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ORIGINAL ARTICLE

HIV-Tuberculosis co-infection in a public health unit in the city of Santo Domingo de los Tsáchilas

Coinfección VIH – Tuberculosis en una unidad de salud pública de la ciudad de Santo Domingo de los Tsáchilas

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ABSTRACT

Introduction: HIV infection has caused significant negative impacts on health due to its high morbidity and mortality. Thus, it is recognized as the ninth leading cause of death globally and the second most prevalent cause due to a single infectious agent, after tuberculosis.
Objective: to describe the clinical behavior of HIV-Tuberculosis co-infection in a Public Health unit in the city of Santo Domingo de los Tsáchilas in the period 2022.
Methods: the design used in this study was descriptive, observational and descriptive. Using methods such as analysis synthesis and observation.
Results: the HIV-Tuberculosis interaction was determined in a series of cases extracted from a databaseofthe Internal Medicine Unit of a public health unitIn the city of Santo Domingo de los Tsáchilas, a series of cases characteristic of a mixed study was used. The main data extracted were: the percentage of affected people, with a higher proportion being male; the diagnostic methods used to confirm HIV-tuberculosis co-infection, among which were BK1, GenExpert and LAM.
Conclusions: the mortality rate of HIV-tuberculosis co-infection within the group was determined, in addition, the main diseases associated with co-infection were determined, which were Syphilis, Covid-19, Histoplasmosis, Acute Renal Failure, in this way the main interactive characteristics of HIV-tuberculosis co-infection in the aforementioned sample were determined.

Keywords: Coinfection; HIV; Tuberculosis.

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RESUMEN

Introducción: la infección por VIH ha provocado importantes impactos negativos en la salud por su elevada morbimortalidad. De esta manera, es reconocida como la novena principal causa de fallecimientos a nivel global y la segunda más prevalente debido a un único agente infeccioso, después de la tuberculosis.
Objetivo: describir el comportamiento clínico de la coinfección VIH-Tuberculosis en una unidad de Salud Pública, en la ciudad de Santo Domingo de los Tsáchilas en el periodo 2022.
Métodos: el diseño empleado en este estudio fue descriptivo observacional y descriptivo. Utilizando métodos como el análisis síntesis y la observación.
Resultados: se determinó la interacción VIH-Tuberculosis representada en una serie de casos extraídos de una base de datos de la unidad de Medicina Interna de una unidad pública sanitaria en la ciudad de Santo Domingo de los Tsáchilas, se empleó un estudio de serie de casos característicos de un estudio mixto, los principales datos extraídos fueron: el porcentaje de personas afectadas que tuvo una mayor proporción fue el sexo masculino; los métodos de diagnóstico utilizados para confirmar la coinfección VIH-tuberculosis entre los cuales estuvieron BK1, GenExpert y LAM.
Conclusiones: se determinó la mortalidad de la coinfección VIH-tuberculosis dentro del grupo, además se determinó las principales enfermedades asociadas a la coinfección las cuales fueron Sífilis, Covid-19, Histoplasmosis, Insuficiencia Renal Aguda, de esa forma se determinaron las principales características interactivas de la coinfección VIH-tuberculosis en la muestra mencionada.

Palabras Clave: Coinfección; VIH; Tuberculosis.

INTRODUCTION

Since its appearance, HIV infection has caused significant negative impacts on health due to its high morbidity and mortality. Thus, it is recognized as the ninth leading cause of death globally and the second most prevalent cause due to a single infectious agent, after tuberculosis.

The interaction between HIV and tuberculosis has represented a problem in the field of health prevention, an interaction determined by the different clinical characteristics of the groups it affects, so determining specific qualities would describe the behavior of the problem in a specific group.

In Ecuador, the Ministry of Public Health, in collaboration with technical support from UNAIDS, reported that by the end of 2019, a total of 47,206 people were affected by HIV. Most of these people are between the ages of 15 and 49 and are male. Regarding the distribution of HIV cases in the different provinces of the country, it is noteworthy that the province of Guayas ranks first with 16,710 cases, followed by Pichincha with 5,452 cases, Los Ríos with 2,941 cases, Manabí with 2,571 cases and finally Esmeraldas with 1,876 cases.

In the Republic of Ecuador, the National Congress officially enacted, according to Law 11, drafted on April 14, 2020, 14 articles aimed mainly at prevention, registration, budgetary delivery, treatment, support and compensation in the corresponding cases related to HIV, measures that were taken due to the seriousness of the situation.

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However, the prevalence of HIV cases in the Province of Santo Domingo has increased, and among the causes of HIV co-infection are the lack of biosecurity measures in the contagion of new patients through sexual contact, dialysis machines, blood banks due to errors in the handling of infected sharp objects, in addition to the lack of knowledge that the patient has about their vulnerability and therefore, there is a lack of care and deficiency in treatment, which increases the probability of HIV-tuberculosis co-infection.

Currently, around 13 million individuals suffer from both pathologies, of which 9,5 million live in sub-Saharan Africa and 2,3 million in South-East Asia. When HIV is present, the clinical symptoms of tuberculosis are aggravated and the detection of the disease at the microbiological level is complicated due to the decrease in the number of bacilli present in the sputum sample.[1]

In 2018, 6,094 cases of susceptible tuberculosis were reported in Ecuador, with a rate of 34,53 per 100,000 inhabitants. Cases of susceptible tuberculosis include both new cases and those that have been previously treated. Since 2012, an increase in the incidence of new tuberculosis cases has been observed, reaching a minimum of 4,903 cases in 2014 and a maximum of 5,960 cases in 2018. In contrast, cases of previously treated tuberculosis have experienced a decrease, going from 663 cases in 2012 to 134 cases in 2018.[2]

According to the 2017 GAM Report, in Ecuador, 92,4 % of PLHIV know their HIV status, 54,20 % of adults and children currently have access to ART, and 78 % of these have a suppressed viral load.

In response to this situation, the Ministry of Public Health (MSP) and the National HIV/AIDS Strategy have implemented a comprehensive, multi-sector response to the spread of the epidemic. This has been achieved through the implementation of various initiatives, such as the free availability of medicines, the promotion of social and community participation, the regular development of national guidelines, and other actions. All of this has been carried out from a perspective that values cultural diversity and seeks equity.

Tuberculosis is one of the most important infectious diseases worldwide, classified as one of the leading causes of death in patients with AIDS co-infection, mainly in poor countries. It is more widely distributed in the world and is one of the leading causes of death in patients with AIDS, especially in poor countries. One third of the world's population is infected with Mycobacterium tuberculosis and every year about 8 million people become ill, of whom approximately two million die. The increase in cases of HIV infection has contributed to the worsening of the impact of tuberculosis. The spread of HIV infection has contributed to the worsening of the impact of tuberculosis.

It is estimated that HIV infection has been linked to around 8 million cases of tuberculosis and 2,9 million deaths attributed to this disease during the period from 1991 to 2000.[1]

It is estimated that people who carry both HIV and M. tuberculosis have a 100-fold higher chance of developing active tuberculosis compared to those who are infected with M. tuberculosis alone and do not have HIV. Tuberculosis negatively affects the progression of HIV infection. Experiments conducted in laboratory settings have revealed that tuberculosis increases the reproduction of the virus to more than 160 copies, leading to chronicity in the development of the infection.

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The cases of HIV-TB co-infection reported in 2020 indicate that, of the 3,823 reported cases with HIV, 522 were diagnosed with active tuberculosis.[2]

Problem.
HIV-Tuberculosis co-infectionin a Public Health unit in the city of Santo Domingo de los Tsáchilas in the period 2022.

General Objective: to write the clinical behavior of HIV-Tuberculosis co-infection in a Public Health unit in the city of Santo Domingo de los Tsáchilas in the period 2022.

METHODS

The design used in this study was descriptive observational of the case series type since the universe and sample were comprised of 16 individuals. The population taken into account in the study were patients from the internal medicine unit of a public health unit; the sample of this study was 16 patients diagnosed with HIV-Tuberculosis co-infection.

In terms of scope, this project is descriptive since it begins by describing the natural history of HIV, how it predisposes to tuberculosis symptoms, and also defines what HIV-tuberculosis co-infection is and their mutual interaction.

The case series is characterized by being a type of document that reports similar characteristics that make them groupable, etiological, anatomical, syndromic, physiological, genetic, histological, molecular, type of treatment, some adverse effect to the treatment or some complementary study. It is taken into consideration that for operational purposes, 2 to 10 cases must be presented in its description.[3]

Techniques and instruments
The information collected by a public health unit is analyzed, the most important points of the information are classified through the synthetic analytical method according to the relevance of the project, using the generative questions as a guide, thus obtaining specific information in order to answer the generative questions and meet the objectives described.

With the information obtained, measures will be proposed to prevent HIV-tuberculosis co-infection, in addition to providing the information obtained to social media.

The place where the information for this project was obtained was both field and bibliographic; field because information will be collected through direct observation of a public health unit using the methodology of case series study (clinical records), bibliographic because different types of sources were used such as Pubmed, Scielo, Elsevier, Ministry of Public Health of Ecuador for the investigation of the origin and evolution of HIV-tuberculosis co-infection.

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RESULTS

Microbiology II

HIV is a retrovirus, which morphologically is a spherical, RNA-containing virus. Its envelope is composed of viral glycoproteins and is formed by budding through the plasma membrane. Its envelope contains a capsid containing two identical copies of the positive-strand RNA genome, located in a dense viral core. In addition, the virion has 10 to 50 copies of the RT and integrase enzymes, as well as two cellular transfer RNAs (tRNAs). These tRNAs pair with each copy of the genome to serve as RT primers. The virion is approximately 80 to 120 nm in size and is enveloped in a spherical shape. In the case of HIV and human T-lymphotropic virus, the positive-strand RNA genome is approximately nine kilobases long. Inside the virion is an RNA-dependent RNA polymerase (reverse transcriptase), two copies of RNA, and protease and integrase enzymes.

The virus's receptor initially determines its tissue tropism. Replication of the virus occurs through a DNA intermediate called a provirus, which integrates randomly into the host cell chromosome and becomes a cellular gene. Transcription of the genome is regulated by the interaction of host cell transcription factors with promoter and enhancer elements in the long terminal repeat portion of the genome. Retroviruses encode tat, rev, net, vif, and vpu in the case of HIV. The virus is assembled and released by budding through the plasma membrane. The main determinant of HIV pathogenesis and disease is the virus's tropism for myeloid cells and CD4-expressing T cells. HIV-induced immunosuppression (AIDS) causes a reduction in the number of CD4 T cells. During sexual transmission, HIV infects a mucosal surface, penetrates it, and rapidly infects cells of mucosal-associated lymphoid tissue, including the gut.

Mycobacterium tuberculosis is a Gram-positive, acid-fast, strict aerobic bacterium. It has a rod-shaped shape and its cell wall contains a layer of mycolic acid. It also has high levels of lipids, which give it unique characteristics and contribute to its resistance to disinfectants, detergents, common antibacterial antibiotics and to the host's immune response. It is an intracellular pathogen that enters the respiratory tract and infectious particles reach the alveoli, where they are digested by macrophages.

However, it has escape and survival mechanisms within macrophages, allowing it to replicate and spread to other tissue, and within granulomas, leading to persistence and reactivation of the infection in the future. Humans are the only natural reservoir, the disease is transmitted by inhalation of infectious aerosols, The likelihood of disease progression depends on both the infectious dose and the patient's immune status. The tuberculin test, IFN-y release tests, microscopy and culture are sensitive indicators of exposure to the microorganism, as well as molecular techniques, such as PCR to detect M. tuberculosis DNA in clinical samples.[4]

Pharmacology

There are four families of antiretroviral drugs, which inhibit enzymes and target structures during HIV viral replication. These families are:

1. Protease inhibitors (PI);
2. Reverse Transcriptase Inhibitors (RTI):
   a. Nucleoside reverse transcriptase inhibitors (NRTIs);
   b. Non-nucleoside reverse transcriptase inhibitors (NNRTIs);
3. Integrase inhibitors (INI);
4. Entry inhibitors:
   a. Fusion inhibitors (FI);
   b. Coreceptor inhibitors (CCR5 antagonists).

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HIV drug treatment recommends starting antiretroviral therapy in all patients diagnosed with HIV infection, regardless of the CD4+ cell count or clinical stage. As shown in Figure 1.

	Régimen	Medicamentos	Posología
Adultos y adolescentes >13 años	**PREFERENTE**		
	2 ITIAN / INI	TDF[1] / 3TC / DTG[2]	300 / 150 / 50 mg, vía oral, una vez al día.
		TDF / FTC + DTG	300 / 200 / 50 mg, vía oral, una vez al día.
	ALTERNATIVAS		
	2 ITIAN + INI	TDF / 3TC + RAL	300 / 150 mg, Vía oral, una vez al día. + 400 mg, Vía oral, dos veces al día.
		TDF / FTC + RAL	300 / 200 mg, Vía oral, una vez al día. + 400 mg, Vía oral, dos veces al día.
	2 ITIAN + ITIANN	TDF / 3TC + EFV[3]	300 / 150 mg, vía oral, una vez al día. + 600 mg, vía oral, una vez al día.
		TDF / FTC/EFV	300 /200/600 mg, vía oral, una vez al día.
	2 ITIAN + IP	TDF / 3TC + DRV/r[4]	300 / 150 mg, vía oral, una vez al día. + 800 mg / 100 mg, vía oral una vez al día.
		TDF / FTC + DRV/r	300 / 200 mg, vía oral, una vez al día. + 800 mg / 100 mg, vía oral una vez al día.
	2 ITIAN + INI	ABC[5] / 3TC + DTG	600 / 300 mg, vía oral, una vez al día + 50 mg, vía oral, una vez al día
	2 ITIAN + INI	ABC / 3TC + RAL	600 / 300 mg, vía oral una vez al día. + 400 mg, vía oral, dos veces al día.
	2 ITIAN + IP	ABC / 3TC + DRV/r	600 / 300 mg, vía oral, una vez al día. + 800 mg/100 mg, vía oral, una vez al día
	2 ITIAN + ITIANN	ABC / 3TC + EFV	600 / 300 mg, vía oral, una vez al día. + 600 mg, vía oral, una vez al día
	2 ITIAN + INI	AZT[6] / 3TC + DTG	300 / 150 mg, vía oral dos veces al día. + 50 mg, vía oral, una vez al día
	2 ITIAN + INI	AZT / 3TC + RAL	300 /150 mg, vía oral dos veces al día + 400 mg, vía oral dos veces al día.

Fig. 1 Antiretroviral therapy in all patients diagnosed with HIV infection.

TDF: tenofovir; 3TC: lamivudine; ABC: abacavir; DRV: darunavir; DTG: dolutegravir; EFV: efavirenz; FTC: emtricitabine; INI: integrase inhibitor; NRTI: nucleoside reverse transcriptase inhibitor; PI/r: ritonavir-boosted protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; RAL: raltegravir; TDF: tenofovir disoproxil fumarate; ATV: atazanavir.(5)

Therapeutic regimens for individuals are classified into two categories: susceptible tuberculosis and resistant tuberculosis, and are prescribed according to the individual's weight.(6)

Treatment for resistant tuberculosis at distances of 4 to 6 kilometers (Am):
Intensive phase: Kanamycin (Km), Moxifloxacin (MFX) at increased doses, Ethionamide (Eto), Isoniazid (H) at high doses, Clofazimine (Cfz), Prirazinamide (Z) and Ethambutol (E). These will be administered daily for four months.

Continuation phase: You will continue with daily administration of Moxifloxacin (MFX), Clofazimine (Cfz), Ethambutol (E) and Prirazinamide (Z) for a period of five months. (6) As shown in Figure 2.

Esquema de tratamiento	Duración	Tipo de Caso TB sensible
2HRZE/4HR	6 meses	Nuevo, **sin evidencia de presentar TB resistente.**
HRZE	9 meses	Pérdida en el seguimiento recuperado, recaídas o fracasos, **con sensibilidad confirmada a rifampicina**

Isoniacida (H), Rifampicina (R), Pirazinamida (Z) y Etambutol (E)

Fig. 2 Treatment for cases with sensitive TB.

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Genetics

The most virulent type of HIV is type I, which is considered to have greater clinical and genetic importance, due to its highGenetic heterogeneity, which is in turn determined by its high mutation rate. In individuals infected with HIV-1, there are 109 to 1012 virions, due to a very high turnover of virions and infected cells. Therefore, the control of infectious diseases caused by RNA viruses (AIDS/HIV) is complex due to the great genetic plasticity and evolutionary potential of HIV-1.

HIV-1 has high resistance due to these mechanisms:
1. Reverse transcriptase without 3' 5' exonuclease activity, which acts as an error corrector.
2. Both structural and functional proteins possess functional plasticity.
3. High replication rate, generating around ¨1010¨ new virions each day.
4. At any given time, all HIV-1 quasi-species coexist in an individual.

General techniques have been established to determine HIV resistance to antiretrovirals: genotypic and phenotypic. Genotypic tests are based on genome analysis to find mutations, and phenotypic tests are based on in vitro replication systems that combine the virus with different concentrations of antiretrovirals, such as commercial phenotypic tests based on measuring drug sensitivity.[7]

Genetic susceptibility to tuberculosis: There are more than 30 genetic polymorphisms related to genetic susceptibility to TB in different populations and regions of the world. Studies of genetic factors associated with pulmonary TB show that innate immunity is essential in the primary host defense mechanism and resistance to TB, where the main risk is related to genes involved in the natural immune response, such as Toll-like receptors (TLRs) in macrophages; the vitamin D receptor (VDR); NRAMP1 (SLC11A1; macrophage activation); INF-γ, TNF-α, DR8-increased risk of TB (immunodeficiency); HLA I (B13-pulmonary tuberculosis) and HLA II (DR3 and DR7-relative protection against TB), among others.[8]

Semiology

Clinical signs and symptoms of tuberculosis (Figure 3) They vary according to the focus of infection, the primary disease is restricted to the lower respiratory tract, with nonspecific symptoms such as malaise, weight loss, cough and night sweats. Sputum may be scant, hemoptysis and purulent. 5 % of people exposed to the Bacillus develop an active disease in the following two years and the rest in later stages. The probability that tuberculosis evolves into an active disease increases with immunosuppression, 10 % of patients infected with HIV and low CD4 T count develop an active disease, due to their deficient immunity they suffer asymptomatic subclinical disease with negative chest X-rays despite the dissemination of the bacillus.[4]

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Presencia de signos y síntomas (Lista de chequeo)	Sexo			
	Femenino		Masculino	
	n = 35	%	n = 92	%
Temores y preocupaciones	25	(71.4)	51	(55.4)
Depresión	21	(60.0)	49	(53.3)
Sed	19	(54.3)	62	(67.4)
Dolor muscular	19	(54.3)	57	(62.0)
Debilidad	19	(54.3)	56	(60.9)
Fatiga	19	(54.3)	50	(54.3)
Dificultad en la concentración	19	(54.3)	38	(41.3)
Pérdida de la memoria	17	(48.6)	38	(41.3)
Dolor de cabeza	16	(45.7)	38	(41.3)
Insomnio	16	(45.7)	33	(35.9)
Formación de morados con facilidad	11	(31.4)	13	(14.1)
Boca seca	9	(25.7)	49	(53.3)
Preocupación por pérdida de peso	9	(25.7)	41	(44.6)
Venas prominentes en las piernas	9	(25.7)	14	(15.2)
Sudores de noche	7	(20.0)	42	(45.7)

Fig. 3 clinical signs and symptoms of tuberculosis.

Pathology

Once the microorganism Mycobacterium tuberculosis, which causes tuberculosis, enters the body, specifically the pulmonary alveoli, a non-specific inflammatory response occurs, causing the accumulation of polymorphonuclear cells and the presence of macrophages.[10]

The first reaction occurs within the alveoli, but it may spread to nearby or distant lymph nodes, as well as to other organs. In the case of primary pulmonary tuberculosis, it is characterized by the presence of a single lesion, in the middle part of the lung lobe and rarely at the apex. This lesion is known as the "Ghon focus".

The dissemination of this focus through the lymphatic pathways resembles a rosary due to the presence of multiple tubercles in a chain along the lymphatic path. The Ghon focus and its drainage towards one or more hilar and/or mediastinal nodes constitute the "primary pulmonary complex" or "Ranke complex".(10)Although highly active antiretroviral therapy (HAART) reduced TB co-infection by 70-90 %, the incidence remains higher even in patients with a high CD4 cell count.[11]

Research and Biostatistics II

Research Design: Descriptive research focuses on investigating a specific topic by asking detailed questions, using appropriate design and data analysis. Descriptive statistics are used to answer the questions about who, what, when, where, and how events occurred.[12]

In the descriptive research process, data describing events is collected and then organized, tabulated, and visually represented using graphs and tables, making it easier to understand the distribution of the information collected.[12]

On the other hand, a database is a set of information organized and presented for a specific purpose.[13]

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DISCUSSION

Within the population studied, we propose a division by biological sex, where there is a higher prevalence of HIV-Tuberculosis positive cases in the male sex compared to the female sex, with a proportion of five female cases and 11 male cases.

Among the diseases associated with HIV-Tuberculosis co-infection within the population studied are: Syphilis, Covid-19, Histoplasmosis, Acute Renal Failure, each with a patient suffering from it.

In the analyzed database consisting of 16 patients, the mortality rate was 6,2 %, which is equivalent to one death in the entire population.

Among those people who suffer from co-infection, their tuberculosis is divided into two general types: pulmonary with 37 % and extrapulmonary with 63 %, among those with extrapulmonary tuberculosis there is miliary tuberculosis with 10 %, lymph node tuberculosis with 10 %, intestinal tuberculosis with 10 % and other varieties of tuberculosis with 70 %:

The diagnostic methods used in the population of this project were BK1, GenExpert and LAM, which diagnosed 18,75 %, 37,5 % and 37,5 % of the confirmed cases respectively.

The results described in this study correlate with studies carried out in other health care facilities, as evidenced in this study carried out in a Peruvian hospital where a sample of 289 patients diagnosed with tuberculosis was taken, of which 75,8 % were male with an average age of 39 years. Pulmonary forms of tuberculosis accounted for 65,1 %.

Of the 101 patients with extrapulmonary TB, the most frequent was that of the central nervous system (33,7 %). The prevalence of TB/HIV co-infection was 30,1 %, of which an analysis of the variables associated with this co-infection was carried out, where factors associated with a higher risk of co-infection were found, which were: male sex, consumption of substances such as: tobacco, alcohol, drugs (César Espinoza-Chiong & Dante M.Whoñones-Laveriano, 2021[(1)]).

Proposal

Raise awareness in the community about the importance of biosecurity measures regarding HIV-tuberculosis co-infection, which will be presented through a scientific infographic to the citizens and student community, the most effective control measures to prevent HIV-tuberculosis co-infection.

CONCLUSIONS

The HIV-tuberculosis interactionand the internal medicine unit of a public health unit,It is determined in the first instance by the lack of therapeutic adherence in those people who already suffered from HIV and therefore had an incompetent immune system, who were also exposed to Mycobacterium tuberculosis, resulting in co-infection in which tuberculosis could affect both the pulmonary and extrapulmonary areas.The most frequent type of tuberculosis in the series of cases suffering from HIV-tuberculosis co-infection was extrapulmonary tuberculosis with 67 %, of which miliary, lymph node and intestinal tuberculosis each represented 10 %.

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