Papua New Guinea Institute of Medical Research

Gonococcal Antimicrobial Susceptibility Survey

Goroka, Eastern Highlands Province

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Abbreviations Used in this Report

AMS	Antimicrobial Susceptibility
CLSI	Clinical and Laboratory Standards Institute
DNA	Deoxyribonucleic Acid
GC	Gonococci
IQR	Interquartile Range
MIC	Minimum Inhibitory Concentration
MICE	Minimum Inhibitory Concentration Evaluator
NDoH	National Department of Health
PNG	Papua New Guinea
PNGIMR	Papua New Guinea Institute of Medical Research
PID	Pelvic Inflammatory Disease
PPNG	Penicillinase-producing *Neisseria gonorrhoeae*
qPCR	Quantitative Polymerase Chain Reaction
STI	Sexually Transmitted Infection
TRNG	Tetracycline Resistant *Neisseria gonorrhoeae*
UDS	Urethral Discharge Syndrome
VDS	Vaginal Discharge Syndrome
VCN	Vancomycin, Colistin Sulphate and Nystatin
WHO	World Health Organization

Purpose of Report

This study was funded through a Papua New Guinea Institute of Medical Research (PNGIMR) Internal Competitive Research Award Scheme with the primary aim of evaluating the current standard treatment regimen for gonococcal infections in Papua New Guinea. Additionally, it was imperative to document patterns of antimicrobial susceptibility among locally circulating gonococci in order to inform the development of future treatment regimens for gonorrhoea in the country.

Key Findings

1. High prevalence of infections with *Neisseria gonorrhoea* (88.2%) and *Chlamydia trachomatis* (31.5%) among males presenting with urethral discharge syndrome (UDS).
2. High proportions of penicillinase-producing *N. gonorrhoeae* (PPNG) (65.0%) and tetracycline resistant *N.* gonorrhoeae (TRNG) (82.8%) were observed among isolates tested.
3. There are limitations in determining susceptibility of gonococcus to amoxicillin-clavulanate. Notwithstanding these limitations, it appears that the majority of isolates (93.9%) were susceptible to amoxicillin-clavulanate (2:1 ratio) but 6.1% had elevated minimum inhibitory concentrations (MIC) (4.0/2.0 µg/ml) to amoxicillin-clavulanate.
4. All isolates tested were susceptible to azithromycin, erythromycin, cefixime, and ciprofloxacin.

5. One isolate (1.5% of 66 isolates tested) was resistant to ceftriaxone by disk diffusion; however this finding should be interpreted with caution as the MIC to ceftriaxone could not be conducted. There is very limited, or no, resistance to cephalosporins in strains of *N. gonorrhoeae* isolated in this study.

Introduction

It has been well documented that sexually transmitted infections (STIs) are a significant health problem in Papua New Guinea (PNG) (1-3). Consequently, the National Department of Health (NDoH) has made it a priority to improve case management in STI clinics throughout the country (4, 5). A barrier to achieving this objective is the limited availability of reliable prevalence and incidence data for common STIs given that the majority of STI clinics do not routinely perform diagnostic tests (1, 2, 6). Gonorrhoea, caused by the Gram-negative coccoid bacterium *Neisseria gonorrhoeae*, remains one of the most common STIs in PNG. The estimated community prevalence of gonorrhoea is 16% in men and 10% in women; with a higher prevalence observed in clinical settings (27% and 74% for women and men respectively) (1-3, 6).

The control of gonorrhoea is potentially compromised by the ability of the causative bacterium to readily develop and acquire resistance genes (7, 8). The last gonococcal antimicrobial susceptibility (AMS) survey that assessed the current standard treatment regimen was conducted over one decade ago. While in that survey all isolates from Port Moresby, Lae, Mt Hagen and Goroka were concluded to be susceptible to amoxicillin-clavulanate therapy (4), it is imperative that the AMS profiles of circulating strains of *N. gonorrhoeae* be assessed at regular intervals to determine if resistance has developed since the last survey. Specifically, it is necessary to document the AMS profiles of *N. gonorrhoeae*

against a spectrum of antimicrobial agents, in order to inform the development of future treatment regimens.

Objectives

Amoxicillin-clavulanate has been used to treat gonorrhoea in PNG for over two decades, raising concern that *N. gonorrhoeae* isolates in current circulation may be developing resistance to the therapy (4). To investigate this, we conducted surveillance of antibiotic resistance in *N. gonorrhoeae* in Goroka, Eastern Highlands Province.

The objectives of this study were to:

(i) Determine the prevalence of infection by *N. gonorrhoeae* and *Chlamydia trachomatis* among males presenting with UDS; and in doing so

(ii) Determine antimicrobial susceptibility patterns of gonococcal isolates collected.

Methods

This prospective cross-sectional study was conducted between 2014 and 2016 in the Sexual Health Clinic at the Eastern Highland Provincial Hospital (Goroka, Eastern Highlands). During the study period, male attendees, ≥18 years of age, presenting at the clinic with UDS were provided information about the study and

invited to participate. Patients who declined to participate in the study were provided the standard care and treatment. Patients willing to participate were asked to provide written informed consent and then underwent a clinical examination where a urethral swab was collected by a health worker. A rayon urethral swab was used to collect urethral discharge and immediately deposited into Amies transport medium without charcoal (Copan Diagnostics, Murrieta, CA). The swab was stored at room temperature until transported to the Bacteriology Laboratory at the PNGIMR in Goroka for processing. The average time in transit for specimens was 4 hours. Following the clinical examination, participants were provided the standard care and treatment for UDS. For men this is a single-dose therapy consisting of 2 g of amoxicillin, 1.25 g amoxicillin-clavunate, 1 g probenecid, 1 g azithromycin and 2 g tinidazole (9).

Isolation of *N. gonorrhoeae*

The urethral swab was used to inoculate a gonococcal (GC) agar plate containing vancomycin, colistin sulphate and nystatin (VCN) selective supplement (Oxoid Limited, Thebarton, SA, Australia). The swab was then used to prepare a smear for Gram stain detection of intracellular diplococci, before being stored at -20°C for molecular detection of *N. gonorrhoeae* and *C. trachomatis.* Inoculated GC-VCN plates were incubated at 37°C in a CO_2 enriched atmosphere (candle jar) for up to 48 hours. The GC-VCN plates were examined for suspected GC colonies after 24 hours up until 48 hours of incubation. GC-VCN plates were discarded after 48 hours of incubation if no

suspected GC colonies were observed. Suspected colonies were presumptively identified as *N. gonorrhoeae* if they were Gram-negative diplococci, oxidase positive and superoxol positive. The rapid carbohydrate utilization test as described by the World Health Organization (WHO) was used to perform confirmatory identification of *N. gonorrhoeae* isolates (8, 10). Detection of ß-lactamase (see below) was performed immediately after confirmatory identification of *N. gonorrhoeae.* Confirmed isolates were stored in skim milk broth at -80°C for later batch testing of antimicrobial susceptibility.

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing of *N. gonorrhoeae* isolates was carried out using the disk diffusion method on Columbia chocolate agar as described by the WHO (8, 10). The antibiotic disks (Oxoid Limited, Thebarton, SA, Australia) used contained amoxicillin and clavulanic acid in a 2:1 ratio (30 µg), azithromycin (15 µg), ceftriaxone (30 µg), cefixime (5 µg), ciprofloxacin (1 µg), erythromycin (15 µg), penicillin G (10 IU), and tetracycline (10 µg). PPNG were identified using a ß-lactamase indicator stick (Oxoid Limited, Thebarton, SA, Australia).The MIC was measured for isolates that displayed a diminished susceptibility to an antibiotic using Minimum Inhibitory Concentration Evaluator (MICE) strips (Oxoid Limited, Thebarton, SA, Australia). Antimicrobial results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines (11). In the absence of CLSI guidelines for azithromycin interpretation, British Society of Antimicrobial Chemotherapy guidelines were used (12). Similar to azithromycin,

an MIC breakpoint of ≤0.5 µg/ml was used for erythromycin (13) since a high correlation has been reported for both agents (14). The MICE strip for amoxicillin-clavulanate contains amoxicillin and clavulanic acid in a 2:1 ratio (Oxoid Limited, Thebarton, SA, Australia). In the absence of amoxicillin-clavulanate disk diffusion interpretive guidelines for PPNG, an MIC breakpoint of 2.0/1.0 µg/ml (i.e. 2.0 µg/ml of amoxicillin and 1.0 µg/ml of clavulanic acid), similar to the breakpoint for penicillin, was used to categorise isolates as susceptible (11, 15, 16).

Molecular Detection of *N. gonorrhoeae* and *C. trachomatis*

Deoxyribonucleic acid (DNA) was extracted from the urethral swabs using NucleoSpin® Tissue Kit (Macherey-Nagel, Germany) and a DNA integrity check was performed by amplifying a 268 base pair (bp) region of the ß-globin gene using the primer pair GH20/PC04 (17). Detection of *N. gonorrhoeae* and *C. trachomatis* was carried out using real-time polymerase chain reaction (qPCR) targeting the *opa* gene and multicopy cryptic plasmid respectively, as per methods previously described (18).

Data Management and Statistical Analysis

Laboratory results were recorded on paper forms and then entered into a study Micriosoft Excel database. Statistical analysis was performed using Stata (StataCorp, College Station, TX) to produce two-by-two tables and to calculate means, ranges, medians and interquartile ranges (IQR).

Ethics and Funding

This study was funded through a PNGIMR Internal Competitive Research Award Scheme. Ethics approval was granted by the PNG Institute of Medical Research Institutional Review Board (IRB 1209) and the PNG Medical Research Advisory Committee (MRAC 12.22).

Results

Study Population and Prevalence of *N. gonorrhoeae* and *C. trachomatis*

A total of 180 male attendees were recruited into the study during the survey period. Two participants were excluded from analysis because an inadequate sample was obtained. Of the resulting 178 participants data on age was available for 163 participants, whose mean age was 25.8 years (range 18-55 years).

The majority of participants were positive for *N. gonorrhoeae* by qPCR (88.2%, n=157) while 31.5% (n=56) were positive for *C. trachomatis*. There was no significant difference in age between males who were positive for *N. gonorrhoeae* and those who were positive for *C. trachomatis*. Double infections were observed in 28.1% (n=50) participants. In total, 91.6% (n=163) of study participants were positive by qPCR for *N. gonorrhoeae* and/or *C. trachomatis*.

Antimicrobial Susceptibility of *N. gonorrhoeae* Isolates

We were able to successfully culture gonococci from 66.9% (n=119) of participants, all of whom were positive for *N. gonorrhoeae* by qPCR. Of the 157 participants positive for *N. gonorrhoeae* by qPCR, viable *N. gonorrhoeae* was isolated (by culture) in 119 participants (75.8%).

Of the 119 isolates, 98.3% (n=117) underwent ß-lactamase testing; with 65% (76/117) determined to be PPNG. Sixty-six isolates (55.4%) underwent AMS testing with the full panel of antimicrobial agents (Table 1). For those of whom AMS testing was carried out, the mean age was 26 years (range 18-50 years).

Table 1 Antimicrobial Susceptibility of *N. gonorrhoeae* Isolates* (n=66)

Antimicrobial Agent (disk concentration)	Susceptible % (n)	Reduced Susceptibility % (n)	Resistant % (n)	Median MIC
Beta-lactams				
Amoxicillin-clavulanate (2:1 ratio) (30 µg)[b]	93.9 (62)	0	6.1 (4)	4 µg/ml
Penicillin G (10 U)[c]	1.5 (1)	13.6 (9)	84.8 (56)	12 µg/ml
Cephlasporins				
Cefixime (5 µg)[c]	100 (66)	0	0	-
Ceftriaxone (30 µg)[c]	98.5 (65)	0	1.5 (1)	-
Macrolides				
Azithromycin (15 µg)[a]	100 (66)	0	0	-
Erythromycin (15 µg)[c]	100 (66)	0	0	-
Quinalones				
Ciprofloxacin (1 µg)[c]	100 (66)	0	0	-
Tetracyclines				
Tetracycline (10 µg)[c]	0	62.1 (41)	37.9 (25)	32 µg/ml

* Interpretation based on disk diffusion results except for amoxicillin-clavulanate where MIC was used.
[a] Determined using British Society of Antimicrobial Chemotherapy guidelines
[b] Determined using CLSI penicillin MIC breakpoints
[c] Determined using CLSI disk diffusion breakpoints

Based on disk diffusion results, all isolates displayed susceptibility to azithromycin, erythromycin, ciprofloxacin, cefixime and ceftriaxone, with the exception of one isolate (1.5%) that was categorised as resistant to ceftriaxone, based on disk diffusion parameters. Confirmation of resistance to ceftriaxone or MIC testing was not conducted on this isolate due to loss of viability. This isolate was also a PPNG and resistant to penicillin.

Susceptibility of *N. gonorrhoeae* to amoxicillin-clavulanate (2:1 ratio) was determined using MIC only, based on breakpoints for penicillin (10, 14, 15) (Table 2). Using this approach, 93.9% (n=59) of isolates were susceptible to

amoxicillin-clavulanate, with MICs less than 2.0/1.0 µg/ml, and 6.1% (n=4) were categorised as resistant, with an MIC of 4.0/2.0 µg/ml. These four resistant isolates were PPNG.

Table 2 Minimum Inhibitory Concentration to Amoxicillin-Clavulanate (n=63)

MIC (µg/ml)	Frequency (%)
0.015/0.0075	1 (1.6)
0.03/0.015	1 (1.6)
0.06/0.03	2 (3.2)
0.12/0.06	4 (6.4)
0.25/0.125	5 (7.9)
0.5/0.25	12 (19.1)
1/0.5	15 (23.8)
2/1	19 (30.2)
4/2	4 (6.4)

Against penicillin, 84.6% of isolates were resistant (n=56), 13.6% (n=9) exhibited reduced susceptibility and 1.5% (n=1) was sensitive by the disk diffusion method. The median MIC for penicillin resistant isolates was 12 µg/ml (IQR 4-32 µg/ml). Of those that were resistant to penicillin, 57.4% (n=31) were PPNG. For isolates with reduced susceptibility to penicillin, the median MIC was 0.5 µg/ml (IQR 0.25-0.5 µg/ml) and 22.2% (n=2) were PPNG. Against tetracycline, 37.9% (n=25) of isolates were resistant and 62.1% (n=41) were less susceptible by the disk diffusion method. Tetracycline MICs were completed for 24.4% (n=29) isolates. Of these, 82.8% (n=24) were classified as TRNG (defined as MIC$\geqslant$16 µg/ml), with the median MIC at 32 µg/ml (IQR 32-64 µg/ml).

Discussion

This study revealed that *N. gonorrhoeae* is commonly detected in males with UDS. Despite the challenges associated with culture of *N. gonorrhoeae*, we isolated the organism in ~76% of samples determined to be positive by PCR. Culture enables AMS testing to be conducted, although maintaining viability remains a challenge in under-resourced settings. Almost all (98.3%) isolates were tested for ß-lactamase production, though only slightly over half of isolates (55.4%) underwent full AMS testing. Most isolates had to be stored at -80°C awaiting procurement of AMS testing reagents during the survey period and were not recoverable primarily because of the fastidious nature of the bacterium (10).

Despite the aforementioned challenges, the findings of this study demonstrate the presence of gonococcal isolates with reduced or diminished susceptibility to commonly used antibiotics in PNG. In particular, the majority of isolates tested were resistant (84.6%) or had reduced susceptibility (13.6%) to penicillin, and high-level resistance to tetracycline was also observed (82.8% of tested isolates were TRNG).

A major contributing factor to resistance to penicillin among isolates of *N. gonorrhoeae* in PNG is the ability to produce penicillinase (also known as β-lactamase). Almost two-thirds (65.0%) of isolates were PPNG, which is a greater proportion than that reported a decade ago (40.0%) (4). Over half (57.4%) of the

penicillin resistant isolates tested in the current study were PPNG and had high MICs (median 12 µg/ml, IQR 4-32 µg/ml).

In PNG amoxicillin-clavulanate remains an important component of the standard treatment for urethral and vaginal discharge (or clinical suspicion of gonorrhoea). In this study 93.9% of isolates were categorised susceptible to amoxicillin-clavulanate while 6.1% were resistant. All resistant strains (6.1%) had elevated MICs (4.0/2.0 µg/ml) to amoxicillin-clavulanate (2:1 ratio) which were above the breakpoint used to determine susceptibility to amoxicillin-clavulanate in this survey (≤2.0/1.0 µg/ml) (14, 15). This is a notable finding since a previous survey in PNG found that all *N. gonorrhoeae* isolates were susceptible to amoxicillin-clavulanate (2:1 ratio) (4).

It is difficult to fully elucidate the public health risk of increasing resistance to amoxicillin-clavulanate in circulating strains of *N. gonorrhoeae* in PNG. The MIC test strip used contained amoxicillin-clavulanate in a 2:1 ratio, while in the current therapy for gonorrhoea in PNG this ratio is 12:1 (5). In clinical applications for treatment of various bacterial infections, the ratio of amoxicillin to clavulanate varies from 2:1 to 16:1 for oral administration. Clavulanate does have some antimicrobial activity, including against *Neisseri*a spp. (19). Thus, at the relatively high concentration of clavulanate used *in vitro*, there may be some increased antimicrobial effect relative to concentrations of clavulanate obtained *in vivo.* This

highlights the need for validated guidelines to evaluate *N. gonorrhoea* susceptibility to amoxicillin-clavulanate in PNG.

We did not seek to determine whether other mechanisms contribute to resistance to β-lactam antibiotics in *N. gonorrhoeae* in PNG. All isolates that were resistant to amoxicillin-clavulanate were PPNG; however, not all penicillin resistant isolates were PPNG. This suggests that penicillin resistance observed in non-PPNG isolates might be chromosomally mediated; and β-lactamase inhibitors such as clavulanic acid have no impact on chromosomally mediated resistant *N. gonorrhoea*. The suitability of amoxicillin-clavulanate as a component of treatment of UDS, vaginal discharge syndrome (VDS) and pelvic inflammatory disease (PID), and thus gonorrhoea, requires ongoing consideration in light of these findings.

While β-lactam antibiotics are an important component of treatment of bacterial STIs in PNG, they are not the only components. Azithromycin forms part of the standard treatment of UDS in PNG; is prescribed for VDS if the patient has risk factors for gonorrhoea or chlamydia; and is recommended for treatment of women with lower abdominal pain (for suspicion of PID) (9). All isolates tested were fully susceptible to azithromycin, and another macrolide antibiotic, erythromycin.

In PNG for disease presentations associated with gonorrhoea infection, if amoxicillin-clavulanate and/or azithromycin are not available alternative treatments are recommended (9). In the absence of amoxicillin-clavulanate, additional amoxicillin is recommended; and in the absence of azithromycin, doxycycline or erythromycin are recommended. On the basis of the high levels of resistance to penicillin and the frequent detection of PPNG, it is unlikely that treatment of gonorrhoea infection with amoxicillin in the absence of clavulanate will be sufficiently efficacious. Although we did not test for susceptibility to doxycycline in this study, based on tetracycline results its use may be similarly ineffective in the treatment of gonorrhoea. No isolates were resistant to erythromycin, suggesting its continued use as an alternative treatment may be effective. However, as opposed to first-line treatment options where a single-dose therapy is administered, a 10-day course of erythromycin is required when the standard treatment is not available. A review of alternative treatment regimens in the absence of first line treatment option is required in PNG.

All isolates were also susceptible to ciprofloxacin and cefixime; and only a single isolate (1.5%) was resistant to ceftriaxone. We must interpret this observed resistance to ceftriaxone with caution, as the isolate lost viability and thus no MIC was conducted to confirm level of resistance. If the treatment regimens currently recommended are, in the future, unsuitable cephalosporins such as cefixime or ceftriaxone could be used as the standard or alternative treatment of UDS/VDS/PID. It is imperative that the current therapy be regularly monitored

through antimicrobial susceptibility surveillance (and potentially clinical studies) to inform the development and rollout of future treatment protocols – should the present standard therapy be deemed ineffective (7).

The continued use of amoxicillin-clavulanate in the standard treatment of gonorrhoea in PNG is a complex issue. Central to the complexity is the lack of current recognised guidelines for the determination of resistance/susceptibility of *N. gonorrhoeae* to this antibiotic. Given the role of amoxicillin-clavulanate in the treatment of UDS/VDS/PID (and thus gonorrhoea) in PNG (9), it was imperative that we included that antibiotic in our testing. To do so we reviewed the limited available literature, and based our cut-off values (that differentiate between resistance and susceptibility) on those for penicillin as suggested in a pharmaceutical prescribing information document (16). A study by Fuchs and colleagues (15) also used an MIC cut-off value equivalent to that state by CLSI for penicillin for *N. gonorrhoeae* MIC testing. Using this approach, our data suggest that amoxicillin-clavulanate continues to be largely effective. Despite the high prevalence of PPNG and thus likely resistance to amoxicillin (65% of isolates), only a small proportion of isolates tested (6.1%) appear to be resistant to amoxicillin-clavulanate.

An additional complexity in the use of amoxicillin-clavulanate is the potential for multiple resistance mechanisms to β-lactams, and the increase of strains resistant to amoxicillin-clavulanate. More work is required to determine the

prevalence of resistance mechanisms in *N. gonorrhoeae* isolates to β-lactam antibiotics in PNG.

Notwithstanding the aforementioned limitations, it appears that the continued use of amoxicillin-clavulanate in the treatment of gonorrhoea (and associated syndromes) may be most appropriate in the absence of compelling data to suggest a change in standard treatment. This conclusion is on account of the low prevalence of resistance to amoxicillin-clavulanate (to the best of our knowledge), and no observed resistance to azithromycin. However, it is acknowledged that the lack of current 'recognised' guidelines to determine resistance of *N. gonorrhoeae* to amoxicillin-clavulanate in itself is an impediment to its use.

We acknowledge that the proposal to continue to use amoxicillin-clavulanate could be considered to contravene WHO recommendations on two fronts. As a general rule, WHO recommends a change in standard treatment when >5% of circulating strains are resistant to the current treatment (7, 20). Secondly, WHO recommends that treatment of gonococcal infections be based on ceftriaxone or cefixime, third generation cephalosporins (20). However, the current combined treatment, which incorporates 1 g of azithromycin coupled with 1 g of probenecid to maintain antibiotic serum levels, is likely to remain effective given that no resistance to azithromycin was observed in this study. Moreover, changing from

amoxicillin-clavulanate, which appears to remain largely effective as a treatment, to the next line of antibiotics may fast-track resistance to the cephalosoprins. Isolates of *N. gonorrhoeae* resistant to ceftriaxone are becoming increasingly prevalent globally, including in nearby Asia, a region that PNG is increasingly engaged with in terms of trade and thus movement of people (21, 22).

Another consideration in changing the standard treatment of gonorrhoea in the country relates to prescriber level restrictions. The NDoH Pharmaceutical Service Standard classifies amoxicillin-clavulanate and ceftriaxone as Category A and B drugs respectively (23). All levels of medical cadre are permitted to prescribe and administer Category A drugs; however, Category B drugs can only be prescribed and administered (either directly or under supervision) by a medical officer. The limited number of medical officers in PNG, particularly in remote and rural areas, will impact the accessibility of treatment if ceftriaxone was adopted to treat gonorrhoea (24). There are almost 10 times more nurses than medical officers in the country (4.7 versus 0.5 personnel per 10,000 population) (25). Prescriber level restrictions add another aspect of complexity when considering a change in the standard treatment of a common condition like gonorrhoea.

This study found that the majority of male participants presenting with UDS were positive for *N. gonorrhoeae* infection (82.8%) and although *C. trachomatis* infection was not as high, almost one-third of participants were positive (31.5%). These findings are similar to the prevalence previously reported among males in

clinical settings (1). The high proportion of double infections (28.1%) as well as the frequent occurrence of either *N. gonorrhoeae* or *C. trachomatis* infection, support the continued treatment of uncomplicated VDS or UDS using a single-dose therapy that targets gonorrhoea, chlamydia and trichomoniasis. This regimen currently consists of a single-dose therapy consisting of 2 g of amoxicillin, 1.25 g amoxicillin-clavunate, 1 g probenecid, 1 g azithromycin and either 2 g tinidazole (men) or 1 g tinidazole twice daily for three days (women) (5).

Given the high prevalence of STIs in PNG, their effective treatment is important for preventing associated and sometimes fatal sequelae, and also as an integral part of stemming the transmission of other important infections like HIV. Although gonorrhoea and chlamydia are easily curable, they continue to be significant STIs in PNG: possibly because the majority of cases are asymptomatic. While regular monitoring of national treatment protocols must continue to be evidence based to ensure effectiveness, the accurate diagnosis and detection of STIs, particularly among those who are asymptomatic, is also crucial to reducing the burden of STIs in PNG (2, 6).

Conclusions

Infection with *N. gonorrhoeae* was very high among males presenting with UDS, providing further evidence of the high burden of gonorrhoea in PNG. It is tempting to attribute treatment failure as the primary driver of this high burden;

however, this study, despite its limitations, does not support such a notion. The current therapy for UDS/VDS/PID seeks to treat gonorrhoea (and other infectious agents), and is based on amoxicillin-clavulanate with probenecid in combination with azithromycin. This treatment is likely to remain effective against *N. gonorrhoeae*. It is vital that gonococcal antimicrobial susceptibility be monitored regularly to guide national treatment protocols, particularly in light of the detection of isolates resistant to amoxicillin-clavulanate in this study. However, other factors that contribute to the high burden of gonococcal disease in PNG need also be considered, such as lack of diagnostics and the high proportion of infections that are asymptomatic.

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