Neisseria gonorrhoaea Infections in Africa - Systematic Review and Meta-Analysis

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Received 24 April 2020 Accepted 28 June 2020

Introduction

Neisseria gonorrhoeae is a Gram-negative Coffee-bean shaped intracellular diplococcus bacterium [1,2] responsible for all gonococcal infections and an exclusively human pathogen that primarily infect the urogenital tracts. If untreated, may lead mild to serious complications such as epididymitis, pelvic inflammatory diseases, opthalmia neonatorum [3-6]. Neisseria gonorrhoeae infections are acquired by sexual contact and usually affect the mucous membranes of the urethra in males and the endocervix and urethra in females [7-10]. In 2016, the World Health Organization (WHO) [11] reported the rate of new N. gonorrhoeae infections to be at 19 per 1000 women and 24 per 1000 men globally. This suggesting the exposure of over 75 million individuals to the infection every year [12] and the African region has the highest rates of gonococcal infections worldwide [13]. In view of this, this paper sought to review the prevalence of Neisseria gonorrhoeae infections with focus on African countries. Gonorrhoea is transmitted through close sexual contacts with an infected individual. Factors such as gender and age may increase the susceptibility to gonorrhea. The rate of gonococcal infections is higher in female than male and also highest among adolescents and young adults at reproductive age [14].

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ABSTRACT

Objective: Despite the classification of Neisseria gonorrhoeae as a 'super bug' by WHO due to the problem of antimicrobial resistance in gonorrhoea treatment globally. This study assesses recent publications on the prevalence of *Neisseria gonorrhoeae* infections in Africa. **Methods:** Systematic review of publications on *Neisseria gonorrhoea* infections in Africa was done in this study. Five databases; PubMed, Plos One, African Journals, ScienceDirect and google scholar were searched from 2000 to 2020. A total of 41 articles were included considering; authors, years of publication, location, study population among other factors

Results: A total of 200 articles were identified from the search engines and only 41 finally passed the eligibility criteria. A total of 15734 participants were screened in the studies from which 1250 only had *Neisseria gonor-rhoeae* infections. The incidence/1000 male subjects infected with *N. gonorrhoeae* was lower compared to the female. In Nigeria, Ethiopia and Ghana higher prevalence was observed among men compared to women. Highest prevalence was found among age group 21-25 years. Altogether 7.9% of subjects (n = 15,734) were positive for *N. gonorrhoeae*. Polymerase chain reaction (PCR) detection method was commonest (n =16) followed by unspecified general nucleic acid amplification assays (n = 11).

Conclusions: Considering the global rate of antibiotics resistance in *Neisseria gonorrhoeae* efforts must be geared towards regional based gonorrhoea control in Africa and elsewhere. Molecular based gold standard techniques complemented with culture where necessary must be adopted for gonorrhoea diagnosis and resistance surveillance.

KEY WORDS:

Neisseria gonorrhoeae Meta-analysis Antibiotics resistance Africa

The effective management of infection with *Neisseria gonorrhoeae* is a challenge in the face of increasing antimicrobial resistance. Gonococcal resistance to antimicrobial agents is a major problem globally.

The resistance of *Neisseria gonorrhoeae* to antimicrobial agents varies in different parts of the world and also changes per time [1,4,15]. *Neisseria gonorrhoeae* exhibits a remarkable ability to adapt to antibiotic pressure through generation of resistance mechanisms. *Neisseria gonor*-

rhoeae has become resistant to almost every antibiotic used for the treatment of its infections [16] which has led to difficulties in clearance treatment because several strains of gonococcus that exhibit resistance to many antibiotics have been discovered. Africa has the highest incidence of gonococcal infections in the world, with an estimated 50–60 new infections per 1000 adults per year. *Neisseria gonorrhoeae* infection may have wide spectrum of symptoms that can affect urogenital, anorectal, pharyngeal, and conjunctiva areas though it can be asymptomatic [17-19].

The proposed systematic review aims to characterize comprehensively the epidemiology of *Neisseria gonor-rhoeae* infections in African countries. The specific objectives are to conduct a systematic review and synthesis of evidence of *N. gonorrhoeae* infections prevalence, and to generate estimates for the prevalence of *N. gonorrhoeae* among the populations, as well as stratified by WHO region, type of assay, sex and populations involved.

Materials and Methods

Search Strategy

A systematic review for the publications on *Neisseria* gonorrhoeae infections in African countries was done in September 2019. The period included for this search was from the year 2000 to 2020 and a standardized protocol was followed. The literature search was done using Pub-Med, Plos One, African Journals, ScienceDirect and google scholar for identification of all published papers on gonococcal infections within the year stated above. The search terms used include the name of locations, 'gonococcus', 'gonococci', 'gonorrhoeae', 'gonorrhoea', 'Neisseria gonorrhoeae infections', 'urethritis', 'opthalmia neonatorum', 'gonococcal conjunctivitis', 'gonococcal infections', and all results were reviewed for relevance. Data were extracted from reports in accordance to inclusion and exclusion criteria

Inclusion and exclusion criteria

Studies included are those that are *Neisseria gonorrhoea* infection within African countries between year 2000 and 2020. While 'articles' that came inform of letters and commentaries, articles are reporting infections outside African countries, not written in English Language and not featured between year 2000 and 2020 were excluded

from the study.

Study Selection and Data Collection Process

Articles were screened to identify duplicates, and then later screened to identify studies for full text evaluation. The full texts were assessed for eligibility, exclusions were made based on exclusion and inclusion criteria. A manual method of data extraction was used for the data extraction. Thirty-seven articles were included in the systematic review and analysis of infections of *Neisseria gonorrhoeae*. The following information was collected: authors, year of publication, country where the study had been carried out, study population, detection method, total number of participants infected, range of age of the participants, total number of study participants, and gender of participants, detection method, total number of participants infected (Figure 1).

Figure 1. Identification of studies included in the review.



Statistical Analysis

Studies based on the overall sample were reported in a table format along with key information pertaining to each study. Distribution includes total number of participants, articles and total number of infected persons were reviewed; population distributions, age distribution and the prevalence of infections in Africa. The 95 % confidence intervals was calculated using GraphPad InStat.

Results

A total of 200 articles were identified from the search engines and 41 articles finally passed the eligibility criteria. From Table 1, the incidence/1000 male subjects infected with *N. gonorrhoeae* was lesser to the female. Only Nigeria, Ethiopia, and Ghana recorded high prevalence of the infection among men (Figure 2).

Figure 2. A map showing the countries in Africa from which the data were collected.



Table 2 shows the prevalence of infections and age range of participants in the study. Some of the journals did not report the age range of participants.

The infection has a high prevalence among youth of age between 21 and 25 years, followed by subjects within 26 years and 30 years and those in the age range between 15 and 20 years.

Table 3 showed the total distributions of infection per country based. A total of 15734 participants were screened in the studies from which 1250 only had *Neisseria gonor-rhoeae* infections. The distribution of the country from where the studies were carries out was also shown in Table 3. The highest number of articles were collected South Africa (n=8) followed by Nigeria (n=7) and Ghana (n=6). Ethiopia and Kenya have 4 and 3 reports respectively.

Countries	Gender	Total screened	Total positive	Incidence/ 1000
Kenya	M	2895	9	3.11
	Г	801	15	18.73
Ghana	М	539	173	320.97
	F	2540	108	42.52
Ethiopia	М	274	17	62.04
-	F	633	26	41.07
Nigeria	М	777	61	78.51
	F	2091	87	41.61
Zambia	М	NS	NS	
	F	116	43	370.69
Zimbabwe	М	NS	NS	
	F	200	48	240
South Africa	Μ	2639	156	59.11
	F	856	220	257.01
Guinea	М	NS	NS	
	F	237	9	37.97
Benin	М	NS	NS	
	F	81	1	12.35
Burkina Faso	М	NS	NS	
	F	367	13	35.42
Mali	М	NS	NS	
	F	114	5	43.86
Cameroon	М	40	40	1000
	F	39	39	1000
Tunisia	М	NS	NS	
	F	188	21	111.70
Central African	М	28	28	1000
Republic	F	2	2	1000
Sudan	М	NS	NS	
	F	151	3	19.87
Madagascar	M	95	95	1000
-	F	31	31	1000
Total	M	7287	579	79.46
	F	8447	671	79.44

Table 1. Prevalence of Neisseria gonorrhoeae infections

in Africa

Table 2. Age distributions of sampled individual.

Age (years)	N = 7244	Prevalence %	Confidence (95 %) Lower	Interval Upper
15 - 20	1206	16.65		
21 - 25	2581	35.63		
26 - 30	1724	23.80	280.67	2134.0
31 – 35	1160	16.01		
36 - 40	437	6.03		
>40	136	1.88		

Guinea and Burkina Faso have 2 reports each while one report each came from Zambia, Zimbabwe, Benin, Mali, Cameroon, Central African Republic, Sudan, Tunisia, and Madagascar. Incidence of infection was reported higher in participants from Ghana while the lowest was from Benin. Table 4 showed where the studies were conducted.

Countries	Appear- ance	Total sam-	Total infect-	Inci- dence/1000
	2	pled	ed	6.40
Kenya	3	3696	24	6.49
Ghana	6	3079	281	91.26
Ethiopia	4	907	43	47.41
Nigeria	7	2868	148	51.60
Zambia	1	116	43	370.69
Zimbabwe	1	200	48	240
South	8	3495	376	107.58
Africa				
Guinea	2	237	9	37.97
Benin	1	81	1	12.35
Burkina	2	367	13	35.42
Faso				
Mali	1	114	5	43.86
Cameroon	1	79	79	1000
Central	1	30	30	1000
Republic				
of Africa				
Sudan	1	151	3	19.87
Tunisia	1	188	21	111.70
Madagas-	1	126	126	1000
car				
Total	41	15734	1250	79.45

Table 3. Total distributions of infection per countrybased.

Table 4. Location of the data and distribution of Neisseria gonorrhoeae infections.

Location	No of	Total no of	Total	Incidence/
	articles	investigated	infected	1000
Community	13	3498	124	35.45
School	3	1143	68	59.49
Hospital	25	11093	1087	97.99
Total	41	15734	1250	79.45

The studies were bases community, school, and hospital. Hospital have the highest number of persons investigated. Some of the reports did not specifically stated the base of the investigation. Table 5 showed the detection method used for identification of the causative agent.

Table 5. Detection method used for identification of organism.

Detection method	Appearance
Culture	14
Nucleic Acid Amplification Test	11
Microscopy	9
Gene probe and Rapid Card Test	2
Polymerase Chain Reaction	16
Transcription Mediated Amplification	6
Strand Displacement and Amplification	2

Discussion

In the data collected, different diagnostic tests were used and populations tested and the test were carried out in different bases. All these factors did not give room for direct comparison of the prevalence of the infection among the nation from which data were drawn. The incidence/1000 male subjects infected with *N. gonorrhoeae* was lower that of the female. This may be due to the nature of the genitourinary tract of females which may have increased their susceptibility to the pathogen. Mengista *et al.* [20] recently reported a prevalence of 5.1 % for gonococcal infection among reproductive age group of women Ethiopia and about 2-15 % in sub-Sahara Africa. The prevalence was lower compared to Southern Mozambique [21].

The incidence of gonorrhea infection among male and female were the same. This is higher on the side of the male because women have been reported to be more vulnerable to the infections than men [8,22]. In most cases gonorrhea infections in women are in most times asymptomatic and the infections are most times not treated due to economic dependency of most African women on their husbands [7].

In this study, it was observed that the infection has a high prevalence among subjects within ages of 21 through 25 years. This range was higher than the range reported by Galadima *et al.* [23]. They reported highest gonorrhoea prevalence of 16 % (n = 1715) for people age group 15 – 20 years. The highest reported prevalence in this study was 35.63 % which is higher than those reported by Alli *et al.* [24] and Ramadhani *et al.* [19] with 25 % and 19.5 % (96/492) respectively.

A total of 15734 participants were screened in the studies from which 1250 only had *Neisseria gonorrhoeae* infections. This account for 7.94 % of prevalence in the study area. Due to economic factors and also lack of appropriate diagnostic facilities and manpower the prevalence of gonorrhoea in Africa has not been adequately captured [25-27. There is still a large reservoir of gonorrhoea in most of the African countries [28].

The data from this study extracted from studies conducted in community, school, and hospital. Hospital have the highest number of persons investigated. Some of the reports did not specifically stated the base of the investigations. Availability of affordable and reproducible rapid screening point of care tests (POCTs) that have high sensitivities and specificities are very adequate for resourcenations [29]. These are mostly immunepoor chromatographic tests which require minimal scientific personnel expertise and laboratory facilities. Cultural detection in biological fluids is the technique in use by most Microbiology laboratories and has been regarded as the gold standard test for gonorrhoea diagnosis [30,31]. Most of the point of care tests used in Africa are mainly immunochromatographic tests which require minimal scientific personnel expertise and laboratory facilities with sensitivities ranging between 60 to 98 % and specificities ranging between 90 to 98 % [29]. Polymerase chain reaction (PCR) is a tool for the diagnosis of infectious, it is fast and reliable that other methods. This method (PCR) should be made mandatory in the clinical diagnoses of gonorrhea.

Conflict of Interest

We declare that we have no conflict of interest.

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