EPIDEMIOLOGICAL SURVEY AND MATHEMATICAL MODELLING OF THE PREVALENCE AND IMPACT OF HIV/AIDS

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Abstract

HIV prevalence studies have widely been carried out in developing countries, and researchers have long appreciated the need to understand the intricacies of the transmission dynamics as well as the cumulative impact of HIV infection in the population. Mathematical modeling provides a more subtle and intuitive mechanism for studying the paradigm and consequences of HIV infection especially in local communities. This study was an epidemiologic survey and mathematical modeling of the prevalence and impact of HIV/AIDS and aims at assessing the transmission dynamics to evaluate the equilibrium condition for continuity and maintenance of the disease among the susceptible population including blood donors, antenatal patients, pre-marriage couples, street children, sex workers/long distance truck drivers and single parents along or near the East-North trucking route of Enugu State. Screening for HIV antibodies was conducted using two enzyme-immuno assays (EIA): the Genie-II and the Q-Spot. Statistical analyses were by ANOVA and the Pearson Chi-square tests. Mathematical modeling of HIV prevalence and impact was carried out using the Routh-Hurwitz Criteria. A steady increase in HIV prevalence was observed across the surveyed areas: from 8.0% in 1999 (in Eha-Alumona) to 22.0% in 2001 (in Enugu urban); with gender prevalence of 15.9% in 1999 to 17.5% in 2000 and 2001 among the males; and 17.3% in 1999 to 20.8% in 2001 among the females (F cal = 5.185; $p < 0.05$). The age bracket most affected was 16-30 years, (28.1%; relative risk, 2.0), followed by those in the 31-45-age range (24.0%). Highest HIV prevalence was however observed among the commercial sex workers (20.1%) and those in multiple sex partnership (17.5%). From mathematical modeling, disparities in HIV prevalence among the population studied are apparent: these are intrinsically linked to their transmission dynamics, chiefly commercial sex networking. The model establishes the failure of the system to achieve the equilibrium conditions necessary for stability, indicating that the stability of the HIV epidemic is not guaranteed, (implying steady increase in HIV infection), and attributing the instability to regular inflow of susceptible individuals to the target population.

Keyword: HIV prevalence, Mathematical modeling, epidemiologic survey, transmission dynamics

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Introduction

HIV/AIDS is one epidemiological event that has generated so much political argument while at the same time uniting mankind in search of remedy. While the index cases were discovered in the United States of America, the underdeveloped world bears the brunt of the epidemic on account of poverty, malnutrition and virtual lack of modern health care facilities. The sub-Saharan African situations particularly highlighted the heterosexual contribution to the epidemiology of the disease. As HIV/AIDS defiled geographical as well as political boundaries and spread across the globe like wildfire, it became epidemiologically important to determine the risk factor for the purpose of planning, education, intervention and prevention measures. This became particularly necessary in the sub-Saharan Africa as the orphanages began to overflow with children of victims. Migrant workers, long distance truck drivers, itinerant traders and all those engaged in occupations that constrained them to leave home for periods of time became identified as vulnerable i.e. at risk of being infected because of their tendency to go into casual sexual partnerships away from home. Vulnerable women or men giving them such companionships, particularly, the commercial sex workers were also identified strongly as groups at risk. Further investigations have since revealed other risk groups and factors predisposing people socially to HIV/AIDS risk behaviours; single women (widows, single mothers, unmarried girls from abjectly poor homes), with no sort of economic empowerment are most tempted and most likely to succumb to sex for money, favour or protection (**Dibua, 2010**;Owuamanam, 1988). Young school leavers or schoolgirls and apprentices living away from home, whose parents cannot afford what they need to belong to the contemporary society, get lured by peers into indulgence in risk behaviours. The under-privileged of the society, children abused in life or so deprived that they turn into "street children" soon get recruited into HIV/AIDS risk behaviours – sex, intravenous drug use, etc. Young men who became successful in business or professional carriers often become identified in association with society girls and HIV/AIDS risk lifestyles (Krueger *et al.*, 1990; Owuamanam, 1988; Ainsworth and Over 1994; Diaz *et al.*, 1994; European Study Group 1989). HIV/AIDS transmission has even been identified with certain population dynamics like settlement along trucking routes, mining camps, fishing ports, refugee camps, etc (Mirjam, 2002; Ainsworth and Over 1994). These became subjects for epidemiologic investigation for a singular purpose of planning education, intervention and prevention strategies.

Modeling of infectious diseases is still a relatively new field. Although the field of epidemiology has a long and well-established history, it is only within the past several decades that mathematicians and immunologists have begun to work together to create models that attempt to predict the progression of disease in an individual. Models permit analyses that extrapolate beyond the limitations of a trial's time constraints, geographic setting, and study population (Over et al., 2004). Model-based analyses synthesize data from multiple sources, permitting decision makers to understand the likely impact of different strategies and to set priorities for clinical trials [1]. The increased efficiency of modern computer techniques has expanded the possibilities of mathematical modeling in an unprecedented way. Since the emergence of the HIV epidemic, mathematical models have been constructed to determine rates of progression to AIDS (5-10). However, medical and biologic research has not taken full advantage of these possibilities especially in developing countries. There are two principal uses of such mathematical models. First, by examining the effects that changes in parameters have on the outcome of the system over time, we can determine which parameters are most important in disease progression, and further, we can determine critical "“threshold values”" for these parameters, which are often crucial in the attempt to control disease. Second, treatment strategies can theoretically be simulated, allowing the design of clinical trials to be streamlined.

The main aim of mathematical model of HIV prevalence is to examine the pattern of the infection including the transmission dynamics in order to establish the likelihood of an epidemic occurrence, as well as the possible consequences or outcomes which can be subtle and counterintuitive; and the available methods for studying this are seldom component of a conventional epidemiology research plan. Mathematical modeling is an excellent way to examine the archetype of HIV infection as well as the determinants or transmission dynamics of the epidemic. Hence, modeling helps in proper understanding and assessment of the dynamics and differences or discrepancies commonly encountered in HIV investigation either globally or locally and provides focus for further research on the epidemic. Hence, in the absence of adequate animal models, mathematical modeling of HIV infection is especially important. Mathematical modeling is therefore a useful research tool in epidemiologic investigation of HIV prevalence alongside laboratory techniques particularly in developing countries.

Materials and Methods

Description of the Project Locations

The epidemiological surveillance study was carried out in Enugu State Nigeria in locations situated along the South-North trucking route (highway). Specific locations in the State chosen for their peculiarities include the 9th-Mile-Corner (Udi Local Government Area), Eha-Alumona (Nsukka Local Government Area), Orba and Obollo-Afor (Udenu Local Government Area). Enugu and Nsukka urban centres were included as reference points for sample populations with no known risk behaviours while the groups in the major locations were selected because of their known HIV/STD risk behaviours.

THE EXPERIMENTAL DESIGN

The investigation was generally aimed at assessing the prevalence of HIV infection among different groups at risk, determining the various factors predisposing the population to the identified risk behaviours as well as evaluating the transmission dynamics and equilibrium conditions for stability by mathematical modeling.

Ethical Procedures

Consent to carry out the study was obtained from the then Enugu State HIV/STD Programme Administrators, Community leaders and Proprietors or Directors of all health institutions used for the survey. Confidentiality was maintained during and after the study. Informed consent (without undue influences) was obtained from participants before their inclusion in the project.

Screening Blood for Human Immunodeficiency Virus antibodies

Blood samples were collected from the general population with no known risk behavior assumed to be leading a normal one partner marital relationship unless otherwise admitted or revealed. Individuals included in this group were the blood donors, couples for pre-marriage counseling and pregnant women attending anti-natal clinics. The rest of the screened blood samples were collected from groups with known risk behaviors including sex-workers, people with multiple partnership sexual relationships, single parents and the young people at the 9 Mile Corner. The third group were those manifesting symptoms of AIDS-related Complex (ARC) or AIDS on routine laboratory screening. Bio-data of the population as well as their social life but not sexual exposures was obtained.

Collection of Blood Samples.

Approximately 5ml of blood was collected from each subjected by vein puncture, using a 10-ml syringe and 18-guage needle and dispensed into 10-ml disposable specimen bottle (sterilin), and appropriately labeled with the patient's code, and allowed overnight in a refrigerator to clot. Subsequently, the serum, which separated from the blood cells and/or clot, was carefully aspirated into another clean specimen bottle and later tested for HIV antibodies.

Serological Assay Procedures for HIV

Two test kits were used for the serological screening namely, Q-SPOT (HI-TECH DIAGNOSTICS, HOUSTON, TEXAS, USA), which does not discriminate between HIV-1 and HIV-2 antibodies; and GENIE –II (Sanofi, Pasteur, France), which detects HIV-1 and HIV-2 separately.

Q-Spot Tests

The Q-Spot kit (Catalogue No. 1544) consisted of a test device (1544D) a 10-ml buffer solution (W & W Buffer, 1544B), a colloidal gold conjugate protein A (1544GC) in 3 ml volumes, a 0.1ml vial of heat-inactivated HIV-1/2 antiserum in sample diluent (1544PC) (which tested non-reactive to both HBsAg and HCV) and disposable pipettes. For the test proper, 2 drops of W & W buffer were placed on the test device and 1 drop of test serum (~50µl) added. The mixture was allowed to stand for 1min to soak completely. Then 3 more drops of W & W buffer were added followed by 2 drops of the gold conjugate. After waiting for 3 min for the added drops to be absorbed, 2 more drops of W & W buffer were added and the experiment was left for 5 min all at room temperature before the result was read. A positive Q-Spot test result consisted of two pink-to-red coloration spots developing within 5min after the last drop of buffer was added. Any colour spot developing ≥10min after completion of assay was discarded as negative. If only one colour spot developed on the left half of the inner circle, absence of HIV-1/2 antibodies was assumed i.e. the test serum was HIV1/2 negative. Development of slight pink colour on the entire surface of the membrane was considered negative.

Genie II Rapid Test

The Genie II is a rapid enzyme immunoassay, which distinguishes between HIV-1 and HIV-2 antibodies. The test kit contained a specimen diluent, washing solution, Streptavidin Alkaline–Phosphatase Conjugate, a chromogenic substrate and a stop solution, microtubes for diluting specimens, disposable pipettor and a disposable test plate as indicated for the Q-Spot. The reaction plate had two cavities or ports, a circular specimen port A and a larger elliptical reaction port B. The biotinylated HIV-1 and HIV-2 antigens respectively provided were immobilized in two separate spots (I and II) on the reaction zone of port B. A third spot (III), containing a mixture of biotinylated HIV-1 and HIV-2 antigens, served as the internal control for both tests.

In the test proper, 150 µl of the Specimen Diluent was dispensed into the provided microtube. To this was added 50µl of the specimen or control fluid and then mixed thoroughly. The entire content of the microtube, approximately 200µl (i.e. all four drops) of the 1 in 4 dilution of the test serum were introduced in port A of the Reaction Device and allowed time to flow along a chromatographic strip into Port B and soak the three spots, I, II, and III. After incubating at room temperature for 3min to allow reaction between serum and antigens, approximately 150µl of Streptavidin-Alkaline Phosphatase conjugate was dropped on the antigen spots in port B until the latter were soaked. Then 3min was allowed for reaction to take place before applying the wash solution. Approximately 100µl of a Chromogenic Substrate was added to Port B and allowed to stand for 3min. Finally, Port B was then filled to the brim with the Stop Solution, allowed to permeate or sip in and then observed for the development of blue-gray colour in two or 3 of the spots in Port B.

THE MODEL

The prevalence of HIV infection in a population with peculiar characteristic chiefly commercial sex working and multiple sex partnering occasioned by the geographic location as major transport route/stopover of commuters via the north-south highway was discussed by this model. This population is a subpopulation of a larger one that serves as a feeder population from which susceptible individuals to HIV infection are regularly fed to the population of interest. There is an observed steady sex working network in this population; with a regular in and outflow of people of the opposite sex who are not only susceptible but are infected by HIV.

The population therefore consists of both infected and susceptible individuals.

The infected are here categorized as <u>infected,</u> <u>infective</u> and <u>full blown AIDS individuals</u>. Hence, we have the stratified population as:

$$N(t) = S + I_1 + I_2 + I_3 + R$$

where S = susceptible

I_1 = infected but cannot transmit the HIV

I_2 = infected and ready to transmit the virus to any

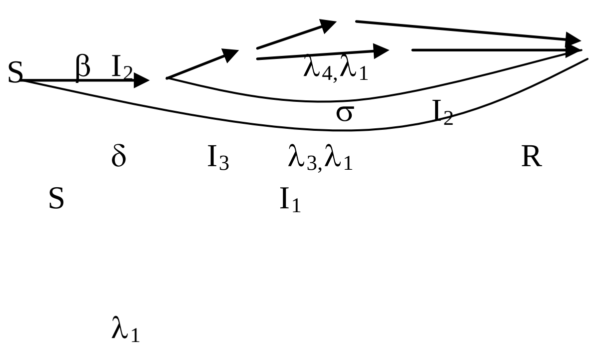
I_3 = infected and have developed to full blown AIDS.

R = removed as a result of death from full blown AIDS or infection (infected/infective class).

THE TRANSMISSION DYNAMICS

In the transmission of the HIV, there is an observed interaction between the infected, (males or females), and in this model, sexual interaction (heterosexual) is considered the source of the disease.

This is diagrammatically presented as:



It is assumed from this diagram, the susceptible individuals get infected (I_1) at a rate β following sexual intercourse. They can also be removed naturally (death) at a rate λ_1 (not induced by the HIV). The infected persons further can develop to infective stage at a rate σ and can be removed (death) either naturally or induced by the disease. At this infectious and infective stage, one could remain infectious till removed or might develop further to full blown AIDS (HIV/AIDS) at a rate δ but could be removed at this stage either naturally or induced by the disease.

This model assumes the presence of the following: sex workers, inflow/outflow of individuals into our population of interest, sexually active and participating individuals (due to poverty, greed, etc.) in the population and none or minimal prevention.

From this assumption, the model showing the transmission dynamic in the stratified population is developed thus:

$$\frac{dS}{dt} = \tau S - \beta S I_2 - \lambda_1 S - kS \qquad (1)$$

$$\frac{dI_1}{dt} = \beta S I_2 - \sigma I_1 - \lambda_1 I_1 - \lambda_2 I_1 + \upsilon I_1 \qquad (2)$$

$$\frac{dI_2}{dt} = \sigma I_2 - \delta I_2 - \lambda_1 I_2 - \lambda_4 I_2 + \xi I_2 \qquad (3)$$

$$\frac{dI_3}{dt} = \delta I_3 - \lambda_1 I_3 - \lambda_3 I_3 \qquad (4)$$

$$\frac{dR}{dt} = (\lambda_1 + k)S + (\lambda_1 + \lambda_2)I_1 + (\lambda_1 + \lambda_4)I_2 + (\lambda_1 + \lambda_2)I_3 \qquad (5)$$

Evaluation of the equilibrium condition for the <u>continuity</u> and maintenance of the disease in the population under study: The transmission rate β of the susceptible to infected is of particular interest and this is indicated as:

β = N+E

where N is the transmission rate in any population

E is the additional transmission rate due to the prevalence of the

regular supply of susceptible population and availability of sex

workers who most of the time are infected.

EQUILIBRIUM STUDY

In considering a set of equations to determine whether the disease transmission can ever attain an equilibrium state (recognizing however the presence of regular in and outflow of both susceptible and infected individuals into and out of our target population), we noted that for equilibrium state to be attained,

$$\frac{dS}{dt} = \frac{dI_1}{dt} = \frac{dI_2}{dt} = \frac{dI_3}{dt} = \frac{dR}{dt} = 0$$

Hence, from equation (1),

$$(\tau - \beta I_2 - \lambda_1 - k)S = 0 \quad \text{and}$$

since $S \neq 0$, then

$$I_2 = \frac{\tau - \lambda_1 - k}{\beta} \qquad (6)$$

From equation (2),

$$\beta S I_2 - (\sigma + \lambda_1 + \lambda_2 - \upsilon) I_1 = 0$$

Similarly,

$$S = \frac{(\sigma + \lambda_1 + \lambda_2 - \upsilon) I_1}{\beta I_2}$$

But $I_2 = \dfrac{\tau - \lambda_1 - k}{\beta}$;

Hence,

$$S = \frac{(\sigma + \lambda_1 + \lambda_2 - \upsilon) I_1}{\tau - \lambda_1 - k} \qquad (7)$$

From equation (3),

$$(\sigma - \delta - \lambda_4 - \lambda_1 + \xi) I_2 = 0$$

$$\Rightarrow \quad \sigma - \delta - \lambda_4 - \lambda_1 + \xi = 0$$

$$\Rightarrow \quad \sigma = (\delta + \lambda_4 + \lambda_1 - \xi) \qquad (8)$$

From equation (4),

$$(\delta - \lambda_1 - \lambda_3) I_3 = 0 \quad \text{and} \quad I_3 \neq 0$$

$$\Rightarrow \quad \delta = \lambda_1 + \lambda_3 \qquad (9)$$

Substituting the value of (9) into (8), therefore,

$$\sigma = (\lambda_3 + \lambda_4 + 2\lambda_1 - \xi) \qquad (10)$$

Finally, for death rate to be constant, (which is practically very difficult and unusual), then, from equation (5)

$$(\lambda_1 + k)S + (\lambda_1 + \lambda_2)I_1 + (\lambda_1 + \lambda_4)I_2 + (\lambda_1 + \lambda_3)I_3 = 0$$

$$\Rightarrow$$

$$I_3 = -\frac{(\lambda_1 + k)S + (\lambda_1 + \lambda_2)I_1 + (\lambda_1 + \lambda_4)I_2}{\lambda_1 + \lambda_3}$$

{11}

From equation (8),

$$\lambda_4 = \sigma - \delta - \lambda_1 + \xi \qquad (12)$$

And substituting (9) and (12) into (11), then,

$$I_3 = -\frac{[(\lambda_1 + k)S + (\lambda_1 + \lambda_2)I_1 + (\sigma - \delta + \xi)I_2]}{\delta}$$

Furthermore, substituting for S and I_2 in this equation, and simplifying, then,

$$I_3 = -\frac{[\beta\{(\lambda_1 + k)(\sigma + \lambda_1 + \lambda_2 - \upsilon) + (\lambda_1 + \lambda_2)(\tau - \lambda_1 - k)\}]I_1 + (\sigma - \delta + \xi)(\tau - \lambda_1 - k)^2}{\beta((\tau - \lambda_1 - k)\delta}$$

(13)

Results

HIV Infection Status

It should however be noted that the results presented are those of the specifically targeted groups in the sentinel areas and not representative of the entire locations. Of the 12,000 subjects screened for HIV, 2199 (18.3%) were HIV positive, while 9801 (81.6%) were seronegative. The specific groups surveyed in each location had peculiar HIV-risk behaviours or exposures (Figure 1); however, no statistical difference was found between the means of the various groups (*P* = .04).

The distribution of HIV across the specific locations surveyed showed increased prevalence rate from 8.0% in Eha-Alumona (1999) to 22.0% in Obollo-Afor (2001), respectively (Figure 2). The t-test analysis showed a significant statistical difference between the means of the locations ($P < 0.05$; $P = 0.43$), thus indicating an increase in pattern of HIV infectivity in these areas during the years of study. Among the group regarded as the general population and therefore the comparative control group, i.e. those with unknown risk behaviours: 579 (19.2%) of the 3001 antenatal attendees were HIV positive 189 (18.4%) of the 1025 premarital couples were HIV positive while 18.1% of 1002 students screened were HIV seropositive (Figure 3).

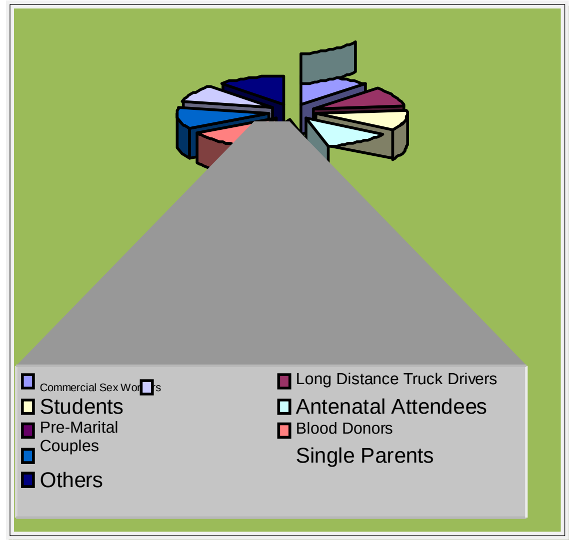


Figure 1: Pattern of HIV Distribution among Targeted Groups

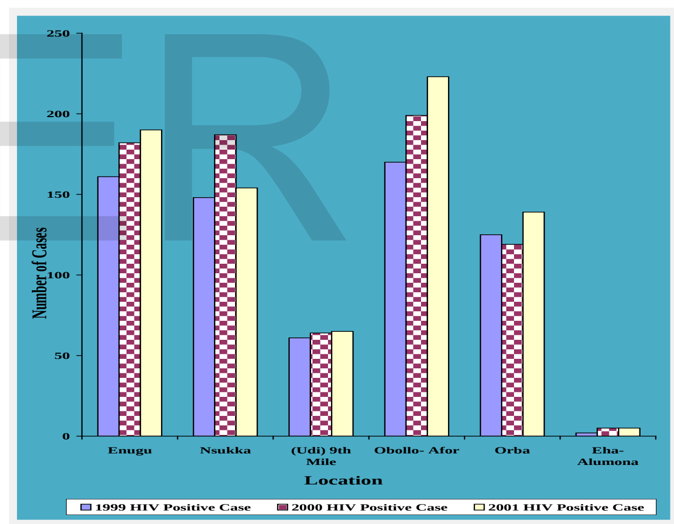


Figure 2: Prevalence of HIV in Surveyed Locations, 1999-2001

HIV status of individuals with known risk behaviours or lifestyles, consisting of Commercial sex workers, Street Children and Single parents similarly had a high prevalence rate. Of the 2,437 Commercial sex workers screened, 491 (20.1%) were seropositive for HIV (frequency distribution of 0.22); while 189 (19.0%) of the Street Children were HIV seropositive. Least prevalence rates were observed among the Single parents: 12 (16.0%) of those surveyed were seropositive for HIV.

A total of 326 of the 2199 blood donors (14.8%) screened during the study were HIV positive. Of the 1,364 screened male blood donors, 197 were seropositive for HIV, and 129 of the 835 female blood donors were HIV seropositive. The prevalence rates for male and female are 14% and 15% respectively. The observed female blood donors were basically those who donated for relatives or friends and not for commercial purposes, since commercial blood donation is not allowed among women due partly to their physiological status. No established significant statistical difference was however found between the means of the male and female blood donors ($P < 0.05$), implying equal chances of exposure of both sexes to HIV infection.

Of the 2199 HIV positive cases, studied, 929 were males (17%), while 1270 were females (19%). An increased HIV prevalence rate from 15.9% in 1999 to 17.5% in 2000 and 2001 respectively was observed among the males; and a similar increase from 17.3% in 1999 to 20.8% in 2001 occurred among the females

Age specific distribution of HIV infections in the surveyed locations showed the highest prevalence among those aged 16-30 years (28.1%), followed by those in the 31-45-age range (24.0%). The least however was among those aged ≥60 years (6.3%). Chi-square and relative risk analyses of age distribution of HIV infection among the subjects studied indicate strong association ($P < 0.05$), 16–30 age group with relative risk (RR) of HIV infection of 2.0; and 31–45 age group (RR = 1.4). These groups are thus considered potential risk groups of HIV infection and transmission. Individuals less than 15 years old had a relative risk of 0.6 of getting infected with HIV. For the group 46-59, the calculated RR was 1.0 and 0.4 for those aged ≥ 60 years.

The analysis of the identified risk factors to HIV infection in the sentinel areas indicated a high association between commercial sex working (20.1%) and multiple sex partnering (17.5%) in HIV disease transmission. However, a correspondingly high prevalence rate of 18.8% was observed among those with no-known-risk lifestyles, the control group (students, premarital couples and antenatal attendees).. The relative risks of commercial sex working, multiple sex partnering and transfusion of blood and blood products were calculated as 1.1, 1.0, and 1.0. Statistical analysis of the mean incidence of HIV infection among these groups showed no significant difference ($P < 0.05$), thus indicating that both commercial sex working and the control groups (e.g. the pre-marital couples and antenatal attendee) (by their clandestine commercial sex lifestyles) are all significant risk factors to HIV infection.

THE EQUILIBRIUM ANALYSIS

In equation (1), the rate constant β could be written more specifically as

$\beta = N + \eta$ where

N is the normal sexual behaviour of the larger population that is the feeder population

η is the further induced sexual behaviour due to poverty or as a sex worker.

In other words if $\eta = 0$, then $\beta = N$ and our population of interest becomes the larger feeder population with the normal sexual behaviour of the population not affected by being a sex worker.

From equation (6), it is observed that the susceptible population will be stable if the infected and infective population (I_2) could be given as

$$I_2 = \frac{\tau - \lambda_1 - k}{\beta}$$

where

τ is the rate of recruitment of the susceptible

λ_1 is the natural death rate of the susceptible

k is the migration rate of the susceptible

β is the rate of interaction between I_2 and S.

In the absence of migration in the population therefore,

$$I_2 = \frac{\tau - \lambda_1}{\beta},$$ and since natural death rate is rather small in the susceptible population; and β is not necessarily small, then I_2 is considered very small (and this is the only condition under which the susceptible population will be in equilibrium).

From equation (7), the condition under which I_1 (infected but not infective) can be in equilibrium state is observed; and this requires that the susceptible population S be given as

$$S = \frac{(\sigma + \lambda_1 + \lambda_2 - \upsilon)I_1}{\tau - \lambda_1 - k}$$

Hence, if $\tau = \lambda_1 + k$, then S will explode implying that there is large inflow of susceptible population and thus not stable. However if S is stable as shown above, then

$$I_1 = \frac{(\tau - \lambda_1 - k)S}{\sigma + \lambda_1 + \lambda_2 - \upsilon}$$

This implies that if $\tau = \lambda_1 + k$, then $I_1 = 0$ and so no further infection and the rest of the population should be stable. However, in reality $\tau \neq \lambda_1 + k$ and so $I_1 \neq 0$ thus there is always infection taking place.

In equation (13), it is observed however, that $I_1 = 0$, does not guarantee $I_3 = 0$ since it is known that I_2 may not be zero and has to still advance to I_3.

Similarly I_2 denotes the totality of AIDS patients in the population. Thus I_3 can only be zero if $I_1 = 0$ and $I_2 = 0$ respectively, implying that there should be no infected as well as infective individuals in the population.

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Finally, it has to be noted that R cannot be zero since death can occur even in the absence of the HIV/AIDS transmission in the population.

THE STABILITY STUDY OF THE PREVALENCE RATE IN THE SYSTEM

For the stability of equation (1) – (5), we can as well look for the steady state of the system, i.e a constant solution of (1) – (5). In this regard we look at the trivial solution of (1) – (5).

Now, suppose the steady state of system (1) – (5) exists, then we observe that

$$\frac{dS}{dt} = \frac{dI_1}{dt} = \frac{dI_2}{dt} = \frac{dI_3}{dt} = \frac{dR}{dt} = 0$$

From (6) the following is obtained:

$$I_2 = \frac{\lambda_1 + k - \tau}{\beta}, \text{ since } S \neq 0 \qquad (6)$$

$$S = \frac{(\sigma + \lambda_1 + \lambda_2 - \upsilon)I_1}{\beta I_2}$$

from equilibrium equation and (6) and (7)

$$\sigma = \delta + \lambda_4 + \lambda_1 - \xi \qquad (8)$$

$$\delta = \lambda_1 + \lambda_3 \qquad (9)$$

$$(\lambda_1 + k)S + (\lambda_1 + \lambda_2)I_1 + (\lambda_1 + \lambda_4)I_2 + (\lambda_1 + \lambda_3)I_3 = 0 \qquad (11)$$

Substituting (9) in (8) then,

$$\sigma = \lambda_3 + \lambda_4 + 2\lambda_1 - \xi \qquad (10)$$

Using equations (7)-(10) in (11), then,

$$I_3 = -\frac{[\beta\{(\lambda_1 + k)(\sigma + \lambda_1 + \lambda_2 - \upsilon) + (\lambda_1 + \lambda_2)(\tau - \lambda_1 - k)\}]I_1 + (\sigma - \delta + \xi)(\tau - \lambda_1 - k)^2}{\beta((\tau - \lambda_1 - k)\delta} \qquad (13$$

Suppose that at the initial stage of the study that no case of full blown AIDS was recorded in the population, this then implies that

$$I_3 = 0 \qquad (14)$$

And if this is the case, then

$$I_1 = \frac{(\delta - \sigma - \xi)(\lambda_1 + k - \tau)^2}{\{(\lambda_1 + k)(\sigma + \lambda_1 + \lambda_2 - \upsilon) + (\lambda_1 + \lambda_2)(\tau - \lambda_1 - k)\}\beta}$$

(15)

Equation (14) substituted in (7) yields

$$S = \frac{(\sigma + \lambda_1 + \lambda_2 - \upsilon)(\delta - \sigma - \xi)(\lambda_1 + k - \tau)}{\{(\lambda_1 + k)(\sigma + \lambda_1 + \lambda_2 - \upsilon) + (\lambda_1 + \lambda_2)(\tau - \lambda_1 - k)\}\beta}$$

(16)

From the steady-state condition of (1) – (4) and the assumption that at the initial time of our study no full blown patient was found, equations (14), (15) and (16) are thus obtained.

From this result then, it is observed that the steady state of (1) – (4) is not all zero solution; hence the steady state of (1) – (4) exists. This point (solution) called the steady state is then denoted by $P\left(\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_3\right) \equiv (\alpha, \gamma, \eta, 0)$, where

$$\alpha = \frac{(\sigma + \lambda_1 + \lambda_2 - \upsilon)(\delta - \sigma - \xi)(\lambda_1 + k - \tau)}{\{(\lambda_1 + k)(\sigma + \lambda_1 + \lambda_2 - \upsilon) + (\lambda_1 + \lambda_2)(\tau - \lambda_1 - k)\}\beta},$$

$$\gamma = \frac{(\delta - \sigma - \xi)(\lambda_1 + k - \tau)^2}{(\lambda_1 + k)(\sigma + \lambda_1 + \lambda_2 - \upsilon) + (\lambda_1 + \lambda_2)(\lambda_1 + k - \tau)\beta},$$

$$\eta = \frac{\lambda_1 + k - \tau}{\beta}$$

Now considering a neighbourhood close to the steady state we have:

$S = \hat{S} + A$, $\quad I_1 = \hat{I}_1 + B$, $\quad I_2 = \hat{I}_2 + C$, $I_3 = \hat{I}_3 + D$.

Expanding (1) – (4) in Taylor's series, about $(\alpha, \gamma, \eta, 0)$, and retaining only the linear terms we get

$$\begin{bmatrix} \frac{dS}{dt} \\ \frac{dI_1}{dt} \\ \frac{dI_2}{dt} \\ \frac{dI_3}{dt} \end{bmatrix} = X \begin{bmatrix} S \\ I_1 \\ I_2 \\ I_3 \end{bmatrix}, \text{ where}$$

$$X = \begin{bmatrix} \tau + \beta I_2 - \lambda_1 - k & 0 & -\beta S & 0 \\ \beta I_2 & 0 & \beta S & 0 \\ 0 & 0 & \upsilon - \sigma - \lambda_1 - \lambda_2 & 0 \\ 0 & 0 & 0 & \delta - \lambda_1 - \lambda_3 \end{bmatrix}$$

The stability of the model is further summarized using the eigenvalues of X. From differential equation, the steady state of system (1) – (4) where $|X| \neq 0$ is observed to be stable if the real part of the eigenvalues of X is all non- negative, and is asymptotically stable if the matrix X has all its eigenvalues of negative real parts. This view (study) is supported by the Routh-Hurwitz criterion:

ROUTH-HURWITZ CRITERION:

The necessary and sufficient condition for the roots of a polynomial equation

$$\sum_{i=1}^{n} a_{n-i} \lambda^i = 0, \qquad (17)$$

for real coefficient $a_i (i = 1,2,...,n)$ to have a negative real parts, is that the principal diagonal matrix $\Delta_i (i = 1,2,...,n)$ of (17) must be positive in the Hurwitz matrix. From this result, it is observed that if (X') should have negative real part, then

(i) $\tau + \beta \hat{I}_2 > \lambda_1 + k$ (18)

(ii) $\upsilon > \sigma + \lambda_1 + \lambda_2$ (19)

(iii) $\sigma + \zeta > \delta + \lambda_1 + \lambda_4$ (20)

(iv) $\delta > \lambda_1 + \lambda_3$ (21)

where

$$X' = \begin{bmatrix} \tau + \beta \hat{I}_2 - \lambda_1 - k & 0 & -\beta \hat{S} & 0 \\ \beta \hat{I}_2 & 0 & \beta \hat{S} & 0 \\ 0 & 0 & \upsilon - \sigma - \lambda_1 - \lambda_2 & 0 \\ 0 & 0 & 0 & \delta - \lambda_1 - \lambda_3 \end{bmatrix}$$

DISCUSSION

The observed prevalence rates in these areas is in consonance with the 2003 UNAIDS global HIV prevalence reports: 20.1% in South Africa, 0.8% in India, 15.0% in Kenya, 33.7% in Zimbabwe (UNAIDS, 2003); as well as the National HIV prevalence, which recorded an increase from 1.4% in 1999 to 4.5% in 1994 and 5.4% in 1999 (FMOH, 1999). The results obtained at Obollo-Afor showing an increase of 16.4% in 1999, 22.0% in 2001; may reflect a steady source of infection, namely the commercial sex workers. Their clients and the ones at the risk of infection are mostly the long distance truck drivers. Kanki *et al.* (1990) had earlier indicated that a common feature of the HIV epidemics is the rapidity of the spread, once the virus finds a foothold in a vulnerable population. The vulnerable population in Obollo-Afor, namely the sex workers had the singular disposition to be infected and to infect others because of the economic importance of the town as a major bus stop (on the North-East highway) and the resultant proliferation of business activities. Nevertheless, the limitation of the survey in Obollo-Afor was that the data obtained could not be regarded as representative of the whole town, since the emphasis/focus of the study was on commercial sex workers and their clients who constituted a majority of the risk groups in the town.

The fairly high prevalence of HIV-positive cases among the antenatal patients in Enugu (17.8% in 1999, and 21.0% in 2001) can be viewed from the perspective of the general population where they were classified. However, it was not possible to particularly pinpoint the sources of infection of some of these patients. It would be assumed that some of them might have been infected through their extramarital activity or by importation of HIV to the home by husbands who keep sexual partners apart from their spouses. It is also possible that many of them may have been infected through patronage of local medicine storekeepers who inject clients, most often, with unsterilized needles and syringes. Ankrah and Rwabukwali (1987); Donnelly *et al.* (1993) and Ogbuagu and Charles (1993), had earlier reported on the problem associated with HIV transmission through spouse as well as other related heterosexual HIV transmissions, thus confirming the impact of extramarital sex on HIV transmission reported in this study.

Other factors enhancing HIV transmission in Enugu is the proliferation of business activities (including sex working) as a result of the presence of several governmental and non-governmental parastatals as well as several large markets, all of which attract huge crowds into the city. There is also an observed high level of poverty as a result of overcrowding and the resultant lack of job, and adequate accommodation in the urban centre of Enugu inspite of the available establishments. These create desperation and subsequently vulnerability of young people (mostly women) to risk behaviours that expose them to HIV infection. This observation is affirmed by similar reports of UNAIDS (2001); Ullrich (2003) and Mirjam (2002) on urban and peri-urban HIV transmission as a result of poverty in sub-Saharan Africa. It was further observed from this study that basically all the social factors or circumstances which directly or indirectly enhance HIV transmission in the otherwise rural areas of Obollo-Afor, Orba and Eha-Alumona are found in the metropolitan city of Enugu, the State Capital. No significant difference was therefore found in the level of HIV prevalence in Enugu urban and other locations in the State. This result is also confirmed by the 2002 National HIV Surveillance Technical Report, which indicated an increase in both rural and urban HIV prevalence. The present observation is also in consonance with the UNAIDS (2003) report indicating that the epidemic is generalized in terms of sex, urban and rural areas as a result of the dynamic movement of people from cities to the villages and vice versa: most workers return from the cities to the villages either weekly or during festivities. Furthermore whatever geographical barrier there would have been between city and village is easily concealed by such movements between those probably infected in the cities that come back to the village to continue their sexual relationships thereby transmitting the virus in the village. This may further explain the observed increase in the rural and urban areas surveyed, as earlier reported by Ulrich (2003) and Mirjam (2002).

HIV infection among single parents/mothers in the Eha-Alumona, a characteristically rural town, was also noted to have a steady increase from 8.0% in 1999 to 20.0% in 2001. This group (though homogenous) was identified during this study to be young ladies whose exposure to HIV infection has been attributed largely to poverty, illiteracy and lack of job opportunities. The observed circumstances that predisposed these ladies to HIV infection as well as the recorded high HIV prevalence rates among them depict a fast growing population of young people with no perceived future, as well as a generalized increasing level of economic deprivation. The high prevalence of HIV infection in Orba (16.6% in 1999 to 18.5% in 2001) may not be divorced from the commercial activities in Orie-Orba, the International Market in Enugu State which attracts several traders from Nigeria and other West African countries. The highlight of this market (as observed from the BSS in another report of this study) is that itinerant traders spend days, weeks or months here outside their homes during which time they constitute notable clients for the local sex workers. In addition, this survey observed that some private laboratories and/or clinics in this location run blood-banking services with doubtful screening records. These are possible sources of HIV infection and transmission in this otherwise rural town.

Nsukka urban on the other hand, had an average prevalence rates of 15.3% during the period. While multiple sex partnering, poverty, illiteracy, polygamy and other socio-cultural factors could impact HIV transmission here, the influence of the University and the liberal social culture it brings could not be overlooked. There are students expressing their freedom from home by unrestricted and clandestine sex associations and some giving sex for money or favours. There are also the local girls who view the University students as pace setters and copy their lifestyle and of course sexual behaviours. These build up to high sexual activity discretely going on in the town and of course multiple sex-partnering, already identified in the BSS to boost the HIV-transmission in the population. The profile of reported HIV cases in the 9th Mile, Udi ranged from 18.4% in 1999 to 19.6% in 2001. Gender specific prevalence of this group ranged from 17.4% among the males to 21.4% among the females. The surveyed group represents youths with no family or societal restrictions on sexual indulgence and who infact have evolved using sex as a means of survival. Thus, their prevalence rates show the level of sexual abuse among themselves and with others in the area either forcefully taken or given for some favour as identified during the socio-cultural studies. Their vulnerability, poverty, illiteracy ignorance and inability to negotiate for safe sex, were considered possible factors responsible for HIV transmission among these Street Children. This factor was also observed by Olaleye (1993), on HIV prevalence among youths, and by Ogbuagu and Charles (1994) on sexual networking among adolescents in Calabar.

Evaluation of the sex distribution of HIV in the area indicated a higher prevalence among the females. The gender prevalence rates observed during the study suggest that females were more exposed to HIV infection than their male counterparts. This could be attributed to a number of factors such as the multiple sex partnering prevalent among the females (as a result of poverty), and exposure to other sexually transmitted infections which can enhance HIV transmission. It was further observed (from the BSS) that with the resultant worsening economic situation, and the tearing apart of social fabric, sexual contacts (notably multiple sex partnering: premarital or extra-marital) which provide immediate cash are becoming increasingly important. Consequently, these women of various classes sought occasional or regular sexual partners to meet their immediate financial needs (as a result of economic recession). These observations were confirmed by the reports of Over (1992) and Cohen (1993) on the socio-economic impact of HIV/AIDS.

Results of the age distribution of HIV infection in the areas of study indicated that individuals aged 16-≤ 30 years appeared to be at greater risk of HIV infection (RR = 1.8). This increase might be related to the level of exposure to society and societal influences; age of freedom from parental controls, influences of peers, age of sexual experimentation, alcohol, smoking and age of consciousness of unemployment. This view was also held by Uwakwe (1994) on the level of HIV infection in the area, and the Federal Ministry of Health's 1999 Technical Report which indicated that individuals aged 15-30 are more at risk of HIV infection (FMOH, 1999). Another observation is that there is presently a reduction in the age of menarche; people are becoming increasingly mature and sexually active at a younger age (than previously) hence there is increased rate of sexual exploitation and exploration and the resultant exposure to HIV infection (Ogbuagu and Charles, 1994). Nevertheless, the observed association between age and HIV infection has serious implications for the future of the area as well as the nation because these young people who are becoming increasingly seropositive are the future hope of the nation; the more they are infected, the more bleak the future, as reported by Abiodun (1993).

Evaluation of the HIV status of the two major classes of people in the surveyed population, namely; those with known risk behaviours: commercial sex workers, and Street Children, and those with unknown risk behaviours: the antenatal attendees, showed no significant difference in the prevalence rates ($P = 0.051$). The HIV prevalence studies among certain occupational groups in the area identified the following as high risk groups and thus risk factors to HIV infection: individuals with known risk behaviours: commercial sex working , multiple sex partnering, transfusion of blood and blood products. Prevalence rates of the control groups: students, premarital couples, and antenatal attendees, prevalence was 18.8%. However, no significant difference was found in their prevalence rates ($p = 0.051$), as the observed HIV prevalence among the control group was equally high. Thus, contrary to the generalized concept that commercial sex working is the major risk factor of HIV infection as earlier reported by several researchers including Ogbuagu and Charles (1993) and Abinbola *et al*. (1991), results of this study indicates that commercial sex working has become a generalized term and includes all those who directly or indirectly sell sex for money or favour and is no longer restricted to those based in the hotels. This view is therefore supported by the observation that students and others in the control group do also engage in clandestine commercial sex working though they are not resident in hotels. The risk of HIV infection has therefore become generalized: anyone who engages in multiple sex partnering is at high risk of HIV infection. This observation finds credence in the clandestine sex lifestyle noted among the single women particularly, whose HIV status was confirmed by laboratory investigations. The stability of HIV infection in the studied population is summarized by the Routh-Hurwitz stability criterion.

DISCUSSION ON THE STABILITY ANALYSIS.

In modelling the prevalence of HIV in the target population, the study assesses the transmission dynamics in order to evaluate the equilibrium conditions for continuity and maintenance of the disease and observes that for the stability of the solution of system (1) to (4), as required by equations (18) to (21) to be guaranteed, the following must exist:

(i). In (18), recruitment rate of the susceptible class and rate at which individuals in the class are infected must be greater than the combination of rate of removal of members of this class.

(i) In Equation (19), it is required that inflow of infected persons into the class of infected but not infective class dominates others in this class.

(ii) Equation (20) states that the rate of conversion from infected to infective and inflow of the infective persons should outnumber the removal rate of persons in this infective class.

(iii) Finally (21) demands that in the class of full blown AIDS; the rate at which the infected and infective progress to full blown AIDS should be greater than the rate at which the AIDS patients die.

For the solution to be stable, then conditions (18) to (21) holds in consonance with the Routh-Hurwitz Criteria (Hurwitz, 1964), which indicates that conditions that are necessary must be satisfied for a system to be stable, but conditions that satisfy these conditions might not all be stable. However, these conditions are not feasible in real life because their actualization implies that the prevalence rate of HIV in our population will be on the increase. This however may be possible in our target population given their peculiar characteristics. Secondly in any HIV population, especially our population of interest, where there is no cure and high risk of infection, it is impossible to satisfy (21). This then indicates that the stability of solution of system (1) to (4) is not guaranteed, hence it could be concluded that the system is unstable. On the contrary, the instability of the system shows that the said solution of this system sometimes diverges to infinity, implying a steady increase in the rate of infection in our target population.

Conclusion

One of the targets of this epidemiologic surveillance was to provide the necessary information to contend with the factors driving HIV infection in the study locations. The study observed that the HIV epidemic is as yet neither stable nor declining. Available results have shown that prevalence rate of HIV is high both in groups with risk behaviours and the general population. These indicate that even in the general population where there were no apparently risk behaviours, there may be known risk behaviours such as the identified sociocultural and socioeconomic behavioural patterns or attitudes that constitute risk factors to these HIV/AIDS and AIDS-related infections: high level of multiple sex partnering mostly expressed in forms of pre and post-marital heterosexual contacts. The prevalence of HIV infection especially among sexually active and reproductive age groups (16-45 years) in the area is a reflection of the prevalence of HIV disease in the country. Targeting of the young people therefore becomes a necessity

The failure to meet the conditions needed for the stability of the system (1) to (4) implies that the prevalence of HIV/AIDS in our target population will always be on the increase. Reversing this ugly trend therefore means reversing some of the assumptions. This can be achieved by

(a). Introducing and improving antiretroviral therapy among other intervention programmes in addition to careful living or behaviour change options.

(b). Creating jobs to help reduce poverty induced sex workers in this population.

(c). Awareness campaign should also be beefed up in this population to further sensitize the populace about the scourge of the disease.

(d). It will also do this population a great help if there should be a regulatory body to control inflow of individuals into its population.

(e). In the face of increasing perenatal HIV transmission, there is need to include short course treatments to prevent mother-to-child HIV transmission. Similarly, care initiatives should aim at providing basic care and support to those living with and affected by HIV/AIDS.

(F). A continued epidemiologic surveillance study or research to unravel other potential socio-cultural and socio-economic behavioural risk factors to HIV infection in the surveyed areas is needed for more effective HIV education and prevention programmes.

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