EPIDEMIOLOGY OF LABORATORY CONFIRMED MUCOSAL AND DISSEMINATED GONOCOCCAL INFECTIONS IN SOUTH AFRICA, FROM 2012 – 2021

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DECLARATION

I, Elfrieda Turkson, declare that this Research Report is my own work. It is being submitted for the Degree of Master of Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

Signature:  **Date:** 05/06/2025

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ABSTRACT

Background

Gonorrhoeal disease, caused by *Neisseria gonorrhoeae* is an important sexually transmitted infection (STI). With global guidelines recommending moving from syndromic management to aetiological screening and diagnostic testing of STIs, laboratory identification of gonococcal infection is of importance. Disseminated gonococcal infections (DGI) are well characterized manifestations of gonococcal infections. In South Africa the extent of DGI and the sites involved as well as overall gonococcal infections has not been fully studied or described.

Methods

This study was a retrospective analysis spanning 10 years, utilizing specimen data obtained from the Laboratory Information System (LIS) of the National Health Laboratory Service (NHLS), covering public health facilities across South Africa. Data was obtained on specimens collected from patients who were 15 years and older at both mucosal and disseminated sites and where *N. gonorrhoeae* testing was requested. Human Immunodeficiency Virus (HIV) status of study individuals was determined based on CD4 count and HIV viral load. South African population data for each study year was collected from PopulationPyramid.net for those 15 years and older and this was used to calculate testing rates expressed per 1 000 000 per population. Testing rates were also calculated for each province also expressed per 1 000 000. Median and Interquartile ranges were used to describe the age of those who tested positive for *N. gonorrhoeae*. Frequencies and percentages were used for sex, province, specimen site, location of infection – mucosal vs disseminated, year of specimen collection and HIV status.

Results

4804 samples were sent to the NHLS laboratories for gonococcal testing over the study period. The highest testing rates were recorded in 2019, reaching 19.7 per 1 000 000 population. 2646 samples had valid results and were used to determine the prevalence. The overall prevalence of laboratory confirmed gonococcal infections was 20% over the 10-year period. Highest percentage of cases was noted in 2015 of 76% and lowest in 2012 of 0%. Females accounted for 60% of total gonococcal infections diagnosed. Disseminated gonococcal infection (DGI) rate was 18% of confirmed gonococcal infections with synovial fluid accounting for the main (61%) disseminated

site. 40% of gonococcal cases had laboratory confirmed HIV positive status, of which 38% were mucosal infections and 49% disseminated infections (p=0.048).

Conclusion

Gonococcal infections remain important STIs. There was varied prevalence over the different provinces and across the years with a predominant female occurrence. The most common DGI specimen was synovial fluid which is in keeping with various studies. Due to limitations with culture testing and laboratory reporting, underreporting of the burden of disease is expected and further studies including clinical data or patient records may allow for further determination of missing data and clinical spectrum related to DGI.

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ABBREVIATIONS

AARMs - Academic Affairs and Research Management System

CDC - Centre for Disease Prevention and Control

CDW - Corporate Data Warehouse

CMID - Clinical Microbiology and Infectious Diseases

DGI - Disseminated Gonococcal Infection

ECDC - European Centre for Disease Prevention and Control

FHC - Fitz-Hugh-Curtis

HIV - Human Immunodeficiency Virus

LIS - Laboratory Information System

MALDI-TOF - Matrix-assisted laser desorption/ionization-time of flight

MSM - Men Who Have Sex with Men

MUS - Male Urethritis Syndrome

NAATs - Nucleic Acid Amplification Tests

NHLS - National Health Laboratory Service

SAHCS - South African HIV Clinicians Society

SOPs - Standard Operating Procedures

STD - Sexually Transmitted Disease

STI - Sexually Transmitted Infection

VDS - Vaginal Discharge Syndrome

WHO - World Health Organization

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CHAPTER 1: BACKGROUND

1.1 Introduction

Gonorrhoea is a sexually transmitted infection caused by *Neisseria gonorrhoeae,* a Gram-negative, fastidious diplococcus. Symptomatic infections usually present as urethritis in men and cervicitis with or without vaginal discharge in women (1).

Gonococcal infections often present with distinct symptoms and are grouped into recognizable syndromes, namely Vaginal Discharge Syndrome (VDS) and Male Urethritis Syndrome (MUS). Most gonococcal infections are treated syndromically, however the 2021 WHO STI guidelines recommend that countries move towards pathogen directed therapy after testing (2). In addition, there are specific indications for testing, and these include persistent or unresolving symptoms and to monitor for antimicrobial resistance (3). Gonorrhoeal infection is the second most reported communicable disease in the United States with an estimated incidence of more than 600 000 cases reported annually (4). Locally, in South Africa, prevalence studies of cases of Male Urethritis Syndrome (MUS) and Vaginal Discharge Syndrome (VDS) in females; where the main aetiology is gonorrhoea, were used to provide an estimated prevalence through a modelling exercise (5). As of 2017 there was an overall estimated female prevalence of 6.6% and an estimated male prevalence of 3.5% in the general population (5). In the same year, the estimated incidence (number of new cases) of gonorrhoea among males and females in the general population was 2.2 million and 2.3 million cases respectively (5). Gonococcal infections are usually limited to the mucosal tissues however, disseminated gonococcal infection (DGI) can occur (6).

1.2 Literature Review

According to the World Health Organization (WHO), gonorrhoea remains a significant public health challenge worldwide, with an estimated 82 million new cases among adults aged 15–49 years in 2020 (2). Both prevalence and incidence of gonorrhoea are higher in priority populations such as men who have sex with men (MSM), female sex workers, adolescent girls and young women as well as pregnant women (2). In addition, there are links noted between HIV infection and gonococcal co-infection. A study conducted by Sheung et al. in Kenya followed 466 female sex workers over a five-year period, during which 35 participants acquired HIV. Notably, 17% of those who became HIV positive also had a gonococcal co-infection, highlighting a potential correlation between HIV and gonococcal infections (7).

The European Centre for Disease Prevention and Control (ECDC) noted that between 2013 and 2022, gonorrhoea notification rates steadily increased, reflecting a rising trend in cases(8). Between this time period there were 397 492 confirmed gonorrhoea cases reported with 4.7 cases per 100 000 population in 2013 to 11.2 cases per 100 000 in 2022 (8). However, in 2020, rates sharply declined to 6.9 cases per 100 000 and this was attributed to the COVID-19 pandemic. In 2021, gonorrhoea notifications increased to 7.6 cases per 100 000.By 2022, cases reached a high record of more than 70 000 gonococcal infections reported across the European Union countries with a 48% annual increase, the largest since 2013. This surge underscored the resumption of testing and services post-pandemic, alongside potentially increased transmission rates (8).

In the USA, the CDC reported an 18.6% increase in reported gonorrhoea cases during the 2016 to 2017 year period (9). In 2021,over 700 000 cases of gonorrhoea were reported to the CDC with an overall increased rate of 4.6% during the 2020 to 2021 period (10).

The current laboratory diagnosis is based on culturing and identification of *N. gonorrhoeae*. Specimens are inoculated onto selective and non-selective media that contain required nutrients to facilitate bacterial growth (11). Presumptive identification is done with the aid of gram stain and biochemical tests (11). With the use of biochemical identification tests or automated instruments such as the VITEK 2 (BioMérieux) and MALDI-TOF (BioMérieux), identification is then confirmed (12). *N. gonorrhoeae* is however a fastidious organism so molecular detection using Nucleic Acid Amplification Tests (NAATs) aids in its identification (12).

Culture-based diagnostic methods enable antimicrobial susceptibility testing, providing critical information for targeted treatment more so with increasing antimicrobial resistance. On the other hand, molecular methods are advantageous for non-culturable samples, offering greater sensitivity and specificity for detecting *N. gonorrhoeae* (12).

The South African HIV Clinicians Society's (SAHCS) 2022 guidelines recommend the use of diagnostic tests for screening of STIs (3). This approach aims to reduce the prevalence of STIs and improve the detection of asymptomatic cases that might otherwise have been overlooked under the existing syndromic management system (3). The WHO in their 2021 STI guidelines likewise recommend that diagnostic tests

for aetiological agents and targeted therapy be done for STI cases in settings or countries where this is possible (2).

DGI is a rare but emerging manifestation of *N. gonorrhoeae* infection characterized by extra-mucosal spread leading to variety of conditions including tenosynovitis, migratory polyarthralgia and dermatitis (4). These manifestations are known as arthritis-dermatitis syndrome or can present as purulent arthritis with or without skin lesions (4,13). Rarely does DGI manifest as endocarditis, meningitis and osteomyelitis (14,15).

DGI affects 0.5 to 3 % of persons with gonococcal infections (4,15). The pathogenesis of DGI is dependent on several host as well as pathogen factors. Host factors include recent menstruation, pregnancy, female gender, complement deficiencies, multiple sexual partners, low socio-economic status, HIV infection and intravenous drug use (4).

DGI typically occurs 2-3 weeks after the primary infection and is a result of disseminated bacteraemia (16). Most patients with DGI may not present with urogenital manifestations thus making this rare presentation a challenge in terms of diagnosis (15). A high index of suspicion is therefore required in patients who are sexually active and present with one or more of these symptoms.

A study done in the USA, revealed that joint involvement was a sustained presentation of DGI among their participants (17). There have been various case reports of varied sites of DGI presentation. A case of pyomyositis of the upper limbs complicated by compartment syndrome secondary to DGI in a male patient in the USA (15), to a female with a case of Fitz-Hugh- Curtis (FHC) syndrome in the background of Systemic Lupus Erythematosus (SLE) in Argentina (18). Additional reported cases were of pre-septal cellulitis of a female patient in the USA (19), a case of aortitis complicated by mycotic aneurysm in a middle-aged male from Finland (20) and cases of septic arthritis complicated by osteomyelitis in a male patient in the USA (21).

The current WHO 2024 STI guidelines recommend Ceftriaxone 1g intramuscularly as a single dose for first line treatment of gonococcal infections (22). This change in increasing the dose is due to the rising anti-microbial resistance of *N. gonorrhoeae.*

Symptoms of gonococcal infections can overlap with other STIs hence laboratory testing assists in distinguishing this (3). Gathering laboratory data enables the determination of prevalence and trends, and the characterization of different infection

sites, allowing for national-level analysis through a centralized data warehouse. In addition, South Africa lacks an electronic medical record system, and without research groups specifically gathering data on clinical gonorrhoea cases, there are no alternative sources of data to estimate the disease burden in the country.

The objectives of this study were to describe the epidemiology of gonococcal infections including HIV status of patients, to determine the gonococcal testing rates and to evaluate dissemination sites based on laboratory data.

1.3 Aims and objectives

1.3.1 Aim of the study

To describe the prevalence of laboratory confirmed mucosal and disseminated gonococcal infections and to characterize patient demographics of these infections over a 10-year period from 2012 to 2021 in South Africa.

1.3.2 Study Objectives

1. To describe gonococcal infection testing rates within the NHLS laboratories countrywide
2. To describe the prevalence of laboratory confirmed mucosal and disseminated gonococcal infections in South African public facilities over the 10-year study period
3. To describe the demographic characteristics - age, sex, location and year- of individuals with gonococcal infections including DGI during the study period
4. To determine the dissemination sites that are involved in individuals with DGI
5. To determine the HIV status of individuals with gonococcal infections including DGI

CHAPTER 2: MATERIALS AND METHODS

2.1 Setting

The NHLS provides laboratory services to all public health providers nationwide. Specimens are collected by clinicians based on clinical signs and symptoms and these specimens are sent to the laboratory for testing. Samples are inoculated onto selective and differential media namely the New York City Agar which allows for growth of Neisseria species (12). Colonies are then further tested to provide definitive identification and speciation either with automated or manual methods according to established standard operating procedures (SOPs). Testing in the NHLS is primarily

done through culture-based methods as described. The laboratory request form including data such as patient name, sex, age and sample type and test requested is captured onto the Laboratory Information System (LIS) where the test results are entered. This test information and results are archived in the Corporate Data Warehouse (CDW) and this data was extracted for the study.

2.2 Study design

This is a descriptive study of data from specimens submitted to the NHLS laboratories for gonococcal testing between January 1, 2012, and December 31, 2021. CD4 cell count and HIV Viral load data were obtained for these individuals for whom gonococcal testing was requested during the study period.

2.3 Study population

2.3.1 Inclusion Criteria:

- All individuals above the age of 15 years who had samples sent to the laboratory for *N. gonorrhoea* testing (culturing) during the study period.

2.3.2 Exclusion Criteria:

- All duplicate cultures from the same patient with the same test dates were excluded
- All samples that had an undocumented or unknown age
- All individuals tested as part of surveillance programs

2.4 Ethical considerations

Approval was obtained from the Academic Affairs and Research Management System (AARMs) to obtain data from the CDW. All data was anonymized with no patient identifiers provided. Ethics approval was obtained from the Wits Human Research Ethics Committee (M230151 MED22-08-110)

2.5 Data collection

Data collected and archived from various NHLS laboratories across South Africa over the study period were extracted from CDW. Data on sample types which included genital swabs, eye swabs, throat swabs, blood, tissue, urine, synovial fluid, respiratory samples and cerebrospinal fluid (CSF) was extracted including the province where testing was done. CD4 count and HIV viral load data was extracted for each patient who had gonococcal testing done and were used as markers for HIV infection. Patients

that had no CD4 count and/ or HIV viral load were assigned as laboratory unconfirmed HIV status and those who had these results were categorised as laboratory confirmed HIV positive.

2.6 Data management and analysis

Data was obtained from the CDW in Excel format and cleaned using STATA software (version 18). Descriptive analysis was subsequently conducted. The yearly gonorrhoea testing rates were calculated by dividing the annual number of gonorrhoea test requests by the total population aged 15 years and above for that year. These rates were then expressed per 1 000 000 population. Population estimates were sourced from PopulationPyramid.net (23). Testing rates were also determined per province as number of gonorrhoea tests requested throughout the 10-year period for each province over the estimated population of that province and expressed as rate per 1 000 000 population. Population data for each province was obtained from Statistics South Africa (24).

Median and Interquartile ranges were used to describe age of those who tested positive for *N. gonorrhoeae* while frequencies and percentages were used for sex, province, specimen site, location of infection – mucosal vs disseminated, year of specimen collection and HIV status. Sensitivity analysis was performed to evaluate the impact of samples with unknown results on the prevalence with assumptions that the unknowns were either all positive or all negative. Prevalence of infection was determined as the proportion of positive gonococcal tests over the number of valid gonococcal test results. Prevalence was also determined for each year of the study and per province. There was further categorisation based on age, sex, province, HIV status and location (mucosal vs disseminated). P-values were determined using Chi-Square Test. P-value of ≤ 0.05 was considered statistically significant. Data was analysed using STATA® version18 [Stata Corporation, College Station, Texas]

CHAPTER 3: RESULTS

3.1 Gonorrhoea testing rates

There were 4827 samples that were sent to the NHLS laboratories from January 2012 to December 2021 across the 9 provinces of South Africa for gonococcal testing. Of these, 23 samples had an unknown age (not documented), and these were excluded from the analysis giving a total of 4804 samples that were sent to the laboratories for gonococcal testing. Testing rates were calculated for each year and results showed a general increase in testing rates (**Figure 3.1**) from a rate of 1.24 per 1 000 000 population in 2012 to 12.74 per 1 000 000 population in 2021. The peak year of testing was in 2019 with a testing rate of 19.70 per 1 000 000 population, however in subsequent years from 2020 the rate dropped, but remained above the 2016 rate.

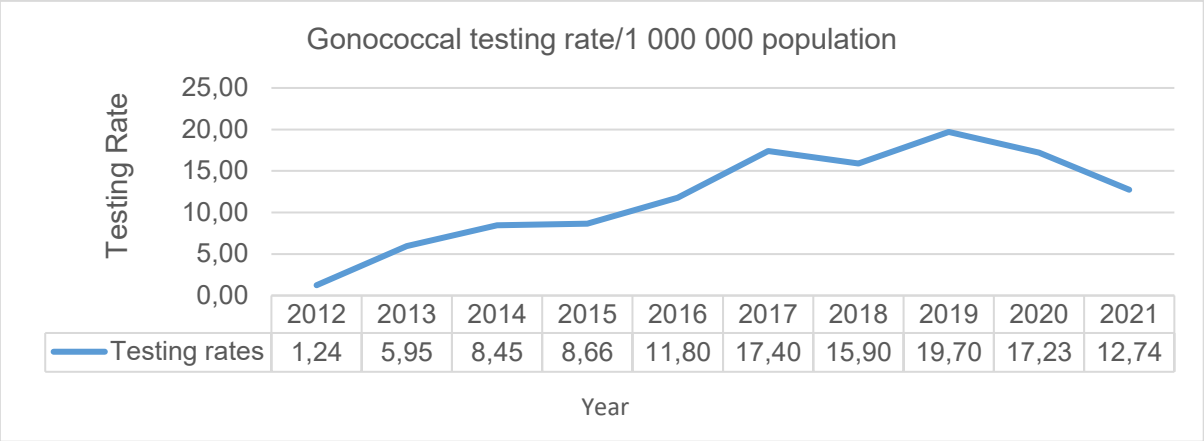


Figure 3.1: Graph showing the gonococcal testing rates per 1 000 000 population from all NHLS laboratories in South Africa from 2012 to 2021

Testing rates were also calculated per province (**Figure 3.2**) and there is wide disparity in gonococcal testing rates with the Free State province having the highest testing rates over the 10-year study period of 435.50 per 1 000 000 population. Gauteng recorded a testing rate of 132.46 tests per 1 000 000 population. Mpumalanga, Northwest and Limpopo recorded the lowest testing rates of 1.22, 0.79 and 0.30 per 1 000 000 population respectively.

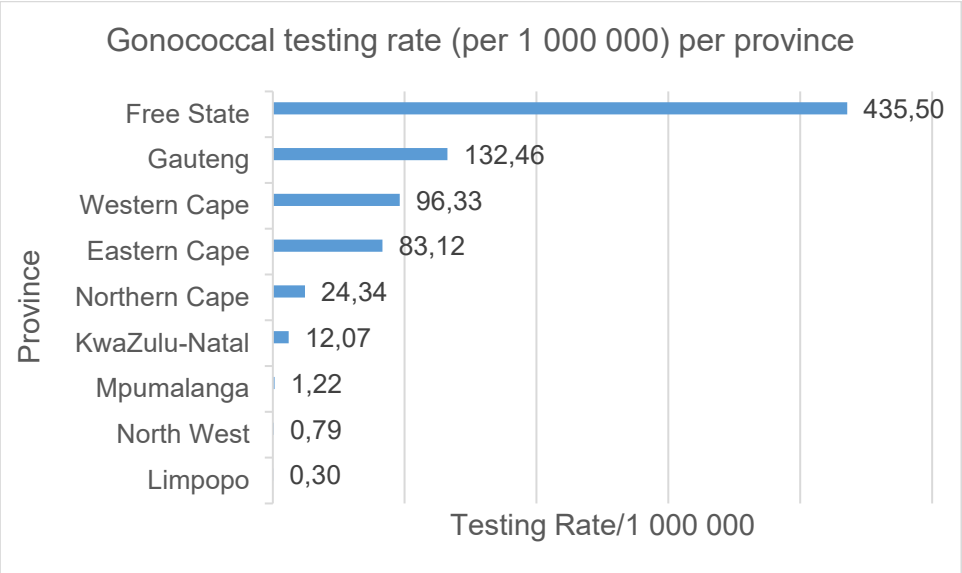


Figure 3.2: Graph showing the gonococcal testing rates per 1 000 000 population from all NHLS laboratories across the 9 provinces in South Africa from 2012 to 2021

3.2 Gonorrhoea prevalence among tested samples

Out of the 4804 samples sent, 532 were positive for *N. gonorrhoea*. There were 2114 negative samples (44%) and 2152 (44.8%) samples that results were unknown. These unknown samples had gonorrhoea testing requested but further information regarding results was not documented or accessible from the CDW due to either incomplete, or lack of information entered on growth or culture results. From the sensitivity analysis (**Table 3.1**) a prevalence of 56% would be expected assuming all unknowns were positive and assuming all the unknowns were negative, prevalence would be 11%. Excluding cases with unknown results and focusing on valid gonococcal test results, it was assumed that the prevalence among those with known and unknown results would be comparable. Under this assumption, the overall prevalence of laboratory-confirmed gonococcal infections was determined to be 20% over the 10-year study period. The unknown samples were distributed throughout all the years of the study and across the different provinces and laboratories. There were 6 (0.1%) isolates that were not tested due to either incorrect sample type sent or samples that had mixed growth and were unable to do further testing for. This resulted in a total of 2646 valid testing results which were used to determine prevalence of infection. The prevalence per year is depicted in **Figure 3.3.**

Table 3.1: Sensitivity Analysis - effect of assumptions of unknown samples on laboratory confirmed gonococcal infections from 2012-2021

Results Scenario	Prevalence (%)
Valid test results	20
Assume all unknowns are positive	56
Assume all unknowns are negative	11

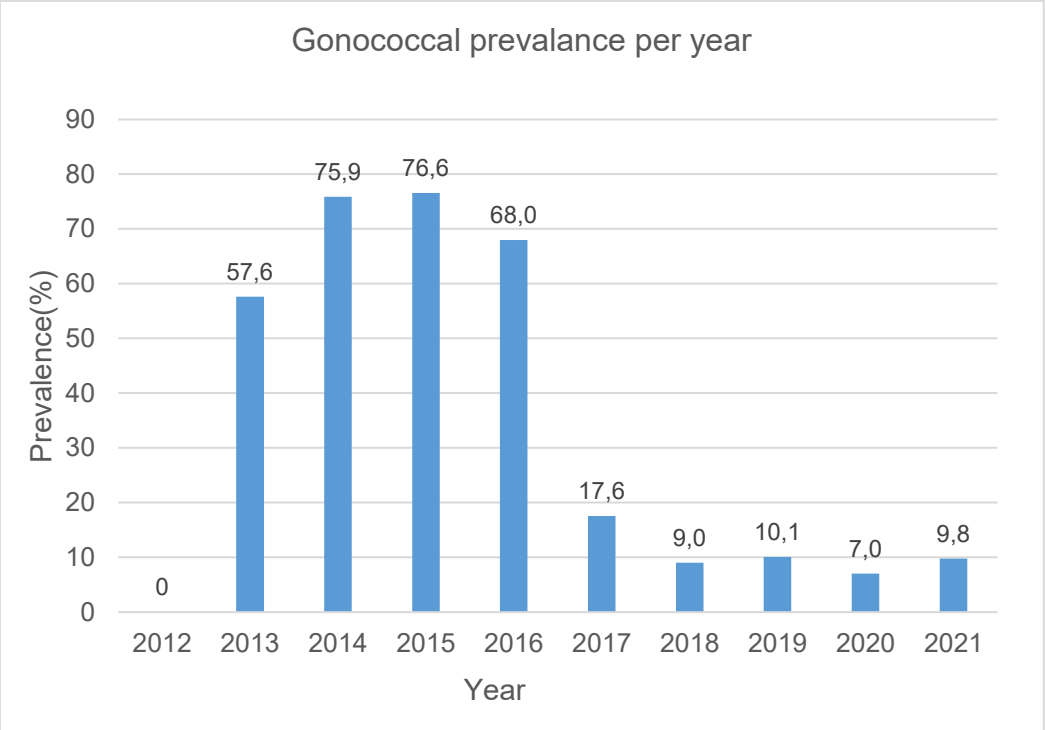


Figure 3.3: Graph showing the Prevalence of Laboratory Confirmed Gonococcal infections per year from 2012 to 2021

The years with the highest prevalence were from 2013 to 2016 with the highest being in 2015 at 76.6%. From 2017 to 2021, prevalence remained less than 20% throughout these years and the lowest prevalence was in 2012 of 0%.

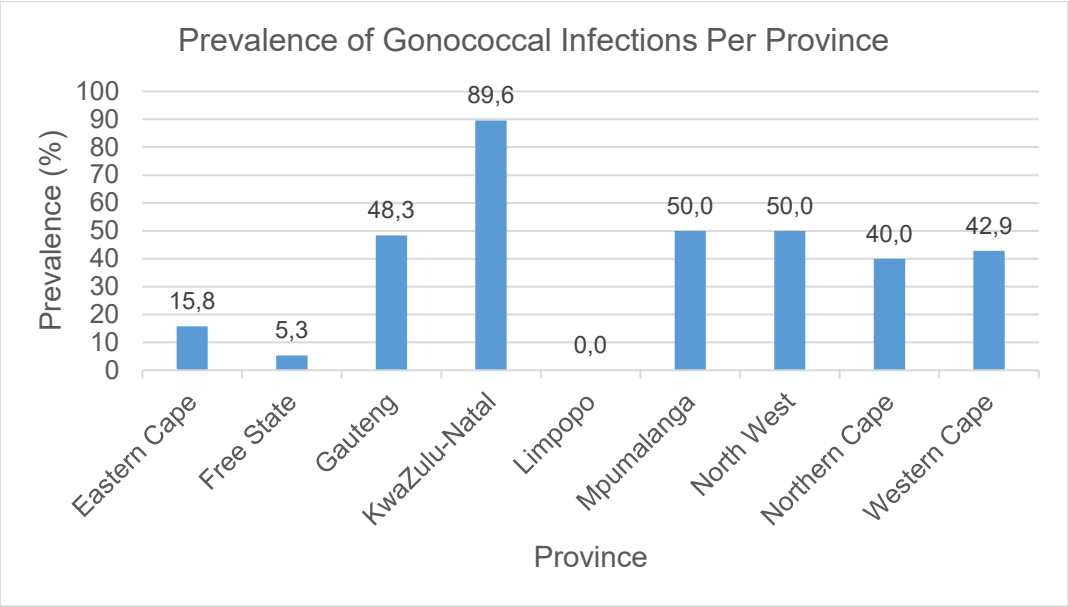


Figure 3.4: Graph showing the prevalence of laboratory confirmed gonococcal infections for each of the provinces over the study period

Figure 3.4 illustrates provincial prevalence of gonococcal infections. KwaZulu-Natal demonstrated the highest prevalence of 89.6% of gonococcal infections, notably markedly higher than the other provinces. Mpumalanga, North West, Gauteng, Northern Cape and Western Cape showed a prevalence in the 40-50% ranges. Limpopo had the lowest prevalence at 0%.

3.3 Demographic and clinical characteristics of gonococcal cases

The demographics of the cases identified are tabulated in **Table 3.2**. From the 532 positive cases, the median age was 29 years, interquartile range of 24-35 years. Of the 532 cases, 347 (65.23%) were females, 178 (33.46%) were males and 7 (1.32%) had unknown/undocumented gender.

Table 3.2: Demographic and clinical characteristics of individuals with laboratory confirmed gonococcal infections from 2012 -2021

		Median (Inter Quartile Range)	
Age in years		29 (24-35)	
		Number	**%**
Age Group (years)	15-25	180	33.83
	26-35	223	41.92
	36-49	103	19.36
	≥ 50	26	4.89
Sex	Males	178	33.46
	Females	347	65.23
	Unknown	7	1.32
Provinces	Eastern Cape	89	16.73
	Free State	74	13.91
	Gauteng	129	24.25
	KwaZulu Natal	120	22.56
	Mpumalanga	1	0.19
	Northern Cape	4	0.75
	North West	1	0.19
	Western Cape	114	21.43
	Limpopo	0	0
Specimen type	Blood	31	5.83
	Mucosal	434	81.58
	Synovial Fluid	60	11.28
	Tissue	7	1.32
HIV status	Laboratory Confirmed	215	40.41
	[1]Laboratory Unconfirmed	317	59.59

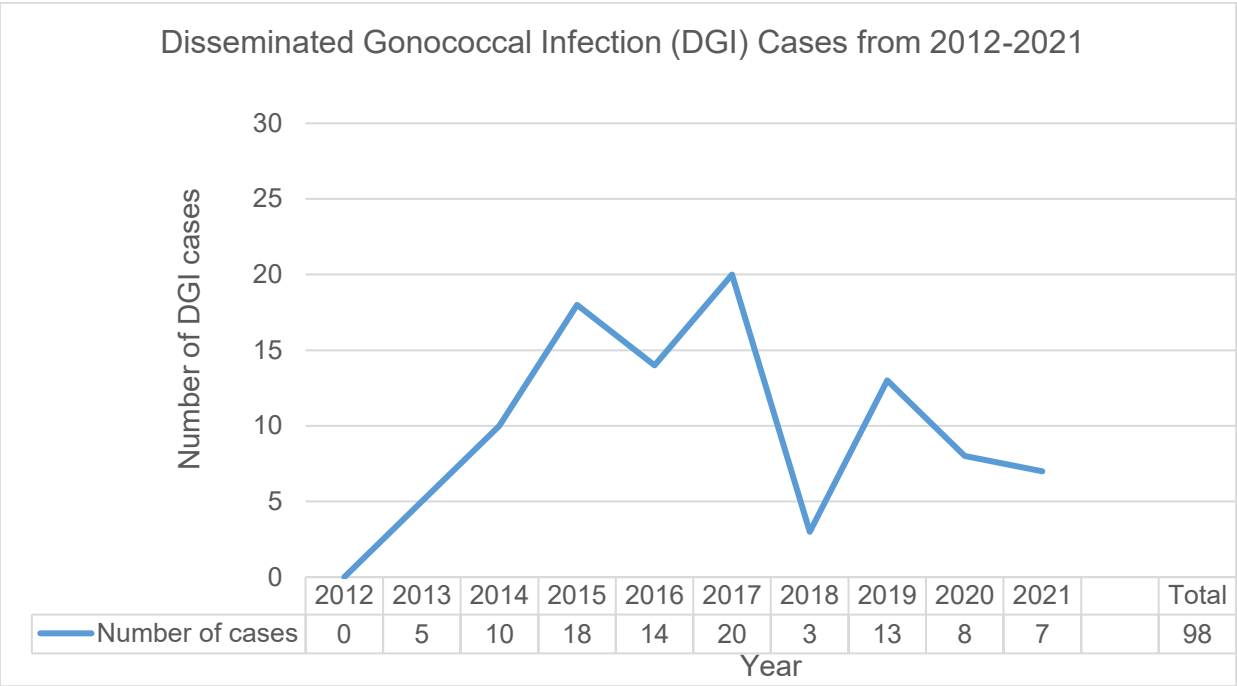
[1] Laboratory confirmed: CD4 count and HIV viral load data available
Laboratory unconfirmed: No CD4 and HIV viral load data available

In terms of provinces, the top three provinces that had the most laboratory confirmed gonococcal infections were Gauteng (24.25%), KwaZulu Natal (22.56%) and Western Cape (21.43%). Mpumalanga, Northern Cape, Northwest and Limpopo reported low cases of less than 1% each.

3.4 Disseminated gonococcal infections

Majority of laboratory confirmed cases were from mucosal specimen types, 434 (81.58%) which were obtained from the genital area, urine, eyes and pharynx. The remaining laboratory confirmed cases were detected from specimens which were categorized as disseminated and accounted for 98 of total laboratory confirmed cases. This gave a DGI rate of 18.42% of laboratory confirmed gonococcal infections. These specimens from which disseminated cases were detected consisted of synovial fluid 60/98 (61.22%), blood 31/98 (31.63%) and tissue 7/98 (7.14%).

Figure 3.4 shows the trend of disseminated gonococcal infections over the duration of the study period. There was an initial increase in cases from 2012 to a peak of 20 DGI cases in 2017. In 2018, the number of laboratory confirmed DGI cases markedly dropped to 3 cases.



	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021		Total
Number of cases	0	5	10	18	14	20	3	13	8	7		98

Figure 3.4: Graph showing the number of Laboratory Confirmed Disseminated Gonococcal infections per year from 2012 to 2021

Table 3.3: Demographics of Laboratory Confirmed Mucosal and Disseminated Gonococcal Infections

	Category	Mucosal (N=434) n (%)	Disseminated (N=98) n (%)	P-value
Age group	15-25	155 (35.71)	25 (25.51)	0.078
	26-35	182 (41.94)	41 (41.84)	
	36-49	80 (18.43)	23 (23.47)	
	≥ 50	17 (3.92)	6 (6.12)	
Sex	Males	148 (34.10)	32 (32.65)	0.568
	Females	282 (64.98)	64 (65.31)	
	Unknown	4 (0.92)	2 (2.04)	
HIV status	Laboratory confirmed	167 (38.48)	48 (48.98)	0.048
	Laboratory unconfirmed	267 (61.52)	50 (51.02)	
Total		434 (100)	98 (100)	

Table 3.3 categorizes mucosal and disseminated infections according to demographics and HIV status. In both mucosal and disseminated infections, the highest number of cases were between the ages of 25-35, accounting for 41.94% and 41.84% respectively. However, there was no statistical difference (p=0.078) among the age groups for mucosal infection versus DGI. In both the mucosal and disseminated cases, females accounted numerically for majority of the cases with 64.98% and 65.31% respectively compared to males who had 34.10% and 32.65% respectively, although there was no statistical difference (p=0.568) between the sex groups when looking at dissemination.

Total patients with gonococcal infections who had laboratory confirmed HIV status were 215 making up 40% of patients. With disseminated gonococcal infections, laboratory confirmed HIV positive patients accounted for 48.98% of cases as compared to 38.48% among those with mucosal gonococcal infections (p-value 0.048).

CHAPTER 4: DISCUSSION

In this retrospective study of *N. gonorrhoea* testing by culture within public sector laboratories during the period 2012- 2021 we found i) low but increasing testing rates for gonococcal infections, ii) decreasing prevalence of gonococcal infections over the years with variability in prevalence over the 9 provinces of South Africa iii) Majority of cases affect young adults and females iv) Synovial fluid was the most common site for DGI and there was an association with HIV status and DGI with higher HIV positivity among those with DGI.

Gonorrhoea testing rates

The gonorrhoea testing rates within the NHLS had increased from 2012 peaking in 2019 and remaining higher than 2016 levels. This could be attributable to increased awareness of STIs and high index of suspicion for complicated cases. There has been a noted increase in gonococcal resistance rates globally (2,5,8) and this could further explain the increase in testing rates as part of susceptibility testing of *N. gonorrhoea* isolated (10,25). Of note is the decline in the testing rates from 2019 and this could be attributed to the COVID-19 pandemic with reduced health seeking behaviour and as a result reduced testing during that period (26).

Prevalence of gonorrhoea

There was an overall prevalence of 20% of laboratory confirmed infections over the 10-year study period. Based on individual prevalence per year, increasing prevalence from 2012 to a peak in 2015 of 76.6% was illustrated. This high prevalence may indicate highly targeted testing during these years where there was a high likelihood that patients tested had gonococcal infection. The increasing trend during this time period has been demonstrated in other studies globally, from surveillance studies in Canada (25) and in the United States of America from the CDC Sexually Transmitted Diseases (STDs) surveillance data of 2018 and 2021 (9,10). Reasons given by these international studies were better detection of infection through molecular methods which would not necessarily be applicable in this study as all isolates were identified using culture-based methods. From 2017, there were significantly lower prevalences than the prior years and the low prevalence in 2020 would again be attributed to the COVID-19 pandemic (26). According to the CDC, in their review of sexually transmitted diseases surveillance 2020, there was reduced screening of STIs and redirection of funds towards the pandemic that resulted in disrupted STI prevention and

underreporting of cases (10,26). In our analysis, the years with the lowest testing rates coincided with the times when the highest prevalence of infections was recorded except for 2012 which had the lowest testing rate of 1.24 per 1 000 000 and a prevalence of 0%. The inverse is also noted with the later years of study where testing rates were higher, but prevalence was lower. In 2015, the national STI guidelines were formally revised and of note was a change in the management of MUS and VDS which are commonly associated with *N. gonorrhoea*e infection (27). This change was the use of Ceftriaxone as first line instead of Cefixime due to the increasing development of resistance of *N. gonorrhoea* (27). This could explain the high burden of disease in the earlier years of the study pre-revision of guidelines.

Profile of patients with gonococcal infections

The median age of individuals with gonococcal infections was 29 years. This indicates that most cases were among young adults, a group that is often at higher risk for STIs (25). There was a female predominance with a M:F ratio of 1:2 and this is varied from different studies where they noted the reverse with a male predominance (9,25,28) and the reasons noted in these studies was an increase in MSM. In our study the possible reasons could be attributed to possibly better health seeking behaviours in the female group. Additionally biological factors such as female anatomy and hormonal changes make females more susceptible to STIs (28). In analysis of mucosal versus DGI, female cases for both mucosal and DGI were almost twice the number noted in males, and this was expected as females had majority of gonococcal infections compared to males, however this difference was not statistically significant (p-value= 0.568).

Gauteng, Kwazulu-Natal and Western Cape were the provinces with the highest proportion of detected gonococcal cases making up more than 60% of cases. In terms of the testing rates for these 3 provinces, they had rates of between 80 to over 100 per 1 000 000 population, second only to the Free State with a testing rate of more than 400 per 1 000 000 population.

KwaZulu-Natal had the highest provincial prevalence of almost 90% and yet one of the lowest testing rates and this could indicate a more targeted testing approach, a higher burden of disease in the province or better isolation of *N. gonorrhoea* and more robust reporting methods of positive results onto the LIS.

In contrast, the Free state province had the highest testing rate of all the provinces but the second lowest gonococcal infection prevalence of 5.3%. Possible reasons could

be that testing was conducted on individuals who may not have had clinical features or presentation suggestive of gonococcal infection, hence the high testing rates but lower prevalence, a low burden of disease in the province, inadequate laboratory testing methods to isolate *N. gonorrhoeae* or poor or inappropriate reporting of positive gonococcal results onto the LIS.

Limpopo, Northern Cape, Northwest and Mpumalanga, all had <1% of positive cases. Consistently Limpopo had the lowest testing rate and the lowest prevalence Underreporting due to limited access to healthcare services or lower population density may be the main causes of these findings (24).

Disseminated gonococcal infections

More than 80% of specimens were mucosal and this reflects that most gonococcal infections present as localized mucosal infections (1,21,29). Disseminated infections, which accounted for 18% of cases, involved specimens from synovial fluid, blood and tissue. This DGI rate is notably higher than what has been estimated in previous studies (4,15,30) of 0.5-3% and the likely explanation for this high DGI rate in our setting is the postulation that the study focused on laboratory-confirmed cases, in which testing would have been done in patients who were unwell or who would have presented with complicated or disseminated disease. The high number of synovial fluid samples noted is consistent with one of the main presentations of DGI; septic or purulent arthritis and joint involvement being a sustained DGI presentation (15,29,30). With regards to the tissue samples, the exact locations of tissue sample collection or the type of tissue sample sent was not elucidated due to this information not being available from the data received. This information would be beneficial as studies have shown DGI presenting with skin lesions, pyomyositis and endocarditis or cardiac manifestations (13,15,29). Specific data of type of tissue received could guide extent of DGI. Further studies could investigate these from clinical data to ascertain the tissue types and characterise the extent of DGI.

The finding that 40% of patients with gonococcal infections had a laboratory-confirmed HIV positive status aligns with previous research that shows an association between HIV and STIs. In this study, women who were HIV infected were more likely to acquire *N. gonorrhoeae* (adj. HR, 2.29; 95% CI, 1.47-3.56) compared with HIV-uninfected women (28). Additionally, gonococcal infections can increase the susceptibility to HIV

transmission due to mucosal disruption and inflammation, which enhances viral acquisition and replication (31).

The distribution of laboratory confirmed HIV status (49%) among DGI patients compared to those with mucosal infections (38%) (p=0.048) was statistically significant (p-value <0.05) suggesting a potential association between HIV infection and the occurrence of DGI. Studies have shown that HIV can modify the immune response, potentially affecting the clinical presentation and severity of gonococcal infections (31,32).

4.2 Limitations

There was a significant amount of incomplete or missing data from the LIS system that was not entered in relation to certain patient demographics and specimen type. And this was evidenced by the number of unknown cases that had to be excluded from further analysis. Exclusion of these specimens may have impacted on the trends reported and this may possibly have led to an over or under estimation of prevalence and dissemination rates.

Furthermore, there was a change in the LIS platform that occurred which coincided with the study period and there was possible loss of data or inability to fully extract all data from the old platform, further attributing to incomplete or missing data.

This study likely under-estimated the epidemiology of gonococcal infections as data is only representing cases who presented to a public health facility and in whom samples were collected for microbiological assessment. It does not account for the patients that were managed syndromically.

Data obtained of *N. gonorrhoeae* isolation was solely culture-based which is less sensitive than nucleic acid amplification tests (11,12) and there may have been missed infections due to non-culturable cases.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

The study demonstrated low but increasing prevalence of gonococcal infections across the years and with varying prevalence across the different provinces of the country. There remains a higher prevalence in females and in the young adults. Disseminated gonococcal infections predominantly involve synovial fluid as the most frequently reported specimen site in keeping with the common clinical presentation of DGI. There is an association between HIV infection and gonococcal infection as well as DGI.

We recommend incorporation of molecular based test results where available to increase yield of laboratory confirmed cases due to the limitations in culture-based diagnostic methods. In addition, the use of clinical data or collection of patient records will aid in determination of more accurate prevalence due to the current syndromic management where not all patients have diagnostics done but will have clinical features suggestive of gonococcal infection. Clinical data will also aid in further categorisation of DGI based on clinical syndrome.

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CHAPTER 7: APPENDICES

Appendix A Protocol

University of the Witwatersrand

Faculty of Health Sciences

(School of Pathology; Clinical Microbiology & Infectious Diseases)

TITLE:

EPIDEMIOLOGY OF LABORATORY CONFIRMED MUCOSAL AND DISSEMINATED GONOCOCCAL INFECTIONS IN SOUTH AFRICA, FROM 2012 - 2021

For the degree MMed

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List of Acronyms

MUS - Male Urethritis Syndrome

DGI - Disseminated Gonococcal Infection

HIV - Human Immunodeficiency Virus

API-NH - Analytical Profile Index- *Neisseria* and *Haemophilus*

MALDI-TOF - Matrix-assisted laser desorption/ionization-time of flight

SAHCS- South African HIV Clinicians Society

WHO- World Health Organization

ECDC - European Centre for Disease Prevention and Control

STI - Sexually Transmitted Infection

MSM - Men Who Have Sex with Men

FHC - Fitz-Hugh-Curtis

NHLS - National Health Laboratory Service

LIS - Laboratory Information System

CDW - Corporate Data Warehouse

CHBAH- Chris Hani Baragwanath Academic Hospital

AARMs - Academic Affairs and Research Management System

CMID - Clinical Microbiology and Infectious Diseases

1. Summary

Gonorrhoeal disease, caused by *Neisseria gonorrhoea* is an important sexually transmitted infection (STI). With guidelines recommending moving from syndromic management to aetiological screening and diagnostic testing of STIs, laboratory identification of gonococcal infection is of importance. Gonococcal infection at extra-genital sites is well documented. There are a number of risk factors associated with disseminated spread of infection and disseminated gonococcal infection (DGI) is considered a common cause of arthralgia and arthritis. In South Africa the extent of DGI and the sites involved as well as overall gonococcal infections has not been fully studied or described. Therefore, this study will aim to describe the epidemiology of laboratory confirmed gonococcal infections and DGI in terms of patient demographics and to characterize sites of infection involved in DGI. This study will be a 10-year retrospective study looking at data obtained from the NHLS LIS from public health facilities across South Africa. Data obtained will include all sites both genital and extra-genital sites which isolated *N. gonorrhoea* from patients who are 15 years and older and data will also be collected on HIV status of individuals based on CD4 count and HIV viral load. Prevalence of gonococcal infection and DGI will be assessed including characteristics related to age, sex, HIV status and clinical sites involved. The possible limitation of this study is incomplete data obtained from various facilities captured onto the LIS.

2. Introduction

Gonorrhoea is a sexually transmitted disease caused by *Neisseria gonorrhoea,* a gram-negative, fastidious diplococcus. Symptomatic infections usually present as urethritis in men and cervicitis with or without vaginal discharge in women (1)

Gonorrhoeal infection is the second most reported communicable disease in the United States with an estimated incidence of more than 600 000 cases reported annually (2). Locally, in South Africa, cases of Male Urethritis Syndrome (MUS); where the main aetiology is gonorrhoea, were used to provide an estimated prevalence. Data was obtained from previous studies of eligible population of adults from 15 years of age for both males and females. As of 2017 there was an overall estimated female prevalence of 6.6% and estimated male prevalence of 3.5% in the general population (3) In the same year, the estimated incidence of gonorrhoea (number of new cases) among men and women in the general population was estimated to be 2.2 million and 2.3 million cases respectively (3) Both prevalence and incidence of gonorrhoea are higher in priority populations such as men who have sex with men (MSM), female sex workers, adolescent girls and young women as well as pregnant women (4).

Gonococcal infections are usually limited to the mucosal tissues but can lead to disseminated gonococcal infection (DGI) (5). The postulated pathogenesis is immune complex mediated however direct infection of the synovium of joints also occurs. (6). DGI is a rare but emerging manifestation characterized by tenosynovitis, migratory polyarthralgia and dermatitis known as arthritis-dermatitis syndrome or presents as purulent arthritis with or without skin lesions (2). The typical rash seen is described as macular-papular in nature and affecting the torso, lower limbs and the

palms of the hand and soles of the feet (7). Rarely does DGI manifest as endocarditis, meningitis and osteomyelitis (8)

DGI affects 1-3 % of persons with gonococcal infection (2). The

pathogenesis of DGI is dependent on several host as well as pathogen factors. Host factors include recent menstruation, pregnancy, female gender, complement deficiencies, multiple sexual partners, low socio-economic status, HIV infection and intravenous drug use (2). Furthermore, there are some features of certain *N. gonorrhoea* species that would make them more prone to cause disseminated disease including those lacking protein II, and those with arginine-hypoxanthine-uracil strains (9).

DGI typically occurs 2-3 weeks after the primary infection and is a result of disseminated bacteraemia (10). Most patients with DGI may not present with urogenital manifestations thus making this rare presentation a challenge in terms of diagnosis (11). A high index of suspicion is therefore required in patients who are sexually active and present with one or more of these symptoms.

The current laboratory diagnosis is based on culturing and identification of *N. gonorrhoea*. Specimens are inoculated onto non-selective and selective agar and presumptive identification is done with the aid of gram stain and biochemical tests. Confirmatory Identification is then made either with API-NH or automated machines such as the VITEK and MALDI-TOF. *N. gonorrhoea* is however a fastidious organism so molecular detection using Nucleic Acid Tests aids in its identification (12).

The South African HIV Clinicians Society (SAHCS) has 2022 guidelines where they provide guide on screening of STI using diagnostic tests which they noted would

assist in reducing prevalence of STIs and detecting asymptomatic patients that would otherwise have been missed using the current syndromic screening STI management system (13). The WHO in their 2021 STI guidelines, recommend that diagnostic tests for aetiological agents and targeted therapy be done for STI cases in settings or countries where this is possible (14). It is therefore valuable to determine the laboratory identified *N. gonorrhoea* cases and assessing the characteristics in terms of specimens sent and determining prevalence based on laboratory data.

A multi-centre retrospective study done in the USA over a 34-year period from 1975 to 2008 looked at the clinical presentation and treatment response of 112 women with DGI at Parkland Memorial Hospital (15). They cohorted patients into pregnant and non-pregnant with confirmed (laboratory diagnosed) DGI or probable with clinical features suggestive of DGI. They reviewed patient medical records. The different specimen types which were analysed included blood, skin lesions, synovial fluid, cervix, rectum and pharyngeal samples. Joint involvement was a sustained presentation in almost all the women in the study with 26% of joint aspirate samples having bacteriologically confirmed *N. gonorrhoea*. They concluded that the prevalence of DGI is on a decline from just over 300 cases per 100 000 women in the mid-1980s to just under 150 cases per 100 000 women in 2008. In the study the reasons as to the decline in these cases was not discussed but they did note that the decline was consistent with decline in infections in the general population in the USA during this same time period from data obtained from the Centres for Disease Control and Prevention. They however concluded that DGI is still an important disease to have a high index of suspicion in patients. Of note, this study only included women and even though they are noted to have more prevalent disease

than in men it would be important to assess both genders to ascertain overall prevalence in that hospital of study.

Birrell et al, 2019, performed a retrospective study in Australia where they looked at the burden of DGI in certain areas in Australia. They identified cases that fit the criteria for DGI over an 8-year period between January 2010 to September 2018 using hospital records and their notifiable disease database. They looked at various sites including blood, synovial fluid, skin and tissue samples. In this study, of the 7540 laboratory-confirmed gonococcal infections identified, 97 were noted to have involved disseminated sites and 10% of septic arthritis cases in this study were caused by gonococcal infection (16).

A study was done in France where they looked at the epidemiology, clinical and microbiological as well as treatment outcomes of DGI over a 3-year period from 2009-2011(17). In this study 20 cultures from 21 patients were identified to have *N. gonorrhoea* and specimens included blood, synovial fluid, pharynx, genital sites and urine. They concluded that during this study period there was an increase in cases from 2 in 2009 to 10 cases by 2011. The increased trend was consistent with data from the European Centre for Disease Prevention and Control (ECDC) on sexually transmitted infections (STIs) in Europe from 2008 to 2012, and they reported a 62% increase in the rate of gonorrhoea cases (18). In the report they attributed the increase to improved diagnosis of gonorrhoea in men particularly Men who have sex with Men (MSM).

Aside from these studies, there have been various case reports of varied sites of DGI presentation. Cases of pyomyositis complicated by compartment syndrome secondary to DGI (11), to cases of Fitz-Hugh-Curtis (FHC) syndrome (19). Others

reported cases of pre-septal cellulitis (20) a case of aortitis complicated by mycotic aneurysm (21) and cases of septic arthritis complicated by osteomyelitis (22). This highlights that the scope of DGI is vast, and dissemination can and may involve almost any tissue or organ.

In the setting of South Africa there is paucity of data and studies characterizing the occurrence and demographics of DGI and various sites reported of DGI and gonococcal infections as a whole. There has not been a study done that provides a descriptive analysis of DGI in South Africa.

Therefore, this study aims to review the epidemiology of laboratory confirmed Gonococcal infections including DGI in South Africa determining the prevalence and patient demographics over a 10-year period.

3. Aims and objectives

3.1 Aim of the study

To describe the prevalence of laboratory confirmed mucosal and disseminated gonococcal infections in South Africa and to characterize patient demographics of mucosal and disseminated gonococcal infections over a 10-year period from 2012 to 2021

3.2 Study Objectives

1. To Describe gonococcal infection testing rates within the NHLS
2. To describe the prevalence of mucosal and disseminated gonococcal infections in South African public facilities over the 10-year study period

3. To describe the demographics in relation to age, sex, location and year of individuals with gonococcal infections including DGI during the study period at public health facilities in South Africa
4. To determine the HIV status of individuals with gonococcal infections including DGI in public health facilities in South Africa during the study period
5. To determine the extra-genital sites that are involved in individuals with DGI during the study period in public health facilities in South Africa

4. Methods

4.1 Setting

The National Health Laboratory Service (NHLS) provides laboratory services to all public health providers nationwide. Specimens are collected by clinicians based on clinical signs and symptoms and these specimens are sent to the laboratory for testing. Information on the laboratory request form regarding patient name, sex, age and sample type and test requested is captured onto the Laboratory Information System (LIS) where the test results are entered. The test information is archived in the Corporate Data Warehouse (CDW) and this data can be extracted for research purposes.

4.2 Design

This study will be a cross sectional study based on retrospective analysis of laboratory data obtained from the NHLS LIS from a period of January 2012 to December 2021 across various laboratories in South Africa.

4.3 Population

Inclusion Criteria:

All individuals above the age of 15 years who had *N. gonorrhoea* detected from both genital and extra-genital specimens during the study period

All samples that were sent to the laboratory for *N. gonorrhoea* testing (culturing) during the study period

Exclusion Criteria:

All duplicate cultures from the same patient within the same presentation period will be excluded

All individuals tested as part of surveillance programs

4.4 Data collection procedures

Data on all samples where *N. gonorrhoea* testing was requested from both genital and extra-genital sites will be extracted. Data extracted will include age and sex of individuals where available of all specimens where *N. gonorrhoea* was requested or culturing and identification. Data will also be extracted on the specimen types or sites such as blood, fluid, tissue and pus and swabs where *N. gonorrhoea* was detected. CD4 count and HIV viral load data will be extracted as markers for HIV infection. Request will be obtained from the Academic Affairs and Research Management System (AARMs) to obtain data from the CDW. All data will be anonymized.

4.5 Sample size

Based on previous literature, the estimated prevalence of DGI from those who had gonococcal infection is between 1-3% (2). At Chris Hani Baragwaneth Academic Hospital (CHBAH), there were an estimated 200 samples received for *N. gonorrhoea* testing in this past year. Looking at the other 13 major laboratories in the country,

assuming similar testing rates as CHBAH, an estimated total of about 29000 samples over a 10-year period would have been sent for *N. gonorrhoea* testing

4.6 Data analysis

Descriptive analysis will be used to describe gonorrhoea testing rates as well demographic and clinical characteristics of individuals included. Mean with standard deviation will be used for continuous variables such as age while frequencies and percentages will be used for categorical data obtained such as sex, location of specimen collection – facility and province, specimen type, location of infection suspected – mucosal vs disseminated, year of specimen collection and HIV status. Overall gonorrhoea testing rate will be determined as number of gonorrhoea tests requested each year divided by the total population and presented as tests / 100 000 population. Prevalence of infection will be determined as the proportion of gonorrhoea test that are positive and will be determined by age, sex, province, HIV status and type of specimen (mucosal vs disseminated). Prevalence will also be determined for each year and trend analysis will be made for each year throughout the study period. Data will be analysed using STATA® software. If appropriate univariable and multivariable logistic regression will be used to determine the factors associated with DGI as opposed to mucosal infection and the observed data will be presented as odds ratios with 95% confidence intervals.

5. Ethical considerations

Ethics approval will be obtained from the Wits Human Research Ethics Committee. Data will be anonymized such that privacy of patient's personal information will be protected. Approval for the collection of data from the NHLS will be obtained through the AARMs

6. Timing

	Sept 2021	Oct 2021	Nov 2021	December 2021	June 2022	July 2022	August 2022	September 2022	October 2022	November 2022	December 2022	January 2023
Literature Review:												
Protocol Write up												
Protocol Assessment												
Ethics Application:												
Data collection:												
Data Analysis:												
Write up:												

7. Funding

Stationary and photocopying costs will be funded by the department of Clinical Microbiology and Infectious Diseases (CMID)- estimated cost of paper and printing- R700.

8. Anticipated Problems/ Limitations

1. Incomplete or missing data from the LIS system that may not have been entered in relation to certain patient demographics and specimen type.

2. The statistics may be an under-estimate of the epidemiology as data is representing only those who presented to a public health facility and in whom samples were collected for microbiological assessment.

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Appendix B Ethics Clearance Certificate

M230151 MED22-08-110

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Elfrieda Turkson

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M230151 MED22-08-110

NAME: (Principal Investigator)	Dr Elfrieda Turkson
DEPARTMENT:	School of Pathology Department Microbiology National Health Laboratory Service (NHLS)
PROJECT TITLE:	Epidemiology of laboratory confirmed mucosal and disseminated gonococcal infections in South Africa, from 2012 -2021
DATE CONSIDERED:	27/01/2023
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr T kufa-Chakezha and Dr M Kolojane

APPROVED BY: CB Penny

Dr C Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 27/06/2023 **EXPIRY DATE:** 27/06/2028

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report** in January each year until study is closed. Failure to submit annual report will result in ethics clearance certificate suspension. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in January and will therefore be due in the month of January each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical). Upload signed copy of this ethics clearance certificate prior to commencing with the study hrec-medical.researchoffice@wits.ac.za

03/07/2023

Appendix C Plagiarism/Turn-it-in Report

Turnitinreport 0701951D-1.docx

ORIGINALITY REPORT

6%	7%	10%	7%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	bmchealthservres.biomedcentral.com Internet Source	1%
2	emedicine.medscape.com Internet Source	1%
3	www.emdocs.net Internet Source	1%
4	researchspace.ukzn.ac.za Internet Source	1%
5	eprints.ucm.es Internet Source	1%
6	journals.plos.org Internet Source	1%
7	Donald E Greydanus, Maria Demma Cabral, Dilip R. Patel. "Pelvic inflammatory disease in the adolescent and young adult: An update", Disease-a-Month, 2021 Publication	1%
8	www.cdc.gov Internet Source	1%

Appendix D AARMS data request approval

Academic Affairs and Research
1 Modderfontein Road, Sandringham, 2031
Tel: +27 (0)11 555 0367/0406
Email: babatyi.kgokong@nhls.ac.za
academic.research@nhls.ac.za
Web: www.nhls.ac.za

29 March 2023

Applicant: Elfrieda Turkson
Institution: NHLS
E-mail Address: elfrieda.turkson@nhls.ac.za
Tel: 011 386 0434 **Cell:** 072 749 6982

Project Title: EPIDEMIOLOGY OF LABORATORY CONFIRMED MUCOSAL AND DISSEMINATED GONOCOCCAL INFECTIONS IN SOUTH AFRICA, FROM 2012 - 2021
Reference Number: PR2340020

Research Application Type(s):
1. Request for Data

RE: APPROVAL LETTER: REQUEST TO ACCESS NHLS RESOURCES FOR RESEARCH PURPOSES

This letter serves to advise that the application requesting permission to conduct the above-mentioned research using the listed NHLS resources has been reviewed and **"Approved"**. Please note that the approval is granted on the condition that you comply with the NHLS Research Material and Data Access Policy and requirements stated below.

1. All material and data requested shall be used as per the research protocol submitted to the NHLS and as approved by the relevant Health Research Ethics Committee (HREC) in South Africa.
2. Access to the NHLS material and/or data shall be limited to the minimum required for successful completion of the approved study and shall be made available ***without patient names and other patient identifiers (including, but not limited to, national identity numbers, hospital/clinic file numbers, addresses and telephone numbers)***.
3. Confidentiality shall be maintained at the participant and institutional level and there shall be no disclosure of personal information or confidential information.
4. Data and/or material shall not be shared with other parties unless approved by the NHLS
5. The material and/or data obtained from the NHLS shall be anonymised and not, for any reason, be used to track or recruit patients as no pre-approval/consent is obtained from patients.
6. Processes shall be discussed with the relevant NHLS departments (i.e. Corporate Data Warehouse (CDW), NHLS Laboratory Management, Operations Office, etc.) and agreed upon.
7. Any amendments to the study requirements, including the use of the material and/or data for purposes not initially disclosed to the NHLS) shall be cleared by an approved HREC and submitted to the NHLS for approval via the AARMS system – https://aarms.nhls.ac.za.
8. The NHLS shall be acknowledged as a source of material and/or data in any output, such as abstracts and journal articles, emanating from the project.
9. A final report of the research study and any published output resulting from this study shall be submitted to the NHLS via AARMS

Please note that this letter constitutes approval by the NHLS Academic Affairs and Research Office. The NHLS entities tasked with providing the material and/data may have additional requirements for access. Data related queries may be directed to NHLS CDW, email: zarina.sabat@nhls.ac.za; contact number: 011 386 6074 and sample related queries (if applicable) shall be directed to the relevant business manager.

Dr Babatyi Malope-Kgokong
National Manager: Academic Affairs and Research

Appendix E AARMS data request form

FORM

Title :	Access to data from CDW FMI0069
Document Number:	FMI0069
Version number :	7

(Changes from previous version highlighed)

Written by :	Zarina Sabat
Checked by :	Maanda Mudau
Approved :	Ephraim Mashaba

Active date : 18-12-2019

Date of next review	Date reviewed	Reviewed by	Action
18-12-2020			

Date withdrawn .....

Q-Pulse5/docs/active/FMI0069v7

NATIONAL HEALTH LABORATORY SERVICE

NATIONAL HEALTH LABORATORY SERVICE HELPDESK
Tel : (011) 386-6125/6/7/9 Fax : (011) 386-6308 email : helpdesk6@nhls.ac.za
ACESS TO DATA FROM CDW FMI0069

NATIONAL HEALTH LABORATORY SERVICE

NATIONAL HEALTH LABORATORY SERVICE HELPDESK
Tel : (011) 386-6125/6/7/9 Fax : (011) 386-6308 email : helpdesk6@nhls.ac.za

ACESS TO DATA FROM CDW FMI0069

Each application will be approved or rejected subject to the ability to extract this data and availability of the data, and subject to the intended usage of the requested data. Applications that are incomplete and/or do not contain supporting documentation, will be rejected.

APPLICANT DETAILS			
Applicant's Name and Surname	Dr. Elfrieda Turkson	**Title**	Dr.
Telephone Number	0113860434	**Cell Phone Number**	0727496982
Email Adress	elfrieda.turkson@nhls.ac.za		
Business Role/Designation		**Name of Laboractory/ Department/External Organisation**	
Supervisor/Manager Name and Surname		**Telephone Number**	
Supervisor/Manager Designation		**Email Adress**	

TERMS AND CONDITIONS

Data/Information is not to be used in contravention of Section 14, 15, 16, and 17 of the National Health Act 61 of 2004 and the Promotions of Access to information Act 2 of 2000 and the Protection of Personal Information (POPI) Act, 2013.

The applicant undertakes to ensure that the data supplied to it by the NHLS is used ethically and solely for the purposes for which it is provided as detailed in this application, and further acknowledges that it shall remain liable for any breaches of this clause by the end user.

If the purpose for the data requested in this application is for research, ethics approval and the full protocol must be attached to this application form. It is the responsibility of the applicant to obtain Ethics clearance from their regional human research ethics committe. to access the requested NHLS data.

The applicant undertakes to the NHLS data in a confidential manner by separating patient identifying details from laboratory data and storing the master list that links patient identifying details to study patient identifiers in a separate, secure location

The applicant undertakes to provide the Academic Affairs and Research office at the NHLS with a copy of any report ,

ACCEPTANCE OF CONDITIONS

By signing this document the requestor and supervisor/Manager accept the terms and conditions as stated above.

Submitted by	Dr. Elfrieda Turkson	**AARMS Submission Date**	09-01-2023
Reviewed by (Supervisor)		**AARMS Submission Date**	20-01-2023

In the event of a dispute concerning this doccument, the electric version stored on Q-Pulse will be deemed to be the correct version

NATIONAL HEALTH LABORATORY SERVICE

NATIONAL HEALTH LABORATORY SERVICE HELPDESK
Tel : (011) 386-6125/6/7/9 Fax : (011) 386-6308 email : helpdesk6@nhls.ac.za

ACESS TO DATA FROM CDW FMI0069

Note: All fields in this section must be completed

DATA REQUEST DETAILS					
Request Type	New	**Data Format**	Excel	**Data Delivery**	Email
Frequency of Extract	Once	**Repeat Frequency**			

DESCRIPTION OF REQUIRED DATA EXTRACT	
Overview of Data required	all samples that were sent to the laboratory for Neisseria gonorrhoea testing or identification - patient details including age, sex - date of specimen collection - sample type - clinical diagnosis - site/laboratory where sample processed - results of the test- organism identified and if present or not CD4 counts and Viral loads of all
Region For data extract e.g (Provice, Laboractory or Facility)	Province: Select All BusinessUnit: All Lab: All
Date range of extract (Period for which data is required)	01-01-2012 **To** 31-12-2021
Fields required (e.g. Test code or method, Episode number, etc.)	**Test Code** / **Test Name** M155 AUTOMATED CULTURE M260 CULTURE ID BACTERIAL M161 CULTURE PUS M156 CULTURE FOR CSF M163 CULTURE RESP/SPUTUM M160 CULTURE STERILE SITES M162 CULTURE TISSUE M157 CULTURE URINE M164 MANUAL BLOOD CULTURE M935 MICROBIOLOGY TESTS REQUESTED V065 HIV VIRAL LOAD H065 CD4 ARV

NATIONAL HEALTH LABORATORY SERVICE

NATIONAL HEALTH LABORATORY SERVICE HELPDESK
Tel : (011) 386-6125/6/7/9 Fax : (011) 386-6308 email : helpdesk6@nhls.ac.za

ACESS TO DATA FROM CDW FMI0069

ADDITIONAL INFORMATION
De-duplication of data requested

DESCRIPTION OF INTENDED USE OF DATA EXTRACT (e.g. research, epidemiology study, cost analysis of service, drug effectiveness, disease surveillance
For research purposes

LIST WHO WILL HAVE ACCESS TO THIS DATA

PROJECT NAME AND REGISTRATION NUMBER (If data is required for a registered research project. Please attach the Ethics Approval and Full Protocol.)	
Registration Number:	PR2340020
Project Name:	EPIDEMIOLOGY OF LABORATORY CONFIRMED MUCOSAL AND DISSEMINATED GONOCOCCAL INFECTIONS IN SOUTH AFRICA, FROM 2012 - 2021

NATIONAL HEALTH LABORATORY SERVICE

NATIONAL HEALTH LABORATORY SERVICE HELPDESK
Tel : (011) 386-6125/6/7/9 Fax : (011) 386-6308 email : helpdesk6@nhls.ac.za

ACESS TO DATA FROM CDW FMI0069

NHLS RESPONSIBILITIES
The NHLS will: **Ascerain if it is possible to extract the required data.** **Register the application and issue a registration number.** **Only release the requested data to the aoolicant whose name is specified on this application form.**
After this application has been completed and approved, please raise a service request with the NHLS IT service Desk (Contact Number: (011) 386-612/6/7/9): **Send an email to helpdesk6@nhls.ac.za,** **Scan this application form and attach it to the email, or fax it to (011) 386-6308**

FOR OFFICE USE					
APPROVAL BY RESEARCH OFFICE (Research data requests only)					
Check List	☐ Data Request reviewed by Supervisor ☐ Ethics Approval attached ☐ Research Protocol Attached				
Recommended by: Manager - Academic Affairs and Research	Dr. Babatyi Malope-Kgokong	**Signature**	eAARMS	**AARMS Submission Date**	23-03-2023
Approved by: Executive Manager: Academic Affairs, Research and Quality Assurance	Prof. Koleka Mlisana	**Signature**	eAARMS	**AARMS Submission Date**	31-03-2023
Endorsed by: Chief Executuve Officer	Dr. Kamy Chetty	**Signature**	eAARMS	**AARMS Submission Date**	
Actioned by : CDW Manager		**Signature**		**Date**	
APPROVAL BY CDW (Non research requests only)					
Approved by : CDW Manager		**Signature**		**Date**	

In the event of a dispute concerning this doccument, the electric version stored on Q-Pulse will be deemed to be the correct version