

# Detection and Identification of Gonococci Resistance to Cephalosporin and Determination the Most Effective Empirical Treatment for Gonococcal Urethritis in Male Human in Egypt

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## Abstract

**Introduction:** Gonorrhoeae and antimicrobial resistance AMR of gonococci is a major health problem today, because emerged resistance to last line empirical treatment for gonorrhoeae cephalosporins in many countries is predictable to be untreatable disease in near future. WHO GASP, WHO GLASS and WHO's global action plan on AMR recommends to expand nationally and internationally to collect data to monitor AMR of gonococci for public health policies. **Objective:** Our aim is to detect resistance of gonococci to Cephalosporins and determine the most effective empirical treatment for uncomplicated gonococcal urethritis in males in Egypt. **Methods:** We depended in our methodology on selected gonococci from male urethral discharge specimens on Thyer Martien medium; collected 33 isolates during three years from 2017 to 2020; used antibiotics with MIC according to international standards and measuring IZD according to antimicrobial susceptibility testing reference ranges in international standards. **Results:** By statistical studies, resistance to cephalosporins was as follows: Cephadrine 97%, Cefaclor 87.9%, Cefoxitin 97%, Ceftriaxone 90.9% and 42.4% to Cefepime, that shows heterogeneity in resistance inside cephalosporin group; while resistance to Macrolides group represented by Azithromycin and Tetracyclins group represented by Doxycycline was as follows: Azithromycin 39.4%, Doxycycline 27.3%; finally fluoroquinolones, the most effective group, resistance, was as: Levofloxacin 15.2%, Ciprofloxacin 15.2% and Ofloxacin 24.2%. **Conclusion:** The most effective empirical treatment for uncomplicated gonococcal urethritis in males in EGYPT is Fluoroquinolone; especially Levofloxacin ranks first susceptibility as 78.8%

and 15.2% resistance followed by Ciprofloxacin susceptibility as 69.7% and 15.2% resistance, finally Ofloxacin susceptibility as 66.7% and 24.2% resistance; for Ceftriaxone not more recommended in EGYPT as empirical treatment for uncomplicated gonococcal urethritis, it is susceptibility as 6.1% and 90.9% resistance; in addition, we can use combination therapy of Fluoroquinolones with Azithromycin or Doxycycline, whose susceptibility is 30.3% for Azithromycin and 42.4% for Doxycycline, while resistance is 39.4% for Azithromycin and 27.3% for Doxycycline. It is worth noting that only Cefepime in Cephalosporins group represents 42.4% susceptibility and 42.4% resistance; in addition to the Carbapenems group, it represents as 42.4% susceptibility for Imipenem and 45.5% resistance, then 42.2% susceptibility for Meropenem and 48.5% resistance, which can play role in combination therapy.

## Keywords

Gonorrhoea, Urethritis, Gonococcal Urethritis, Sexually Transmitted Diseases, Resistance to Antibiotics in Human Gonococcal Urethritis in Male in Egypt, Resistance to Cephalosporins, Resistance to Ceftriaxone, Empirical Treatment for Gonococcal Urethritis, *Niesseria gonorrhoeae*

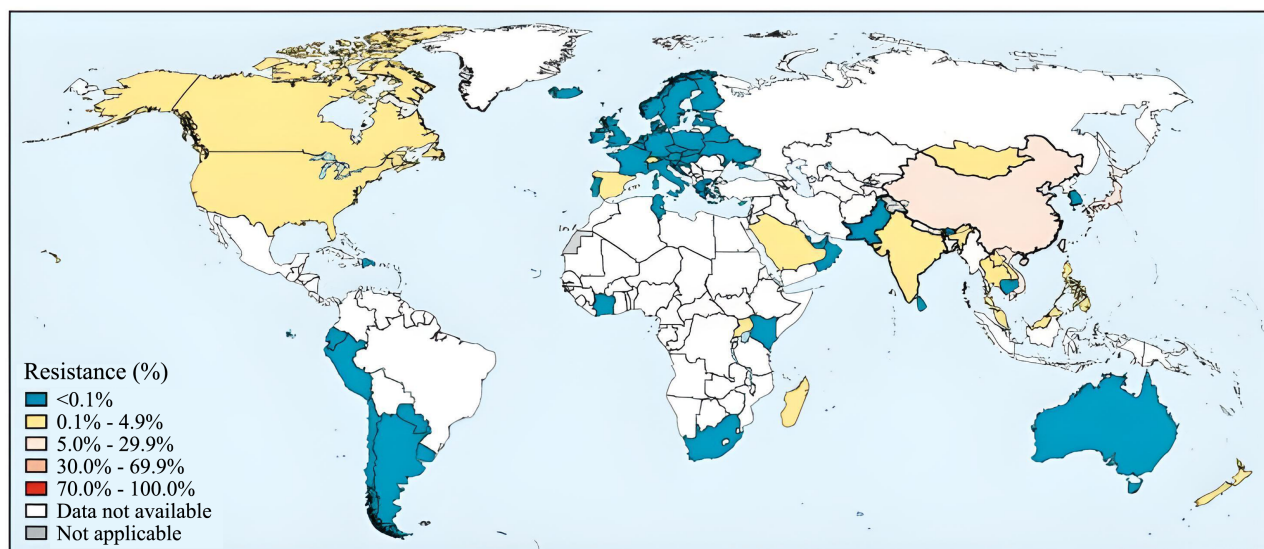
## 1. Introduction

Gonorrhoea is an ancient disease mentioned in the third book of Moses in the Bible, also in the 18th dynasty of Luxor in Egypt [1] [2] [3]. Gonorrhoea is the second prevalent sexually transmitted disease [4] [5]. WHO considered gonorrhoea as a major health problem, Center of Disease Control and prevention (CDC) mentioned gonorrhoea as a Super Bug [6] [7] [8] [9] [10], since gonorrhoea has remarkable ability to cause repeated infection in the same host and has extraordinary ability to develop resistance to all clinically used antibiotics [11] [12] [13]. However, Cephalosporins especially 3<sup>rd</sup> generation Ceftriaxone is still considered the first line empirical treatment for gonorrhoea worldwide, but resistance is reported globally in many countries [14]-[20].

In 2010, WHO GASP Program (WHO Global Gonococcal Antimicrobial Surveillance Program) proposed to monitor (AMR) Anti-Microbial Resistance of gonococci [6] [21] [22]; also in 2012 WHO published a global action plan to control the spread and impact of AMR in *Niesseria gonorrhoeae* which is in line with WHO's global action plan on AMR; then in 2015 WHO supported Global Antimicrobial resistance Surveillance System (GLASS) [19] [23] [24]. WHO recommended GASP, GLASS and Global Action Plan on AMR of gonococci to expand nationally and internationally to collect data from countries all over the world to monitor AMR of gonococci [19] [23] [24]. Egypt has no data about gonorrhoea according to GASP map [19] as shown in (Figure 1); this study is to report some data in EGYPT.

## 2. Materials and Methods

During three years 2017-2020 33 clinical isolates were collected (urethral



**Figure 1: Percentage of isolates with decreased susceptibility or resistance to Ceftriaxone reported to WHO Global Antimicrobial Surveillance Programme and Global Antimicrobial Resistance Surveillance System in 2018**

For Bahrain, China, Ecuador, New Zealand, Tunisia, and Vietnam, data are from 2017 (no data reported in 2018). Due to the low number of isolates in several countries (appendix pp 1-3), interpretations of antimicrobial resistance levels in these countries should be done with great caution. Disputed territories (Western Sahara, Jammu, and Kashmir) were not applicable and no data were available from these regions. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any county, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

**Figure 1.** GASP map for Ceftriaxone resistance that shows EGYPT from region with data not available (Magus *et al.*, 2021).

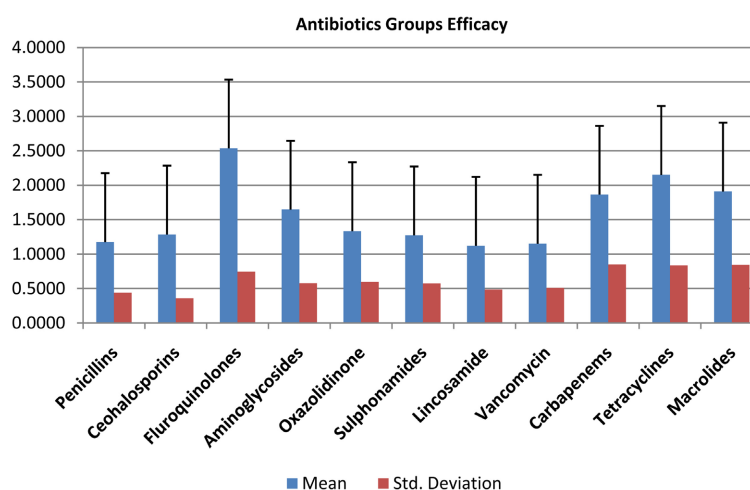
discharge swab) from male patients in varying ages diagnosed as uncomplicated gonococcal urethritis (UGU) obtained from National Institute of Urology and Nephrology in Cairo with disease diagnostic sheet and full history to each patient. Urethral discharge collected by the physician after cleaning urethral meatus with gauze soaked in physiological saline (0.9% w/v), at least one hour before voiding [25] [26]. Sample taken by inserting Rayon swab gently 2 - 3 cm into the anterior urethra and rotated from side to side [25], the purulent discharge expressed out by pressing at the base of the penis before inserting swab [24] [26] [27]; kept swab in Amies transport medium equipped in medical center [25] [28]; transporting to microbiology lab within 24 hours [27] [28] [29]; Make a fresh smear of urethral discharge specimens for Identification of polymorphic intraleukocytes kidney shape diplococci by microscopic examination and Gram staining so Gram staining is very high specific & diagnostic tool for symptomatic male urethritis, the sensitivity of gram stain is up to (95%) and specificity is up to (97%) [12] [25] [26] [28] [30]; urethral discharge isolates was cultivated on selective media (Modified Thyer Martine medium with (VCNT) supplement) at optimal conditions, Bacterial culture is still considered the gold standard to diagnosis *Neisseria gonorrhoeae* especially in urogenital specimens, bacterial culture is high sensitive and high specific, sensitivity may reach (85% - 95%) under optimal conditions, and specificity up to (100%) considered diagnostic test [12] [19] [25] [26] [28] [30] [31]; Identification of tested organism by Colonies morphological features, biochemical tests of gonococci (Oxidase test, Catalase

test and Carbohydrate fermentation test) and Gram staining of bacterial colonies to detect Gram-negative kidney shape diplococci [25] [28] [32]; then by disc diffusion method applied Antimicrobial susceptibility testing according to (Clinical Laboratory Standard Institute, CLSI) using antibiotics with MIC according to international standards and measuring IZD according to antimicrobial susceptibility testing reference ranges in international standards [12] [25] [26] [28] [31] [32] [33]; selected anti-biotic discs represent all functional anti-biotic groups as: Penicillins (first generation): Penicillin G, 10 IU, Aminopenicillins (3 red generation of penicillins): Amoxycillin, 10 µg; Amoxicillin/clavulanic acid, 30 µg; Ampicillin 10 µg/sulbactam 10 µg, 20 µg, Uredopencillins (4th generation of pencillins): piperacillin, 100 µg, Cephalosporins (1st generation): Cephadrine, 30 µg, Cephalosporins (2nd generation): Cefaclor, 30 µg; Cefoxitin, 30 µg, Cephalosporins (3rd generation): Ceftriaxone, 30 µg, Cephalosporins (4th generation): Cefepime, 30 µg, Fluroquinolones (2nd generation): Ofloxacin, 5 µg; Ciprofloxacin, 5 µg, Fluroquinolones (3rd generation): Levofloxacin, 5 µg, Aminoglycosides: Amikacin, 30 µg; Tobramycin, 10 µg; Gentamicin, 10 µg, Oxazolidinone: Linezolid, 30 µg, Sulphonamides: Trimethoprim 1.25 µg/sulphamethoxazol 23.75 µg, 25 µg, Lincosamide: Clindamycin, 2 µg, Vancomycin: Vancomycin, 30 µg, Carbapenems: Imipenem, 10 U; Meropenem, 10 U, Tetracyclines: Doxycycline, 30 µg, Macrolides: Azithromycin, 15 µg [12] [25] [26] [28] [31] [32] [33].

### 3. Results

Our results according to statistical analysis provide the most effective antibiotic group and the most effective antibiotic drug, the most effective group were as follows:

Fluroquinolones ranks first effective followed by Tetracyclin, Macrolides, Carbapenemes, Aminoglycosides, and oxazolidinon in sixth rank, followed by Cephalosporin, Sulphonamides, Penicillins, Vancomycin and Lincosamide was the least effective, show ranks mean and st. deviation values as in (Table 1 and Figure 2).



**Figure 2.** Diagrams show the ranking of the most effective antibiotic group gradually from the most effective to the least.

**Table 1.** Final ranking of antibiotic groups.

	N	Minimum	Maximum	Mean	Std. Deviation	C.V %	Rank
<b>Fluroquinolones</b>	33	1	3	2.5354	0.74507	29.387365	1
<b>Tetracyclines</b>	33	1	3	2.15	0.834	38.749996	2
<b>Macrolides</b>	33	1	3	1.91	0.843	44.144039	3
<b>Carbapenems</b>	33	1	3	1.8636	0.85030	45.625894	4
<b>Aminoglycosides</b>	33	1	3	1.6465	0.57699	35.043915	5
<b>Oxazolidinone</b>	33	1	3	1.33	0.595	44.633928	6
<b>Cephalosporins</b>	33	1	3	1.2848	0.35718	27.799191	7
<b>Sulphonamides</b>	33	1	3	1.27	0.574	45.104753	8
<b>Penicillins</b>	33	1	3	1.1758	0.43806	37.257426	9
<b>Vancomycin</b>	33	1	3	1.15	0.508	44.074037	10
<b>Lincosamide</b>	33	1	3	1.12	0.485	43.222123	11
<b>Valid N (listwise)</b>	33						

(N: Number of cases; the minimum value = 1 compensation for resistant cases; maximum value = 3 compensation for susceptible cases; Std. Deviation: standard deviation; C.V: coefficient of variation;  $1 \leq \text{Mean} = \text{Weighted average} \leq 3$ )

The most effective antibiotic drug inside Flouroquinolones group is Levofloxacin, so ranking of drugs both overall ranking and internal ranking inside each group, which provide homogeneity and heterogeneity inside each group were as show in (Table 2 and Figure 3).

From statistical studies there are two groups, less resistant group represented by 11 cases and more resistant group represented by 22 cases show in cluster analysis in (Figure 4); this table provides Frequencies and percent of susceptibility to each group and to total cases show in (Table 3).

## 4. Discussion

Drug resistance in *Neisseria gonorrhoeae* is considered according WHO collected data a major health concern [6] [7] [8] [9] [10], the AMR of gonococcal isolates reported to WHO by 73 countries in 2017-2018 is that each country collects at least 100 gonococcal isolates per year. WHO, findings was decreased susceptibility or resistance to Ceftriaxone was (31%) of 68 reporting countries and to Cefixime (47%) of 51 reporting countries.

Resistance to Azithromycin was reported by (84%) of 61 countries. Interpretation in many countries showed exceedingly high resistance to Ciprofloxacin (100%) of 70 reporting countries [6] [7] [12] [19] [23] [24].

In 2016 WHO estimated that: 6.9 million incident cases of gonorrhoeae occurred in adults, while in 2020 was 82.4 million, the first line empirical treatment was Ceftriaxone as monotherapy in most countries. However resistance to Ceftriaxone has been spread and continues to emerge globally [6] [7] [12] [19] [23] [24].

**Table 2.** Final ranking of antibiotic drugs.

	N	Minimum	Maximum	Mean	Std. Deviation	C.V %	Rank over all	Rank Internal
Penicillin G	33	1	3	1.12	0.485	43.222123	17	2
Amoxycillin	33	1	3	1.06	0.348	32.826072	18	3
Amoxicillin/clavulanic acid	33	1	3	1.12	0.485	43.222123	17	2
Ampicillin 10 µg/sulbactam 10µg	33	1	3	1.12	0.485	43.222123	17	2
pipracillin	33	1	3	1.45	0.711	48.889025	12	1
Cephadrine	33	1	3	1.06	0.348	32.826072	18	4
Cefaclor	33	1	3	1.18	0.528	44.646872	15	2
Cefoxitin	33	1	3	1.03	0.174	16.895772	19	5
Ceftriaxone	33	1	3	1.15	0.508	44.074037	16	3
Cefepime	33	1	3	2.00	0.935	46.770717	5	1
Ofloxacin	33	1	3	2.42	0.867	35.768625	3	3
Ciprofloxacin	33	1	3	2.55	0.754	29.612721	2	2
Levofloxacin	33	1	3	2.64	0.742	28.159453	1	1
Amikacin	33	1	3	1.73	0.674	39.032624	9	1
Tobramycin	33	1	3	1.48	0.667	44.929836	11	3
Gentamicin	33	1	3	1.73	0.761	44.074037	10	2
Linezolid	33	1	3	1.33	0.595	44.633928	13	1
Trimethoprim 1.25 µg/ sulphamethoxazol 23.75 µg	33	1	3	1.27	0.574	45.104753	14	2
Clindamycin	33	1	3	1.12	0.485	43.222123	17	4
Vancomycin	33	1	3	1.15	0.508	44.074037	16	3
Imipenem	33	1	3	1.97	0.951	48.30561	6	1
Meropenem	33	1	3	1.76	0.830	47.241065	8	2
Doxycycline	33	1	3	2.15	0.834	38.749996	4	
Azithromycin	33	1	3	1.91	0.843	44.144039	7	
Valid N (listwise)	33							

(N: Number of cases; the minimum value = 1 compensation for resistant cases; maximum value = 3 compensation for susceptible cases; Std. Deviation: standard deviation; C.V: coefficient of variation;  $1 \leq \text{Mean} = \text{Weighted average} \leq 3$ )

**Table 3.** Frequencies and percent of susceptibility to each group and to total cases.

Penicillins	Group A		Group B		Total	
	Frequency	%	Frequency	%	Frequency	%
PG:						
Sensitive	1	4.5	1	9.1	2	6.1

**Continued**

Moderate	-	-	-	-	-	
Resistance	21	95.5	10	-90.9	31	93.9
Mean Ranks	17.25		16.5			
Mann-Whitney Test	(Z = 0.508), Sig. = 0.611, (N.S, P > 0.05)					
AML:						
Sensitive	1	4.5	-	-	1	3
Moderate	-	-	-	-	-	-
Resistance	21	95.5	11	100	32	97
Mean Ranks	16.75		17.5			
Mann-Whitney Test	(Z = 0.707), Sig. = 0.480, (N.S, P > 0.05)					
AMC:						
Sensitive	1	4.5	1	9.1	2	6.1
Moderate	-	-	-	-	-	-
Resistance	21	95.5	10	90.9	31	93.9
Mean Ranks	17.25		16.50			
Mann-Whitney Test	(Z = 0.508), Sig. = 0.611, (N.S, P > 0.05)					
SAM:						
Sensitive	1	4.5	1	9.1	2	6.1
Moderate	-	-	-	-	-	-
Resistance	21	95.5	10	90.9	31	93.9
Mean Ranks	17.25		16.50			
Mann-Whitney Test	(Z = 0.508), Sig. = 0.611, (N.S, P > 0.05)					
PRL:						
Sensitive	2	9.1	2	18.2	4	12.1
Moderate	4	18.2	3	27.3	7	21.2
Resistance	16	72.7	6	54.5	22	66.7
Mean Ranks	18.05		14.91			
Mann-Whitney Test	(Z = 1.055), Sig. = 0.291, (N.S, P > 0.05)					
Cephalosporins						
CE:						
Sensitive	1	4.5	-	-	1	3
Moderate	-	-	-	-	-	-
Resistance	21	95.5	11	100	32	97
Mean Ranks	16.75		17.50			
Mann-Whitney Test	(Z = 0.707), Sig. = 0.480, (N.S, P > 0.05)					

**Continued**

<b>CEC:</b>						
Sensitive	1	4.5	1	9.1	2	6.1
Moderate	1	4.5	1	9.1	2	6.1
Resistance	20	90.9	9	81.8	29	87.9
Mean Ranks	17.5		16.0			
Mann-Whitney Test	(Z = 0.741), Sig. = 0.459, (N.S, P > 0.05)					
<b>FOX:</b>						
Sensitive	-	-	-	-	-	-
Moderate	-	-	1	9.1	1	3
Resistance	22	100	10	90.9	32	97
Mean Ranks	17.5		16.0			
Mann-Whitney Test	(Z = 1.414), Sig. = 0.157, (N.S, P > 0.05)					
<b>CRO:</b>						
Sensitive	1	4.5	1	9.1	2	6.1
Moderate	-	-	1	9.1	1	3
Resistance	21	95.5	9	81.8	30	90.9
Mean Ranks	17.73		15.55			
Mann-Whitney Test	(Z = 1.225), Sig. = 0.220, (N.S, P > 0.05)					
<b>FEP:</b>						
Sensitive	5	22.7	9	81.8	14	42.4
Moderate	3	13.6	2	18.2	5	15.2
Resistance	14	63.6	-	-	14	42.4
Mean Ranks	20.89		9.23			
Mann-Whitney Test	(Z = 3.553), Sig. = 0.000, (Sig at 0.01, P < 0.01)					
<b>Fluoroquinulones</b>						
<b>OFX:</b>						
Sensitive	12	54.5	10	90.9	22	66.7
Moderate	2	9.1	1	9.1	3	9.1
Resistance	8	36.4	-	-	8	24.2
Mean Ranks	19.18		12.64			
Mann-Whitney Test	(Z = 2.208), Sig. = 0.027, (Sig at 0.05, P < 0.05)					
<b>CIP:</b>						
Sensitive	14	63.6	9	81.8	23	69.7
Moderate	3	13.6	2	18.2	5	15.2



**Continued**

Resistance	5	22.7	0	-	5	15.2
Mean Ranks	18.23	14.55				
Mann-Whitney Test	(Z = 1.274), Sig. = 0.203, (N.S, P > 0.05)					
<b>LEV:</b>						
Sensitive	15	68.2	11	100	26	78.8
Moderate	2	9.1	-	-	2	6.1
Resistance	5	22.7	-	-	5	15.2
Mean Ranks	18.75		13.50			
Mann-Whitney Test	(Z = 2.064), Sig. = 0.05, (Sig at 0.05, P < 0.05)					
<b>Aminoglycosides</b>						
<b>AK:</b>						
Sensitive	3	13.6	1	9.1	4	12.1
Moderate	9	40.9	7	63.6	16	48.5
Resistance	10	45.5	3	27.3	13	39.4
Mean Ranks	17.73		15.55			
Mann-Whitney Test	(Z = 0.673), Sig. = 0.501, (N.S, P > 0.05)					
<b>TOB:</b>						
Sensitive	2	9.1	1	9.1	3	9.1
Moderate	7	31.8	3	27.3	10	30.3
Resistance	13	59.1	7	63.6	20	60.6
Mean Ranks	16.77		17.45			
Mann-Whitney Test	(Z = 0.221), Sig. = 0.825, (N.S, P > 0.05)					
<b>CN:</b>						
Sensitive	3	13.6	3	27.3	6	18.2
Moderate	9	40.9	3	27.3	12	36.4
Resistance	10	45.5	5	45.5	15	45.5
Mean Ranks	17.41		16.18			
Mann-Whitney Test	(Z = 0.372), Sig. = 0.710, (N.S, P > 0.05)					
<b>Oxazolidinone</b>						
<b>LZD:</b>						
Sensitive	1	4.5	1	9.1	2	6.1
Moderate	5	22.7	2	18.2	7	21.2
Resistance	16	72.7	8	72.7	24	72.7
Mean Ranks	17.07		16.86			
Mann-Whitney Test	(Z = 0.074), Sig. = 0.941, (N.S, P > 0.05)					

## Continued

Sulphonamides						
SXT:						
Sensitive	1	4.5	1	9.1	2	6.1
Moderate	5	22.7	-	-	5	15.2
Resistance	16	72.7	10	90.9	26	78.8
Mean Ranks	16.11		18.77			
Mann-Whitney Test	(Z = 1.045), Sig. = 0.296, (N.S, P > 0.05)					
Lincosamide						
DA:						
Sensitive	1	4.5	1	9.1	2	6.1
Moderate	-	-	-	-	-	-
Resistance	21	95.5	10	90.9	31	93.9
Mean Ranks	17.25		16.50			
Mann-Whitney Test	(Z = 0.508), Sig. = 0.611, (N.S, P > 0.05)					
Vancomycin						
VA:						
Sensitive	1	4.5	1	9.1	2	6.1
Moderate	1	4.5	-	-	1	3
Resistance	20	90.9	10	90.9	30	90.9
Mean Ranks	17.02		16.95			
Mann-Whitney Test	(Z = 0.038), Sig. = 0.969, (N.S, P > 0.05)					
Carbapenems						
IPM:						
Sensitive	4	18.2	10	90.9	14	42.4
Moderate	3	13.6	1	9.1	4	12.1
Resistance	15	68.2	-	-	15	45.5
Mean Ranks	21.34		8.32			
Mann-Whitney Test	(Z = 4.006), Sig. = 0.000, (Sig at 0.01, P < 0.01)					
MEM:						
Sensitive	2	9.1	6	54.5	8	42.2
Moderate	4	18.2	5	45.5	9	27.3
Resistance	16	72.7	-	-	16	48.5
Mean Ranks	21.32		8.36			
Mann-Whitney Test	(Z = 3.930), Sig. = 0.000, (Sig at 0.01, P < 0.01)					

Continued

Tetracyclines						
DO:						
Sensitive	6	27.3	8	72.7	14	42.4
Moderate	8	36.4	2	18.2	10	30.3
Resistance	8	36.4	1	9.1	9	27.3
Mean Ranks	19.68		11.64			
Mann-Whitney Test	(Z = 2.407), Sig. = 0.016, (Sig at 0.05, P < 0.05)					
Macrolides						
AZM:						
Sensitive	7	31.8	3	27.3	10	30.3
Moderate	7	31.8	3	27.3	10	30.3
Resistance	8	36.4	5	45.5	13	39.4
Mean Ranks	16.50		18.00			
Mann-Whitney Test	(Z = 0.447), Sig. = 0.655, (N.S, P > 0.05)					

(PG: Penicillin G, AML: Amoxicillin, AMC: Amoxicillin/clavulanic, SAM: Ampicillin 10 µg/sulbactam 10 µg, PRL: piperacillin CE: Cephadrine, CEC: Cefaclor, FOX: Cefoxitin, CRO: Ceftriaxone, FEP: Cefepime, OFX: ofloxacin, CIP: ciprofloxacin, LEV: levoflox- aic, AK: Amikacin, TOB: Tobramycin, CN: Gentamicin, LZD: Linezolid, SXT: Trimethoprim 1.25 µg/sulphamethoxazol 23.75 µg, DA: Clindamycin, VA: Vancomycin, IPM: Imipenem, MEM: Meropenem, DO: Doxycycline, AZM: Azithromycin)

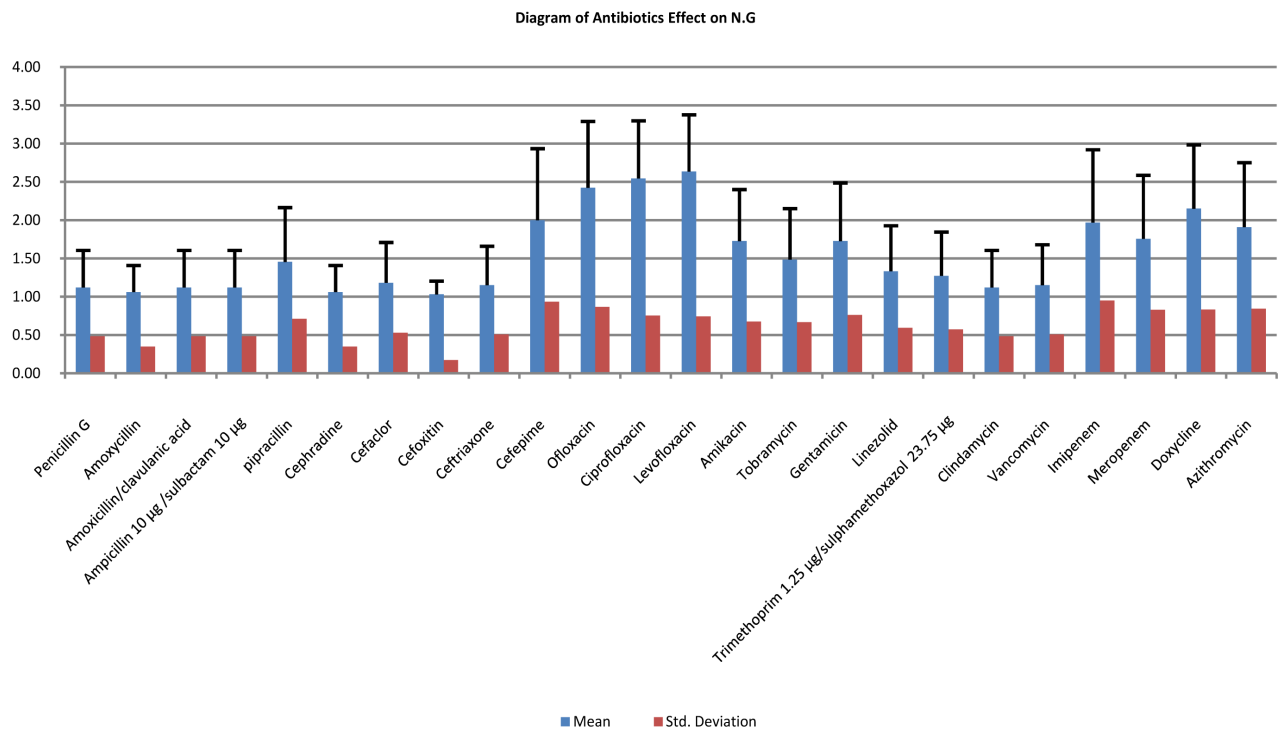
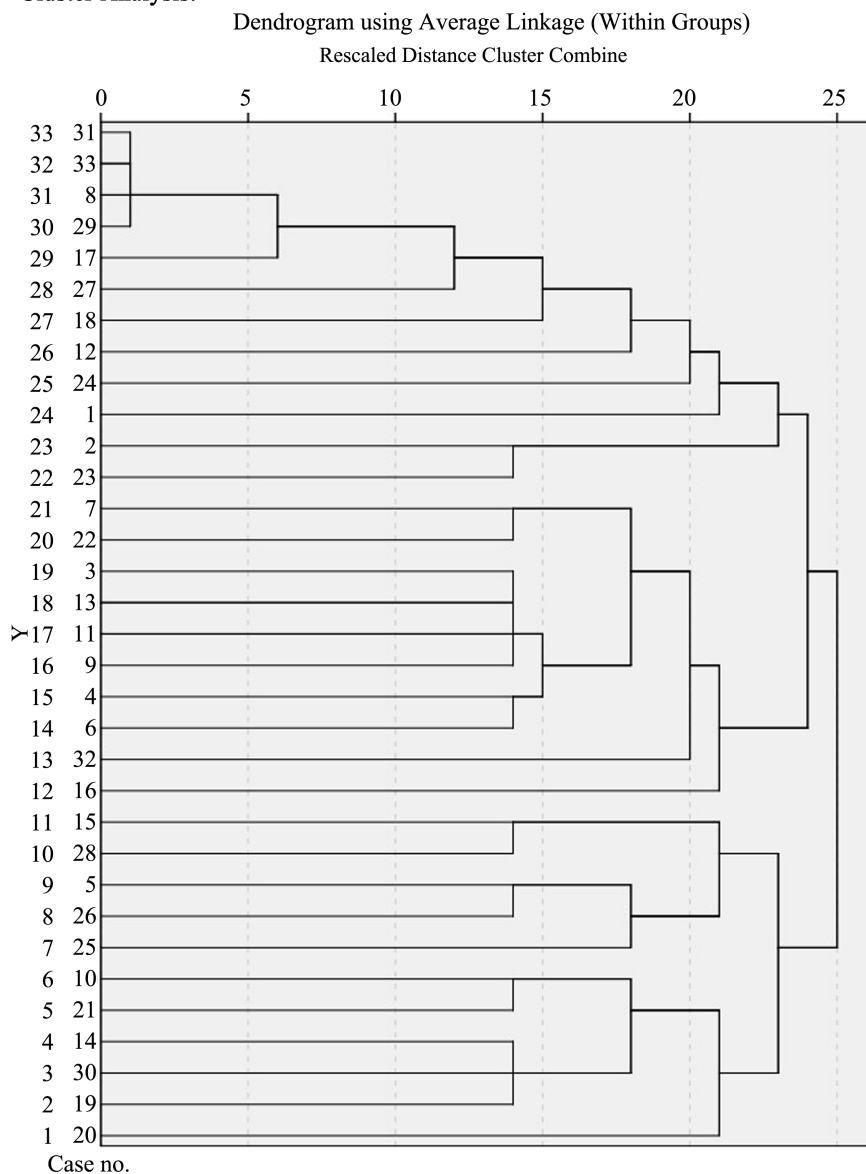


Figure 3. Diagrams show the ranking of the most effective antibiotic drug gradually from the most to the least.

## Cluster Analysis:



**Figure 4.** Dendrogram using average linkage (within groups).

In UK and Australia the first strain with resistance to Ceftriaxone was isolated in 2010. In Asia several Ceftriaxone resistance strains appeared [6] [7] [12] [19] [23] [24].

According to our results in the study done in EGYPT to detect the antimicrobial resistance to *Neisseria gonorrhoeae* and the most effective empirical treatment for non-complicated gonococcal urethritis in adult males, Flouroquinolones ranks first effective followed by Tetracyclin, Macrolides, Carbapenemes, Aminoglycosides, and oxazolidinon in sixth rank, followed by Cephalosporin, Sulphonamides, Penicillins, Vancomycin and Lincosamide was the least effective, show ranks as in previous (**Table 1**).

Inside Flouroquinolones Group Levofloxacin was the most effective followed

by Ciprofloxacin, and Ofloxacin represented ranks as in (Table 4).

The mean level of Ciprofloxacin resistance in WHO regions ranged from 49% (European region) to 93% (South East Asia region), overall 12 countries in five WHO regions reporting more than 90% resistance to Ciprofloxacin [7] [12] [19] [23] [24]. This shows resistance to Ciprofloxacin is higher than EGYPT that equals 15.2% according to our results shows as in (Table 5).

From GASP Map for Ciprofloxacin resistance that shows EGYPT from region with data not available as shows in (Figure 5).

Resistance to Chephalosporins in our results were reported as 90.9% for Ceftriaxone, Cefoxitine 97%, Cefaclor 87.9%, Cefradine 97%, while Cefepime 42.4% Which mean heterogeneous resistance in the Chephalosporin group show as in (Table 6).

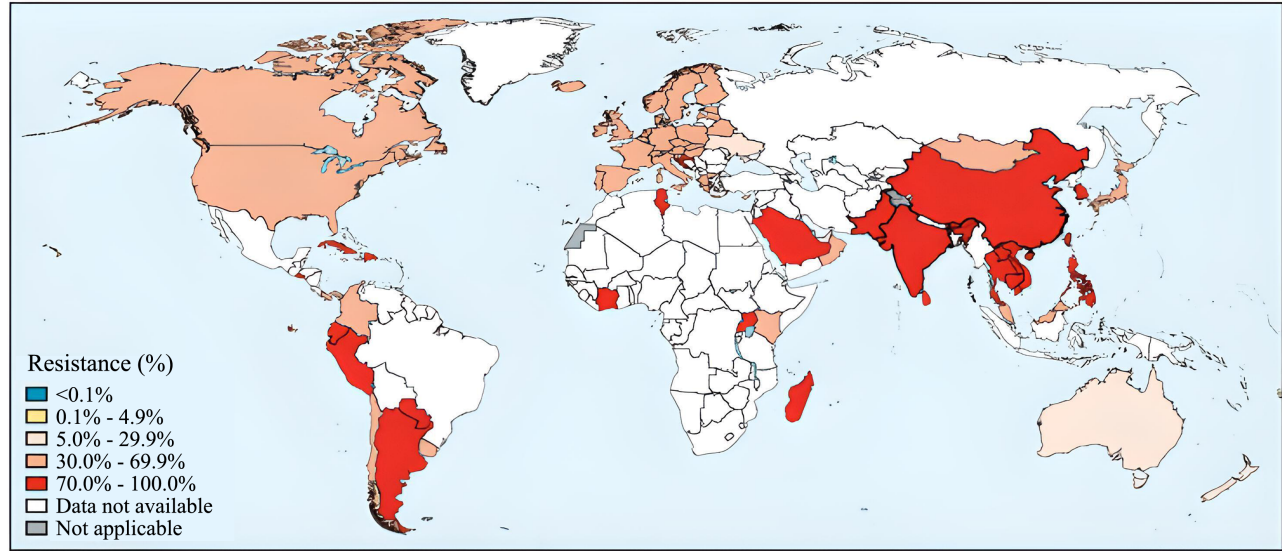


Figure 4: Percentage of isolates with resistance to ciprofoxacin reported to WHO Global Antimicrobial Surveillance Programme and Global Antimicrobial Resistance Surveillance System in 2018

For Bahrain, China, New Zealand, El Salvador, Tonga, and Vietnam, data are from 2017 (no data reported in 2018) Due to the low number of isolates in several countries (appendix pp 1-3), interpretations of antimicrobial resistance levels in these countries should be done with great caution. Disputed territories (Western Sahara, Jammu, and Kashmir) were not applicable and no data were available from these regions. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines o maps represent approximate border lines for which there may not yet be full agreement

Figure 5. GASP Map for Ciprofloxacin. (Magus *et al.*, 2021).

Table 4. Internal ranking of Fluroquinolones.

	N	Minimum	Maximum	Mean	Std. Deviation	C.V %	Rank over all	Rank Internal
Ofloxacin	33	1	3	2.42	0.867	35.768625	3	3
Ciprofloxacin	33	1	3	2.55	0.754	29.612721	2	2
Levofloxacin	33	1	3	2.64	0.742	28.159453	1	1

(N: Number of cases; the minimum value = 1 compensation for resistant cases; maximum value = 3 compensation for susceptible cases; Std. Deviation: standard deviation; C.V: coefficient of variation;  $1 \leq \text{Mean} = \text{Weighted average} \leq 3$ )

**Table 5.** Frequencies and percent of susceptibility to each drug in Fluroquinolones.

Fluoroquinulones	Frequency	%
<b>OFX:</b>		
Sensitive	22	66.7
Moderate	3	9.1
Resistance	8	24.2
Mann-Whitney Test	(Z = 2.208), Sig. = 0.027, (Sig at 0.05, P < 0.05)	
<b>CIP:</b>		
Sensitive	23	69.7
Moderate	5	15.2
Resistance	5	15.2
Mann-Whitney Test	(Z = 1.274), Sig. = 0.203, (N.S, P > 0.05)	
<b>LEV:</b>		
Sensitive	26	78.8
Moderate	2	6.1
Resistance	5	15.2
Mann-Whitney Test	(Z = 2.064), Sig. = 0.05, (Sig at 0.05, P < 0.05)	

(OFX: Ofloxacin, CIP: Ciprofloxacin, LEV: Levofloxaic)

**Table 6.** Frequencies and percent of susceptibility to each drug in Cephalosporins.

Cephalosporins	Frequency	%
CE:		
Sensitive	1	3
Moderate	-	-
Resistance	32	97
Mann-Whitney Test	(Z = 0.707), Sig. = 0.480, (N.S, P > 0.05)	
CEC:		
Sensitive	2	6.1
Moderate	2	6.1
Resistance	29	87.9
Mann-Whitney Test	(Z = 0.741), Sig. = 0.459, (N.S, P > 0.05)	
FOX:		
Sensitive	-	-
Moderate	1	3
Resistance	32	97
Mann-Whitney Test	(Z = 1.414), Sig. = 0.157, (N.S, P > 0.05)	

**Continued**

<b>CRO:</b>		
Sensitive	2	6.1
Moderate	1	3
Resistance	30	90.9
Mann-Whitney Test	(Z = 1.225), Sig. = 0.220, (N.S, P > 0.05)	
<hr/>		
<b>FEP:</b>		
Sensitive	14	42.4
Moderate	5	15.2
Resistance	14	42.4
Mann-Whitney Test	(Z = 3.553), Sig. = 0.000, (Sig at 0.01, P < 0.01)	

(CE: Cephadrine, CEC: Cefaclor, FOX: Cefoxitin, CRO: Ceftriaxone, FEP: Cefepime)

These results is different, according to WHO (GASP) resistance to Ceftriaxone in Africa 40%, Americas 22%, Estern Mediterranean 14%, Europe 10%, South-East Asia 50%, Western Pacific 38%, with total Resistance 22% Resistance to Ceftriaxone in EGYPT we were recorded 90.9% which is much higher [6] [7] [12] [19] [23] [24].

From GASP Map for Ceftriaxone resistance that shows EGYPT from region with data not available as shows in (previous **Figure 1**).

Ceftriaxone in EGYPT is shelf medicine given by pharmacist and given in an-inappropriate dose and short course; this attributes the high incidence of resistance, while Flouroquinolons are usually prescribed by physician, also most patients asked medical advice late after chronicity. Ceftriaxone is in injection form and non-compliant patients discontinue the injection once they improve and do not complete the treatment, while most of Flourquinolons are in tablet form this will encourage the patient to complete the course of treatment, moreover in EGYPT sexually transmitted diseases are considered shameful and the patient easy ask advice from friend or colleague and Ceftriaxone injection is given, so our result in EGYPT is slightly different due to regulations of medicine administration and socioeconomic habits.

## 5. Conclusion

The most effective empirical treatment for uncomplicated gonococcal urethritis in male in EGYPT is Fluoroquinolones; especially Levofloxacin ranks first susceptibility as 78.8% and 15.2% resistance followed by Ciprofloxacin susceptibility as 69.7% and 15.2% resistance, finally Ofloxacin susceptibility as 66.7% and 24.2% resistance. Ceftriaxone not more recommended in EGYPT as empirical treatment for uncomplicated gonococcal urethritis, susceptibility as 6.1% and 90.9% resistance. We can use combination therapy of Fluoroquinolones with Azithromycin or Doxycycline, which is susceptibility as 30.3% for Azithromycin and

42.4% for Doxycycline, while resistance as 39.4% for Azithromycin and 27.3% for Doxycycline. It is worth noting that: only Cefepime in Cephalosporins group whose susceptibility represents as 42.4% and 42.4% resistance, in addition to the Carbapenems group (represented by Imipenem and Meropenem) whose susceptibility represents as 42.4% for Imipenem and 45.5% resistance, then 42.2% susceptibility for Meropenem and 48.5% resistance. Those can play role in combination therapy.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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