v. 3, n. 44, 2023

International Journal of Health Science

IMPORTANCE OF *Salmonella* SURVEILLANCE AGAINST THE ANTIBIOTIC RESISTANCE: A BRIEF LITERATURE REVIEW

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Keywords: *Salmonell*a, prevalence, bacterial typing, resistance antibiotic, safety.

INTRODUCTION:

Salmonella is a genus of bacteria that belongs to the Enterobacteriaceae family, formed by gram-negative bacilli, facultative anaerobes, with peritrichous flagella and that do not develop a capsule (except the species *S.* typhi) or spores. They are mobile bacteria that produce hydrogen sulfide (H2S). They ferment glucose because they have a specialized enzyme and do not produce urease. (Ryan and Ray 2004).

From the epidemiological point of view, *Salmonellas* can be classified into three groups: those that do not have a preference for any host (they infect both humans and animals), those that arise only in humans: *S.* Typhi, *S.* Paratyphi A and *S.* Paratyphi C. and those that are adapted to a host in animal species such as *S.* Abortusovis (cattle), *S.* Abortusequi (equine) and *S.* Gallinarum (birds).

The possibility of an infection when consuming a food containing *Salmonella* depends on numerous circumstances, among which are the resistance of the consumer and the number of microorganisms ingested.

Less pathogenic or at least less powerful *Salmonellas*, such as *Salmonella* pullorum, must be in the millions or billions to be capable of producing an infection. Of the more pathogenic species, such as *Salmonella* enteritidis, such high numbers are not necessary. *Salmonella* can be found in extraordinary numbers without appreciably altering the smell or taste of food. The greater the number of participating microorganisms, the greater the chances that the consumer will be infected (De la rosa and prieto 1997).

FOOD SAFETY

The concept of Food Safety is defined as "the guarantee of doing no harm as a shared responsibility, which adds value to both the producer and the consumer so that it is sustainable over time".

FOOD SAFETY, QUALITY FOR CONSUMPTION

An adequate diet is essential for health. Food provides the energy and essential nutrients that all human beings need to maintain a good nutritional status. Contrary to what many believe, Health is not the absence of disease, but must be understood as a complete state of physical, mental and social well-being. The contribution of healthy food is essential to properly nourish ourselves, but it is also essential to avoid getting sick from its consumption (Om et Jammer 1991).

A faulty preparation, cooking or storage of a food, are the main causes for the appearance of bacteria in any dish of food, which begin to multiply and make the consumption of food dangerous to health. The presence of bacteria is not always visible in food, they do not always present changes in taste, smell or even changes in their appearance.

The objective of hygiene in this sense is to guarantee the production and preparation of food that is innocuous and clean. A safe food is the guarantee that it will not cause harm to the consumer when it is prepared or eaten, in accordance with hygienic-sanitary requirements. Food safety is a process that ensures quality in the production and preparation of food products. It guarantees the obtaining of healthy, nutritious and hazard-free food for the consumption of the population. The preservation of safe food implies the adoption of methodologies that allow the identification and evaluation of the potential dangers of contamination of food in the place where it is produced or consumed, as well as the possibility of measuring the impact that a disease transmitted by contaminated food can cause to human health (Ingraham

1998).

As established by the Codex Alimentarius (code that regulates the quality and safety of food) a food is considered contaminated when it contains: live agents (viruses or parasites that are hazardous to health); toxic or organic chemical substances foreign to their normal composition and toxic natural components in concentrations greater than those allowed

FOOD CONTAMINATED WITH *Salmonella*

The prevalence of this bacterium can be found in a wide variety of birds and animals, but the most important source of infection for man is poultry, however all raw meats are treated as contaminated, it can also be present in milk without pasteurize and eggs.

Insects, rodents, and pets that are interacting with contaminated birds can spread this bacteria onto food. It is also recommended to wash your hands before eating and after going to the bathroom since this bacterium lives in the human intestine. (Pascual et calderón 2000).

MOLECULAR AMPLIFICATION TECHNIQUE (ISOLATION)

Currently, molecular techniques have been widely used as an epidemiological and clinical tool. The usefulness of genomic amplification (PCR) as a diagnostic tool for the identification of pathogens has been well documented in the world literature, being widely used in samples from food, environmental and clinical matrices in an increasing way.

PCR has been used as a tool for investigating outbreaks of food outbreaks and the identification of responsible etiological agents. This technique presents high sensitivity, specificity and less processing time. The realization of the detection by the PCR method depends, in part, on the extraction of the DNA, and the specificity of the primers. The environmental, food and clinical matrices are very complex, mainly due to the high amount of existing proteins, carbohydrates and lipids, as well as the presence of other microorganisms present; this contributes to limitations of the technique.

Inhibitors are one of the major problems within the analyzes made by PCR; For this, pre-enrichment steps of the samples to be analyzed have been devised.

Tetrathionate and rappaport-vassidialis have been used mainly in food laboratories. The purpose of these media is to dilute the interferents and increase the number of viable microorganisms, thereby increasing the number of DNA copies, increasing the sensitivity of the technique (Van Belcum et al. 2001).

MICROBIAL RESISTANCE TO ANTIBIOTICS

Antibiotic resistance is the ability of a microorganism to resist the effects of an antibiotic. Resistance occurs naturally by natural selection through random mutations, but it can also be artificially induced by applying selective pressure to a population. Once the genetic information is generated, the bacteria can transmit the new genes through horizontal transfer (between individuals) by exchange of plasmids. If a bacterium carries several resistance genes, it is called multi-resistant or, informally, a superbug.

Antibiotic resistance is a consequence of evolution via natural selection. The antibiotic action is an environmental pressure: those bacteria that have a mutation that allows them to survive will reproduce. They will pass this trait on to their offspring, which will be a fully resistant generation (G. Guilfoile Patrick 2007).

A strain is a set of microorganisms that derive from well-defined progenitors, have a similar genetic endowment and retain certain

characteristics that they maintain for several successive generations; it is a pure culture derived from a single isolate. A clone is a culture made up of the descendants of a single bacterium isolated by micromanipulation.

GENETICS OF MICROBIAL RESISTANCE

The genetic changes that explain resistance can be produced by several mechanisms that involve either chromosomal DNA, as in mutation, or by the acquisition of extrachromosomal genetic material, by transduction, transformation, or conjugation.

In the mutation, changes appear in the chromosome that may be due to chance or to the influence of physical or chemical agents and in fact not necessarily due to exposure to the antimicrobial, as demonstrated by the observation that many microorganisms isolated before the appearance of antibiotics have had mutations that have made them insensitive to antibiotics after they were discovered. Although the antimicrobial is not the cause of the mutation, it nevertheless has an important role in the selection of resistant strains, since when the antimicrobial is administered to a patient with a bacterial culture in which there are sensitive strains and others with mutations that confers resistance to them, the antimicrobial will eliminate sensitive microorganisms, leaving only the resistant ones. The speed of appearance of the mutant strains is highly variable and can occur very quickly in some cases or, on the contrary, very slowly and gradually, over the years.

More commonly, the genetic alteration that determines resistance is produced through the acquisition, by the microorganism, of genes carried in extrachromosomal plasmids, through transduction, transformation or conjugation (G. Guilfoile Patrick 2007).

During transduction, a bacteriophage virus transfers bacterial extrachromosomal DNA incorporated into its protein coat, from an insensitive bacterium to a sensitive one, which acquires resistance and the ability to transfer it to its offspring, as has been observed in *Staphylococcus* aureus strains that acquires resistance to penicillins.

In the transformation process, sensitive bacteria can incorporate DNA from the environment and if the environment possesses genes that code for resistance, the bacterium becomes resistant to one or more antimicrobials. The origin of DNA from the environment would lie in the fact that some bacteria, in certain phases of their growth, are capable of excreting DNA.

Conjugation is an important mechanism for the acquisition of microbial resistance and consists of the passage of genes (R determinants) from a resistant bacterium to a sensitive one, through direct coupling between the bacteria through the formation of a sexual pili. R factors can contain information to provide resistance to several antimicrobials at once, and this happens very quickly, in a single step. For conjugation between bacteria and the formation of sexual pili to occur, the intervention of another group of genes called resistance transfer factor is necessary, without which the process cannot take place. The R determinant complex plus the resistance transfer factor is known as the R factor. The emergence of resistance mediated by R factors is very important among gram-negative bacteria, especially among Enterobacteriaceae. Microorganisms capable of transferring this type of resistance to sensitive bacteria include *Escherichia coli, Salmonella, Shiguella, Klebsiella,* and *Pseudomonas* aeruginosa. This mechanism produces resistance to tetracyclines, chloramphenicol, sulfonamides, penicillins, and aminoglycosides.

STRAIN TYPING, PRINCIPLES AND METHODOLOGY

These bacterial typing methods are capable of discriminating between strains belonging to the same bacterial species in different clone lines, that is, groups of bacteria originating from the same initial clone. Based on this definition of a bacterial clone, different bacterial isolates from different times and locations that present identical results by a number of different typing methods most likely belong to the same clonal line. According to this definition, clonality implies the high probability that two isolates are related, the confidence of this probability increasing the more typing methods are used. It is therefore desirable in epidemiological research to use a variety of typing methods.

PRINCIPLES OF BACTERIAL TYPING

A typing method is one that can be used to differentiate bacterial strains belonging to the same species. The essence of using these methods is to be able to compare isolates and group strains with identical results into the same group. When two studied isolates yield different results according to one or more typing methods, it can generally be concluded that they derive from different clonal lines. However, to be able to locate different isolates in the same clonal line, coincident results in more than one typing method are required.

Obtaining epidemiologically valid conclusions is facilitated if there is knowledge of the distribution of relevant types in a given geographical area, which makes it possible to lay the foundations for establishing which typification results can be compared.

Typing methods must meet three essential requirements: 1) typing power (being able to classify any isolate into a given type); 2) Discriminatory power (being able to discriminate between unrelated isolates); 3) reproducibility (being able to provide reproducible results between different assays and stable for a given strain obtained from different origins) (Hyo Bi Kim et al., 2011).

When evaluating a typing method, in addition to considering these requirements, the simplicity of its implementation and interpretation of results is also considered.

Typing methods fall into two broad categories: phenotypic and genotypic. The first are those that characterize the products of gene expression to differentiate strains, studying biochemical and antigenic properties, sensitivity to phages, antimicrobials, etc. These properties have a tendency to vary with culture conditions, growth phase, occurrence of spontaneous mutations, etc., since they are the result of gene expression.

On the other hand, genotypic methods are those based on the analysis of the genetic structure of an organism, and include polymorphisms in DNA restriction patterns by endonucleases, gene amplification profiles, and plasmid profiles. These methods are less subject to natural variation, although they may be affected by chromosomal DNA insertions or deletions, extrachromosomal DNA gain or loss, or random mutations that may create or delete restriction sites, for example (Yujuan Jin et al., 2009).

In general, phenotypic methods have limited typing power, since each one is applicable to a small number of bacterial species (eg, serotyping, phage typing), while genotypic methods are generally applicable to any bacterial taxon (A.H. Moon et al., 2011).

The reproducibility of a technique can be affected both by variations in the method and by biological variations, which are more easily detectable in the case of phenotypic methods. Over time (from weeks to years depending on the strain), the typing patterns produced with DNA-based methods present minor variations in some cases, so when analyzing the results

it is important to consider the time elapsed since their isolation (Van Belkum 2001).

The main advantage of genotypic methods over traditional ones is their discriminatory capacity, managing in many cases to differentiate between absolutely identical strains in phenotypic terms (Chibundu Ngozi et al., 2011).

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