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Review Article

Non Typhoidal Salmonellae and its aetiological spectrum-An overview with Indian perspective

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ABSTRACT

Background: Non Typhoidal Salmonellae (NTS) is emerging as a major health problem. NTS serovars have a wide variety of host range varying from domestic animals, aquatic fauna, reptiles, arthropods, leafy vegetables and many more. This zoonotic infection manifests as self limited gastroenteritis associated with food poisoning to fatal extra intestinal invasive infections.
Aim & Objective: In this overview, an attempt is made to compile the documented reports due to NTS from Indian subcontinent for the last 5 decades, searching the available databases. These reports emphasizes the role of NTS in diverse clinical infections and the possible links of transmission.
Conclusion: Prophylactic measures such as adoption of quality measures in fish and meat processing units, vaccination of farm animals, serotyping of all NTS strains, above all health education and public awareness program should be made mandatory to minimize the incidence of NTS in our country.

1. Introduction

Non Typhoidal Salmonellae (NTS) which excludes S.Typhi & S.Paratyphi- is emerging as a major health problem across the globe. Salmonellae species are widely distributed in the environment and commonly found in farm effluents, human sewage as well as any material that is subjected to faecal contamination. These infections are also acquired through contact with pet animals or from veterinary clinics, zoological gardens, farm environments as a part of occupation. NTS species are mainly responsible for the food borne infections, gastroenteritis acquired through direct or indirect animal contact or by consumption of foods such as meat, sea foods, poultry products, leafy vegetables. Salmonellosis in animals always presents a potential zoonotic threat as these infected animals serve as a source of infections to humans. Subclinical infection in farm animals may lead to the contamination of meat, eggs or milk. It can also cause secondary contamination of fruits and vegetables fertilized or irrigated with water containing faecal wastes. Bovine Salmonellosis manifests clinically resulting in septicemia, acute or chronic enteritis and abortion. Hence, Salmonellosis in farm animals will cause a huge economic burden to the farmers for the management of these infections.

There are many contributory factors in India for the development of NTS infections such as occupation, geographic and climatic conditions. Agriculture being the main occupation in India, contact with farm animals and inadequate sanitary conditions occur very often. Poultry and dairy farming are two important means of livelihood for numerous people in India. Indian peninsula is surrounded by water bodies such as lakes, river, sea, hence fish and seafood are used as a common accompaniment.

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Many species of NTS were reported to cause extra intestinal, invasive infections such as meningitis, septicaemia, bacteremia, septic arthritis as reported by various investigators from India. The severity of the NTS infection may vary from self limiting diarrhoeal diseases to fatal invasive infections which are more commonly found in immunocompromised patients or those who are with underlying diseases. In addition, many gastrointestinal outbreaks due to consumption of diverse foods were also documented in the literature.

Genus Salmonella includes more than 2500 serotypes which are potential human and animal pathogen. Taxonomy of Salmonella is complicated and undergoes periodical revisions. The designation of Salmonella serovars got the present Nomenclature status as adopted in WHO International Centre for Salmonella and the Centres for Disease Control and Prevention (CDC) which use shortened serovar nomenclatures. For example, S.enterica serotype typhimurium may be written as Salmonella Typhimurium for convenience. According to this, the name of the genus is written in italics but not the serotype name which starts with a capital letter.

In this overview, an attempt is made to compile the mushrooming, documented reports regarding gastroenteritis, extra intestinal infections and outbreaks due to NTS from Indian subcontinent for the last 5 decades , searching the available databases. The documented reports of NTS from India are shown in Table 1. As NTS infections are not notifiable and many of the isolates are not serotyped, this may be an underestimated data**.** All these report**s** are arranged in the alphabetical order of the Salmonella Serotypes, each report in the chronological order of occurrence and citing the reference number in the order that appears in the text.

2. NTS Infections Reported from India

As reported in most of the studies from other countries and also the results of our findings, S.Typhimurium was the most frequenly encountered NTS in India followed by S.Senftenberg and S.Weltevreden. S.Typhimurium mainly causes outbreaks of Gastroenteritis, primarily in children.[1–6] Few extra intestinal manifestations are also reported which include neonatal septicemia[7] neonatal septic arthritis[8] scalp abscess[9] and meningitis.[10] In our study one isolate of S.Typhimurium was obtained from a suspected case of bacteremia. We have encountered a sporadic outbreak of food poisoning associated with S.Typhimurium due to consumption of squid, during a get together in a reputed restaurant in Mangalore.

S.Senftenberg was the second most common NTS reported from India. It was responsible for Extraintestinal infections such as Septicemia[11,12] Lung Abscess,[13] Pleuro pulmonary infection[14] Empyema,[15] and ear infection.[16] Many outbreaks were also documented, especially in neonatal or paediatric wards.[17]

S. Weltevreden is another predominant NTS responsible for outbreaks of Gastroenteritis and foodpoisoning.[18–20] An outbreak investigation of S.Weltevreden foodpoisoning in a tea garden of Assam was reported by Saikia et al[21] Extra intestinal infections include enteric fever like infection, cholecystectomy surgical site infection.[22] Sepsis in two newborns was reported by Patil[23] and ulcerative skin lesions by Desikan[24] An outbreak of food poisoning due to S. Weltevreden involving many nursing students had been occurred in our institute due to a non vegetarian dish, in a get togthrer.[25]

E Enteritidis is usually causing extra intestinal manifestations and reported as aetiological agents of Septic arthritis,[26] complicated Aortic aneurism, meningitis,[27] polyserositis, arthritis following trauma in a child with Thalassemia Major.[28] Gastroenteritis due to S.Enteritidis was reported by Vijaya et.al.[29] We also experienced a small outbreak due to S.Enteritidis, probably associated with consumption of egg.

2.1. Rarely encountered NTS

S.Newport & S. Worthington are also reported from India, but not so frequently like other NTS. S Newport was mainly causing Gastrointestinal epidemics[30,31] and few Extraintestinal infections such as Neonatal septicemia.[32] S. Worthington was more commonly encountered in Extraintestinal manifestations such as septicemia, meningitis[33–35] An Outbreak of S.Worthington in a neonatal ward in a general hospital was reported by Muley et.al.[36]

S.Oranienberg was responsible for Gastrointestinal outbreaks.[37,38] S.Dublin was exclusively isolated from invasive infections like meningitis.[39] Dias et.al reported S.Dublin bacteremia mimicking Enteric fever from our institute.[40] S.Bareilly was isolated from pediatric infections,[41] neonatal poly arthritis and septicemia[42] by various investigators. It was reported as the second

highest organism isolated from faecal samples in Goa by Verenkar. Two case reports on S.Virchow causing invasive infections such as meningitis,[43] septicemia in an infant[44] were also documented in the literature. Devi from Manipal and Jesudason from Vellore isolated S.Agona from Gastroenteritis cases.[45,46] In our experience one strain of Agona was isolated from a gastroenteritis case.

Panhotra et.al reported an outbreak of S.Anatum infection from a premature nursery at Chandigarh.[47] We could isolate S.Anatum from a bacteremia case in our institute. The rare isolates of NTS reported from our country include fatal gastroenteritis in an infant with microcephaly due to S.Arizona by Mahajan et.al,[48] S.Bornheim causing UTI in a diabetic patient with aplastic anemia,[49] S.Branderup,[50] S.Cerro causing pyaemia,[51] S.Havana from a case of neonatal meningitis.[52] S.Mbandeka, a rare serotype was isolated in Ambajogai, rural area by Fule and Kaundinya.[53] S.Newbrunswick causing infection in an old man was reported by Shriniwas in a hospital from Delhi.[54] Other unique strains of NTS reported include S.Roan from bacteraemia,[55] S.Tamilnadu from a gastroenteritis in a child.[56] A case of invasive gastroenteritis with acute kidney injury and hemiplegia was reported by Ballal et.al due to S.Wangata.[57] Three rare isolates such as S.Augstenborg, S.Indiana, S.Regent were reported by Basu et.al for the first time in India. In a 16 year study Basu et al described the prevalence of various new Salmonella serotypes in India.[58] A very interesting finding in this study was that out of 99 serotypes obtained from 8027 strains of Salmonella, 13 were isolated only from man and 49 exclusively from animals with S.Weltevreden being the commonest serotype. S.Typhimurium was the commonest species isolated from animals. Jain P et.al reported a blood and urine culture positive bacteremia by S.Choleraesuis for the first time in India.[59] A rare case of Pyogenic meningitis caused by Salmonella choleraesuis var. Kunzendorf had been reported by Prakash and Ray in 1970.[60]

A South Indian Study describing the Seroprofiling of NTS isolated from Gastroenteritis, few rare serovars were reported which included S.Bovismorbificans**,** S.Schleissheim, S.Wangata and Ciprofloxacin resistant S.Kentucky. More recently, a case of Gastroenteritis in a 10 year old child , complicated by Severe Acute Kidney Injury and neurological dysfunction due to a new NTS species S.Decatur was reported by Krishnamurthy & Mandal from Pondicherry.[61] Occasional reports regarding the changing pattern of Salmonella serovars from various geographical areas also appeared in the literature. Another rare serotype S.Wien, one of the epidemic clones which spread from North Africa through Europe in the 1970s was isolated from 10 cases of gastroenteritis in our hospital.[62]

For the last 10 years duration, 145 NTS were isolated from feces and 8 strains of NTS from suspected cases of bacteremia, including 4 outbreaks occurred in our institute was presented in GISICON, 2021**.** S.Oslo was not so commonly reported from India. However in the recent past there was a sudden change in the pattern of NTS where we observed the emergence and prevalence of S.Oslo for a certain period of time. Rare serotypes such as S.Bareilly**,** S.Anatum**,** S.Infantis**,** S.Hadar, S.Dunkuwa and S.Kentucky were also obtained from Gastroenteritis cases during this period. Prevalence of S.Oslo was reported by Ballal et.al in Cancer patients, from a neighbouring district of Mangalore, Dakshina Kannada.[63]

Emergence of multi drug resistance in NTS strains is a major concern nowadays. Many investigators reported MDR Salmonellae from various States in India.[64] A detailed Review describing the various mechanisms involved in the resistance in NTS is done by Bhaskar & Harish from Pondicherry.

3. Conclusions

The documented reports from Indian Subcontinent emphasizes the role of NTS in diverse clinical infections and the possible links of transmission. There are many contributory factors in our country for the occurrence of these infections. As NTS is widely distributed in animals and sea foods, it is very essential to adopt stringent quality measures in the poultry, fish, dairy and meat processing units. A structured questionnaire to the patients and the family, Vaccination of Farm animals and inclusion of NTS in the list of notifiable diseases will definitely be helpful to understand the magnitude of the problem. Many of the NTS species are biochemically similar, hence serotyping of all the isolates are to be made mandatory. In addition, strategies should be formulated by health education and public awareness program to sensitize the population and thereby minimising the incidence of NTS in our country.

Table 1: Documented Reports of NTS Infections from India:

Serotype	Clinical Manifestation	Author	Ref No.
S.Agona	Gastroenteritis	DeviJN et.al(1985)83	45
	Gastroenteritis	Jesudasan M,(1988)	46
S.Anatum	Outbreak in Chandigarh	Panhotra et.al, (1979)	47
S.Arizona	Fatal Gastroenteritis	Mahajan et.al, (2003)	48
S.Augstenborg	First case from India	Basu S et al., 1972	58
S.Bareilly	Paediatric Infections	Aggarwal et.al, (1983)	41
	Septicaemia	Gupta et.al, (1997)	42
S.Bornheim	UTI in DM & Aplastic Anaemia	Snehalatha et.al (1992)	49
S.Bovismorbificans	Gastroenteritis	Ballal	63
S.Braenderup	First case from India	Devi. JNS et.al, (1988)	50
S.Cerro	Pyaemia	Bhore et.al (1980)	51
S.Choleraesuis	Isolation from blood & urine	Jain P et.al,2014	59
S. Decatur	Gastroenteritis	Krishnamurthy &, Mandal2020	61
S.Dublin	Meningitis	Diwan et.al (1997)	39
	Bacteremia	Dias et.al (2009)	40
S.Enteritidis2	Bilateral septic Arthritis	John et.al (1993)	26
	Meningitis	Varaiya et.al (2001)	27
	Arthritis	Behera et.al (2010)	28
	Gastroenteritis	Vijaya et.al, (2012)	29
S.Havana	Meningitis	Menon et.al, (1994)	52
S.Indiana	First report from India	Basu et.al., 1975	58
S.Infantis	gastroenteritis	Taneja	64
S.Kentucky	gastroenteritis	Ballal	63
S. Kunzendorf	Pyogenic Meningitis	Prakash & Ray, 1970	60
S.Mbandeka	Isolation of a rare serotype	Fule & Kaundinya, (1985)	53
S.New Brunswick	Infection in an old man	Shriniwas et.al (!(1983)	54
S.Newport	Nursery Outbreak	Kumari S et.al (1980)	30
	Epidemic	Dravid et.al (1989)	31
	Neonatal Septicaemia	Rao MR et al, (1991)	32
S.Oranienburg	Gastroenteritis	Aggarwal et.al (1980)	37
	Outbreak in NICU	Mehta et.al (1982)	38
S.Oslo	Gastroenteritis	Ballal	63
S.Regent	First report from India	Basu et.al , 1973	58
S.Roan	Bacteraemia	Sundaram et.al (1983)	55
S.Schleissheim	gastroenteritis	Ballal	63
S.Senftenberg	Nosocomial outbreak	Narang et al (1985)	17

Continued on next page

Table 1 continued

	Septicemia	Saigal et.al (1989)	11
	Septicaemia	Gupta P et.al, (1993)	12
	Lung Abscess	Gupta JP, (1994)	13
	Pleuropulmonary Infection	Nair D, (1999)	14
	Hospital acquired Empyema	Ramanathan et.al (2000)	15
	Ear Infection	Bairy I et.al (2000)	16
S.Tamilnadu	Gastroenteritis in a child	Nath ML et.al (1970)	56
S.Thompson	gastroenteritis	Taneja	64
	Nosocomial epidemic	Puri et.al, (1980)	1
	Outbreak of gastroenteritis	Bhat & Macaden(1983)	2
	Outbreak in Paediatric ward	Chaturvedi et.al, (1985)	3
	Outbreak in Solapur	Fule et.al (1988)	4
S.Typhimurium	Protracted diarrhoea in infants	Koshoo et.al (1990)	5
	Neonatal septicaemia	Rao PS (1993)	7
	Nosocomial outbreak	Mahajan R et.al, (1995)	6
	Neonatal septic arthritis	Sarguna &Lakshmi,(2005)	8
	Scalp Abscess	Baliga S et.al(2011)	9
	Meningitis in infancy	Adhikary R,(2013)	10
S.Virchow	Meningitis in an infant	Sachdeva et.al(1963)	43
	Sepsis in an infant	Randhawa et.al(2006)	44
S.Wangata	Invasive Gastroenteritis	Ballal et.al(2015)	57
	Outbreak of Gastroenteritis	Y.K.Chitkara,M K Gill(1976)	18
	Outbreak of food poisoning	Aggarwal,(1985)	19
	Post cholecystectomy surg.site inf.	Ashok R.et.al,(2005)	22
	Sepsis in 2 Newborns	Patil BA et.al,(2006)	23
	Sporadic outbreak of food poisoning	Antony.B.et.al,(2009)	24
	Ulcerative skin lesion	DesikanP et.al,(2009)	25
	Outbreak of food poisoning	Priyanka Jain, (2015)	20
	Outbreak in Tea Estate	Saikia et.al, (2015)	21
S.Wien	Gastroenteritis -10 cases	Antony B.et.al, (2009)	62
	Meningitis & septicaemia	Ayyagari et.al, (1990)	33
S.Worthington	Outbreak of Neonatal septicaemia	Rodrigues et.al, (1994)	34
	Outbreak of Neonatal Meningitis	Udani et.al, (1999)	35
	Neonatal outbreak	Muley et.al ,(2004)	36

4. Conflicts of Interest

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