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Diagnostic discordance in Neisseria gonorrhoeae: negative culture and positive PCR

Bachelor's degree of Biochemistry and Molecular Biology

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This work is based on patient data obtained during the external curricular practices carried out at the Hospital Clínico de Valencia under the supervision of Dr. Javier Colomina.

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ABBREVIATIONS

PCR: Polymerase chain reaction

PMNs: Polymorphonuclear cells

MALDI-TOF: Matrix-Assisted Laser Desorption/Ionization

qPCR: Real-time quantitative PCR

STI: Sexually transmitted infections

ESC: Extended spectrum β-lactamases

HIV: Human immunodeficiency virus

STD: Sexually transmitted diseases

CT: Cycle of quantification

OR: Odds-ratio

CI: Confidence range

ABSTRACT

Introduction: *Neisseria gonorrhoeae* is a gram-negative coccobacillus and infection is the etiologic cause of gonorrhea. Gonorrhea is the second most prevalent sexually transmitted disease with an annual incidence of 86.9 million adults. Microscopic inspection of Gram-stained tissues, bacterial culture, and a nucleic acid amplification test are required for the diagnosis of *N. gonorrhoeae*.

For many years, infections caused by *N. gonorrhoeae* were thought to be fairly simple to cure; nevertheless, resistance to all therapeutic medications used to treat the disease, such as penicillin, ciprofloxacin, or azithromycin, has evolved progressively. The necessity of better diagnosis is highlighted by the rising incidence of *N. gonorrhoeae* infection and developing resistance to medicines such ceftriaxone. Therefore, in this study we discuss possible causes that may result in a negative Thayer-Martin culture but positive PCR.

Materials and methods: The aim of the study is to analyze the cases of positive PCR and negative culture for *N. gonorrhoeae* detected during the years 2018-2022 in the Clínico-Malvarrosa Health Department (Valencia). To identify possible causes, a retrospective analysis was performed using binary logistic regression using IBM SPSS software.

Results and conclusion: The results suggest that there are risk variables that can lead to *N. gonorrhoeae* cases with a positive PCR but a negative culture. The absence of symptoms in the patient at the time of sampling, a CT>27 (CT: cycle of quantification) on PCR, and antibiotic administration prior to sampling are the most important aspects that have been described. As a result, these parameters should be considered in order to avoid unfavorable culture and to improve *N. gonorrhoeae* diagnosis and therapy.

INTRODUCTION

1. *Neisseria gonorrhoeae*

Neisseria gonorrhoeae is an aerobic, facultative intracellular, gram-negative coccobacillus that clusters in pairs (diplococci) [1]. *N. gonorrhoeae* lack flagella and spores and are producers of oxidase and catalase, factors that facilitate their identification [2]. It is considered an obligate human pathogen that can grow and multiply in mucous membranes including the cervix, uterus and fallopian tubes in women, as well as in the male urethra. Although it can also be found in the mouth, pharynx and anus [3].

N. gonorrhoeae infection is the etiologic cause of gonorrhea. Gonorrhea is the second most prevalent sexually transmitted disease after *Chlamydia trachomatis* infection [4]. It is transmitted by sexual and vertical (birth canal) transmission. It can produce a urogenital infection that in the male causes purulent urethritis, in the female the infection is asymptomatic in about 50% of cases. In addition, it is capable of producing bacteremia (especially in pregnancy and in situations of C5-C9 complement deficiency). It can also cause endocarditis, pericarditis, meningitis and neonatal purulent conjunctivitis [1].

If the *N. gonorrhoeae* infection goes unnoticed and untreated or if it is inadequately treated, the infection can move up into the upper genital tract and lead to a complicated gonococcal infection (e.g., pelvic inflammatory disease [PID] and related sequelae such as ectopic pregnancy and infertility) in women and penile edema and epididymitis in men. Conjunctivitis can occur in adults, but ocular infection most often presents as ophthalmia neonatorum in the newborn [2].

N. gonorrhoeae is estimated to have an annual incidence of 86.9 million adults [5]. The World Health Organization (WHO) estimated the pooled 2016 global prevalence of urogenital gonorrhea (the proportion of the world's population with gonorrhea in a given year) to be 0.9% in women and 0.7% in men. Incidence rate, a measure of new infections or diagnoses in a specific time period, was 20 per 1000 women and 26 per 1000 men globally in 2016, translating into 86.9 million new cases [6]. In Spain there has also been an increase in the number of cases of *N. gonorrhoeae*, as shown in the graph (Figure 1), where there are now 25 cases per 1000 habitants [7].

By age and sex, the rates in men were higher than those in women in all age groups. The highest rates in both sexes were observed between 20 and 24 years of age (177.45 cases per 100,000 in men and 65.75 cases per 100,000 in women), followed by the 25-34 year age group (159.94 cases per 100,000 in men) and from 15 to 19 years of age in women (37.96 cases per 100,000) [7].

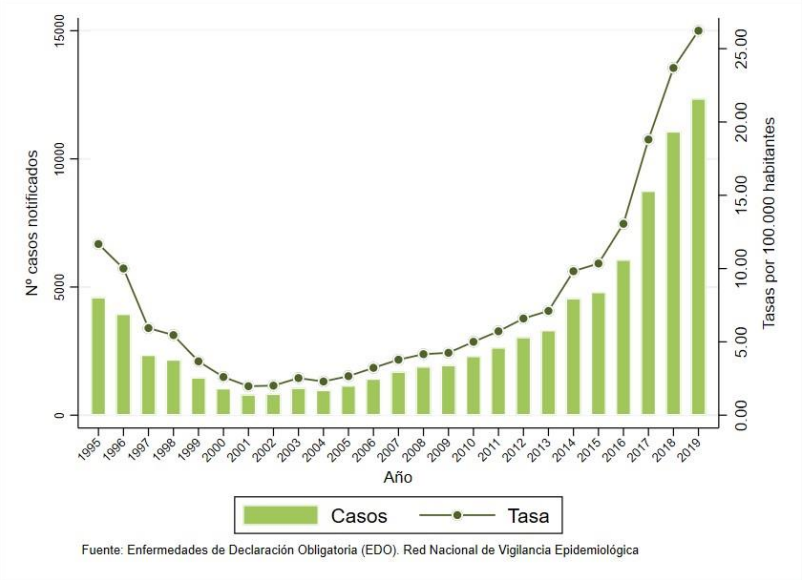

Figure 1. Incidence of gonococcal infection. Number of cases and rates per 100,000 population, Spain, 1995-2019 [7].

2. *Neisseria gonorrohoeae* diagnosis

For the diagnosis of *N. gonorrhoeae*, sample collection, transport and processing are very important, especially for culture, since *N. gonorrhoeae* is very sensitive to environmental conditions. Previously it was thought that the survival of gonococcus was superior at room temperature, but recent studies have shown that the preservation and survival of gonococcus is much higher if the swabs are kept refrigerated (4°C) [8].

The ideal anatomical site for specimen collection depends on sex, age and sexual behavior of the individual; the clinical manifestations of infection and the diagnostic test method. In women, the main location for collecting specimens for culture and microscopy is the endocervical canal; for nucleic acid amplification testing, it is the endocervical canal or the vagina. Other secondary locations are the urethra, rectum and oropharynx [2].

In heterosexual men, samples for culture and microscopy should be collected from the urethra, and for PCR (polymerase chain reaction), a urine sample should be collected. In men who have sex with men, and in women and men with clinical signs indicative or who engage in oral or anal sex should also be taken from the rectum and oropharynx [2].

To take the samples, a swab is generally introduced into the cavity to a depth of about 2-3 centimeters where it will be rotated. In case of an oropharyngeal sample, the posterior part of the pharynx should be swabbed above the tonsillar crypts [2].

For confirmation of the diagnosis of *N. gonorrhoeae*, microscopic examination of Gram-stained specimens, bacterial culture and nucleic acid amplification test are necessary [5].

a) Microscopic examination of the Gram stain of the smear specimen
Microscopic examination by Gram stain or methylene blue should be performed [8]. The sample should be spread on the slide. The sample should then be heat-fixed and a Gram stain of the sample smear should be performed [2]. If a quantity ≥ 2 PMNs (polymorphonuclear cells) per field and gram-negative diplococci are observed at x1000 magnification (Figure 2), it allows a rapid diagnosis of gonococcal urethritis to be made with good sensitivity (>95%) and specificity [8].

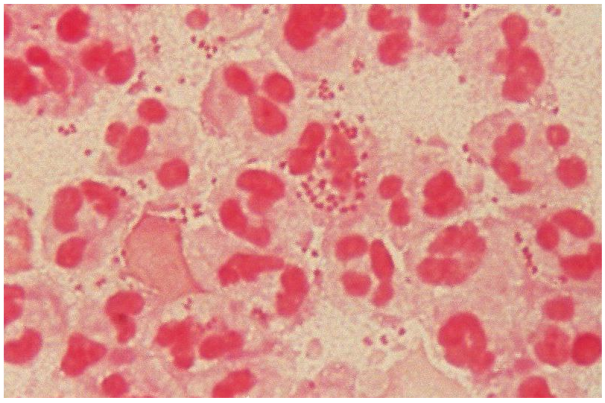

Figure 2. Presence of PMN and diplococci in Gram staining [2].

In contrast, the sensitivity of Gram staining in asymptomatic males, endocervical exudates and rectal and pharyngeal exudates is low, so it is not a useful tool to rule out these infections [8].

b) Culture
The diagnosis of *N. gonorrhoeae* is made by isolation and identification of the microorganism in culture [8]. Although not all patients in whom *N. gonorrhoeae* is detected by real time PCR are isolated in culture, this is the only diagnostic test that allows antimicrobial sensitivity studies to be performed. Therefore, it is essential for detecting and monitoring antimicrobial resistance [9].

N. gonorrhoeae should be cultured at 35-37°C under 5% CO2 atmosphere for 24-72 hours. It is considered a demanding bacterium as it requires cysteine, glucose, pyruvate or lactate as a carbon source. The medium used to isolate colonies of this bacterium is Thayer-Martin, which is the selective medium of choice for isolation when working with clinical samples with accompanying microbiota [3].

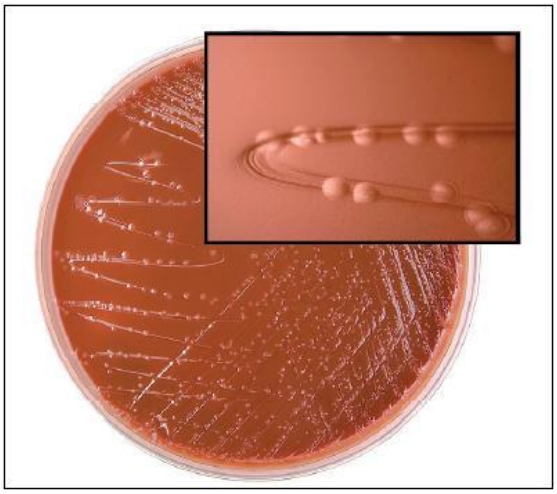

Figure 3. Morphology of *N. gonorrhoeae* colonies in Tayer-Martin culture medium [3].

Thayer-Martin Selective Agar was developed for the primary isolation of *N. gonorrhoeae* and *N. meningitidis* from samples with mixed flora extracted from the throat, vagina, rectum and urethra. Composed of Chocolate agar with vancomycin, colistin and nystatin, it is formulated to minimize the growth of contaminants so that they do not outgrow gonococci, to suppress the growth of saprophytic Neisseria species and to promote the growth of pathogenic Neisseria [10].

From the colonies isolated on Thayer-Martin culture medium, identification of the microorganism is performed by MALDI-TOF [1]. MALDI-TOF is a mass spectrometer that allows the identification of a microorganism by comparing its protein profile with a database. It allows identification to genus and species level with good sensitivity and specificity [11].

MALDI-TOF has replaced the identification of *N. gonorrhoeae* by biochemical gallery or enzymatic tests that had more limitations, identification errors and were more expensive. The most important advantages of MALDI-TOF are: 1) requirement of only a small amount of biological material, 2) a fast and easy measurement protocol, and 3) high specificity in species differentiation [12].

c) Real-time PCR

Currently, in addition to culture of specimens for the diagnosis of *N. gonorrhoeae*, real time PCR (real-time polymerase chain reaction) is performed [1]. They are currently recommended for the detection of urogenital infections in women and men with and without symptoms. They have a great advantage in that they detect non-viable organisms and this allows for increased sensitivity. The high sensitivity has allowed the use of less invasive samples for the patient, such as first urine in men and vaginal smears in women [8].

The real-time PCR performed in this study is the REALQUALITY RQ-SevenSTI PCR that allows the detection of *Chlamydia trachomatis, Neisseria gonorrhoeae* and *Mycoplasma genitalium* in the first amplification and the detection of

Thrichomonas vaginalis, Mycoplasma hominis, Ureaplasma urealyticum and *Ureaplasma parvum* in the second amplification.

For *N. gonorrhoeae* detection the targets are the porA pseudogene and the multi-copy opa gene. The porA pseudogene encodes a porin and the opa gene encodes for opacity proteins, so called because of their contribution to the opacity of colonies during bacterial growth on agar plates. The opa genes are multicopy genes harboring conserved regions and encode proteins with biological functions, integral outer membrane proteins. Therefore, they are suitable as target sequence for real-time PCR [4].

Real-time quantitative PCR (qPCR) is a technique used to monitor the PCR reaction in real time [13]. qPCR uses a Taq polymerase, which is a thermostable DNA polymerase, and two flanking primers for the amplification of a target nucleic acid sequence. qPCR reactions are performed under thermal cycling conditions allowing dissociation and extension cycles of a target duplex [14].

Real-time quantitative PCR combines PCR and fluorescent reporter chemistry to monitor template amplification with higher sensitivity and specificity [13]. This kit uses JOE fluorophore for quantitative analysis of *N. gonorrhoeae* in samples. The multiplex qPCR assay also includes an internal control (IC) for assessing potential sample-related inhibition, in this kit the internal control is beta-hemoglobin.

The combined analysis of *N. gonorrhoeae* and *Chlamydia Trachomanis* by real-time PCR is carried out because co-infection is very common (and can be as high as 50%), therefore it is often more efficient and cost effective to simultaneously process and detect *C. Trachomanis* and *N. gonorrhoeae* from suspected patient specimens [14].

The primers used in this specific kit are not in the public domain as they are under trade secret. Due to this situation, the primers referred to are from literature-based kits with *N. gonorrhoeae* determinations by qPCR. Therefore, the primers used in qPCR are:

- PorA pseudogene (Bio-Rad qPCR probe reagent kit):

  F-primer- 5'- CAGCATTCAATTTGTTCCGAGTC- 3'

  R-primer- 5'- GAACTGGTTTCATCTGATTACTTTCCA- 3' [14]

- Opa gene (COBAS Amplicor NG test):

  F-primer- 5'-TTGAAACACCGCCCGGAA-3'

  R- primer- 5'- TTTCGGCTCCTTATTCGGTTTAA- 3' [15]

3. *Neisseria gonorrhoeae* treatment

For many years, infections caused by *N. gonorrhoeae* were considered to be relatively easy to treat; however, resistance has emerged successively to all therapeutic agents used in treatment of the disease, e.g., penicillin, ciprofloxacin

or azithromycin [16]. As no gonococcal vaccine is available, prevention relies on promoting safe sexual behaviours and reducing STI-associated stigma (sexually transmitted infections- associated stigma), which hinders timely diagnosis and treatment thereby increasing transmission [5].

Currently, the treatment of choice for *N. gonorrhoeae* is ceftriaxone (third generation cephalosporin) [1]. Although, there is a worldwide problem which is the emergence of *N. gonorrhoeae* strains resistant to extended-spectrum cephalosporins (ESC), such as injectable ceftriaxone and oral cefixime [16].

Especially dangerous are multi-resistant strains which are resistant simultaneously to ESC and azithromycin. These strains, were isolated for the first time in 2018. Moreover, in 2018, the first ESBL (extended spectrum β-lactamases) was described in *N. gonorrhoeae* and that makes the threat of appearing the ESBL mechanism of resistance in *N. gonorrhoeae* more real, even though the strain was sensitive to ceftriaxone [16].

Finally, it should be emphasized that infection with *N. gonorrhoeae* is known to increase the risk of human immunodeficiency virus (HIV) infection. Odds ratio (OR) estimates for increased risk of HIV infection due to previous infection with an STD (sexually transmitted diseases) vary from 3.5 to 9.0 for *N. gonorrhoeae*. Additionally, infection with *N. gonorrhoeae* may also be associated with an increased risk of HIV seroconversion [4].

This scenario has generated worldwide concern, due to the increase in cases of gonorrhea associated with the increase of multi-resistant strains. Therefore, it is very important to evaluate the sensitivity of the isolated strains, carry out an accurate diagnosis to avoid bacterial dissemination, especially in asymptomatic cases, prescribe a good treatment and implement health campaigns in the population [3].

In summary, the increasing incidence of *N. gonorrhoeae* infection and increasing resistance to antibiotics such as ceftriaxone reflects the importance of improving diagnosis [6]. Therefore, in this study we discuss possible causes that may result in a negative Thayer-Martin culture but positive PCR. As discussed above, diagnosis by culture could not be eliminated since it is the only diagnostic method that allows the assessment of antibiotic sensitivity.

HYPOTHESIS AND OBJECTIVES

The aim of the study is to analyze the cases of positive PCR and negative culture for *N. gonorrhoeae* detected during the years 2018-2022 in the Clínico-Malvarrosa Health Department (Valencia).

The objective is to identify possible triggering factors of this diagnostic situation by using descriptive and retrospective analysis through binary logistic regression performed with IBM SPSS software. The specific objectives are:

1. To evaluate whether the presence of antibiotic treatment prior to sampling may result in a negative culture.

2. To analyze whether an asymptomatic patient is more likely to have a negative culture.
3. To examine whether the presence of coinfections is a risk factor for obtaining a negative culture.
4. To assess whether an elevated CT (cycle of quantification) on real-time PCR can result in a negative culture.

MATERIALS AND METHODS

1. Cohort

The data for this statistical analysis were obtained from patients in the Clínico-Malvarrosa Health Department (Valencia) during the period 2018-2022. Data about the presence of *N. gonorrhoeae* was obtained from the departmental application Gestlab, where both culture and PCR results are recorded. According to the Swedish health criteria of National Board of Health and Welfare in 2008 is considered positive for *N. gonorrhoeae* when: 1) a positive culture is present in a specimen, 2) positive qPCR is present in a specimen or 3) findings of Gram-negative intracellular diplococci from urethra smear from men [18].

During this period there are samples that will be used as control (positive culture and positive PCR, n=89) (Annex 1) and samples where the factors will be evaluated, problem samples (negative culture and positive PCR, n= 86)(Annex 2).

The information on previous antibiotic treatment was obtained from the Orion-Clinic application in case the sample came from the hospital and from the Abucasis application in case the sample came from a health center or outpatient clinic. In the same way, information on the presence of symptoms in patients is also obtained from Orion-Clinic in the case of hospital samples and from Abucasis in the case of out-of-hospital samples.

In the case of co-infection information with *Chlamydia trachomatis* or *Mycoplasma genitalium* or the presence of HIV in the same patient can be obtained within the Gestlab program, as previous serologies and PCRs are found. Finally, general patient information such as age and gender can also be found in Gestlab.

2. Analyses

Descriptive, cross-sectional and retrospective analysis of *N. gonorrhoeae* infections diagnosed by molecular biology technique (AriaDx Real-Time PCR system, Agilent Technologies) and with negative cultures. The detected cases

are compared by binary logistic regression performed with IBM SPSS software, with a similar group of PCR and culture-positive infections (randomly selected in the same period).

We have not excluded samples where we do not have all the information such as the serology that determines if the patient has HIV, the information provided by the physician about the symptoms or the previous antibiotic treatment (annex 1).

Main outcome variable is defined as a positive PCR but negative follow-up culture (+-) and will hereafter be referred to as discordant cases. Odds-ratios (OR) with ninety-five percent confidence intervals were assessed in the model building process.

Binary logistic regression was carried out with each of the variables to be analyzed: sex, age, presence of coinfections determined by molecular biology (PCR), the presence of symptoms, the PCR CT value, the presence of antibiotic treatment prior to sample collection and whether the patient was HIV positive or negative.

Binary logistic regression is used because it is useful in cases where it is desired to predict the presence or absence of a characteristic or outcome based on the values of a set of predictors. Binary logistic regression is the statistical technique that aims to test hypotheses or causal relationships when the dependent variable (outcome) is a binary variable (dichotomous, dummy).

N. gonorrhoeae culture is analyzed as a dependent variable and all possible risk factors as independent variables. In the independent variables, the situation that according to the hypothesis is more likely to result in a negative culture is taken as a reference. For example, in the case of PCR CT, a CT>27 is taken as a reference because it is considered to be a higher risk (marked in Table 1 as ref).

RESULTS

In total, 175 samples were included in this study, 86 of which were culture negative and 89 were culture positive (Table 1). Among the samples 139 are men and 36 are women. 44, 6% of the men with positive PCR were culture negative, therefore, they were discordant cases. In the case of women the value increases to 66,7% of discordant cases. In the study population most of the cases are in people younger than 30 (median age of the patients), also 51,9 % of the discordant cases are found in this age range.

No differences in discordant cases were seen between individuals with and without *Chlamydia trachomatis* or *Mycoplasma genitalium* co-infection. Regarding the presence of symptoms, 90,9% of the patients who had no symptoms when the sample was taken are discordant cases, but this decreases to 49,9% of culture-negative samples when the patient presents symptoms related to *N. gonorrhoeae.*

Table 1. Descriptive information of gonorrhea PCR positive cases included in the study.

Variables		Negative culture	%	Positive culture	%	Total
PCR positiva						
Total		86		89		
Gender	Man (ref)	62	44,6	77	55,4	139
	Women	24	66,7	12	33,3	36
Age	<30 (ref)	56	51,9	52	48,1	108
	>30	30	44,8	37	55,2	67
Co-infections	Yes (ref)	38	48,1	41	51,9	79
	No	48	50,0	48	50,0	96
Symtoms	Yes	57	39,9	86	60,1	143
	No (ref)	20	90,9	2	9,1	22
CT	<27	20	23,0	67	77,0	87
	>27 (ref)	66	75,0	22	25,0	88
Prior treatment	Yes (ref)	35	76,1	11	23,9	46
	No	48	38,1	78	61,9	126
VIH positive	Yes (ref)	7	53,8	6	46,2	13
	No	57	49,1	59	50,9	116

Analyzing the CT presented by the sample in the PCR, it can be observed that in the cases with a CT >27 (mean of the CT values of the samples) 75% are discordant cases, whereas when presenting a CT <27, the percentage of discordant cases decreases to 23%. The presence of antibiotic treatment prior to sampling increases the number of samples with a negative culture, from 38,1% in the case of no treatment to 76,1% in the case of treatment. Finally, there is no significant difference between the patient's HIV infection or not in the occurrence of more discordant cases.

The results of the statistical analysis are interpreted as follows: the greater than 1 is the OR, the greater is the relationship between the dependent variable and the independent variable. Therefore, the higher the OR, the stronger the relationship between the two variables and the more likely that a negative culture of *N. gonorrhoeae* will occur in the presence of the independent variable (e.g., presence of symptoms).

In contrast, an OR of less than 1 represents a significant difference but with an inverse relationship, in which case the independent variable is considered protective, thus avoiding a negative culture of *N. gonorrhoeae*.

The CI (Confidence Interval) analysis is important to evaluate the real significant difference of the independent variable. In the case of including the value 1 between the minimum and maximum value of the interval, it is considered a non-significant difference, and therefore, there is no relationship between the dependent variable and the independent variable.

To sum up, an OR value greater than 1 with a CI that does not include 1 is considered a significant difference, and therefore a risk factor for a negative culture. In contrast, an OR less than 1 with an CI that does not include the value 1 in the interval is considered a protective factor.

After statistical analysis using IBM SPSS we obtained that in the population analyzed being male is a protective factor against a negative culture (OR: 0.403; 95% CI 0.18-0.869), therefore, women are more likely to be culture negative (Table 2). Regarding the age group, no significant difference was found between the two groups (younger and older than 30 years) (OR: 1.328; 95% CI 0.72-2.449). Neither was a significant difference found between the presence or not of coinfections, therefore, the presence of a coinfection by *Chlamydia trachomatis* or *Mycoplasma genitalium* is not a risk factor for a negative culture (OR: 0,843; 95% CI 0,464-1,532).

Table 2. Binary logistic regression modeling risks for gonorrhea PCR positive, culture negative cases, presented as Odds ratio with 95% confidence intervals.

	Odds ratio	Confidence range	
Variables		Lower	Superior
Gender	0,403	0,187	0,869
Age group	1,328	0,72	2,449
Co-infections	0,843	0,464	1,532
Symptons	15,088	3,395	67,053
CT	10,05	5,019	20,126
Prior treatment	5,104	2,369	10,995
VIH positive	1,208	0,383	3,812

Concerning the presence of symptoms in the patient prior to sampling, the absence of symptoms is a risk factor for obtaining a negative culture (OR: 15.088; 95% CI 3.395-67.053). When a sample has a CT greater than 27 on PCR it is more likely to have a negative culture, therefore, a CT> 27 is a risk factor for a negative culture (OR: 10.05; 95% CI 5.019-20.126).

Prior antibiotic treatment leads to more discordant cases, and therefore, prior antibiotic administration results in an increase in negative cultures in PCR-positive samples (OR: 5.104; 95% CI 2.369-10.9995). In contrast, no significant

difference was found when the patient had HIV or not, with respect to an increase in negative cultures (OR: 1.208; 95% CI 0.383-3.812).

DISCUSSION

The purpose of this study is to evaluate possible risk factors that may result in a negative culture even though there is a positive PCR. The study of these risk factors is important because although *N. gonorrhoeae* can be diagnosed by PCR alone, antibiotic resistance testing can only be performed using the colonies obtained in the primary culture. Therefore, it is imperative to evaluate these factors to avoid erroneous treatment of gonorrhea due to increasing resistance [17].

As mentioned above, women are more likely to have a negative culture, and therefore to be discordant cases. Some of these gender discrepancies could be explained by biological causes. The genus Neisseria includes *N. gonorrhoeae*. Other Neisseria species (for example, *N. lactamica* or *N. subflava*) can exist in vaginal normal flora and are not pathogenic, but they can cross-react with *N. gonorrhoeae*, decreasing PCR specificity for women depending on the circulating genus-types in the population tested [18].

In addition, it has been observed that the absence of symptoms in the patient at the time of sampling results in an increase in discordant cases (Figure 4). It can be seen that many of the discordant samples come from women who do not present symptoms. This situation may be due to the fact that about 50% of gonococcal cervicitis is symptomless, while 90-95% of men who contract gonorrhea present symptoms such as urethritis, dysuria or purulent excretion [17].

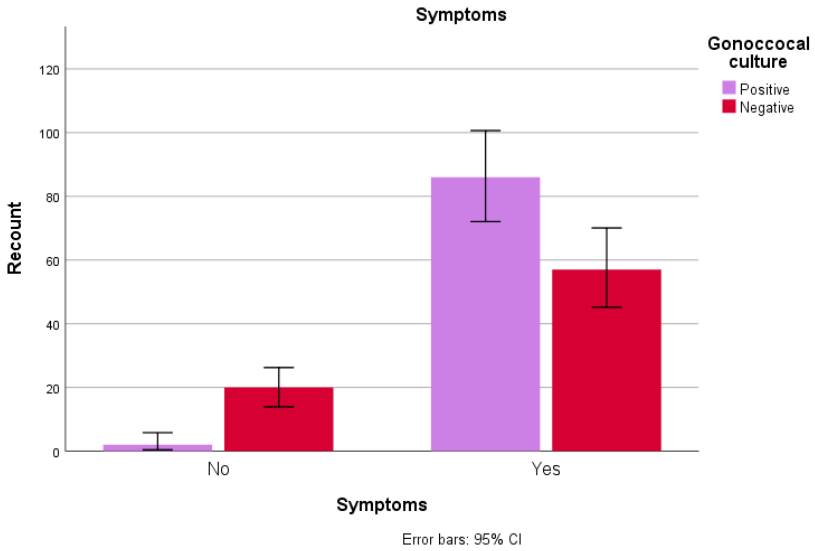

Figure 4. Representation of gonococcal culture in the presence of symptoms in the patient

In regard to the presence of coinfection as a possible risk factor for presenting a negative culture, this study shows that there is no significant difference. This conclusion is in agreement with previous studies where no direct relationship was found between a negative culture and co-infection of the patient with *C. Trachomatis* [17]. Neither has a significant difference been found in HIV infection in the patient, therefore, HIV infection cannot be considered as a risk factor that could result in negative culture with a positive PCR.

An elevated CT (>27) on PCR does directly correlate with a higher percentage of discordant cases (Figure 5). Therefore, an elevated CT is a risk factor for a negative culture. The PCR CT is indirectly proportional to the DNA load in the sample.

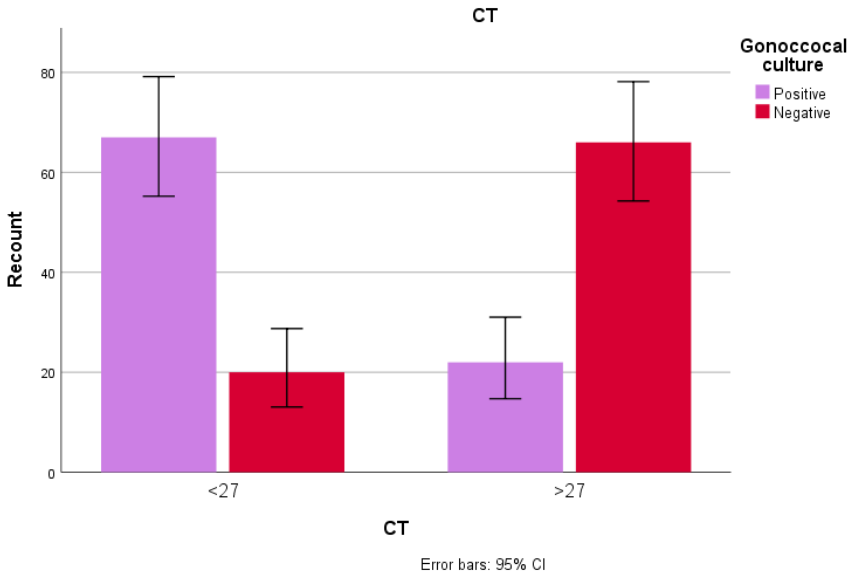

Figure 5. Representation of gonococcal culture and CT on PCR

It's worth noting that gonorrhea screening with PCR has a significant false-positive rate, especially in a low-prevalence community [19]. Because of the relationship between specificity, disease prevalence, and positive predictive value, it's critical to evaluate the latter before testing on a large scale [17]. Low-level positive results should be regarded with caution, according to one study, because none of the low-level results were confirmed by culture or confirmatory PCR in that study [19].

Finally, antibiotic treatment prior to sampling significantly increases the percentage of discordant cases (Figure 6), therefore, it can be considered a risk factor for a negative culture with positive PCR. Prior antibiotic administration has been associated with negative cultures in urine samples for STI testing [20].

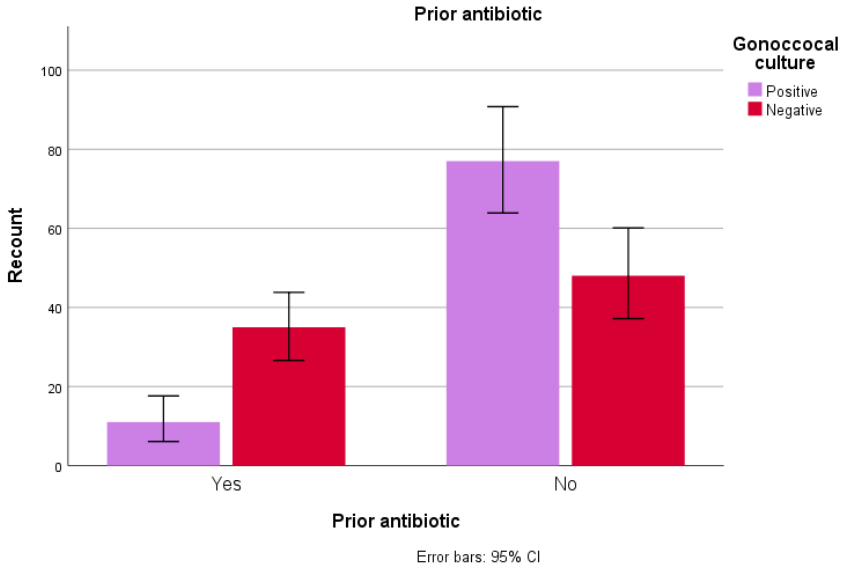

Figure 6. Representation of gonococcal culture and prior antibiotic

CONCLUSIONS

This study concludes that there are risk factors that can lead to discordant cases of *N. gonorrhoeae*, where a positive PCR but a negative culture is present. The most important factors that have been described are absence of symptoms in the patient at the time of sampling, a CT>27 (CT: cycle of quantification) on PCR and the administration of antibiotics prior to sampling. Therefore, these factors should be taken into account to avoid negative culture and to improve the diagnosis and treatment of *N. gonorrhoeae*.

In addition, it has been determined that there is no relationship between the variables of age, presence of co-infections, HIV infection and the occurrence of a negative *N. gonorrhoeae* culture, therefore, they are not considered as a risk factor. Finally, it has been found that women are more likely to result in a negative culture with positive PCR than men.

The study has certain limitations since the sample is limited and studies with a larger cohort would be necessary to obtain more convincing conclusions. In addition, the antibiotics that most interfere with the growth of *N. gonorrhoeae* should be studied in greater depth to avoid their administration before taking the sample.

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ANNEXES

Annex 1: PCR positive and culture positive data

Muestra	Edad	Sexo	Tipo muestra	Diagnóstico	Cultivo de Neisseria gonorrhoeae	Neisseria gonorrhoeae - DNA*	CT	VIH	Antibiotico previo	Coinfecciones	Síntomas
1	21	H	Exudado uretral	Uretritis	POSITIVO.	POSITIVO (ciclo positividad PCR=20)	20	Negativo	No	Si	Si
2	21	H	Exudado uretral	CISTITIS	POSITIVO.	POSITIVO (ciclo positividad PCR=22.4)	22	Negativo	No	Si	Si
3	39	H	Exudado uretral	URETRITIS	POSITIVO.	POSITIVO (ciclo positividad PCR=25.4)	25	Negativo	No	No	sI
4	21	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO (ciclo positividad PCR=22.2)	22	Negativo	No	Si	Si
5	26	H	Exudado uretral	uretritos	POSITIVO.	POSITIVO (ciclo positividad PCR=20.8)	21	Negativo	No	Si	Si
6	26	M	EXUDADO CERVIX	RIESGO ITS	POSITIVO.	POSITIVO (ciclo positividad PCR=30.0)	30	Negativo	No	Si	Si
7	32	H	Exudado uretral		POSITIVO.	POSITIVO (ciclo positividad PCR=20)	20	Negativo	No	Si	sI
8	42	M	Exudado cervicovaginal	cultivos	POSITIVO.	POSITIVO (ciclo positividad PCR=21)	21	Negativo	No	No	Si
9	25	H	Exudado uretral	OTRA URETRITIS NCOC	POSITIVO.	POSITIVO (ciclo positividad PCR=22)	22	Negativo	No	No	Si
10	19	H	Exudado uretral	URETRITIS	POSITIVO.	POSITIVO (ciclo positividad PCR=.22)	22	Negativo	No	Si	Si
11	26	H	Exudado uretral	BALANITIS	POSITIVO.	POSITIVO (ciclo positividad PCR=.21)	21	Negativo	Si, doxi	No	Si

Muestra	Edad	Sexo	Tipo muestra	Diagnóstico	Cultivo de Neisseria gonorrhoeae	Neisseria gonorrhoeae - DNA*	CT	VIH	Antibiotico previo	Coinfecciones	Síntomas
12	21	H	Exudado uretral	EPIDIDIMITIS	POSITIVO.	POSITIVO (ciclo positividad PCR=.....24)	24	No consta	No consta	Si	No consta
13	35	M	Exudado cervicovaginal	EPI	POSITIVO.	POSITIVO (ciclo positividad PCR=30)	30	No consta	No	Si	Si
14	25	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO (ciclo positividad PCR=23)	23	Negativo	No	No	Si
15	20	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO (ciclo positividad PCR=22.)	22	Negativo	Si, ceftriaxo	Si	Si
16	31	H	Exudado uretral	uretritis	POSITIVO.	24	24	No consta	No	No	Si
17	24	H	Exudado uretral	uretritis	POSITIVO.	21) = ALTA carga.	21	No consta	No	Si	Si
18	26	M	Exudado cervicovaginal	epi subclinica	POSITIVO.	24	24	Negativo	No	Si	Si
19	31	H	Exudado uretral	OTRA URETRITIS NCOC	POSITIVO.	26	26	Negativo	No	Si	Si
20	23	H	Exudado uretral	SOSPECHA URETRITIS	POSITIVO.	.23..	23	No consta	No	No	Si
21	25	H	Exudado uretral	URETRITIS GONOCOCICA	POSITIVO.	POSITIVO (CT22.	22	Negativo	No	No	Si
22	54	H	Exudado uretral	exudado uretral blanquecino	POSITIVO.	24.4 = alta carga.	24	Negativo	No	No	Si
23	30	H	Exudado uretral	OTRA URETRITIS	POSITIVO.	25) =ALTA . carga.	25	Negativo	Si, ceftriaxo	No	Si
24	24	H	Exudado uretral	secrecion uretral	POSITIVO.	POSITIVO (CT27,5.) =ALTA. carga.	28	No consta	No	Si	Si

Muestra	Edad	Sexo	Tipo muestra	Diagnóstico	Cultivo de Neisseria gonorrhoeae	Neisseria gonorrhoeae - DNA*	CT	VIH	Antibiotico previo	Coinfecciones	Síntomas
25	22	M	Exudado cervicovaginal	ULCERA	POSITIVO.	25) = ELEVADA carga.	25	Negatuvo	No	Si	No
26	17	H	Exudado uretral	urettritis	POSITIVO.	27	27	Negativo	No	Si	Si
27	25	H	Exudado uretral	uretritis	POSITIVO.	29	29	No consta	No	No	Si
28	25	H	Exudado uretral	URETRITIS	POSITIVO.	24) = ALTA. carga.	24	Negativo	No	Si	Si
29	18	H	Exudado cervicovaginal	vaginosis	POSITIVO.	27) = ALTA. carga.	27	Negativo	No	No	Si
30	36	H	Exudado uretral	uretritis	POSITIVO.	24.) = alta. carga.	24	Negativo	No	Si	Si
31	34	H	Exudado uretral	sospecha uretritis	POSITIVO.	21	21	Negativo	nO	Si	Si
32	58	H	Exudado uretral	exudado pene	POSITIVO.	POSITIVO (CT26.) = .ALTA CARGA	26	Negativo	nO	Si	Si
33	35	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO. Ct: 24	24	Negativo	No	No	Si
34	22	H	Exudado uretral	CISTITIS AGUDA	POSITIVO.	25	25	Negativo	Si, doxi	No	Si
35	26	H	Exudado uretral	uretritis	POSITIVO.	27.) =ALTA carga	27	Negativo	No	No	Si
36	24	H	Exudado uretral	uretritis	POSITIVO.	22) =ALTA carga.	22	Negativo	No	Si	Si
37	16	H	Exudado uretral	OTRA URETRITIS	POSITIVO.	25	25	Negativo	No	No	Si

Muestra	Edad	Sexo	Tipo muestra	Diagnóstico	Cultivo de Neisseria gonorrhoeae	Neisseria gonorrhoeae - DNA*	CT	VIH	Antibiotico previo	Coinfecciones	Síntomas
38	21	H	Exudado uretral	URETRITIS	POSITIVO.	30	30	Negativo	No	Si	Si
39	19	H	Exudado uretral	Sospecha de uretritis	POSITIVO.	22	22	Negativo	No	No	Si
40	21	H	Exudado uretral	relacion de riego, exudado uretral	POSITIVO.	25	25	No consta	No	No	Si
41	47	H	Exudado uretral	gota uretral, SIDA	POSITIVO.	POSITIVO (CT28..	28	Positivo	No	No	Si
42	36	M	Exudado cervicovaginal	FLUJO	POSITIVO.	28	28	Negativo	No	Si	No
43	42	H	Exudado uretral	uretritisi	POSITIVO.	22	22	No consta	No	Si	Si
44	27	H	Exudado uretral	uretritis	POSITIVO.	20	20	No consta	No	No	Si
45	20	H	Exudado uretral	Disuria y secreción uretral	POSITIVO.	20	20	Negativo	No	Si	Si
46	21	H	Exudado uretral	uretritis	POSITIVO.	26	26	No consta	No	No	Si
47	33	H	Exudado uretral	uretritis	POSITIVO.	22	22	Negativo	Si, fosfomicina	Si	Si
48	26	H	Exudado uretral	OTRA URETRITIS	POSITIVO.	25	25	Negativo	No	No	Si
49	29	H	Exudado uretral	uretritis	POSITIVO.	23	23	No consta	No	Si	Si
50	28	H	Exudado uretral	uretritis	POSITIVO.	24	24	Negativo	No	Si	Si

Muestra	Edad	Sexo	Tipo muestra	Diagnóstico	Cultivo de Neisseria gonorrhoeae	Neisseria gonorrhoeae - DNA*	CT	VIH	Antibiotico previo	Coinfecciones	Síntomas
51	17	H	Exudado uretral	uretritis	POSITIVO.	21	21	No consta	No	No	Si
52	28	H	Exudado uretral	URETRITIS	POSITIVO.	27	27	No consta	No	No	Si
53	19	H	Exudado uretral	OTRA URETRITIS	POSITIVO.	25	25	Positivo	Si, ceftriaxo	Si	Si
54	31	H	Exudado uretral	uretritis	POSITIVO.	19	19	No constra	No	Si	Si
55	37	H	Exudado uretral	uretritis	POSITIVO.	23	23	Negativo	No	No	Si
56	44	M	Exudado cervicovaginal	ENFERMEDAD INFLAMATORIA PELVICA	POSITIVO.	POSTIVO (CT31)= ALTA CARGA	31	Negativo	Si, ceftriaxo	Si	Si
57	27	H	Exudado uretral	uretritis	POSITIVO.	23	23	Negativo	No	No	Si
58	30	M	Exudado cervicovaginal	sospecha EPI	POSITIVO.	25	25	Negativo	Si, fosfomicina	Si	Si
59	41	H	Exudado uretral	exudado purulento pene	POSITIVO.	21	21	Negativo	No	Si	Si
60	40	H	Exudado uretral	Uretritis	POSITIVO.	25	25	Negativo	No	No	Si
61	26	H	Exudado uretral	uretritis tras RS de riesgo	POSITIVO.	25	25	No consta	No	Si	Si
62	30	H	Exudado uretral	ETS	POSITIVO.	23	23	Negativo	No	Si	Si
63	21	H	Exudado uretral	OTRA URETRITIS NCOC	POSITIVO.	30	30	Negativo	No	No	Si

Muestra	Edad	Sexo	Tipo muestra	Diagnóstico	Cultivo de Neisseria gonorrhoeae	Neisseria gonorrhoeae - DNA*	CT	VIH	Antibiotico previo	Coinfecciones	Síntomas
64	21	H	Exudado uretral	ets	POSITIVO.	23	23	Negativo	No	No	Si
65	58	H	Exudado uretral	SECRECION PURULENTA	POSITIVO.	28	28	Negativo	No	No	Si
66	32	H	Exudado uretral	uretritis	POSITIVO.	24	24	No consta	No	No	Si
67	22	H	Exudado uretral	URETRITIS AGUDA	POSITIVO.	34) = MODERADA carga.	34	Negativo	No	No	Si
68	33	H	Exudado uretral	uretritis	POSITIVO.	23	23	Negativo	No	No	Si
69	27	H	Exudado uretral	uretritis	POSITIVO.	21	21	Negativo	No	No	Si
70	22	M	Exudado cervicovaginal	epi	POSITIVO.	29	29	No consta	No	Si	Si
71	40	H	Exudado uretral	URETRITIS AGUDA	POSITIVO.	27	27	Positivo	Si, doxi	No	Si
72	32	H	Exudado uretral	uretritis	POSITIVO.	25	25	No consta	No	No	Si
73	20	H	Exudado uretral	URETRITIS	POSITIVO.	POSITIVO (CT26) =ALTA. carga.	26	Negativo	Si, Azitro	Si	Si
74	25	H	Exudado uretral	Uretritis	POSITIVO.	28) = MODERADA carga.	28	No consta	No	No	Si
75	24	H	Exudado uretral	OTRA URETRITIS	POSITIVO.	23) = ALTA carga.	23	No consta	Si, ceft y azitro	No	Si
76	42	H	Exudado uretral	INFECCION URINARIA EN EL HOMBRE	POSITIVO.	27) =MODERADA carga.	27	Negativo	no	No	Si

Muestra	Edad	Sexo	Tipo muestra	Diagnóstico	Cultivo de Neisseria gonorrhoeae	Neisseria gonorrhoeae - DNA*	CT	VIH	Antibiotico previo	Coinfecciones	Síntomas
77	25	H	Exudado uretral	uretritis	POSITIVO.	27	27	Negativo	No	No	Si
78	57	M	Exudado cervicovaginal	moles	POSITIVO.	POSITIVO (Ct =22).	22	Negativo	No	No	Si
79	35	H	Exudado uretral	CRIBADO ETS. VIH CONFIRMADO	POSITIVO.	POSITIVO (Ct = 25).	25	Positivo	No	Si	Si
80	20	M	Exudado cervicovaginal	fluijo alterado	POSITIVO.	POSITIVO (Ct =33).	33	No consta	No	Si	Si
81	29	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO (Ct =24).	24	Negativo	No	No	Si
82	36	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO (Ct =25).	25	Negativo	No	No	Si
83	19	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO (Ct =25).	25	Negativo	No	No	Si
84	31	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO (Ct =31).	31	Negativo	No	No	Si
85	30	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO (Ct =22).	22	Negativo	No	Si	Si
86	25	H	Exudado uretral	Uretritis	POSITIVO.	POSITIVO (Ct = 22).	22	Positivo	No	Si	Si
87	56	M	Exudado cervicovaginal	SOSPECHA ITS	POSITIVO.	POSITIVO (Ct =20).	20	No consta	No	No	Si
88	30	H	Exudado uretral	uretritis	POSITIVO.	POSITIVO (Ct = 23).	23	No consta	No	No	Si
89	36	H	Exudado uretral	urettritis	POSITIVO.	POSITIVO (Ct = 22).	22	Positivo	No	No	Si

Annex 2: PCR positive and culture negative data

Muestra	Edad	Sexo	Tipo muestra	Diagnóstico	Cultivo de Neisseria gonorrhoeae (gonococo)*	Neisseria gonorrhoeae - DNA*	CT	VIH	Antibiotico previo	Coinfecciones	Síntomas
1	17	H	**Exudado uretral**	Uretritis - Secreción uretral	Negativo.	POSITIVO (ciclo positividad PCR=41)	41	Negativo.	No	UP	Si
2	30	H	**Semen**	uetritis	Negativo.	POSITIVO (ciclo positividad PCR=37.5)	38	No consta	No	0	No consta
3	24	M	**Exudado cervicovaginal**	Contacto riesgo / Cribado ITS	Negativo.	POSITIVO (CT:29) =ALTA carga.	29	Negativo.	No	UP CT	Asintomática
4	32	H	**Exudado uretral**	URETRITIS	Negativo.	POSITIVO (CT:36) = BAJA carga.	36	Negativo.	Si	0	Asintomático
5	28	H	**Exudado uretral**	URETRITIS AGUDA	Negativo.	POSITIVO (CT:24) = ALTA carga.	24	Negativo.	Si, azitro y ceftriaxona	UU UP TV	No consta
6	18	M	**Exudado cervicovaginal**	EPI	Negativo.	POSITIVO (CT:43) = BAJA carga.	43	Negativo.	No	0	Dolor abdominal
7	46	M	**Exudado cervicovaginal**	vulvovaginitis	Negativo.	POSITIVO (CT:44) = BAJA carga.	44	Negativo.	No	0	Secreción vaginal
8	22	M	**Exudado cervicovaginal**	VAGINITIS	Negativo.	POSITIVO (CT:39) = BAJA carga.	39	Negativo.	No	UP. C.albicans	Asintomática
9	10	H	**Exudado uretral**		Negativo.	POSITIVO (CT:31) = ALTA carga.	31	No consta	No consta	0	No consta
10	20	H	**Exudado uretral**	Contacto sexual riesgo	Negativo.	POSITIVO (CT:36) = MODERADA carga.	36	Negativo.	Si, ciprofloxacino	0	Asintomática
11	22	H	**Exudado uretral**	uretritis	Negativo.	POSITIVO (CT:22) = ALTA carga.	22	No consta	No	CT UU	Secreción uretral y disuria

12	33	M	**Exudado cervicovaginal**	EPI	Negativo.	POSITIVO (CT:33) = MODERADA carga.	33	No consta	No	TV MH	Dolor abdominal
13	24	M	**Exudado cervicovaginal**	Piosalpinx izquierdo	Negativo.	POSITIVO (CT:25) = ALTA carga.	25	Negativo.	No	CT MH	Dolor abdominal
14	19	M	**Exudado cervicovaginal**	EPI	Negativo.	POSITIVO (CT:26) = ALTA carga.	26	Negativo.	Si, azitromicina	UU UP	Dolor abdominal y fiebre
15	24	M	**Exudado cervicovaginal**	CANDIDIASIS VULVAR Y VAGINAL	Negativo.	POSITIVO (CT:45) = BAJA carga.	45	Negativo.	No	MH UP	Secreción vaginal
16	23	H	**Exudado uretral**	URETRITIS AGUDA	Negativo.	POSITIVO (CT:31) =MODERADA carga.	31	Negativo.	Si, azitromicina	0	Secrecion uretral y disuria
17	17	M	**Exudado cervicovaginal**	Contacto sexual riesgo	Negativo.	POSITIVO (CT: 17) = ALTA carga.	17	Negativo.	Si, azitromicina	CT UP	Asintomática
18	22	M	**Exudado cervicovaginal**	CONTACTO CON GONORREA	Negativo.	POSITIVO (CT32) = MODERADA carga.	32	Negativo.	Si, azitro y ceftriaxona	UP	Disuria
19	47	H	**Exudado uretral**	URETRITIS	Negativo.	POSITIVO (CT:40) = BAJA carga.	40	Si	No	CT H. parainfluenza	Secreción uretral
20	24	H	**Exudado uretral**	uretritis	Negativo.	POSITIVO (Ct = 24 ALTA CARGA	24	Negativo	No	CT	Secreción uretral
21	18	H	**Exudado uretral**	CISTITIS Y URETRITIS GONOCÓCICA, NO ESPECIFICADA	Negativo.	POSITIVO (Ct = 33 MODERADA CARGA	33	Neggativo	Si, doxi y azitro	0	Secreción uretral
22	21	M	**Exudado cervicovaginal**	EPI	Negativo.	POSITIVO (Ct = 32 MODERADA	32	No consta	No	UP CT	Dolor abdominal
23	36	H	**Exudado faringeo**	Cribado ITS	Negativo.	POSITIVO (Ct = 39 BAJA CARGA	39	Si	No	-	No consta
24	32	H	**Exudado uretral**	URETRITIS GONOCOCICA	Negativo.	POSITIVO (Ct = 41 Baja carga	41	Negativo	Si, ceftriaxona y doxi	0	Secreción uretral
25	36	H	**Exudado faringeo**	Cribado ITS	Negativo.	POSITIVO (Ct = 40	40	Si	No	-	No consta
26	26	H	**Exudado uretral**	URETRITIS	Negativo.	POSITIVO (Ct = 38	38	Si	Si ceft y azitro	0	Secreción uretral

27	50	H	**Exudado uretral**	OTRAS URETRITIS	Negativo.	POSITIVO (Ct = 35	35	Negativo	Si ceft y azitro	0	Secreción uretral
28	21	H	**Exudado uretral**	OTRAS URETRITIS	Negativo.	POSITIVO (Ct = 21	21	No consta	Si ceft y azitro	0	Secreción uretral
29	31	M	**Exudado cervicovaginal**	CONDUCTAS GENERADORAS DE SALUD (ESPECIFICAR)	Negativo.	POSITIVO (Ct = 30	30	Negativo	No	C. albicans	Asintomática
30	23	H	**Exudado uretral**	OTRAS URETRITIS	Negativo.	POSITIVO (Ct = 27	27	Negativo	Si,azitro	0	Secrecion uretral y disuria
31	46	H	**Exudado uretral**	OTRAS URETRITIS	Negativo.	POSITIVO (Ct = 22 ALTA CARGA	22	Negativo	Si, azitro	0	Secreción purulenta
32	33	H	**Exudado uretral**	URETRITIS GONOCOCICA	Negativo.	POSITIVO (Ct = 40	40	Negativo	No	UU	secreción purulenta
33	24	M	**Exudado cervicovaginal**	CONTACTO PARA CRIBADO DE INFECCIONES DE TRANSMISIÓN PREDOMINANTEMENTE DE TIPO SEXUAL	Negativo.	POSITIVO (Ct = 32, MODERADA CARGA	32	Negativo	Si, doxi	CT UP UU	Asintomática
34	19	M	**Exudado cervicovaginal**	Cribado ITS	Negativo.	POSITIVO (Ct = 34, moderada carga	34	No consta	No	MH UP	Asintomática
35	26	H	**Exudado uretral**	SECRECION URETRAL	Negativo.	POSITIVO (Ct =30, alta carga	30	Negativo.	No	H. parainfluenza	Secreción uretral
36	27	M	**Exudado cervicovaginal**	VAGINITIS	Negativo.	POSITIVO (Ct =37, MODERADA CARGA	37	Negativo	No	MH UU UP	Asintomática
37	23	H	**Exudado uretral**	URETRITIS GONOCOCICA	Negativo.	POSITIVO (Ct =40, BAJA CARGA	40	Negativo	Si, ciprofloxacino	0	asintomático
38	25	M	**Exudado cervicovaginal**	portadora diu	Negativo.	POSITIVO (Ct =36, moderada carga	36	Negativo	No	MH UP	Asintomática
39	35	H	**Exudado uretral**	uretritis	Negativo.	POSITIVO (Ct = 40, BAJA CARGA	40	No consta	Si, azitromicina	CT	Secreción Uretral
40	22	H	**Exudado uretral**	Secreción uretral	Negativo.	POSITIVO (Ct = 25, ALTA CARGA	25	Negativo	Si, azitromicina	-	Secreción Uretral

41	26	H	**Exudado uretral**	Secreción uretral	Negativo.	POSITIVO (Ct = 32	32	Negativo	No	H. parainfluenza	Secreción Uretral
42	39	M	**Exudado cervicovaginal**	SANGRADO DESPUES DE COITO	Negativo.	POSITIVO (Ct =32,5 MODERADA CARGA	33	Negativo	No	MH UP	flujo vaginal
43	16	M	**Exudado cervicovaginal**	R	Negativo.	POSITIVO (Ct = 29,5	30	Negativo	No	MH UU	flujo vaginal
44	21	H	**Exudado uretral**	riesgo ITs	Negativo.	POSITIVO (Ct = 39,8 Baja carga	40	Negativo	No consta	CT UU	No consta
45	24	H	**Exudado uretral**	INFECCION DE VIAS URINARIAS SITIO NEOM	Negativo.	POSITIVO (Ct = 39.5 Baja carga	40	Negativo	No	C. albicans	Disuria
46	29	H	**Exudado rectal**	prep	Negativo.	POSITIVO (Ct = 39 Baja carga.	39	Negativo	No	CT MG	No consta
47	21	H	**Exudado uretral**	uretritis	Negativo.	POSITIVO (Ct = 29 Moderada carga.	29	Negativo	Si, ceftriaxona y azitromicina	0	Secreción uretral
48	22	H	**Exudado uretral**	OTRAS URETRITIS	Negativo.	POSITIVO (Ct = 23 Alta carga.	23	Negativo	Si, azitro	0	Disuria
49	28	H	**Exudado uretral**	Uretritis	Negativo.	POSITIVO (Ct = 31 Moderada carga	31	No consta	Si, azitromicina	0	Secreción uretral
50	24	H	**Exudado uretral**	secreción uretral amarillenta y disuria	Negativo.	POSITIVO (Ct = 26 Moderada carga.	26	No consta	No	0	Secreción uretral
51	36	M	**Exudado cervicovaginal**	INFECCION ORINA	Negativo.	POSITIVO (Ct =32.4 MODERADA	32	No consta	Si, fosfomicina	CT MG	Disuria
52	18	H	**Exudado rectal**	CONSEJOS SOBRE OTRAS ENFERMEDADES DE TRANSMISION SEXUAL	Negativo.	POSITIVO (Ct = 30	30	No consta	no	0	Asintomacito
53	18	H	**Exudado faringeo**	CONSEJOS SOBRE OTRAS ENFERMEDADES DE TRANSMISION SEXUAL	Negativo.	POSITIVO (Ct = 27	27	No consta	no	0	Asintomacito
54	28	H	**Exudado uretral**	relacion sexual de riesgo orquiepididimitis + uretritis	Negativo.	POSITIVO (Ct = 26 Alta carga	26	Negativo	No	MG	Secreción uretral

55	30	H	**Exudado uretral**	URETRITIS	Negativo.	POSITIVO (Ct =38	38	Negativo	Si, ceftriaxona	0	Disuria
56	39	H	**Exudado rectal**	vih descartar ITS	Negativo.	POSITIVO (Ct =33.41	33	Si	No consta	UP	No consta
57	37	H	**Exudado uretral**	prep	Negativo.	POSITIVO (Ct =38	38	Negativo	No	0	Asintomático
58	41	H	**Exudado uretral**	OTRAS URETRITIS	Negativo.	POSITIVO (Ct = 35	35	No consta	Si, doxi	0	Secreción uretral
59	23	H	**Exudado uretral**	uretritis	Negativo.	POSITIVO (Ct = 31	31	Negativo	Si. Amoxi-Clav, Ceftriaxona, Azitro	0	Secreción uretral.
60	14	M	**Exudado cervicovaginal**	APP	Negativo.	POSITIVO (Ct = 32	32	Negativo	Si. Cefuroxima	UP UU	Flujo amarillento (?)
61	31	H	**Exudado uretral**	uretritis	Negativo.	POSITIVO (Ct = 23.2	23	Negativo	No	UU	Secreción uretral, disuria
62	42	H	**Exudado rectal**	inici prep	Negativo.	POSITIVO (Ct = 33	33	Negativo	No	CT UU	Asintomático
63	22	M	**Exudado cervicovaginal**	contacto sexual riesgo	Negativo.	POSITIVO (Ct =37	37	No consta	No	MH, Gardnerella	Asintomática
64	23	H	**Exudado uretral**	Uretritis	Negativo.	POSITIVO (Ct = 26.48	26	Negativo	No	0	Secreción uretral
65	28	H	**Exudado uretral**	OTRAS URETRITIS	Negativo.	POSITIVO (Ct = 27	27	Negativo	Si, doxi	0	secreción uretral
66	16	M	**Exudado cervicovaginal**	CHEQUEO MEDICO SALUD	Negativo.	POSITIVO (Ct =31	31	Negativo	No	CT	Asintomatica
67	28	H	**Exudado uretral**	uretritis	Negativo.	POSITIVO (Ct = 33	33	No consta	No	0	Secreción uretral y disuria
68	38	H	**Exudado uretral**	vih, despistaje its	No crecimiento.	POSITIVO (Ct = 25	25	Si	Si, ceftriaxona y azitromicina	0	No consta
69	32	H	**Exudado uretral**	uretritis	No crecimiento.	POSITIVO (Ct = 24	24	Negativo	No	0	Secreción uretral y disuria

70	47	H	**Exudado uretral**	Uretritis	Negativo.	POSITIVO (Ct = 27	27	Negativo	No	0	Secreción uretral
71	22	M	**Exudado cervicovaginal**	Cribado ITS /Contacto rieso	Negativo.	POSITIVO (Ct = 37	37	Negativo	Si, no consta cual	Gardnerella	Asintomática
72	28	H	**Exudado uretral**	orquiepididimitis	Negativo.	POSITIVO (Ct = 38	38	Si	No	CT	Dolor uretral
73	19	M	**Exudado cervicovaginal**	EPI	Negativo.	POSITIVO (Ct = 28	28	No consta	Ceftriaxona y Azitro	C. glabrata, MH, UP	Dolor abdominal
74	26	H	**Exudado uretral**	OTRAS URETRITIS	Negativo.	POSITIVO (Ct = 23	23	Negativo	No	0	disuria
75	26	H	**Exudado uretral**	OTRAS URETRITIS	Negativo.	POSITIVO (Ct = 23).	23	Negativo	No	0	Uretritis
76	20	H	**Exudado uretral**	URETRITIS	Negativo.	POSITIVO (Ct = 30).	30	No consta	Si, cefixima y azitro	0	Secreción uretral
77	23	H	**Exudado uretral**	uretritis	Negativo.	POSITIVO (Ct = 26).	26	No consta	No	0	Secreción uretral
78	23	H	**Exudado uretral**	UG	Negativo.	POSITIVO (Ct = 29).	29	Negativo	No	CT	Exudado uretral
79	34	H	**Exudado cervicovaginal**	Flujo abundante	Negativo.	POSITIVO (Ct = 27).	27	No consta	No	0	Flujo alterado
80	30	H	**Exudado uretral**	ITS / INFECCION DE TRANSMISION SEXUAL	Negativo.	POSITIVO (Ct = 28).	28	Negativo	Si, azitro y cefixima	Haem	Secreción uretral
81	20	H	**Exudado rectal**	prep	Negativo.	POSITIVO (Ct = 35).	35	Negativo	No	0	Asintomático
82	48	H	**Exudado uretral**	sospecha uretritis	Negativo.	POSITIVO (Ct =28).	28	Negativo	Si, azitro	0	Secreción uretral
83	28	H	**Exudado rectal**	prep	Negativo.	POSITIVO (Ct = 38).	38	Negativo	No	UU	Asintomatico
84	30	H	**Exudado uretral**	Uretritis	Negativo.	POSITIVO (Ct = 38.6).	39	Negativo	Si, cipro, ceftriaxona, azitro	0	Secreción uretral, dolor inguinal

85	24	H	**Exudado uretral**	URETRITIS	Negativo.	POSITIVO (Ct = 26).	26	No consta	No	0	Secreción uretral
86	20	H	**Exudado uretral**	gonococic	Negativo.	POSITIVO (Ct = 22).	22	No consta	no	0	Secreción uretral
87	30	H	**Exudado uretral**	.	Negativo.	POSITIVO (Ct = 32).	32	Negativo	Si, doxi	0	Secreción