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Original Research Article

Ocular Chlamydia Trachomatis Prevalence in Jamaica

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ABSTRACT

Objectives: To determine the prevalence of ocular *Chlamydia trachomatis* infections among patients with infectious conjunctivitis and assess the Trachoma spectrum manifestations in Jamaica.
Method: Cross-sectional sampling of suspect cases of person's aged ≥1 month, was conducted over a 4 month period at 3 health care facilities. Patients with conjunctivitis were recruited and conjunctival swabs were collected. Molecular detection with extraction of DNA from conjunctival swabs using Sacace™ Chlamydia trachomatis DNA-Sorb-A (REF K-1-1/A) was done. Amplification and qualitative detection was performed using the Sacace™ Chlamydia trachomatis Real-TM assay. Samples were tested for the presence of other bacterial pathogens using standard microbiological protocols.
Results: Seventy eight eye swabs were collected. Female to male distribution was 52.9% and 47.1% respectively. Of the 78 cases, 34 were randomly tested by PCR for the presence of Chlamydia. PCR Chlamydia tests were positive in 11.8% (4/34). Gram positive bacteria (GPB) and gram-negative bacteria (GNB) were detected in 55.1% (43/78) of cases. Of these 60.5% (26/43) were GPB and 32.6% (14/43) were GNB. Mixed infections (GPB and GNB) accounted for 7% (3/43) of cases. Coagulase-negative staphylococci (CoNS) was the most commonly detected organism in 41.8% (18/43) of cases. *Pseudomonas aeruginosa*, most frequently detected GNB was in 35.7% (5/14) of cases.
Conclusion: The prevalence of *Chlamydia trachomatis* infection was 11.8% amongst chronic conjunctivitis. Jamaica is in accordance with the World Health Organization Ultimate Intervention Goals for blinding trachoma elimination status. Monitoring and laboratory detection of ocular *Chlamydia trachomatis* needs to be continued.

Keywords: *Chlamydia trachomatis, conjunctivitis, trachoma, Jamaica*

INTRODUCTION

Ocular *Chlamydia trachomatis* infections continue to be of public health concern in developing countries. Although there has been a reduction in the global prevalence of the end spectrum of this disease known as blinding trachoma, it remains as one of the leading neglected infectious causes of blindness in 1.8 million persons and is endemic in 51 countries. [1-3] *Chlamydia trachomatis* eye infections can present initially with foreign body sensation, keratoconjunctivitis and a moderately

mucoid discharge, then progress to scarring, corneal opacity and blindness.

It is one of the priority diseases of the Global Initiative Vision 2020, of the World Health Organization (WHO) and the International Agency for the Prevention of Blindness. [1] The WHO has been actively working to reduce Ocular Chlamydia trachomatis by implementing the Alliance for the Global Elimination of Blinding Trachoma by 2020 (GET 2020) protocol which uses the SAFE Strategy; Surgery, Antibiotics, Facial cleaning and Environmental improvement. [4] The last reported prevalence of *Chlamydia trachomatis* eye infections in Jamaica was in 1967, when the prevalence of *Chlamydia trachomatis* among school children in the rural areas of Jamaica was 11.9%. [5]

In countries which have reported a Trachoma free status, ongoing surveillance and evaluation is important in maintaining and preventing re-emergence. The aim of this study was to determine the frequency of ocular *Chlamydia trachomatis* infections amongst patients with infectious conjunctivitis and to re-evaluate the status of Trachoma manifestation spectrum in Jamaica.

METHODOLOGY

A cross-sectional sampling of suspect cases of person's aged 1 month and older over a period of 4 months was conducted at the three selected health care facilities (HCF). Samples were systematically collected along with corresponding data by trained health care workers using the WHO Guidelines for Trachoma. A proposed sample size of 79 was determined for the study duration based on a national average report of 4,500 conjunctivitis cases per year, an assumed prevalence of less than 0.08, a confidence level of 95% and detection sensitivity and specificity each of 0.9%. [6,7] Inclusion criteria included all patients aged 1 month of age or greater, presenting with clinical signs of chronic conjunctivitis. Exclusion criteria were patients younger than 1 month of age, patients with non-ocular acute or chronic systemic infections.

Sample collection and laboratory methodology

Patients were assessed by the attending Ophthalmologists at the UHWI for evidence of conjunctivitis, folliculitis, and signs of Trachoma using the WHO Simplified Grading Scheme. [2,8] Following standard procedures, sterile swabs were rolled three times across the tarsal plate to obtain a specimen. Conjunctival swabs were placed in Chlamydia Transport Media for storage and transport. Samples were processed immediately after collection and stored at 2–8 °C for no longer than 24 hours, or stored at –20/80°C for durations greater than 24hours. In addition to testing for the presence of Chlamydia, samples were tested for the presence of other bacterial pathogens using standard microbiological protocols.

Study Setting

All specimens were sent to the Microbiology Laboratory at the University of the West Indies (UWI) from two tertiary HCF and one secondary HCF in Kingston, the capital and largest city of Jamaica. These HCFs included: The University Hospital of the West Indies (UHWI), which serves an immediate population of ~96,052 in addition to wider population of 555,828 in St. Andrew, an adjacent geographic region. The socio-demographic profile of the population served by this hospital is diverse, ranging from the affluent to the very poor and homeless; located in close proximity to the UHWI is The Foundation for International Self Help Development (FISH Clinic). This clinic is a non-profit organization which offers ophthalmology services in addition to other medical services. In contrast to the UHWI, this clinic is a secondary HCF whose population although diverse has an increased number of patients of the lower socio-demographic profile; The study also included the government laboratory, the National Public Health Laboratory. This laboratory participated in the study as a center for referral of patient samples from 73 health

care sentinel sites within all 14 parishes of Jamaica.

Chlamydia trachomatis detection

Molecular detection included the extraction of DNA from conjunctival swabs using Sacace™ Chlamydia trachomatis DNA-Sorb-A (REF K-1-1/A). Amplification and qualitative detection was performed using the Sacace™ Chlamydia trachomatis Real-TM assay. This assay is an in vitro nucleic acid amplification test for qualitative detection of Chlamydia trachomatis DNA using broad based primers which detect all serovars by means of real-time hybridization-fluorescence detection. A Ct value of <30 was considered as positive. DNA from samples positive for Chlamydia trachomatis was re-extracted from the original specimen using the QIAamp DNA Mini Kit (Qiagen) and further purified for analysis by sequencing for identification of the specific Chlamydia strain (serovar). Data was analyzed using the Statistical Package of Social Science (SPSS) version 17.

Ethical approval was obtained through the University Hospital of the West Indies, University of the West Indies, Faculty of Medical Sciences (UHWI/UWI/FMS) Ethics Committee. Approval was also obtained from the administration of UHWI and The Foundation for International Self Help Development (FISH) Medical Clinic and the Ministry of Health, National Public Health Laboratory.

RESULTS

A total of 78 eye swabs were submitted for investigation with a female to male distribution of 52.9% and 47.1% respectively. Forty three (43/78, 55.1%) cases were submitted from the UHWI and FISH Health Centre and 44.9% were submitted from sentinel sites in the 14 parishes. Ten (10) cases were omitted from the age analysis as the date of birth could not be confirmed. Children <1yr comprised 76.5%, (52/68) and represented the majority of cases included in the study.

Laboratory investigations for other bacterial pathogens were performed on all 78 cases. Gram positive bacteria (GPB) and Gram-negative bacteria (GNB) were detected in 55.1% (43/78) of cases, Gram positive bacteria in 60.5% (26/43), Gram negative bacteria in 32.56% (14/43) and no pathogens or negative growth was documented in 41.0% (32/78). Mixed infections with GPB and GNB were detected in 7% (3/43) of cases. Among positive isolates, coagulase-negative staphylococci (CoNS) were detected in 41.8% (18/43), followed by *Staphylococcus aureus* in 18.6% (8/43) and Streptococcus species in 18.6% (8/43). The most frequently detected Gram negative bacteria included *Pseudomonas aeruginosa* in 35.7% (5/14) followed by Enterobacter species in 28.6% (4/14) and *Haemophilus influenza* in 14.3% (2/14). Bacterial co-infections with Gram positive and Gram-negative pathogens were documented in 7% (3/43) of cases, and 7% (3/43) of cases had more than 3 bacterial pathogens isolated.

Of the 78 cases, 34 were randomly selected for PCR testing for the presence of Chlamydia. The majority of the patients were <10 years old (Figure 1). Samples tested by PCR were positive for Chlamydia in 11.8% (4/34). Of these, 75% of patients positive for Chlamydia were in the <1year age group.

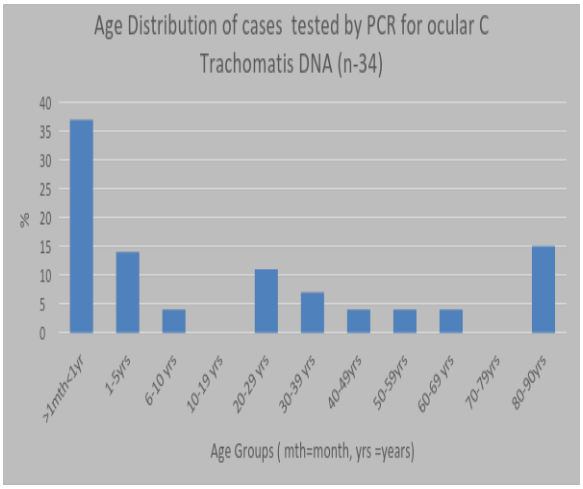

Figure 1: Frequency of Age groups tested by PCR for ocular C trachomatis

Co-infection of one Chlamydia positive case with *Staphylococcus aureus* was detected, however on further analysis Chlamydia positive cases were not associated with bacterial co-infections and were more likely to be associated with a negative bacterial culture (χ^2= 31, p=0.0005). Due to budget limitations the identification of specific Chlamydia serovars (strains) by sequencing was not performed.

Further analysis showed a significant association between cases with conjunctivitis and the detection of Chlamydia trachomatis DNA (χ^2, 8.23, p=0.041). Chlamydia DNA was detected in one of the two cases in which follicular conjunctivitis was documented (Figure 2a and 2b). There were no cases of trachomatous lid scarring nor corneal opacification associated with the chronic conjunctivitis.

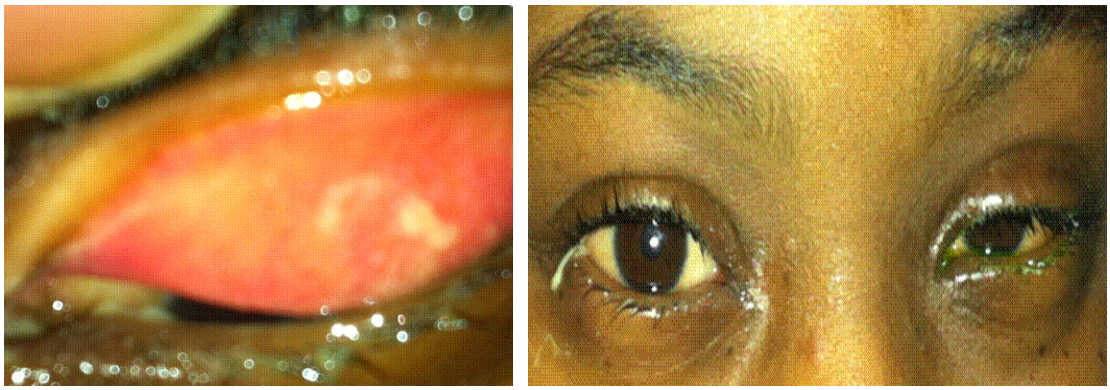

Figure 2: Follicular conjunctivitis

DISCUSSION

The organism *Chlamydia trachomatis* is an obligate intracellular Gram-negative bacterium human pathogen and is one of three bacterial species in the genus Chlamydia. *C. trachomatis* includes three human biovars which are further sub-divided into: 1) serovars Ab, B, Ba, or C – which cause Trachoma, 2) serovars D-K - associated with genital tract infections and neonatal conjunctivitis and 3) serovars L1, L2 and L3 – the causative agents of lymphogranuloma venereum (LGV). The disease process of Trachoma begins in early childhood with recurrent *Chlamydia trachomatis (*Serovars A, B, B1, and C). [9,10]

Many evaluation programs rely primarily on the clinical presentation and examination as Chlamydia tests are expensive and not readily available in developing countries. Studies have indicated that clinical examination alone is not representative of the disease presence, particularly in areas of low prevalence. [11] Infected individuals present initially with sub-clinical manifestations of sticky, itchy and/ or painful eyes. Infection of the conjunctival epithelium provokes a follicular conjunctivitis, known as 'active trachoma'. After repeated infections, when scarring of the conjunctiva has occurred, the patient may complain of a feeling of 'sand or grains' in the eyes. [10]

The WHO and the International Agency for the Prevention of Blindness (IAPB) have included Trachoma as one the priority diseases using the criteria for priority diseases as; diseases with a greater potential for elimination and diseases that can be drastically reduced with available tools. Challenges of socioeconomic development, inadequate hygiene and access to water in developing countries continue to be risk factors which predispose to the ongoing transmission of *Chlamydia trachomatis.* [1,10]

Results of this study showed a prevalence of infection of 11.8%, which compares with the overall prevalence of

11.9% reported by Dawson in 1967 [5]. In this study Chlamydia was detected mainly in patients with specimens negative for other bacteria. Trachoma can be associated with other bacterial infections which can contribute to the inflammation, conjunctival scarring and corneal opacification. [12] As in similar studies, co-infection of Chlamydia and Staphylococcus was detected in 25% of Chlamydia positive cases. [12,13] In Jamaica, patients present with a chronic conjunctivitis, which can be follicular. However, the advanced full spectrums of the trachomatous disease (with lid scarring, trichiasis and corneal scarring) are not present as compared to African countries.

Studies using molecular detection methods show improved sensitivities of C trachomatis ribosomal RNA-based nucleic acid amplification tests (NAATs) compared to DNA-based NAATs. [14] In a NAAT comparative study by Keenan *et al*, RNA-based NAAT was found to be detected in ocular chlamydial infection in more children (6.9%) compared with Chlamydia DNA-based test (4.2%). [15,16] Another study by Keenan et al., in which the prevalence of ocular chlamydia RNA was documented as 7.1%, comparison of a DNA-based NAAT reported a sensitivity of 61.0%, specificity of 100% and a positive predictive value of 100%. This compared with a RNA-based gold standard NAAT sensitivity of 100% and specificity of 99.6 %. [15,16]

Such studies suggest the possible under detection of Chlamydia in this study which may have been associated with the use of the Sacace™ Chlamydia trachomatis DNA assay. Other limitations associated with the use of the Sacace assay included the inability of the broad based primers to differentiate serovars A, B, Ba and C. Follow-up sequencing to identify serovars A, B, Ba and C was not done due to budget constraints. Although the sample used in this study was statistically acceptable for countries with low endemic levels of C. trachomatis, bias may have been introduced by the small sample size

The methods used for the detection of *Chlamydia trachomatis* in Dawson's study of 1967 included cytology, immunofluorescence and isolation with embryonated hens eggs. [5] Confirmation of positive findings was through collaboration with the WHO Reference Centre for Trachoma and the San Francisco Laboratories of the Reference Centre. These methods are known to have sensitivities and specificities which are lower than that of PCR. It is possible therefore, that the prevalence of C trachomatis reported by Dawson may have been underestimated.

One of the proxy targets used for monitoring the elimination of blinding trachoma, refer to the WHO Ultimate Intervention Goal (UIGs) of a prevalence of active trachoma (TF) in children aged 1–9 years of <5%. Although there was no detection of Chlamydia DNA among children in the 1-9 age group in this study, Chlamydia DNA was detected in 30% of children between the ages of 1 month to 1 year. Caution however, should be taken in the interpretation of Chlamydia negative DNA results, as reports by Keenan *et al* have suggested that chronic inflammation and progressive scarring of Trachoma may be present in the absence of Chlamydia detection. [15,16]

The absence of trichiasis or cicatrical entropion among children in this study was similar to findings of Dawson's report. Dawson's report documented the manifestations of trachoma as being mild with minimal corneal involvement with an overall prevalence of 11.9% (N=1000 school children), and an increased active trachoma frequency of 21% and 13% in the parishes of St. Thomas and St. Andrew respectively.

Several countries reported to the WHO in 2011 that they had achieved the 2 proxy targets of the Ultimate Intervention Goals (UIGs) used for monitoring the elimination of blinding trachoma. The UIGs has been defined as; 1) <1 case of trichiasis per 1000 population and, 2) a prevalence of Active Trachoma (TF) in children aged 1–9

years of <5%. (World Health Organization, Trachoma Fact Sheet, 2015) While there has been a decline in blinding trachoma worldwide, there has been a corresponding increase in the number of trichiasis cases indicating a continued degree of endemicity of this agent in populations. [17]

Documentation by Nichols *et al*., in 1976 of clinical Trachoma caused by serotypes A and B in Caribbean countries such as Haiti support the need for continued surveillance of *Chlamydia trachomatis* in the Caribbean region. [2] Risk factors for the continued circulation of *Chlamydia trachomatis* in Jamaica include the presence of over 700 squatter settlements which comprise an estimated 20% of Jamaica's population of which 10% are associated with environmentally poor sanitation. [18] Susceptible populations, overcrowding, urbanization, poor hygienic practices, sub-standard physical infrastructures and inadequate access to safe water are associated with squatter settlements and are known risk factors for *Chlamydia trachomatis* transmission. [2,19]

Gaynor *et al*, sought to clarify the implications of the use of the terms eradication and elimination in reference to the post-endemic surveillance of *Chlamydia trachomatis.* [20] Whereas the goal of elimination of blinding trachoma may be feasible, the elimination of its causative agent is not. Ongoing surveillance is critical as the Ultimate Intervention Goals (UIGs) of blinding trachoma permits for the continued presence of trachoma in a population at a level which does not adversely impact on public health.

It must be remembered that Trachoma presents itself as a spectrum of progressive clinical manifestations. It is therefore necessary that countries ensure that ongoing ophthalmic and laboratory services are available to monitor the spectrum of this disease. The association of the detection of *Chlamydia trachomatis* DNA with conjunctivitis across different age groups in this study suggests the need for renewed awareness and continued surveillance of this disease.

CONCLUSION

Results of this study showed an overall prevalence of *Chlamydia trachomatis* ocular infections of 11.8 %. The typical clinical presentation in Jamaica is a chronic conjunctivitis with absence of the lid and corneal scarring. Chlamydia DNA was detected by PCR in association with cases of different age categories presenting with conjunctivitis. Interpretation of the results of this study in accordance with the UIGs fulfilled the requirement for blinding trachoma elimination status in Jamaica. It is recommended that the monitoring and specific laboratory detection of ocular *Chlamydia trachomatis* be continued in Jamaica.

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