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Predicting Chlamydia Trachomatis Infection in a Mining Community in Western Ghana

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Abstract: Chlamydia Trachomatis (CT) infection among females in a mining community in Western Ghana is a major medical issue. Screening using laboratory test results have been the usual control and prevention of STI globally but have been found to have its own limitations due to delay in test results leading to further transmission of genital infections. Consequently, a statistical model is formulated to predict the incidence of Chlamydia Trachomatis (CT) infection among females in the community. The model used a Modified Univariate Normal Discriminant Function, a Logistic Regression Model and specific symptoms associated with Chlamydial infection as part of the explanatory variables. Samples were taken from 186 patients consisting of 40 males and 146 females from two hospitals in the Tarkwa Nsuaem Municipality, a mining community in Western Ghana. The model was validated using a sensitivity analysis test and Apparent Error Rate (APER). The model predicted decreasing infection rate of patients with increasing age. The most reported and significant symptoms among the female patients diagnosed was vaginal discharge, ($p<0.05$). The study predicted a patient as positive or infected with Chlamydial, if the result of the model evaluated gave a positive value, otherwise the patient was declared free of infection. Further analysis of the proposed Statistical Chlamydia Trachomatis (SCT) model gave a sensitivity of 84% which was consistent with other research findings like the rapid point of care (POC) diagnostic test for Chlamydial infection with sensitivity range of 55–85% for high prevalence populations. The study observed that young females in mining communities are at risk of acquiring Chlamydial T infection if presenting with vaginal discharge. Identifying these risk factors associated with Chlamydial infection among young women in the mining communities would help inform health care officials the rate of infection in the Municipality, and accordingly mount public educational health campaign in the Municipality aimed at minimizing the spread of chlamydial infections and any other STI.

Keywords: Chlamydia Trachomatis, Symptoms, Univariate, Discriminant, Logistic, Sensitivity, Prediction

1. Introduction

Chlamydia Trachomatis (CT) infection, is caused by the bacteria called Chlamydia trachomatis (CT). Centers for Disease Control [1]; CT is transmitted from person to person through sexual contact with an infected person through the vagina, penis, mouth, anus or through the birth canal of an infected mother to child [2]. Chlamydia Trachomatis and other sexual transmitted diseases have been a major health problem globally especially in Africa regions [3]. In 2011, the World Health Organization (WHO) estimated that 50 million women were infected with Chlamydia trachomatis worldwide, of which 34 million were in Sub-Saharan Africa and Southeast Asia [4, 5]. The asymptomatic nature of the disease enhances its spread because it is difficult to detect and hence remains untreated for long periods. Research shows that about 75% of affected females hardly show any

symptoms. A study in Uganda by Orroth et al.[6] estimated that only 11% of infected males and 6% of infected females developed symptoms. According to the CDC's STI Fact sheet, more than 1 million Sexually Transmitted Infections (STIs) are acquired every day worldwide. Studies have shown that each year, there are approximately, 357 million new infections with 1 out of every 4 STIs includes; chlamydia, gonorrhea, syphilis and trichomonas [7].

Hussen et al. [8], reviewed the systematic and meta-analysis of the prevalence of chlamydia trachomatis infection among reproductive-age women in sub-Saharan Africa, with higher rates observed in other African countries, mostly among the rural folks. Ghana had recorded incidence of 4.9% [9], Tanzania with 5.9% among antenatal care unit [10], while a prevalence of 26.5% among women aged 15 to 49 years had been reported for Uganda [11].

In Ghana, the incidence of urogenital chlamydia infections among selected patients in Kumasi, was evaluated using an immunofluorescent monoclonal antibody technique. According to the findings, Chlamydia Trachomatis was found in 4 out of 110 patients who were presenting for prenatal care and 2 out of 55 female patients were identified with the issue of infertility [12]. However, the incidence of chlamydia infections among asymptomatic patients was seen to be relatively low as compared to high prevalence rate of Chlamydia infection among female sex workers and non-sex workers residing in major cities in Accra and Kumasi [12-14].

The diagnosis and control of chlamydial infections among patients especially in developing countries has always been a challenge, although there are many tests available to detect chlamydial infections. However, most test require laboratory facilities such as Test kits for screening, and these kit are so expensive and scarce. Modern PCR methods using urine or vulvar swab samples can also be self-sampled at home and this has been shown to raise participation in screening 15]. Other methods for diagnosing Chlamydia Trachomatis infection include antigen detection, culture, antibody detection and serology. Mathematical modelling on the contrary can be explored effectively as a tool in predicting and evaluating effectiveness of chlamydial screening in various forms. This provides accurate information on how different infection parameters such as transmission probability, incidence, prevalence, age, and gender affect assessment [16]. Moreover, primary prevention of Chlamydia Trachomatis infection is notably through health education and screening, and these have been the usual control strategies worldwide but has its own setbacks. Consequently, a rapid point of care (POC) diagnostic test was introduced to enable patients to be diagnosed and treated at a single visit to avoid the delay between testing and treatment and further transmission of any other infections other than CTI [17]. The POC diagnosis tests for *Chlamydia trachomatis* in women has a sensitivity ranging from 55–85% for high prevalence populations [18] and 25–49% for low prevalence. In 2020, Verwijs et al. compared the performance of the Women's Improvement of Sexual and Reproductive Health (WISH) algorithms and the WHO vaginal discharge and lower abdominal pain algorithms with gold standard testing had 71% sensitivity and 100% specificity for *Chlamydia trachomatis* [19].

In 1998, the World Health Organization (WHO) recommended the use of a syndromic approach for the management of urethral discharge in men and vaginal discharge and lower abdominal pain in women. While the syndromic approach appears to be satisfactory in men, it has several important limitations in women [18]. Furthermore, studies evaluating the syndromic approach in women have shown that it generally has a poor sensitivity (30–80%) and specificity (40–80%) for the diagnosis of Neisseria gonorrhea and Chlamydia trachomatis. Such tests would permit the screening of asymptomatic women and would reduce the false diagnosis and overtreatment of symptomatic women inherent in the currently recommended syndromic management algorithms, [17, 20]. Olaleye et al. enrolled a diversity of women between (18-24) years with low to high risk for acquiring *Chlamydia trachomatis* infection and few of the infected women was found to met the syndromic management criteria for treatment, leaving a high number of them at risk of developing severe upper genital tract disease and likelihood of transmitting the pathogen to their partners [21].

This study reports on a model developed to address the issue of re-infection, wrong diagnosis due to misclassification, massive overtreatment and social complications of misdiagnosis. The model predict the incidence and infectious status of patients, thus enabling immediate treatment to curb further spread of CTI from loss of follow-up.

2. Material and Methods

A sample of One Hundred and Eighty Six (186) patients were screened, with One Hundred and Forty-Six (146) being females and Forty (40) males. The female patients were between the ages of 15-50 years, attending the usual routine checkup at two different hospitals in the Tarkwa-Nsuaem Municipality in the Western Region of Ghana. The common symptoms identified among the female patients diagnosed included; Vaginal Discharge (VD), Vulva Vaginitis (VV), and Pelvic Inflammatory Disease (PID). The dependent variable considered was the infectious status of the patient, which is either positive or negative. A female patient was coded '1' if she tested positive and '0' if she is negative. The independent variables were age and specific symptoms diagnosed. The symptoms were also coded '1' for VD, '2' for VV and '3' for PID.

3. Formulating the SCT Model

The Statistical Chlamydia Trachomatis (SCT) Model was developed by considering a Univariate Discriminant Model of two normal probability density functions, $f_1(x)$ and $f_2(x)$, which were associated with the random variable x_i. The variable π_i takes the value π_1 when a patient is diagnosed with positive Chlamydia Trachomatis infection and π_2 if a patient has no infection. p_1 and p_2 represent

the prior probabilities for π_1 and π_2 respectively such that, $p_1 + p_2 = 1$.

The analysis of the SCT model was derived using an Expected Cost of Misclassification (ECM) by Johnson and Richard [22] as defined in Equation (1)

$$ECM = C(\pi_2 \mid \pi_1)P(\pi_2 \mid \pi_1)P_1 + C(\pi_2 \mid \pi_1)P(\pi_2 \mid \pi_1)P_2 \quad (1)$$

However, the region R_1 represent the likelihood of an individual being diagnosed with chlamydia infection (π_1) with respect to x and R_2 is when a patient is diagnosed negative of chlamydia infection (π_2) with respect to x. The ECM for both R_1 and R_2 are defined by the following inequalities indicated as Equation (2);

$$R_1 = \frac{f_1(x)}{f_2(x)} \geq \left(\frac{C(\pi_1/\pi_2)}{C(\pi_2/\pi_1)}\right)\left(\frac{P_2}{P_1}\right) \quad (2)$$

and Equation (3)

$$R_2 = \frac{f_1(x)}{f_2(x)} < \left(\frac{C(\pi_1/\pi_2)}{C(\pi_2/\pi_1)}\right)\left(\frac{P_2}{P_1}\right) \quad (3)$$

An individual with a particular symptom (x_0) diagnosed with CT infection (π_1) given that the patient has no infection (π_2) is represented by the inequality given by Equation (4).

$$\frac{f_1(x_0)}{f_2(x_0)} \geq C(\pi_1 \mid \pi_2)p_2 / C(\pi_2 \mid \pi_1)p_1 \quad (4)$$

We denote Ω, to represent the population to be and R_1 represents the conditions with respect to x, the likelihood of an individual from the population acquiring the disease is classified as π_1 and it implies $R_2 = \Omega - R_1$, an individual not having CT infection π_2. If R_1 and R_2 mutually exclusive events and each patient can be assigned to either π_1 or π_2, then, $P(\pi_2 \mid \pi_1)$ denotes the conditional probability of classifying an individual as π_2 when, in fact, the person belongs to π_1. Equation (5) represents the conditional probability of classifying an individual as π_2

$$P(\pi_2 \mid \pi_1) = P(X \in R_2/\pi_1) = \int_{R_2} f_1(x)dx \quad (5)$$

Similarly, the conditional probability $P(\pi_1|\pi_2)$ of classifying an individual as π_1 when in actual fact, the patient belongs to π_2 is given as in Equation (6):

$$P(\pi_1 \mid \pi_2) = P(X \in R_1/\pi_2) = \int_{R_1} f_2(x)dx \quad (6)$$

where the integral sign in Equations (5) and (6) represents the number of patients with an infection under the density function $f_1(x)$ over region R_2 and those without the infection with density function $f_2(x)$ over the region R_1 respectively.

Now, for clarity of interpretation, we define the probability functions of misclassification as:

where the integral sign in Equations (5) and (6) represents the number of patients with an infection under the density function $f_1(x)$ over region R_2 and those without the infection with density function $f_2(x)$ over the region R_1 respectively.

Now, for clarity of interpretation, we define the probability functions of misclassification as:

$$P \text{ (a patient is misclassified as } \pi_1) = P(X \in R_1/\pi_2)P(\pi_2) = P(\pi_1 \mid \pi_2)p_2$$

$$P \text{ (a patient is correctly classified as } \pi_1) = P(X \in R_1/\pi_1)P(\pi_1) = P(\pi_1 \mid \pi_1)p_1$$

$$P \text{ (a patient is misclassified as } \pi_1) = P(X \in R_1/\pi_2)P(\pi_2) = P(\pi_1 \mid \pi_2)p_2$$

$$P \text{ (a patient is correctly classified as } \pi_2) = P(X \in R_2/\pi_2)P(\pi_2) = P(\pi_2 \mid \pi_2)p_2$$

$$P \text{ (a patient is misclassified as } \pi_2) = P(X \in R_2/\pi_1)P(\pi_1) = P(\pi_2 \mid \pi_1)p_1$$

3.1. Model Assumptions

The three main assumptions for the proposed model are:

The number of patients belonging to π_1 and π_2 are considered to be independent

The number of patients belonging to π_1 and π_2 are normally distributed

Estimated success probability $\hat{p}_i$, is also considered as the dependent variable.

Again, under the Univariate Discriminant Model, the paper considered a number of patients screened of CT infection with π_i, $i = 1, 2$, representing patients who tested positive and negative as defined earlier. If the mean (μ_i) and variance of these two groups of patients are from normally distributed populations, then the density ratio of the two groups that is, diagnosed of CT infection (π_1) and those without the infection, (π_2) would be modelled as Equation (7):

$$D(x)=\frac{f_1(x)}{f_2(x)}=\frac{\frac{1}{\sqrt{2\pi\sigma_1^2}}e^{-\frac{1}{2}\left(\frac{x-\mu_1}{\sigma_1}\right)^2}}{\frac{1}{\sqrt{2\pi\sigma_2^2}}e^{-\frac{1}{2}\left(\frac{x-\mu_2}{\sigma_2}\right)^2}} \quad (7)$$

Rearranging Equation (7) we obtain Equation (8)

$$D(x)=\frac{\sigma_2}{\sigma_1}e^{-\frac{1}{2}\left\{\left(\frac{x-\mu_1}{\sigma_1}\right)^2-\left(\frac{x-\mu_2}{\sigma_2}\right)^2\right\}} \quad (8)$$

Again, suppose we consider a situation where the variance of the two groups π_1 and π_2 are equal then, it can be inferred that, the variance, $\sigma_1^2=\sigma_2^2=\sigma^2$. Thus, Equation (8) becomes (9):

$$D(x)=e^{-\frac{1}{2\sigma^2}\left\{(x-\mu_1)^2-(x-\mu_2)^2\right\}} \quad (9)$$

where $D(x)$ denotes the discriminant function of the normal distribution. Simplifying (9) further yields (10),

$$D(x)=\exp\left[-\frac{1}{2\sigma^2}\left\{2(\mu_1-\mu_2)x+\left(\mu_1^2-\mu_2^2\right)\right\}\right]$$

$$D(x)=\exp\left[\frac{1}{\sigma^2}\left\{(\mu_1-\mu_2)x-\frac{1}{2}\left(\mu_1^2-\mu_2^2\right)\right\}\right] \quad (10)$$

Comparing (4) and (10) to a patient, (x_{CS}), with Chlamydia symptoms (CS), the inequality in (11) is established.

$$(\mu_1-\mu_2)x_{CS}-\frac{1}{2}\left(\mu_1^2-\mu_2^2\right)\le s^2\ln\left[\frac{c(\pi_1/\pi_2)p_2}{c(\pi_2/\pi_1)p_1}\right] \quad (11)$$

Equation (11) is the modified normal discriminant function of the study, and the sample population of the discriminant function in the study area is as shown in (12)

$$(\bar{x}_1-\bar{x}_2)x_{cs}-\frac{1}{2}\left(\bar{x}_1^2-\bar{x}_2^2\right)\le S_p^2\ln\left[\frac{c(\pi_1/\pi_2)p_2}{c(\pi_2/\pi_1)p_1}\right] \quad (12)$$

Equation (12) is the sample modified Linear Univariate Discriminant Function, where, $\bar{x}_1$ is the mean value of patients infected with CT whilst $\bar{x}_2$ denotes the mean value of patients who are not infected with CTI. The pooled sample variance, for the two population groups is given as Equation (13);

$$S_p^2=\frac{(n_1-1)s_1^2+(n_2-1)s_2^2}{n_1+n_2-2} \quad (13)$$

Where n_1, n_2 and s_1, s_2 are the total number of infected and non-infected patients and their standard deviations respectively.

The Statistical Chlamydia Trachomatis (SCT) model thus evolves from (12) where the actual values of the means $(\bar{x}_1 \text{ and } \bar{x}_2)$ derived from an independent sample T-test computed were substituted likewise the values for the estimated Pooled Sample Variance $\left(S_p^2\right)$, the prior probabilities (p_1, p_2), the Estimated Cost of Misclassifying (ECM) and the individual patient's success probabilities, $\hat{p}_i$.

3.2. Application of the Model

The paper sampled, diagnosed and screened 146 female patients who have related Chlamydia symptoms. 121 (83%) and 25 (17%) tested negative and positive to Chlamydia Trachomatis infection respectively as shown in Table 1.

Table 1. *Female Patients Diagnosed and Screened of Chlamydia Trachomatis Infection.*

Symptoms	Number of Patients Diagnosed	Number of Patients Testing Negative to CTI	Number of Patients Testing Positive to CTI
Vaginal Discharge	69	52	17
Pelvic Inflammatory Disease (PID)	17	14	3
Vulva vaginitis	30	26	4
Candidiasis	11	10	1
STIs	19	19	
Total	146	121	25

Source: Nyarko et al. [2]

The SCT model was finally obtained by substituting all the parameters in (12) to obtain the desire SCT model. The manipulation using (12) is as shown in (15);

$$(0.2418-0.1570)\hat{p}_i-\frac{1}{2}\left(0.2418^2-0.1570^2\right)\ge 0.00976\ln\left[\frac{(2.3333)(0.8288)}{(0.4286)(0.1712)}\right] \quad (14)$$

With reference from Equation (13), the proposed SCT model was obtained as shown in Equation (15)

$$Pooled\ sample, S^2 = \frac{(25-1)0.1296^2 + (121-1)0.0914^2}{25+121-2} = 0.00976$$

$$0.0848\hat{p}_i - 0.00823 \geq 0 \tag{15}$$

The prior probabilities $p_1 = 0.17123$ and $p_2 = 0.82877$ were derived from the ratio of the number of female patients who had chlamydia infection and those who had no infection over the total number of female patients screened respectively. The estimated cost of misclassifying a patient who had an infection (π_1) as though she had no infection (π_2) is assumed to be twice as serious as not having the infection. (π_1) was assigned a value of 10 and (π_2) as 5. The calculation was done manually and confirmed using Matrix Laboratory (Math Lab). The $\hat{p}_i$ in Equation (15) is the fitted probability which depends on the patient's age and type of symptom diagnosed. The infectious status of a patient is predicted by the SCT model, ($0.0848\hat{p}_i - 0.00823 \geq 0$), if the result of the model evaluated at $\hat{p}_i$ gives a positive value, otherwise the patient is declared free of infection, see as shown in Table 2.

Table 2. *Empirical Analysis of Statistical Chlamydia Trachomatis (SCT) Model.*

Age	Infectious Status Before SCT Model	Type of Symptoms (codes)	$\hat{p}_i = \frac{\exp(Z)}{[1+\exp(Z)]}$	Computing of SCT $0.0848\hat{p}_i - 0.00823 \geq 0$	Infectious Status after modeling with (SCT)
18	1	1	0.388885	0.024745	Infected
20	1	3	0.203428	0.018589	Infected
22	1	1	0.320578	0.019683	Infected
23	1	1	0.314967	0.018479	Infected
25	1	1	0.287614	0.03753232	Infected
28	1	2	0.194504	0.009021	Infected
32	0	1	0.174941	0.004271	Infected
38	0	2	0.111947	0.001772	Infected
40	0	1	0.132156	-0.000309	Not Infected
42	0	1	0.117948	-0.00198	Not Infected

The results show that likelihood of CT infection reduces with age and type of symptoms diagnosed. See figure 1.

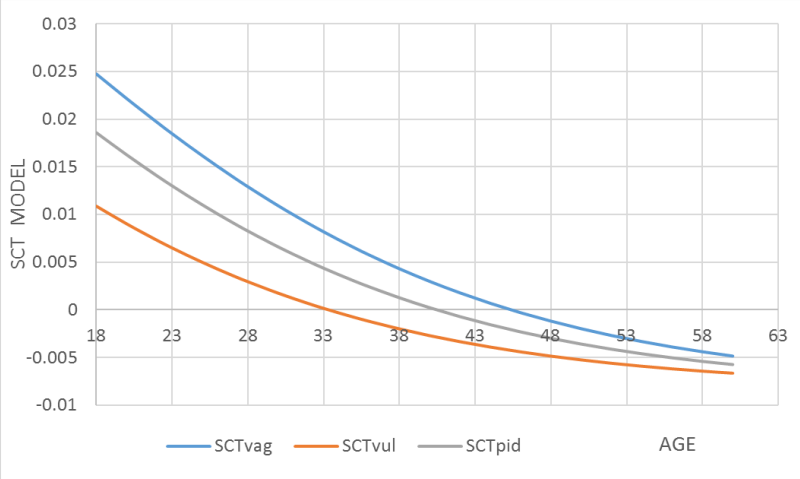

Figure 1. *Graphical Presentation of SCT Model with Symptoms Diagnosed.*

Table 3. *Validation of the SCT Model by APER.*

Diagnosis	Predicted Group Membership		Total (%)
	No (%)	Yes (%)	
No	34 (28.1)	87 (71.9)	121
Yes	4 (16.0)	21 (84.0)	25
Total	38 (26.1)	108 (74.0)	146
Estimated Error Rate	87 (71.9)	4 (16.0)	91 (62%)
Total Percent Classified	34	21	(38%)

Further analysis using SAS confirms the sensitivity of the SCT model as 84% and a precision of 77% which indicates that the SCT model is a very good model and significantly, consistent with other research findings.

4. Discussions of Results

The study observed that female patients who were diagnosed of vaginal discharge and presenting with Chlamydial infection were young females below the age of 25 years which is with other researchers findings [12, 21, 23]. The SCT model

derived had a sensitivity of 84% which is consistent with the gold standard test and the rapid point of care (POC) diagnostic test having sensitivity ranging from 90% and 55-85% for *C. trachomatis* respectively for high prevalence populations and 25–49% for low prevalence populations [17, 24]. We, however, observed a high error rate for the SCT model and attributed its high sensitivity nature to its ability to detect even the slightest infection in patients. A graphical presentation of the SCT model confirms a downward trend as age of infected patients increase with respect to type of symptoms diagnosed.

The study further noticed that, the required sensitivity of the SCT model depends highly on the number of female patients diagnosed of Chlamydial related symptoms and being young, This study supports the findings of POC tests by ensuring a high return rate avoid of further CTI transmission especially during delay in using laboratory tests results. Significantly, the SCT model also enables all symptomatic and asymptomatic patients who visit health facilities to be treated immediately after diagnoses without loss to follow up. However, depending on severity and likelihood of patients acquiring the infection, some of the patients could be diagnosed using a SCT model and others with more accurate laboratory tests especially after re-infection. Furthermore, to avoid social complications associated with women who go through serious issues due to misdiagnoses and misclassification the SCT model is capable of identifying and consequently treating those infected with Chlamydial easier than using syndromic approach. Lowndes *et al.* had considered the use of syndromic approach among sex workers in Cotonou (Benin Republic), and had a prevalence of 24.7% cervical infection, had sensitivity and specificity for cervical infection as 48.3% and 74.7% [17], respectively, which implied that twice as many uninfected women were wrongly diagnosed as having cervical infection (92 women) than those correctly diagnosed (57 women). Thus, the risk associated with wrong diagnosis needs serious attention especially when it relates to heath issues.

5. Conclusion

The developed model had a sensitivity of 84% and 77% prediction ability, and could therefore be used to predict the incidence of CT infection. It was observed that young females in mining communities are most at risk of acquiring Chlamydial Trachomatis infection if presenting with vaginal discharge. Identifying these risk factors associated with Chlamydial infection among young women in the mining communities would help inform health care officials the rate of infection in the Municipality, and take remedial measures to minimize the spread of chlamydial infections.

Furthermore, STI centers established in all of the rural mining communities in Ghana would ensure ready access to testing facilities and treatment.

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Disclosure Statement

The authors report no conflict of interest.

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