrub typhus

was noted in 7(14.2%) cases which includes malaria in 4 cases, dengue positive in 2 cases and leptospirosis in 1 case. Acute rheumatic fever criteria positive in one case of scrub typhus serology positive case. 6 out of 7 cases with co infection showed significant morbidity(85.7%) with one mortality.

ACUTE RHEUMATIC FEVER	1
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Complications^(Table 3) like moderate to severe Anemia noted in 5(10%) cases, thrombocytopenia in 40(81.6%), which is another important clue in diagnoses of scrub typhus. Hypotension noted in 3(6.1%) cases, transient hypertension in 1 case. Pneumonia in 8(16.3%) cases, meningoencephalitis in 7(14.2%) cases, myocarditis, hepatitis and shock in 2 cases each. Other complications includes seizure, bradyarrhythmias, CCF, pleural effusion, ARDS, Acute Kidney injury & DIC.

TABLE 3: COMPLICATIONS OF SCRUB TYPHUS

COMPLICATIONS		FREQUENCY	PERCENTAGE(%)
ANEMIA	MILD (7-11gm/dl)	37	75.5
	MODERATE (4-7gm/dl)	4	8
	SEVERE(<4gm/dl)	1	2
THROMBOCYTOPENIA(<150000)		40	81.6
SEVERE <50,000		12	24.4
<20,000		9	18.3
HYPOTENSION		3	6.1
HYPERTENSION(TRANSIENT)		1	2
MENINGOENCEPHALITIS		7	14.2
SEIZURE		1	2
DIFFUSE CEREBRAL ATROPHY		1	2
MYOCARDITIS		2	4
TRANSIENT BRADYARRHYTHMIA		1	2

CONGESTIVE CARDIAC FAILURE	1	2
PNEUMONIA	8	16.3
PLEURAL EFFUSION	1	2
ARDS	1	2
HEPATITIS	2	4
RENAL IMPAIRMENT	1	2
SHOCK	2	4
DIC	1	2
MORTALITY	3	6.1

Mortality is seen in 3cases(6.1%).Causes of death being ARDS,cardiogenic shock,Encephalopathy.

DISCUSSION

Out of 49 children, 35 cases were diagnosed serologically and 14 cases were diagnosed clinically based on criteria formulated by Rathi et al(5).Scrub typhus constitutes about 9.8% of cases with acute febrile illnesses.

DISTRIBUTION

Mean age of infection in my study is 6years which is school going age group and most commonly affects boys of rural population. All these findings are similar to studies like Bhat NK et al, Kalal BS et al, Kumar M,et al, Thomas R et al, Rathi N,Rathi A et al. The seasonal period in which scrub typhus infection occurred in my study is between August to January similar to studies like Thomas R et al and Rathi N et al.

TABLE 4:COMPARISION OF VARIOUS STUDIES FOR DISTRIBUTION:

STUDY	Bhat NK, Dhar M, et al (2011-2012)	Kalal BS et al, (2011-2012)	Kumar M, Krishnamurthy S, Delhikumar CG, et al (2011)	Thomas R, Puranik P,, et al (2008-2012)	Rathi N, Rathi A (2009)	MY STUDY
Sample population	<18yrs	<18yrs	<12yrs	<18yr	<20yr	<12yrs
Sample size	66	53	35	147	23	49
Duration of study	2yr	2yr	1yr	4yr	1yr	1yr
Mean Age	8.8 yr	7.5yr	6.3yr	5yr	5yr	6yr
MC sex	M>F(1.44:1)	M>F	M>F(1.39:1)	M>F(1.56:1)	M>F(2.2:1)	M>F(1.57:1)
Residence	Rural>urban	Rural>urban	Rural>urban	Rural>urban	Rural>urban	Rural>urban
Season	September-November	August – November	September - February	September to January	September to January	August - January

SYMPTOMATOLOGY^(TABLE 5)

Fever is present in 91.8% of patients at the time of admission whereas history of fever is present in all the patient. Lymphadenopathy documented in 22.4% cases which is lower than the cases reported in studies like Bhat NK et al(38%),Kalal BS et al(49%),Rathi N et al(41%) and similar to the study done by Thomas R et al.

Eschar is documented in 26.5% of cases similar to studies like Bhat Nk et al,Kalal BS et al.Rash is uncommonly present in my study(4%) which is in contradiction with the studies done by Thomas R et al where rash is reported in 50% of cases and Rathi N et al which reported 59% of cases with rash.

TABLE 5:COMPARISION OF VARIOUS STUDIES FOR SYMPTOMATOLGY:

STUDY	Bhat NK, Dhar M, et al (2011-2012)	Kalal BS et al., (2011-2012)	Kumar M, Krishnamurthy S, Delhikumar CG, et al (2011)	Thomas R, Puranik P., et al (2008-2012)	Rathi N, Rathi A (2009)	MY STUDY
Fever	100%	100%	100%	100%	100%	95.9%
Lymph adenopathy	38%	49%	37%	21.8%	41%	22.4%
Eschar	20%	36%	11%	5.7%	7%	26.5%
Rash	20%	26.4%	20%	50%	59%	4%

CLINICAL PRESENTATION^(TABLE 6)

My study ,similar to other studies showed commonly hepatomegaly(82.7%),but it is associated with or isolated splenomegaly is present in 75.5% cases which is higher than other studies like Bhat NK et al, Vivekanandan M et al studies.Anemia(85.5%) and or thrombocytopenia(81.6%) is documented in my study which is higher than other studies like

Rathi N et al, Bhat NK et al, Vivekanandhan M et al. Hyponatremia is noted in my study, similar to other studies.

TABLE 6: COMPARISON OF VARIOUS STUDIES FOR CLINICAL PRESENTATION

STUDY	Bhat NK, Dhar M, et al (2011-2012)	Vivekanandan M, Mani A, Priya YS, et al (2011-2012)	Kumar M, Krishnamurthy S, Delhikumar CG, et al (2011)	Thomas R, Puranik P., et al (2008-2012)	Rathi N, Rathi A (2009)	MY STUDY
Hepatomegaly	82%	67.9%	91%	87%	99%	82.7%
splenomegaly	59%	32.1%	60%	50%	Not included	75.5%
Anaemia	62%	69.8%	Not mentioned	68.7%	71%	85.5%
Thrombocytopenia	53%	66.7%	31%	Not included	68%	81.6%
Electrolyte imbalance	Not documented	Hyponatremia (<125meq/dl) 5.6%	Hyponatremia 17%	Hyponatremia 11.5%	64% hyponatremia	36.7% Hyponatremia (20.4%) Hypocalcemia (24.4%)
Average no of hospital day	7days	7 days	6days	7days	7days	7days

COMPLICATIONS (TABLE 7)

61.2%(n=30) cases showed complications. Severe anemia(<6gm/dl) is seen in 4% cases which is less when compared to studies like Thomas et al. Bhat NK et al. Severe thrombocytopenia (<50,000) is seen in 42.7% which is less than the study done by Kalal BS et al, more than the studies like Bhat NK et al, Kumar M et al. Meningoencephalitis is

documented in 14.2% cases which is similar to the study by Rathi A et al, Kala BS et al, Kumar M et al. Pneumonia is seen in 16.3% which is higher than studies done by Kumar M et al, Thomas R et al. Hypotension is seen in 6.1% cases in my study which is higher than studies like Thomas M et al, Rathi N et al but lower than the studies like Kalal BS et al and Kumar M et al. Other rare complications are transient hypertension(2%), simple febrile seizures(2%), Diffuse cerebral atrophy(2%), myocarditis(4%), transient bradyarrhythmias(2%), Congestive cardiac failure(2%), pleural effusion(2%), ARDS(2%), Renal impairment(2%), Hepatitis(4%), DIC(2%), shock(4%). Mortality is seen in 3 cases(6.1%) due to ARDS, Cardiogenic shock and encephalopathy respectively which is similar to studies like Rathi et al, Bhat NK et al and higher than the studies done by Kumar M et al and Thomas R et al.

In addition to these findings, my study documented co infection of scrub typhus with other infections (Fig 3) in total of 7 cases (14.2%). Co infection with malaria in 4 cases, dengue in 2 cases and leptospirosis in 1 case. One peculiar finding is that one of the serologically positive cases showed features of Acute rheumatic fever which was diagnosed based on Modified Jones criteria and the case died due to cardiogenic shock despite the necessary cardiac support. 6 out of 7 cases with co infections showed severe morbidity and mortality.

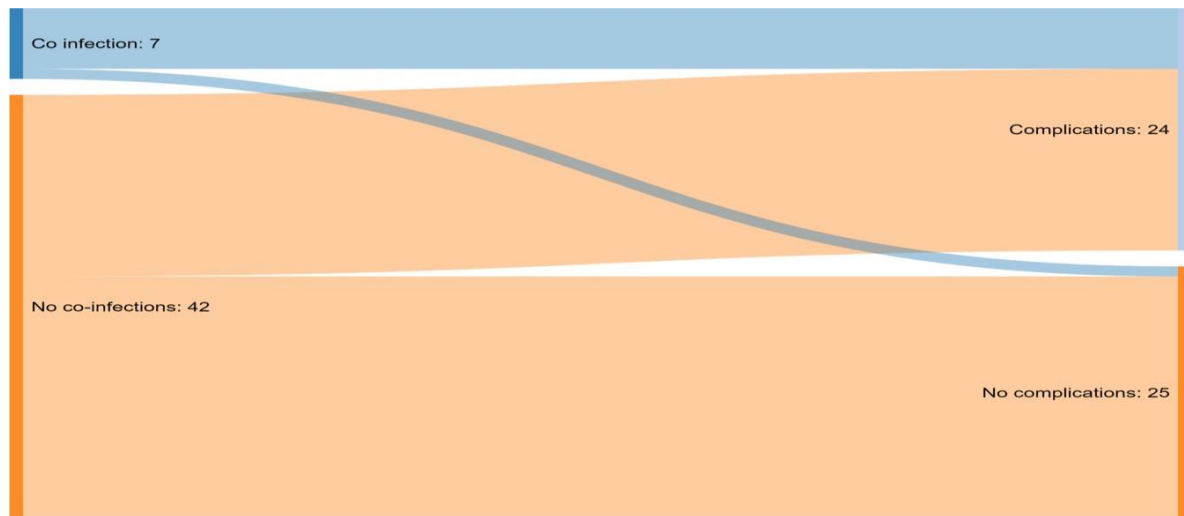
One more important finding includes even the infants (n=5) can acquire scrub typhus, despite less outdoor activities and they are prone to develop severe complications which is 80% (n=4) and mortality in 40% (n=2) mainly due to endothelial damage and vascular leaking.

TABLE 7: COMPARISON OF VARIOUS STUDIES FOR COMPLICATIONS:

COMPLICATIONS	Bhat NK, Dhar M, et al (2011-2012)	Kalal BS et al., (2011-2012)	Kumar M, Krishnamurthy S, Delhikumar CG, et al (2011)	Thomas R, Puranik P., et al (2008-2012)	Rathi N, Rathi A (2009)	MY STUDY
SEVERE ANEMIA (<6g/dl)	6.1%	(<11g/dl) 69.8%	Not included	68.7%	71% (<9g/dl)	4%

SEVERE THROMBOCYTOPENIA (<50000)	27.2%	66.7%	31% (<1,00000)	Not included	Not included	42.7%
HYPOTENSION	Not mentioned	10%	34%	1%	3%	6.1%
HYPERTENSION (TRANSIENT)	Not mentioned	0	0	Not included	0	2%
MENINGO ENCEPHALITIS	30.3%	17%	17%	28%	15%	14.2%
SIMPLE FEBRILE SEIZURE	Not mentioned	15%	0	Not included	0	2%
DIFFUSE CEREBRAL ATROPHY	Not mentioned	0	0	Not included	0	2%
MYOCARDITIS	9.1%	0	34%	Not included	5%	4%
TRANSIENT BRADYARRHYTHMIA	Not mentioned	0	0	0	0	2%
CONGESTIVE CARDIAC FAILURE	Not mentioned	0	0	0	0	2%
PNEUMONIA	10.6%	0	3%	6.1%	21%	16.3%
PLEURAL EFFUSION	9.1%	0	14%	Not included	0	2%
ARDS	12.1%	0	9%	1%	5%	2%
HEPATITIS	13.6%	81.1%	31%	0	Not included	4%
RENAL IMPAIRMENT	16.7%	0	20%	0.4%	5%	2%
SHOCK	25.8%	10%	34%	1.9%	5%	4%
DIC	1.5%	0	9%	Not included	5%	2%
MORTALITY	7.5%	0%	2.8%	1.9%	8%	6.1%

Fig 3: Sankey diagram depicting distribution of participants developed complications in co-infections



CONCLUSIONS

1. In cases of Acute febrile illness especially after monsoon season ,consider the diagnoses of Scrub typhus,
2. Consider empirical treatment with Doxycycline as delay in the treatment after complications may leads to serious morbidity and mortality.
3. Main clinical clues includes persistent fever, hepatosplenomegaly, thrombocytopenia, anemia along with leak signs like edema with or without eschar ,in endemic area consider the first differential diagnosis as Scrub typhus.
4. In resource limited settings,consider starting Doxycycline if the clinical clues points towards Scrub typhus as drastic response will be seen.
5. Although duration of fever doesn't correlate with the complications, delay in treatment may lead to serious complications.
6. Like other hemorrhagic fever, **Infants** are high risk group for complication and mortality as 80% of them showed complications and 66% mortality. Other risk factor includes **co infections** (14.2%).Consider doing investigations for other infections also for better outcome.

CONFLICT OF INTEREST – None

SOURCE OF FUNDING- NIL



INSTITUTIONAL ETHICS COMMITTEE

Siddhartha Medical College & Govt General Hospital (IEC SMC & GGH)

(Authorized by govt Siddhartha Medical College & Govt General Hospitals)

Govt Siddhartha Medical College Campus, Ring Road, Gunadala, Vijayawada -520008, Andhra Pradesh, India

Registration Number: ECR\633\INST\AP\2014\RR-19

Communication of Decision of Ethics Committee SMC & GGH

Reference Number:IEC\2020\062\SMC

Date: 04-03-2021

Protocol Title	AN EMERGING INFECTION "SCRUB TYPHUS"- A DETAILED CLINICAL PROFILE AND COMPLICATIONS AMONG CHILDREN IN A TERTIARY HOSPITAL
Investigator Name	Dr VISHNU PRIYA RAMASAMY
Guide Name	Dr B SUNEETHA ASSOCIATE PROFESSOR,DEPARTMENT OF PAEDIATRICS, SIDDHARTHA MEDICAL COLLEGE, VIJAYAWADA
Institute Name	SIDDHARTHA MEDICAL COLLEGE,NEAR DR YSR UNIVERSITY,GUNADALA,VIJAYAWADA -520008, ANDHRA PRADESH, INDIA.
Review Type	FULL REVIEW
Date of Review Meeting	04-03-2021
Decision of the IEC SMC & GGH	APPROVED
Comments	NIL

Dr. PADMAVATHI,

The chairperson,

IEC SMC &GGH-Vijayawada.



Govt Siddhartha Medical College Associated Hospitals:

- ❖ New Govt General Hospital, Govt. Siddhartha Medical College Campus Gunadala, Vijayawada-520008, Andhra Pradesh, India.
- ❖ Old Govt Hospital, Two Town, Hanumanpet, Vijayawada-520002, Andhra Pradesh, India.
- ❖ Yarlagadda Venkanna Chowdary oncology wing & Research Center [YVCOW], Chinnakani, Guntur -522503 AP India.

REFERENCES

1. Thomas R, Puranik P, Kalal B, Britto C, Kamlesh S, Rego S, *et al.* Five-year analysis of rickettsial fevers in children in South India: Clinical manifestations and complications. *J Infect Dev Ctries.* 2016;10:657-61. from untreated scrub typhus (*Orientia tsutsugamushi*). *PLoS Negl Trop Dis.* 2015;9:e0003971.
2. Taylor AJ, Paris DH, Newton PN. A systematic review of mortality from untreated scrub typhus (*Orientia tsutsugamushi*). *PLoS Negl Trop Dis.* 2015;9:e0003971.
3. Vivekanandan M, Mani A, Priya YS, *et al.* Outbreak of scrub typhus in Pondicherry. *J Assoc Physicians India* 2010;58:24-8.
4. Reller ME, Dumler JS. Scrub Typhus (*Orientia tsutsugamushi*). In: Kleigman RM *et al.*: *Nelson Textbook of Pediatrics.* 19th ed. Philadelphia: Elsevier. 2011; Pp: 1045-6.
5. Rathi N, Rathi A. Rickettsial infections: Indian perspective. *Indian Pediatr* 2010;47(2):157-64.
6. Bhat NK, Dhar M, Mittal G *et al.* Scrub typhus in children at a tertiary hospital in North India: Clinical profile and complications. *Iran J Pediatr.* 2014;24(4):387-392.
7. Huang CT, Chi H, Lee HC, *et al.* Scrub typhus in children in a teaching hospital in eastern Taiwan, 2000-2005. *Southeast Asian J Trop Med Public Health* 2009;40(4):789-94.
8. Digra SK, Saini GS, Singh V, *et al.* Scrub typhus in children: Jammu experience. *JK Science* 2010;12:95- 99
9. Mathai E, Lloyd G, Cherian T, *et al.* Serological evidence of continued presence of human rickettsiosis in southern India. *Ann Trop Med Parasitol* 2001;95(4): 395-8.
10. Palanivel S, Nedunchelian K, Poovazhagi V, *et al.* Clinical Profile of Scrub Typhus in Children. *Indian J Pediatr* 2012;79(11):1459-62.
11. Kumar M, Krishnamurthy S, Delhikumar CG, *et al.* Scrub typhus in children at a tertiary hospital in southern India: Clinical profile and complications. *J Infect Public Health* 2012;5(1):82-8.