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Review Article

Mutation occur in salmonella typhi due to abuse antibiotic

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Abstract

Salmonella is a zoonotic disease, and it's a multi-system disease. It is a deadly disease in developing countries, and Iraq is considered one of the countries where salmonella is widespread. Due to incorrect use, it has led to some mutations in bacteria, and the bacteria to become more resistant to antibiotics through various mechanisms including mutation in the chromosome, activation of the efflux pump, inactivation of the antibiotic, circumvention of the target, reduced penetration of the antibiotic, and horizontal gene transfer. The aim to study of mutation, occur in Salmonella serovar Typhi due to abuse antibiotic

Keywords: *Salmonella typhi*, antibiotic resistance, mutation

Introduction

Salmonella serovar typhi occasion bacterial infection called typhoid, characteristic of bacteria are gram-negative, rod in shape, and have flagellum

that having capsule which affords bacterial virulence thru keeping thereof phagocytosis(1). Transmission of S. typhi during route oral-fecal and patient suffer from elevation of fever, nausea and belly pain (1). In Iraq, there are thousands of people who infected with S.typhi, which are difficult to treat (2). Due to abuse of antibiotics, make the patient resistant to several antibiotics (3). Salmonella have numerous factor to cause disease comprise invasion which including flagella, fimbriae and protein, bacterial load and evasion host immune response (4).

Resistance of mechanisms are varied and difficult, comprising efflux pumps (which play lively role in disseminating drug, thus averting the gathering of drug indoors the cell, then may well source resistance to various antibiotics), horizontal gene transfer, mutation in gene, and changed target sites(5).

Furthermost antibacterial resistance is attributable to change in genetic of organism, due to acquisition of external genes during mutation in chromosome or plasmid (6). This aim to study of mutation, occur in Salmonella serovar Typhi due to abuse antibiotic

Literature Review

Pathogenicity of salmonella

Salmonella has ability to source diseases depends on some aspects, comprising ability for invasion (relating flagella, effector protein an fimbriae), burden of bacteria , and the evasion of host immune response (7).

Propagation of infection in S. typhi is owing to capability of bacteria to emission from IS besides arrive gallbladder and procedure biofilm inner it plus dates to stagnation formal that empowers it to prevaricate defenses of body deprived of viewing slightly symptoms (8). Unique of the central features, which S. typhi owns is its estates of Vi antigen (capsule) that shows a vital role in ingestion resistance (9).

On one occasion Salmonella are gulped in host cell that encapsulated be-

sides vacuole is made everywhere from the constituents membrane of the host cell, besides bacteria incidence in cell encourages immune response of the host cell (10). The fusion of lysosome prevented through this gap, which permits bacteria to continue besides reproduce inside the host cells. In addition, to enable the bacteria to persist in phagocytic cells, which convey them to parts of IS (11, 12).

Strains of Salmonella are ability to continue in host cell that fundamental for pathogenesis, for example strain missing this aptitude are nonvirulent (13). Subsequent the Salmonella are engulfed to host cell; that are encased in membrane compartment termed vacuole that are constituted to membrane of host cell. In standard situations, occurrence of foreign body in bacteria would trigger to host cell IR, consequence the combination of lysosomes plus emission of digesting enzyme to damage intracellular bacteria. Nevertheless, *Salmonella* consumptions SSIII to insert further effector proteins to vacuole, initiating modification of the part structure. Modification of vacuole masses the fusion of lysosome and this allow to intracellular persistence plus imitation of bacteria indoors host cells. Competence of bacteria toward remain in macrophages agrees them designate implemented in RES (14, 15).

Resistance and mutation that occur in Salmonella

Salmonella is institute within the gut and bowel tract (16). Causative agent of enteric fever. The estimated incidences worldwide (17).

The rise frequency of antibiotic resistance is recognized to the discourteous use of antibiotic for treating infection of *Salmonella* (18, 19).

Salmonella has done resistance alongside antibiotic by acquiring sole or various foreign elements of DNA, otherwise plasmids through horizontal gene transfer otherwise by inducing definite mutations in diverse loci in genes of chromosome , transformation and conjugation (20, 21)

Various approaches are laboring in antibiotic resistance mechanism in *Sal-*

monella, comprising mutation in chromosome, activation of efflux pump, inactivation of antibiotic, target circumvent, diminished permeation of antibiotic, and horizontal gene transfer (19, 22).

Resistance of Quinolone resistance due to mutation in chromosome, which code for targeted enzyme, for instance DNA gyrase and topoisomerase. Moreover, plasmid encoded gene. There are PMQR contain qnr families comprise (A,B,C,D,E,S,VC) for efflux pumps accustomed eradicate antibiotic from the body, and responsible for modifying antibiotics that make spread and more difficult to treat infection (23).

In Salmonella plasmid-mediated resistance derived as of foreign plasmids on altered plasmid As *oqxAB* and *aac*(*6'*)*Ib-cr* that mutual per distinct mutation of *gyrA* in *S. typhimurium* could yield plenty ciprofloxacin resistance (24), which may be realized by HGT25)). Aminoglycosides, tetracyclines, macrolides predominantly bind to ribosome of bacteria to impede the creation protein of bacteria, which resistance of bacteria resulting in to antibiotic. Generally, *gyrA*, *gyrB*, *parC*, and *parE* organize fluoroquinolone resistance antibiotic determining region, then modification of *gyrA* resulting in variation in binding site of antibiotics, lead to progress of antibiotic resistance (25, 26).

Resistance of antibiotic has risen, and then genes convening antibiotic resistance of antibiotic in *Salmonella* are nowadays current as selective pressure utilized exhausting antibiotics in production of poultry besides veterinary medicine aimed at development advertising and hindrance (27, 28).

Multi-drug resistance *Salmonella* be able to skirt inhibitory effect to trimethoprim consuming family gene of *dfr* that encode dihydrofolate reductases. Furthermore, trimethoprim resistance that confer via incidence of plasmid, which conjugative otherwise no conjugative designated IncHI1/ non-IncHI1. Per se, plasmids hold whole transposon, which harbors several genes resistance for instance ampicillin resistance blaTEM-1, streptomycin resistance *strAB*, trimethoprim-sulfamethoxazole resistance *sul1*, *sul2*,

dfrA7, and chloramphenicol resistance *catA1* .This plasmid is accountable for incidence of S.typhi multidrug resistance in H58 haplotype (21, 29,30).

The MDR designs of *Salmonella* to diverse antibiotic classes (expressly tetracyclines, sulfonamides, aminoglycosides, and penicillin) previously verified by numerous investigations (31,32-35).

The prevalence of the aadA1 gene was detected in several isolate of *S. typhi* and existence of silent mutation in Iraqi isolate. The first isolate was almost just similar the isolates of each of the countries Korea, Iran, India, and Madagascar, but The second Iraqi isolate was the share of correspondence between them at 99% at position G. The gene of aadA1 was existent in isolate of *S. typhi* from blood, while in isolate from stool of human, and the noticed mutation did not affect (3).

Sequencing of *aadA1* gene showed replacement of cytosine nucleotide to guanine nucleotide at position (408). Nucleotide substitution causes one silent mutation and no changed amino acid from Arginine. Furthermore, the sequencing of *bla-TEM1* gene showed eight mutations were recorded, five mutations from them were point mutation with transvertional changes and three were silent mutation transversional changes and Alterations in nucleotide sequence of gene bla-*TEM1* cause five mutations that change sequence of amino acids (2).

Conclusion

Salmonella is a multi-system disease. It is display in developing countries such as Iraq. Due to incorrect use, it has led to some mutations in bacteria that are more resistant to antibiotics through various mechanisms including mutation by acquiring sole or various foreign elements of DNA, otherwise plasmids by horizontal gene transfer or else by inducing definite mutations in diverse loci of chromosomal gene, transformation and conjugation. Sequencing of *aadA1* gene showed replacement of cytosine nucleotide to guanine nucleotide that causes one silent mutation and no changed amino

acid from Arginine. In addition, the sequencing of *bla-TEM1* gene showed eight mutations five mutations from them were point mutation and three were silent mutation and Alterations in nucleotide sequence of gene bla-*TEM1* cause five mutations that change sequence of amino acids.

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