

**EPIDEMIOLOGI MOLEKULAR *Salmonella typhi*,
PENYEBAB DEMAM TIFOID ASAL WILAYAH ENDEMIK
KABUPATEN SUMBA BARAT DAYA NUSA TENGGARA TIMUR**

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ABSTRAK

Kabupaten Sumba Barat Daya merupakan daerah endemik tifoid dengan angka kesakitan diperkirakan mencapai 725/100.000 penduduk pertahun. Angka kesakitan tersebut melebihi angka kesakitan untuk rata-rata kejadian demam tifoid di daerah pedesaan Indonesia (358/100.000 penduduk), bahkan mendekati angka kesakitan untuk penduduk perkotaan (810/100.000). Selain angka kesakitan yang tinggi, informasi terkait dengan epidemiologi molekular penyakit ini belum diketahui. Dalam hubungannya dengan epidemiologi molekular, ketersediaan data yang akurat dan memiliki kemampuan diskriminatif tinggi sangat penting. Untuk itu perlu dilakukan kajian diversitas strain anggota *S. typhi* dengan pendekatan sistematik polifasik. Pendekatan ini sangat bermanfaat untuk mengetahui persebaran strain berdasarkan tipe dan hubungan antar strain sehingga dapat diketahui strategi pencegahan demam tifoid yang tepat.

Penelitian ini bertujuan untuk (1). Mengungkap diversitas strain anggota *S. typhi* yang berasal dari Kabupaten Sumba Barat Daya, NTT menggunakan pendekatan sistematik polifasik, (2). Mengetahui peta penyebaran *S. typhi* berdasarkan variasi dan hubungan antar strain hasil isolasi dari penderita demam tifoid di wilayah Kabupaten Sumba Barat Daya, NTT, dan (3). Mengetahui hubungan antara diversitas dan sebaran strain-strain anggota *S. typhi* di Kabupaten Sumba Barat Daya, NTT.

Pendekatan sistematik polifasik untuk mengkaji diversitas strain anggota *S. typhi* ditentukan berdasarkan analisis data fenotipik dan genotipik. Sifat fenotipik yang diteliti meliputi karakter biokimiawi sel menggunakan perangkat API20E- dan API 50CHB/E dan analisis profil protein menggunakan SDS-PAGE sedangkan data genotipik diperoleh dari sekuen gen 16S rRNA. Peta sebaran strain *S. typhi* berdasarkan hubungan similaritas dan hubungan kekerabatan antar strain anggota *S. typhi* dilacak melalui pemetaan lokasi tempat tinggal penderita dengan menggunakan alat bantu sistem navigasi satelit (*Global Positioning System/ GPS*).

Hasil penelitian menunjukkan bahwa diversitas strain anggota spesies *S. typhi* dan persebarannya melalui pendekatan sistematik polifasik secara jelas mampu menggambarkan pola distribusi ragam strain yang berada di Kabupaten Sumba Barat Daya, NTT. Strain *S. typhi* Biotipe I (D-xilosa +, L-arabinosa -) dominan terdapat di semua area sedangkan strain *S. typhi* Biotipe III (D-xilosa +, L-arabinosa +) hanya terdapat di Kecamatan Wewewa Timur. Hasil analisis sistematik numerik fenetik memiliki tingkat resolusi diskriminatif sampai level strain dan dapat digunakan untuk klasifikasi strain anggota *S. typhi*. Empat kluster beranggotakan 17 strain terbentuk berdasarkan kemiripan karakter biokimiawi, 12 strain di antaranya dengan nilai indeks similaritas 94,9% mengelompok di kluster

I, 4 strain dengan nilai indeks similaritas 94,5% mengelompok di klaster II, dan 2 strain sisanya terpisah sebagai anggota klaster III pada nilai indeks similaritas 92,8% dan IV pada nilai indeks similaritas 86,3%. Seluruh strain membentuk pusat diversitas baru dalam spesies *S. typhi* berdasarkan profil protein dan memiliki kemiripan tipologis dengan karakter biokimiawi. Demikian pula untuk analisis filogenetik, seluruh strain membentuk suatu pusat keanekaragaman yang terpisah dengan strain acuan *S. typhi* ATCC 19430^T. Empat *clade* terbentuk pada pohon filogeni dan beranggotakan strain dari berbagai wilayah geografis di Kabupaten Sumba Barat Daya, NTT. Hasil analisis filogenetik sangat mendukung hasil identifikasi menggunakan pendekatan sistematik numerik fenetik. Dengan demikian, terbukti bahwa identitas strain yang diteliti berkerabat dengan *S. typhi* ATCC 19430^T. Pemetaan berdasarkan posisi koordinat tempat tinggal penderita menggunakan GPS membuktikan tingginya diversitas strain di Kecamatan Wewewa Timur baik berdasarkan hubungan fenetik (similaritas) maupun hubungan filogenetik (kekerabatan). Dari wilayah ini diduga kuat terjadi penyebaran dengan pola seperti lima jari tangan menuju wilayah Wewewa Utara, Kota Waikabubak, Wewewa Selatan, Wewewa Barat, Kodi Bangedo, Kodi, Kodi Utara, dan Laura.

Kata kunci: epidemiologi molekular, *S. typhi*, sistematik polifasik, numerik fenetik, filogenetik.

THE MOLECULAR EPIDEMIOLOGY OF *Salmonella typhi*, THE CAUSE OF TYPHOID FEVER IN THE ENDEMIC REGION OF THE SOUTHWEST SUMBA DISTRICT, EAST NUSA TENGGARA

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ABSTRACT

Typhoid fever is highly endemic in the Southwest Sumba District, East Nusa Tenggara Province with the incidence rate approximately 725/100,000 per year. It is greater than the standard incidence in rural areas (358/100,000), and it is nearly the same as the total number of the annual incidence in urban areas (810/100,000). Besides its high incidence, there is not much known about the molecular epidemiology of the disease. Accurate data are necessary to scrutinize its distinctive features. Thus, it needs to pursue diversity studies on *S. typhi* strains through a polyphasic systematic approach, which helps to know the distribution of the strains based on their types and interrelations to get a precise prevention strategy.

The aims of this research are to (1) unravel the diversity of the strains belonging to the species *S. typhi* taken from the typhoid fever patients in the Southwest Sumba District, East Nusa Tenggara using a polyphasic systematic approach, (2) understand the spread of *S. typhi* based on its varieties and the interrelations among the strains isolated from the typhoid fever patients in the endemic region, the Southwest Sumba District, East Nusa Tenggara, and (3) to identify the relations among its diversities and the spread of *S. typhi* strains in the Southwest Sumba District, East Nusa Tenggara.

This study uses polyphasic systematic approach to assess the strain diversity belonging to *S. typhi* species using phenotypic and genotypic data analyses. The phenotypic characteristics are identified through biochemical tests using API 20E and API 50CHE diagnostics and by whole-cell protein patterns of SDS-PAGE. The genotypic data are derived from the analysis of 16S rRNA gene sequence. The identification of areas infected by *S. typhi* is based on the residence of the infected patients using Global Positioning System (GPS). Diversity of the strains based on the phenetic numerical analysis and the phylogenetic relationships is mapped by their spread according to their places using GPS.

The results show that, through the polyphasic systematics approach, diversity of strains within the species *S. typhi* and their spread can clearly describe the spread pattern of the strain diversity in the Southwest Sumba District, East Nusa Tenggara. Biotype I (D-xylose +, L-arabinose -) exists in every area in the endemic region, while biotype III (D-xylose +, L-arabinose +) exists only in East Wewewa Subdistrict. As the results of the phenetic numerical analysis, dendrogram has a discriminative resolution until strain level and can be used to classify *S. typhi* strains. There are four clusters with 17 strains based on their similar biochemical characteristics. The first cluster consists of 12 strains with the

similarity value of 94.9%, four strains with the similarity value of 94.5% are of the second cluster, and the remaining two strains belong to the third and the last cluster with the similarity value of 92.8% and 86.3% respectively. All of the strains form a new center of protein diversity within the *S. typhi* species, and it has a similar typology with dendrogram, which is formed using biochemical characteristics. The similar finding is obtained for the phylogenetic analysis. All of the strains form apparent center of diversity with the reference strain of *S. typhi* ATCC 19430^T. There are four clades formed on the phylogeny tree that comprises of strains from many geographical areas in the Southwest Sumba District. The results of the phylogenetic analysis strongly support the identification results using the phenetic numerical approach. Thus, it proves that all of the isolates belong to the species of *S. typhi* suggesting by their relatedness with the type strain of *S. typhi* ATCC 19430^T. Mapping based on the geographical spread of the disease shows that the diversity of the strains of *S. typhi* species is very high in East Wewewa Subdistrict based on the phenetic similarity and phylogenetic relationships. Using GIS technology, the pattern of its spread looks like a finger pattern. It strongly indicates that the spread of the strains begins in East Wewewa Subdistrict and then reaches out to nearby areas such as North Wewewa Subdistrict, Waikabubak, South Wewewa, West Wewewa, Kodi regions (Kodi Bangedo, Kodi, and North Kodi) and Laura.

Keywords: molecular epidemiology, *S. typhi*, polyphasic systematic, phenetic numerical systematic, phylogenetic relationships.