INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
Mail : ICDDR,B, GPO Box 128, Dhaka-1000, Bangladesh
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ICDDR,B CENTRE FOR HEALTH AND POPULATION RESEARCH

Memorandum

23 August 1999

To : Dr. Motiur Rahman
Laboratory Sciences Division

From : Professor Mahmudur Rahman
Chairman, Ethical Review Committee

Sub : Protocol # 99-013

This has reference to your memo of 18th August 1999 along with the modified copy of your protocol # 99-013 entitled "Prevelance of treatment failure due to ciprofloxacin and ceftriazone in gonorrhoea among Bangladeshi female sex workers" (revised title). I am pleased to inform you that the protocol is hereby approved upon appropriate your addressing of the issues raised by the Committee in its meeting held on 4th August 1999.

Thank you.

copy:- Chairman
Research Review Committee

- Division Director
Laboratory Sciences Division

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CENTRE FOR HEALTH AND POPULATION RESEARCH

Date: August 18, 1999

To: Chairman
Ethical Review Committee, ICDDR,B

From: Dr. Motiur Rahman
Assistant Scientist
LSD, ICDDR,B

Motiur Rahman

Sub: Resubmission of protocol for ERC approval.

Dear Sir,

Enclosed please find the revised version of the proposal entitled " **Prevalence of treatment failure due to ciprofloxacin and ceftriaxone in gonorrhea among Bangladeshi female sex workers**" for ERC approval.. The proposal has been revised and corrected as advised by ERC in consultation with Dr. Halida A. Akthar.

Encl:

Revised version of the proposal

Cc: Chairman RRC
Division Director, LSD.

Dear Mr. Chairperson, ERC, ICDDR,B.
The changes made by the PI in the proposal was done in consultation with me and comply with the suggestions made by the ERC. The proposal may now be approved.
Thanks.
19/8/99

Attachment 1

APPROVED COPY

(FACE SHEET) **ETHICAL REVIEW COMMITTEE, ICDDR,B.**

Principal Investigator: Motiur Rahman.

Application No. 99-013

Title of Study: Prevalence of treatment failure in gonorrhea due to ciprofloxacin and ceftriaxone among Bangladeshi female sex worker's.

Trainee Investigator (if any): _____

Supporting Agency (if Non-ICDDR,B) _____

Project Status: _____

[X] New Study

[ ] Continuation with change

[ ] No change (do not fill out rest of the form)

Circle the appropriate answer to each of the following (If Not Applicable write NA)

1. Source of Population:
   - (a) Ill subjects — (Yes) No
   - (b) Non-ill subjects — (Yes) No
   - (c) Minor or persons under guardianship — Yes (No)

2. Does the Study Involve:
   - (a) Physical risk to the subjects — (Yes) No
   - (b) Social risk — (Yes) No
   - (c) Psychological risks to subjects — (Yes) No
   - (d) Discomfort to subjects — (Yes) No
   - (e) Invasion of privacy — (Yes) No
   - (f) Disclosure of information damaging to subject or others — (Yes) No

3. Does the Study Involve:
   - (a) Use of records (hospital, medical, death or other) — Yes (No)
   - (b) Use of fetal tissue or abortus — Yes (No)
   - (c) Use of organs or body fluids — (Yes) No

4. Are Subjects Clearly Informed About:
   - (a) Nature and purposes of the study — (Yes) No
   - (b) Procedures to be followed including alternatives used — (Yes) No
   - (c) Physical risk — (Yes) No
   - (d) Sensitive questions — (Yes) No
   - (e) Benefits to be derived — (Yes) No
   - (f) Right to refuse to participate or to withdraw from study — (Yes) No
   - (g) Confidential handling of data — (Yes) No
   - (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — (Yes) No

5. Will Signed Consent Form be Required:
   - (a) From subjects — (Yes) No
   - (b) From parents or guardian (if subjects are minor) — Yes (No)

6. Will precautions be taken to protect anonymity of subjects — (Yes) No

7. Check documents being submitted herewith to Committee:
   - ___ Umbrella proposal - Initially submit an with overview (all other requirements will be submitted with individual studies
   - X Protocol (Required)
   - X Abstract Summary (Required)
   - X Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw) (Required
   - X Informed consent form for subjects
   - ___ Informed consent form for parent or guardian
   - X Procedure for maintaining confidentiality
   - ___ Questionnaire or interview schedule*

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary

1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy
2. Example of the type of specific questions to be asked in the sensitive areas
3. An indication as to when the questionnaire will be presented to the Committee for review

We agree to obtain approval of the Ethical Review Committee for any changes involving the rights and welfare of subjects before making such change.

Motiur Rahman 18/8/99

Principal Investigator

Trainee

Abstract for ERC

Sexually transmitted infections (STIs) represent a major public health problem in the developing countries. The burden of disease represented by STIs including HIV is not known; however, it is estimated that there are 333 million new cases (Trichomoniasis 170 million, Genital Chlamydia 89 million, Gonorrhea 62 million, and Syphilis 12 million) of STIs per annum and 10 to 15 million people are infected world wide with HIV every year. The estimated magnitude of new cases of human papillomavirus (HPV), herpes simplex virus (HSV) and chancroid are 30, 20 and 7 million respectively per annum. The major focus for STIs is South East Asia with an estimated 150 million new cases in 1995(WHO report 1995).

Commercial sex workers are the major reservoir of STIs including AIDS and remains as the potential source of infection for the society. It has recently been shown that co-infection of HIV with bacterial and parasitic agents of STIs/RTIs, increases the release of virion particles in the semen and ulcers in the genital region and thus increases the risk of both transmission and acquisition of HIV by patients with STIs.

The prevalence of sexually transmitted infection (STIs) including gonorrhea is high among female sex workers (FSWs) in Bangladesh. Available data shows that 35% to 40% of FSWs are culture positive for *N. gonorrhoeae*. Ciprofloxacin is recommended by WHO for the treatment of uncomplicated gonorrhea and is extensively used in Bangladesh as a part of syndromic management. Ongoing studies in our lab indicates that as much as 11% of *N. gonorrhoeae* isolates from FSWs currently show in vitro resistance and 35% had reduced susceptibility to ciprofloxacin. The appearance of large number of *N. gonorrhoeae* isolates with reduced susceptibility to ciprofloxacin strongly suggests the need to study the prevalence of treatment failure due to ciprofloxacin and study the efficacy of an alternate drug (ceftriaxone) recommended by CDC for the treatment of gonorrhea in Bangladesh.

A prospective randomized study will be conducted among FSWs in Dhaka city. Subjects with suspected gonorrhea will be treated with either ciprofloxacin or ceftriaxone and endocervical and high vaginal swab will be collected. Endocervical swab will also be collected from asymptomatic subjects and will be treated similarly, if found to be culture positive for *N. gonorrhoeae*. All subjects will be requested to attend the clinic after 7 days for follow up. A second endocervical swab will be collected from all subjects and treatment will be altered according to laboratory findings or WHO syndromic management guideline. Swabs will be used for culture of *N. gonorrhoeae*, diagnosis of *Chlamydia trachomatis* and *Trichomonas vaginalis*. Antimicrobial susceptibility and minimum inhibitory concentrations (MICs) of *N. gonorrhoeae* isolates to fluoroquinolones and cephalosporins will be determined by disk diffusion and agar dilution or E-test. Treatment failure will be considered if a patient is found to be culture positive with the same isolate one week after treatment.

Clarification of other points (as requested in attachment 1a)

1. This study aims at evaluation treatment failure due to ciprofloxacin in gonorrhea among female sex workers therefore sex worker will be enrolled in the study.
2. There is no potential risk for the patients as we will collect specimen for routine diagnosis.
3. Autoclaved vaginal speculum will be used and only standard clinical examination will be performed.
4. All data obtained during clinical examination as well as laboratory finding are strictly confidential.
5. a. Signed consent form will be obtained.
   b. Patient will be informed about the results.
6. Not applicable
7. Patient will get free diagnosis of their disease and will get free treatment. This study will provide us data regarding the prevalence treatment failure in gonorrhea and efficacy of ceftriaxone for the treatment of gonorrhea.
8. This study will require endocervical swab.

Principal Investigator: Last, first, middle Rahman Motiur

International Centre for Diarrhoeal Disease Research, Bangladesh

RESEARCH PROTOCOL

FOR OFFICE USE ONLY
Protocol No: Date:
RRC Approval: Yes/ No Date:
ERC Approval: Yes/No Date:

1. **Title of Project (Do not exceed 60 characters including spaces and punctuation's)** Prevalence of treatment failure due to ciprofloxacin and ceftriaxone in gonorrhea among Bangladeshi female sex workers.

2a. Name of the Principal Investigator(s) (Last, Middle, First).	2b. Position / Title	2c. Qualifications
Motiur Rahman	Asstt. Scientist	MBBS, Ph. D

3. **Name of the Division/ Branch / Programme of ICDDR,B under which the study will be carried out.**
Laboratory Science Division (LSD)

4. **Contact Address of the Principal Investigator**
4a. Office Location:
Laboratory Science Division

4b. Fax No: 872529
4c. E-mail: motiur@cis.icddrb.org
4d. Phone / Ext: 2405, 2408

5. **Use of Human Subjects** Yes [X] No [ ]
5a. Use of Live Animal Yes [ ] No [X]
5b. If Yes, Specify Animal Species

6. **Dates of Proposed Period of Support** *(Day, Month, Year - DD/MM/YY)*
01 - 07 – 99 to 31 - 12 - 2000

7. **Cost Required for the Budget Period**
7a. 1st Year ($): 45,400 *2nd Year ($):* 10,150 *3rd Year:*
7b. Direct Cost ($) 55,550 **Total Cost ($)**

8. **Approval of the Project by the Division Director of the Applicant**

The above-mentioned project has been discussed and reviewed at the Division level as well by the external reviewers. The protocol has been revised according to the reviewer's comments and is approved.

Name of the Division Director Signature Date of Approval

9. **Certification by the Principal Investigator**

I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

10. Signature of PI Motiur Rahman

Date: 18/8/99

Principal Investigator: Last, first, middle Rahman Motiur

Table of Contents

X Check here if appendix is included

Principal Investigator: Last, first, middle Rahman Motiur

PROJECT SUMMARY: Describe in concise terms, the hypothesis, objectives, and the relevant background of the project. Describe concisely the experimental design and research methods for achieving the objectives. This description will serve as a succinct and precise and accurate description of the proposed research is required. This summary must be understandable and interpretable when removed from the main application. (TYPE TEXT WITHIN THE SPACE PROVIDED).

Principal Investigator: **Motiur Rahman**

Project Name: **Treatment failure due to ciprofloxacin in gonorrhea among Bangladeshi female sex workers.**

Total Budget	Beginning Date	Ending Date
55,550	July 1999	December 2000

Hypotheses:

1. Treatment failure due to ciprofloxacin in gonorrhea will be high in Bangladesh.
2. Treatment failure occurred due to appearance of *N. gonorrhoeae* clones resistant to fluoroquinolones.
3. Treatment failure will be less in ceftriaxone therapy as compared to ciprofloxacin.
4. Ceftriaxone is effective against gonorrhea in Bangladesh and should be included as first line therapy in the treatment guideline for syndromic management.

Aims of the study:

1. To study the treatment failure due to ciprofloxacin and ceftriaxone in gonorrhea.
2. To study the efficacy of ceftriaxone in the treatment of gonorrhea and its comparison with currently used ciprofloxacin.
3. To study the prevalence of ciprofloxacin resistance in *N. gonorrhoeae* among female sex workers (FSWs).

Background: The prevalence of sexually transmitted infection (STIs) including gonorrhea is high among female sex workers (FSWs) in Bangladesh. Available data shows that 35% to 40% of FSWs are culture positive for *N. gonorrhoeae*. Ciprofloxacin is recommended by WHO for the treatment of uncomplicated gonorrhea and is extensively used in Bangladesh as a part of syndromic management. Ongoing studies in our lab indicates that as much as 11% of *N. gonorrhoeae* isolates from FSWs currently show in vitro resistance and 35% reduced susceptibility to ciprofloxacin. The appearance of large number of *N. gonorrhoeae* isolates with reduced susceptibility to ciprofloxacin strongly suggests the need to study the prevalence of treatment failure due to ciprofloxacin and study the efficacy of an alternate drug (ceftriaxone) recommended by CDC for the treatment of gonorrhea in Bangladesh.

Materials and Methods: A prospective randomized study will be conducted among FSWs in Dhaka city. Subjects with suspected gonorrhea will be treated with either ciprofloxacin or ceftriaxone and endocervical high vaginal swab will be collected. Endocervical swab will also be collected from asymptomatic subjects and will be treated similarly, if found to be culture positive for *N. gonorrhoeae*. All subjects will be requested to attend the clinic after 7 days for follow up. A second endocervical swab will be collected from all subjects and treatment will be altered according to laboratory findings or WHO syndromic management guideline. Swabs will be used for culture of *N. gonorrhoeae*, diagnosis of *Chlamydia trachomatis* and *Trichomonas vaginalis*. Antimicrobial susceptibility and minimum inhibitory concentrations (MICs) of *N. gonorrhoeae* isolates to fluoroquinolones and cephalosporins will be determined by disk diffusion and agar dilution or E-test. Treatment failure will be considered if a patient is found to be culture positive with the same isolate one week after treatment.

Principal Investigator: Last, first, middle Rahman Motiur

KEY PERSONNEL (List names of all investigators including PI and their respective specialties)

Name	Professional Discipline/ Specialty		Role in the Project
1. Motiur Rahman	MBBS, Ph D.	Microbiologist & Molecular biologist	Principle investigator
2. M. John Albert	Ph D., MRCPath	Microbiologist	Coinvestigator
3. Dr. Shahnaoaz Alam	MBBS, MPH	Coordinator Concern Bangladesh	Coinvestigator
4. Dr. M. A. Salam	MBBS	Chief Physician, CRSC CSD, ICDDR,B	Coinvestigator

DESCRIPTION OF THE RESEARCH PROJECT

Hypothesis to be tested:

Concisely list in order, in the space provided, the hypothesis to be tested and the Specific Aims of the proposed study. Provide the scientific basis of the hypothesis, critically examining the observations leading to the formulation of the hypothesis.

Hypotheses:

1. Treatment failure due to ciprofloxacin in gonorrhea will be high in Bangladesh.
2. High treatment failure is related to high prevalence of fluoroquinolone-resistant *N. gonorrhoeae.*
3. Treatment failure will be less in ceftriaxone therapy as compared to ciprofloxacin.
4. Ceftriaxone will be effective against gonorrhea in Bangladesh, which should be the first line therapy in the treatment guideline for syndromic management.

Specific Aims:

Describe the specific aims of the proposed study. State the specific parameters, biological functions/ rates/ processes that will be assessed by specific methods (TYPE WITHIN LIMITS).

Aims of the study:

1. To study the treatment failure due to ciprofloxacin and ceftriaxone in gonorrhea.
2. To study the efficacy of ceftriaxone in the treatment of gonorrhea and its comparison with currently used ciprofloxacin.
3. To study the prevalence of ciprofloxacin resistance in *N. gonorrhoeae* among female sex workers (FSWs).

Background of the Project including Preliminary Observations

Describe the relevant background of the proposed study. Discuss the previous related works on the subject by citing specific references. Describe logically how the present hypothesis is supported by the relevant background observations including any preliminary results that may be available. Critically analyze available knowledge in the field of the proposed study and discuss the questions and gaps in the knowledge that need to be fulfilled to achieve the proposed goals. Provide scientific validity of the hypothesis on the basis of background information. If there is no sufficient information on the subject, indicate the need to develop new knowledge. Also include the **significance and rationale** of the proposed work by specifically discussing how these accomplishments will bring benefit to human health in relation to biomedical, social, and environmental perspectives. (DO NOT EXCEED 5 PAGES, USE CONTINUATION SHEETS).

Background

Sexually transmitted infections (STIs)/ reproductive tract infections (RTIs) represent a major public health problem in the developing countries. Despite the sharp decline in the incidence of gonococcal infection in developed countries during the last decade, gonorrhoea remains as one of the most common venereal diseases in developing countries and a global health problem (De Schryver *et al.*, 1990). The problem is compounded by development of resistance to antimicrobials in *N. gonorrhoeae*, which is a result of both wide dissemination of resistant clones and the emergence of strains with novel mechanism(s) of resistance (Ison *et al.*, 1992). The advent and increase of human immunodeficiency virus (HIV) infection during the last decade has highlighted the importance of infections spread by the sexual route (Michael *et al.*, 1996). The burden of disease represented by STIs including HIV is not known; however, it is estimated that there are 62 million new cases of gonorrhea per anum and most of them are in South Asia and Africa (WHO report 1995).

Neisseria gonorrhoeae, the causative organism of gonorrhoea, is transmitted from person to person by direct, close and usually sexual contact (Knapp *et al.*, 1994). STIs including gonorrhoea have a major demographic, economic, and social impact and cause substantial morbidity and mortality. Most men (95%) who are infected with *N. gonorrhoeae* develop symptomatic urethritis, while infected women (40%) are usually asymptomatic or have mild and nonspecific symptoms, thus remain untreated for a long period. The symptoms that usually develop in females are cervicitis, urethritis, endometritis, vaginal discharge and vaginitis. Besides the acute symptoms of gonorrhoea, gonococcal infection causes upper genital tract infection (pelvic inflammatory disease) and its medical sequelae including infertility, ectopic pregnancy and chronic pelvic pain in women; and urethritis, epididymidis and their complications, stricture urethra and infertility in man and proctitis, pharyngitis, conjunctivitis and disseminated gonococcal infections in both sexes (De Schryver *et al.*, 1990; Sherrard *et al.*, 1995).

There has been growing evidence during recent years of the epidemiological synergism between HIV infection and STIs. A recent study has demonstrated that control of STIs in a high prevalence rural area of Tanzania reduced seroconversion to HIV by 40%. In a number of recent studies it has been shown that co-infection of HIV with bacterial and parasitic agents of STIs/RTIs, increases the release of viron particles in the semen and ulcers in the genital region and thus increases the risk of both transmission and acquisition of HIV by patients with STIs (Hoffman *et al.*, 1996; Wasserheit *et al*,. 1992). Gonococcal infection is also considered to act as an independent cofactor in the transmission of HIV infection (Anaya *et al.*, 1994).

Female sex workers (FSWs) serve as the largest reservoir of sexually transmitted disease in the society (Arya *et al.*, 1988). In most parts of Asia and Africa, 80% to 90% of the venereal infections, including gonorrhoea originate from FSWs (WHO 1963). FSWs were found to be the source of 60% of the gonococcal urethritis in men in Kenya (Adler *et al.*, 1996).

Recent data suggest that, in developing countries bacterial pathogens are the most reported causes of STIs and in STIs mixed bacterial pathogens frequently occur (Adler *et al.*, 1996). Syndromic approach to patient management as recommended by WHO is widely used but has obvious limitations. This approach has proven to have lesser predictive values in the diagnosis of chlamydial and gonococcal infections in high prevalence populations especially in women where asymptomatic carriage of the organism can be as high as 70% (Laga *et al.*, 1996).

Antimicrobial resistance of *N. gonorrhoeae* is an increasing public health problem. Gonococci, a highly adaptable pathogen, showed a demonstrable capacity to develop drug resistance. Therefore, gonococcal control strategies have relied on the use of highly effective and often single dose therapy administered at the time of diagnosis. Resistance to penicillin caused by penicillinase-producing *N. gonorrhoeae* (PPNG) was reported in early 1976 in the United States (Ashford *et al.*, 1976) and in the United Kingdom (Philips *et al.*, 1976). Since then, penicillinase-producing *N. gonorrhoeae* have been reported from many countries of South-east Asia and the Pacific. For more than a decade, tetracycline has been one of the preferred drugs for the treatment of uncomplicated gonorrhoea. High level plasmid mediated resistance to tetracycline in *N. gonorrhoeae* was first reported in 1985 (Morse *et al.*, 1986). Due to the appearance and subsequent increase in the prevalence of penicillinase-producing *N. gonorrhoeae* and to the chromosomally mediated resistance to penicillin and tetracycline (CMRNG ^{PT}), the Center for Disease Control, Atlanta, GA USA has advocated third generation cephalosporins or selected fluoroquinolones including ciprofloxacin and ofloxacin, as the first line therapies for uncomplicated gonorrhea (CDC 1993). Since the introduction of fluoroquinolones for the treatment of uncomplicated gonococcal and non-gonococcal urethritis, ciprofloxacin and ofloxacin have been extensively used in Africa and Asia. Fluoroquinolones (ciprofloxacin) have been extensively used in Bangladesh as a part of syndromic management of suspected gonorrhea, irrespective of susceptibility testing. *N. gonorrhoeae* strains with decreased susceptibility to the quinolone group of antimicrobial agents were reported as early as mid-1980s and the incidence of such strains has increased world wide since then (Clendennel *et al.*, 1992; Abeyewickerme *et al*, 1996).

Fluoroquinolones, derivatives of nalidixic acid, have a broad spectrum of antimicrobial activity including activity against *N. gonorrhoeae.* Fluoroquinolones inhibit DNA gyrase, the enzyme that maintains bacterial DNA in a negatively supercoiled state. Two types of quinolone resistance mutants have been described: (i) permeability mutants and (ii) gyrase mutants (Karl *et al.*, 1997). Permeability mutants show reduced accumulation of quinolones and either reduced or enhanced permeability to unrelated drugs. Mutations in the target enzyme, gyrase have been found in both Gram-negative and Gram-positive bacteria. Resistance to fluoroquinolone in neisseria occurs as a result of point mutation in the DNA gyrase (*gyr*A) gene and the topoisomerase IV (*par*C) gene. Among the mutations analyzed so far, alteration of the *gyr*A subunit of DNA gyrase particularly serine -91 and Asp-95 has a central role in conferring high-level quinolone resistance in *N. gonorrhoeae.* In addition to this, an alteration at Ser-88 and/or Gly -91 in the *par*C subunit of DNA topoisomerase IV has been reported to be responsible for an increase in resistance to fluoroquinolones in laboratory mutants.

The relationship between dosage, minimum inhibitory concentration (MIC) of the infecting isolate, and therapeutic failure was unknown when ciprofloxacin was introduced as the first line therapy for gonorrhea. Subsequently, low level resistance was reported for *N. gonorrhoeae* isolates for which MICs were 0.06-0.5μg/ml, followed by reports of high level resistance in isolates for which MICs were >1μg/ml (Ison *et al.*, 1998). An MIC of 1 μg/ml has been suggested as indicating resistance to ciprofloxacin and an MIC of 0.125-0.5 μg/ml has been classified as intermediate resistance (NCCLS). Strains exhibiting reduced susceptibility to ciprofloxacin (intermediate resistance) has been reported from Hong Kong, the Republic of the Philippines and Thailand (Knapp *et al.*, 1997). Recent reports suggested that 16 - 17.5 % of *N. gonorrhoeae* isolates in Cleveland, Ohio shows reduced susceptibility to ciprofloxacin (Knapp *et al.*, 1996). The correlation between treatment failure in gonorrhea due to ciprofloxacin and in-vitro resistance of the isolates to ciprofloxacin has

not been evaluated. However, therapeutic failure with 500 mg dose of ciprofloxacin has been reported in three of the 18 patients with isolates for which the MIC was 0.12 – 0.5μg/ml (Ison *et al.*, 1998). High-level quinolone resistance indicates adaptive mutations of *N. gonorrhoeae* under selective antibiotic pressure. *N. gonorrhoeae* rapidly develops resistance to most antimicrobial agents and most recently to quinolones used for treatment of the diseases. Inappropriate therapy because of self-medication and poor compliance is common among patients with gonorrhea and these are the factors that enhance the development of resistance. Resistance to ciprofloxacin is chromosomally mediated, affects all the members of the fluoroquinolone group of antibiotics and is apparently incremental.

CDC has recently published the 1998 STD treatment guidelines and recommended Cefixime 500 mg single dose; or Ciprofloxacin 500 mg single dose; or Ofloxacin 400 mg single dose; or Ceftriaxone 125 mg single dose I.M as first line therapy for gonorrhea (Zenilman *et al.*, 1998; http://www.cdc.gov/nchstpp/dstd/dstdp.html). Unfortunately, Cefixime is not available in Bangladesh and if available, it extremely expensive.

Ceftriaxone, a third generation cephalosporin, is one of the most active of all antimicrobial agents against *N. gonorrhoeae*. The minimum inhibitory concentration (MICs) of ceftriaxone for both PPNG and penicillinase negative *N. gonorrhoeae* are < 0.0001 – 0.063 μg/ml (Handfeild *et al.*, 1983). Ceftriaxone has a very long plasma half life of 8 to 16 hours (Seddon *et al.*, 1980). The efficacy of ceftriaxone against *N. gonorrhoeae* has extensively been evaluated. A comparative study of ceftriaxone and spectinomycin for the treatment of uncomplicated gonorrhea among patients attending a STD clinic showed that 100% of 59 men treated with either 125 mg or 250 mg ceftriaxone and 97% of 58 men treated with spectinomycin were both symptomatically and microbiologically cured of gonorrhea (Handfeild *et al.*, 1983). Although neither of the drugs caused perceptible toxicity, patient acceptance was greater for ceftriaxone than for spectinomycin. A similar study among Ugandan population has documented a 99% (71/72) cure of gonorrhea by ceftriaxone (Hellmann *et al.*, 1995). Ceftriaxone, a single dose of 125 mg was found to be effective against uncomplicated urethral and anorectal gonorrhea (Handfeild *et al.*, 1981). Efficacy of ceftriaxone has also been evaluated against PPNG and non-PPNG isolates in children. Twenty-eight children were treated with 125 mg single dose ceftriaxone, and this eradicated *N. gonorrhoeae* from the pharynx, rectum, urethra, vagina and conjunctiva (Rawstron *et al.*, 1989). 125 mg of ceftriaxone was found to be as effective as any known single dose reginm for the treatment of uncomplicated genital or anorectal gonococcal infection, and it has added advantage of efficacy against PPNG infection, excellent acceptance by patients, and low toxicity. Ceftriaxone is also expected to be effective against incubating syphilis. In vitro susceptibility of *N. gonorrhoeae* isolates to ceftriaxone were subsequently studied. Sixty-four PPNG and 24 non-penicillinase producing isolates collected form different parts of Asia were evaluated for their in vitro susceptibility. All isolates were found to be susceptible to ceftriaxone (Ng *et al.*, 1983). In a subsequent study 112 PPNG and the same number of non-PPNG gonococcal isolates were tested for their in vitro susceptibility to β-lactum antibiotics and spectinomycin. Although all cephalosporins had good in vitro activity against both PPNG and non-PPNG isolates, ceftriaxone had lowest MICs and 4% of the PPNG isolates were resistant to spectinomycin (Waghorn *et al.*, 1986).

In Bangladesh the prevalence and etiology of RTIs and STIs among general and high risk population are not well documented. Lack of adequate laboratory infrastructure, trained health workers and motivation hamper proper diagnosis and management. In a well documented study with adequate laboratory methodology Wasserheit *et al.* (1985) have shown that 22% of 1929 women reported symptoms of RTI, and of them 68% had clinical and laboratory evidence of RTIs. In a similar study among patients attending a women(s) clinic, the prevalence of bacterial vaginosis was 44%, *C. trachomatis* and *N. gonorrhoeae* were 2% and syphilis was 2% (J. Bogaerts, personal communication). A cross sectional study among the slum dwellers in Dhaka city has shown that the prevalence of *N. gonorrhoeae* was 5% and syphilis was 11.5%. (Sabin *et al.*, 1997). There are approximately 100,000 FSWs in Bangladesh. They are almost ubiquitous in distribution, urban, semi-urban and rural. They are either organized in brothels or work as floating sex workers (Choudhury *et al.*, 1996).

We have conducted a point prevalence study among FSWs in Dhaka city during the summer '97 and have examined 224 FSWs for gonorrhoea and syphilis. 94 (40%) of FSWs were found to be culture positive for gonorrhea and 76 (34%) were found to be positive for syphilis (Bhuiya *et al.*, 1998). In a subsequent study, the antimicrobial susceptibility of the isolates was studied. Among the gonococcal isolates, 66% and 60% were resistant to penicillin and tetracycline respectively, 10% of the isolates were resistant and 26% had reduced susceptibility to ciprofloxacin and 99% of isolates were susceptible to ceftriaxone (Bhuiya *et al.*, 1999). We are currently conducting a study among FSWs in Dhaka city and have examined them for gonorrhea, syphilis, trichomoniasis and chlamydia infection. Of the one hundred fifty FSWs examined so far, 35% were found to be culture positive for gonorrhea (Rahman *et al.*, unpublished results). Of the 53 isolates tested so far, 11% of the isolates were resistant and 35% had reduced susceptibility to ciprofloxacin.

Although ciprofloxacin is extensively used in Bangladesh, treatment failure due to ciprofloxacin in gonorrhea has never been studied in Bangladesh. Ongoing studies in our laboratory indicates that as much as 35% of the gonococcal isolates are currently shows reduced susceptibility to ciprofloxacin. Study of treatment failure due to ciprofloxacin (500 mg/single dose) in gonorrhea and the efficacy of an alternate therapy for gonorrhea are essential for control and management of STIs/RTIs. In this proposal, we will study the treatment failure due to ciprofloxacin in gonorrhea and the efficacy of ceftriaxone (125 mg/single dose, I.M) will be compared with that of ciprofloxacin.

Significance:

Early and correct diagnosis and proper treatment of STIs including gonorrhea are essential not only to prevent complications associated with the infection, but also to control the spread of HIV infection. The prevalence of sexually transmitted infection (STIs) including gonorrhea is high among female sex workers (FSWs) in Bangladesh. Ciprofloxacin is recommended by WHO for the treatment of uncomplicated gonorrhea and is extensively used in Bangladesh as a part of syndromic management. However, treatment failure due to ciprofloxacin in gonorrhea has never been studied in Bangladesh even though, we have seen in vitro resistance and reduced susceptibility to ciprofloxacin in up to 46% of isolates. Therefore, study of treatment failure due to ciprofloxacin in gonorrhea and guideline for alternate therapy for the treatment of gonorrhea is essential. The results of this study will help Government of Bangladesh, WHO and CDC to suggest alternate first line therapy for the treatment of gonorrhea, in developing countries where ciprofloxacin may no longer be effective against gonorrhea.

Principal Investigator: Last, first, middle Rahman Motiur

Research Design and Methods

Describe in detail the methods and procedures that will be used to accomplish the objectives and specific aims of the project. Discuss the alternative methods that are available and justify the use of the method proposed in the study. Justify the scientific validity of the methodological approach (biomedical, social, or environmental) as an investigation tool to achieve the specific aims. Discuss the limitations and difficulties of the proposed procedures and sufficiently justify the use of them. Discuss the ethical issues related to biomedical and social research for employing special procedures, such as invasive procedures in sick children, use of isotopes or any other hazardous materials, or social questionnaires relating to individual privacy. Point out safety procedures to be observed for protection of individuals during any situations or materials that may be injurious to human health. The methodology section should be sufficiently descriptive to allow the reviewers to make valid and unambiguous assessment of the project. (DO NOT EXCEED TEN PAGES, USE CONTINUATION SHEETS).

Materials and methods

Study site and design: This study will be conducted in Health Care Clinic of Concern Bangladesh, at Mirpur Vagrant Home. FSWs attending this clinic include floating sex workers and sex workers form residential hotels. All FSWs attending the clinic both with and without signs and symptoms of STIs will be included in the study.

Inclusion criteria for enrollment includes:

a. Age between 18 to 50 years.
b. Non pregnant.
c. Not treated with antibiotic in the preceding two weeks.
d. Not allergic to carboxiquinolone or cephalosporines
e. With or without symptoms of STIs

Exclusion criteria:

a. Age below 18 and above 50 years.
b. Pregnancy and nursing mother.
c. Antibiotic treatment in the preceding two weeks.
d. Allergic to carboxiquinolone or cephalosporines
e. Chronic or acute intercurrent infection which would compromise treatment evaluation.
f. Any neurological or convulsive disorder in past.

FSWs will be informed about the objective of the study and those who give written consent and are willing to come for follow up will be included in the study (See Annex 1). Subjects with uncertain last menstrual date will be screened for pregnancy by rapid dipstick test before enrollment and will be excluded if found pregnant. Subjects will be randomly assigned to treatment with ceftriaxone (125 mg I.M single dose, as recommended by CDC or ciprofloxacin (500 mg single dose, as recommended by WHO) according to a computer generated random table (CDC 93; WHO 91). Subjects presenting with signs and symptoms of gonorrhea (urethral discharge or dysuria or cervical infection with mucopus and/or Gram staining of endocervical swab showing Gram negative intracellular diplococci in polymorphonuclear leucocytes) will be randomized to either ciprofloxacin or ceftriaxone after specimen collection. Enrolled subjects will be asked to visit after one week for follow up. Subjects with suspected gonorrhea, from whom *N. gonorrhoeae* was not isolated (culture negative) in the first instance will be treated for other STI and will be dropped from the study. During follow up visit, patients will be asked about relief of symptoms of gonorrhea and clinical cure will be assessed. A patient will be considered clinically cured if the symptoms of gonorrhea (urethral discharge or dysuria or cervical mucopus and/or Gram staining of endocervical swab showing Gram negative intracellular diplococci in polymorphonuclear leucocytes) were found to be absent during follow up. A second endocervical swab will be collected and the patient will be treated for other STIs if identified by laboratory diagnosis. If signs and

symptoms were not relieved, treatment will be modified according to laboratory results for other STIs pathogens (as recommended by WHO) and susceptibility of the gonococcal isolate, and the patient will be asked to visit the clinic after one week for assessment of clinical cure. During the second follow up, if the patient is found cured, then she will be considered to have initial sign and symptoms due to gonorrhea and/or other STIs.

For asymptomatic subjects, an endocervical swab will be collected and will be asked to come back after 48 hour for the results. Asymptomatic subjects with culture positive for gonococcus will be treated as described earlier and will be asked to come back for a follow up after one week. Asymptomatic subjects with culture negative for gonococcus will be treated for other STIs if present and will be dropped from the study. During follow up visit (asymptomatic culture positive cases) a second endocervical swab will be collected and treatment will be adopted according to laboratory finding (as recommended by WHO) and susceptibility of the gonococcal isolate.

The subjects who are culture positive for gonorrhea will be provided counseling and condom will be supplied. They will be advised to persuade their clients to use condoms till the follow up sample is collected. The outcome of treatment will be studied after one week. Each isolate will be analysed for its susceptibility to fluoroquinolones and cephalosporins. Treatment failure will be considered if a patient was found to be culture positive with the same isolate one week after treatment. Each enrolled subject will be asked about the side effect and discomfort for the therapy.

Sample size: Assuming that 95% of patients treated with ceftriaxone and 75% treated with ciprofloxacin will be cured, the minimum number of patients required for this study will be 116 (58 in each group) (confidence level of 95% with 80% power). According to our previous study, the prevalence of gonococcal infection among the FSWs is 40%. Considering a 40% prevalence and 30% drop out, a total of 377 FSWs will be included in the study.

Sample collection and diagnosis: Each subject will undergo a clinical examination of the external genitalia as well as examination with a vaginal speculum by a female physician and specimen will be collected. Specimens include two endocervical swabs and a high vaginal swab. One endocervical swab will be stored immediately in 0.5 ml PBS and stored at -70C and used for PCR.

Treatment: If the subject is found to be culture positive for gonorrhea, treatment will be randomized to either 500 mg single dose ciprofloxacin or 125 mg I.M single dose of ceftriaxone at the clinic. If the subject is found to culture negative for gonorrhea, she will be treated for her symptoms according to syndromic management guideline (WHO 1991).

Laboratory diagnosis:
A Gram staining of endocervical smear will be made for detection of Gram negative intracellular diplococci in polymorphonuclear leucocytes. Endocervical swab will be immediately inoculated onto pre-warmed Modified Thayer –Martin medium (MTM) and will be incubated at 37 C in candle extinction jars. The plates will be examined after 24 hours and a presumptive identification of *N. gonorrhoeae* will be made on the basis of colony morphology, Gram staining, oxidase and superoxol test of suspected gonococcal colonies (WHO 89).

Serotype and serovar analysis: Identity and serotype of the organism will be confirmed by Phadebact GC monoclonal kit and Padebact GC serovar test kit. *N. gonorrhoeae* isolates obtained before and after treatment will be analyzed for their serotype and serovar by Phadebact GC monoclonal kit and Padebact GC serovar test kit. If the isolates before and after treatment belong to same serotype and serovar it will be considered as a treatment failure and if the serotype and serovar differs between the pre and post treatment isolates it will be considered as re-infection rather than treatment failure.

PCR RFLP of the isolates: Chromosomal DNA was extracted from overnight culture of the isolates. The *por* gene of the isolates was amplified by PCR using specific primers from conserved region of the gene. Primer POR1 ATG AAA AAA TCC CTG ATT GCC C and POR2 TTA GAA TTT GTG GCG CAG A were used to amplify *por* gene. In PIA expressing isolates the amplified product will be 0.9 –1.0 kb compared to 1.1kb in PIB expressing isolates. Amplification of the *por* gene consisted of 35 cycles of 1 min at 94 C, 2 min at 45 C and 3 min at 70 C. An initial and final step of 5 min at 94 C and 10 min at 72 C were included. The amplified products were analyzed by 0.8 agarose gel electrophoresis. 10 ml of the PCR product was digested with MspAII restriction enzyme and run on 6% non-denaturing polyacrilamide gel. After ethidium bromide staining the banding pattern were analyzed. Isolates with treatment failure will have identical banding pattern.

T. vaginalis infection will be identified through a microscopic examination of a wet mount preparation with high vaginal swab. A whiff test will be carried out using a 10% solution of KOH and pH of the vaginal fluid will be measured during speculum examination. Presence of clue cells will be determined by gram staining of vaginal swab. Bacterial vaginosis will be defined as the presence of any three of the following four signs in the absence of trichomonas vaginitis: i. White homogeneous discharge; ii. Clue cells (>20% of epithelial cell) on vaginal wet mount; iii. Vaginal pH >4.5; or iv. Positive whiff test (amine odour using 10% potassium hydroxide on vaginal secretions). *C. trachomatis* will be diagnosed by *C. trachomatis* enzyme immunoassay (EIA) (Chlamydia EIA test, Syva Company, Palo Alto, CA). Confirmatory diagnosis will be made by PCR using primers specific for major outer membrane protein (MOMP). Endocervical swab stored at -70 C will be thawed and centrifuged at 13000xg for 15 minute. DNA extracted from the bacterial pallet will be used for PCR as described elsewhere (Class *et al.*, 1990).

Antimicrobial susceptibility and MIC determination: The antimicrobial susceptibility of the gonococcal isolates to ciprofloxacin, ofloxacin, trovofloxacin, cefuroxime, ceftriaxone, penicillin, tetracycline, aztreonam and spectinomycin will be determined by disk diffusion method and MIC for each of the antimicrobial agent will be determined by agar dilution or E-test using standard protocol (NCCLS).

Facilities Available

Describe the availability of physical facilities at the place where the study will be carried out. For clinical and laboratory-based studies, indicate the provision of hospital and other types of patient's care facilities and adequate laboratory support. Point out the laboratory facilities and major equipments that will be required for the study. For field studies, describe the field area including its size, population, and means of communications. (TYPE WITHIN THE PROVIDED SPACE).

This study will be carried out in health clinic of Concern in Mirpur and LSD, ICDDR,B. The clinic has sufficient infrastructure for interviewing, examination and sample collection. The support required for the clinic is one simple microscope, refrigerator, slides, cover slip, cotton swab, transport medium, needle, syringe, stationary and medicine. The following equipment's are needed for ICDDRB. One refrigerator, Co_2 incubator, biohazard hood, microscope and bench top centrifuge.

Data Analysis

Describe plans for data analysis. Indicate whether data will be analyzed by the investigators themselves or by other professionals. Specify what statistical software's packages will be used and if the study is blinded, when the code will be opened. For clinical trials, indicate if interim data analysis will be required to monitor further progress of the study. (TYPE WITHIN THE PROVIDED SPACE).

Data generated by the project will be analyzed by suitable statistical program. Primary data will be analysed by SPSS or Epi-Info program.

Principal Investigator: Last, first, middle Rahman Motiur

Ethical Assurance for Protection of Human Rights

Describe in the space provided the justifications for conducting this research in human subjects. If the study needs observations on sick individuals, provide sufficient reasons for using them. Indicate how subject's rights are protected and if there is any benefit or risk to each subject of the study.

Social worker will explain the aim of the study to the subject and written consent will be taken from all the patients. All data obtained during clinical examination as well as laboratory finding are strictly confidential. Only standard clinical examination will be performed. Diagnosis will be done according to WHO syndromic management flow chart and standard treatment regimens will be given.

Use of Animals

Describe in the space provided the type and species of animal that will be used in the study. Justify with reasons the use of particular animal species in the experiment and the compliance of the animal ethical guidelines for conducting the proposed procedures.

No laboratory animal will be used in this study.

Literature Cited

Identify all cited references to published literature in the text by number in parentheses. List all cited references sequentially as they appear in the text. For unpublished references, provide complete information in the text and do not include them in the list of Literature Cited. There is no page limit for this section, however exercise judgment in assessing the "standard" length.

Reference:

1. Abeywickereme I, Senaratine L, Prithivira VB. Rapid emergence of 4- fluoroquinolone resistance with associated decline in penicillinase-producing *Neisseria gonorrhoea* in Colombo, Sri Lanka. Genitourin Med 1996; 72:302.

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5. Bhuiya, B., Rahman, M., Miah, R.A., Rahman, M . and Albert, M.J. (1998) High prevalence of Ciprofloxacin resistant *Neisseria gonorrhoeae* among the Commercial Sex Workers in Bangladesh. J Antimicrob Chemother. 48(5):675-76.

6. Bhuiya, B., Rahman, M., Miah, R.A., Nahar, S., Islam, N., Ahmed, M., Rahman, K.M., Albert, M.J. (1999) Antimicrobial susceptibility, and plasmid content of *Neisseria gonorrhoeae* isolated from commercial sex

workers in Dhaka, Bangladesh: Emergence of high level ciprofloxacin resistance. J. Clin Microbiol. 37(4):1130-36.

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Dissemination and Use of Findings

Describe explicitly the plans for disseminating the accomplished results. Describe what type of publication is anticipated: working papers, internal (institutional) publication, international publications, international conferences and agencies, workshops etc. Mention if the project is linked to the Government of Bangladesh through a training programme.

It is hoped that the project will generate data that will have national and international impact. These data will help the Government of Bangladesh, WHO and CDC to suggest alternate first line therapy for the treatment of gonorrhoea, in developing countries where ciprofloxacin is no longer effective against gonorrhoea. The data generated by this project will be presented in national and international conferences and will be published in international journals.

Collaborative Arrangements

Describe briefly if this study involves any scientific, administrative, fiscal, or programmatic arrangements with other national or international organizations or individuals. Indicate the nature and extent of collaboration and include a letter of agreement between the applicant or his/her organization and the collaborating organization. (DO NOT EXCEED ONE PAGE)

This project is collaborative one between Concern Bangladesh and ICDDR, B. The investigators from each institute will interact closely. Concern clinic will take the responsibility of patient enrollment, follow up visit and will ensure treatment compliance. Investigators in ICDDR, B will be responsible for interviewing, management of patients and collection of swab, training personnel, carrying out the diagnostic tests, data analysis and dissemination of the results. Investigators will meet monthly and will discuss the progress of the project. (See Annex 2)

Principal Investigator: Last, first, middle Rahman Motiur

Biography of the Investigators

Give biographical data in the following table for key personnel including the Principal Investigator. Use a photocopy of this page for each investigator.

Name	Position	Date of Birth
Motiur Rahman	Asstt. Scientist	21st Dec 1961

Academic Qualifications (Begin with baccalaureate or other initial professional education)

Institution and Location	Degree	Year	Field of Study
Rangpur medical college, Rangpur Bangladesh.	MBBS	1985	Medicine Surgery
Microbiology & tumorbiology Centre Karolinska Institute, Stockholm, Sweden.	Ph. D	1977	Microbiology & Molecular biology

Research and Professional Experience

Concluding with the present position, list, in chronological order, previous positions held, experience, and honours. Indicate current membership on any professional societies or public committees. List, in, chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. **(DO NOT EXCEED TWO PAGES, USE CONTINUATION SHEETS).**

Professional experience

Sept'85 to Sept'86:	Assistant surgeon, Rangpur Medical college Hospital. Rangpur, Bangladesh.
March'95 to March'97:	Research Assistant, Microbiology & Tumorbiology Centre, Karolinska Institute, Stockholm, Sweden.
From April'97:	Assistant Scientist, LSD, ICDDR'B, Bangladesh.

Principal Investigator: Last, first, middle Rahman Motiur

Publications:

1. Bhuiya, B., **Rahman, M.**, Miah, R.A., Rahman, M . and Albert, M.J. (**1998**) High prevalence of Ciprofloxacin resistant *Neisseria gonorrhoeae* among the Commercial Sex Workers in Bangladesh. **J Antimicrob Chemother**. 48(5):675-76.

2. Bhuiya, B., **Rahman, M.**, Miah, R.A., Nahar, S., Islam, N., Ahmed, M., Rahman, K.M., Albert, M.J. (**1999**) Antimicrobial susceptibility, and plasmid content of *Neisseria gonorrhoeae* isolated from commercial sex workers in Dhaka, Bangladesh: Emergence of high level ciprofloxacin resistance. **J. Clin Microbiol.** 37(4):xx-yy.

3. **Rahman, M.**, Bhuiya, B., Miah, R.A., Islam, N., Rahman, K.M., J., Albert, M.J. (**1997**) Molecular epidemiology and plasmid profile of *Neisseria gonorrhoeae* isolated from commercial sex workers in Dhaka city. **ASCON** 1998, ICDDR'B, Dhaka, Bangladesh.

4. **Rahman, M.**, Jonsson, A.-B., and Holme, T. (**1998**) Monoclonocal antibodies to the α-Gal-(1-4)-β-Gal-(1- epitope of *Moraxella catarrhalis* lipopolysaccharide react with the type IV pili of *N. meningitidis.* **Microbial pathogenesis**. 24(5):299-300.

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11. Jönsson, I,. Holme, T,. Krook, A,. **Rahman, M,.** and Thorén, M. (1992) Variability of surface-exposed antigens of different strains of *Moraxella catarrhalis.* **Eur. J. Clin. Microbiol. Infect. Dis**. 11: 919-922.

12. **Rahman, M,**. and T. Holme, (1996) Antibody response in rabbits to serotype-specific determinant in lipopolysaccharides from *Moraxella catarrhalis.* **J. Med. Microbiol. *44: 1-7.***

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18. **Motiur Rahman** (1997) Characterization of surface components of *Moraxella catarrhalis* and pathogenic *Neisseria*. **ISBN- 91-628-2314-0**.

Manuscripts submitted

1. Borelli, S,. **Rahman, M**,. Holme, T,. Alf, A, Lindberg,. and P, -E, Jansson. (1996) *Moraxella* (*Branhamella*) *catarrhalis* and *Haemophilus influenzae* lipopolysaccharides express distinct Galα1-4Galβ epitopes as determined by the binding of specific *H. influenzae* anti-Galα1-4Galβ monoclonal antibodies. Submitted to Microbial pathogenesis.

2. Holme, T., **Rahman, M**., Jansson P.E., and Vidmalm, G. (1998) The lipopolysaccharides of *Moraxella Catarrhalis*: structural relationship and antigenic properties. Submitted to **Infection and Immunity**.

Principal Investigator: Last, first, middle Rahman Motiur

International Centre for Diarrhoeal Disease Research, Bangladesh
Voluntary Consent Form

Title of the Research Project: **Treatment failure due to ciprofloxacin in gonorrhea; among Bangladeshi female sex workers.**

Principal Investigator: Motiur Rahman

Before recruiting into the study, the study subject must be informed about the objectives, procedures, and potential benefits and risks involved in the study. Details of all procedures must be provided including their risks, utility, duration, frequencies, and severity. All questions of the subject must be answered to his/ her satisfaction, indicating that the participation is purely voluntary. For children, consents must be obtained from their parents or legal guardians. The subject must indicate his/ her acceptance of participation by signing or thumb printing on this form.

See Annex 3 and 4

Signature of Investigator/ or agents
Date:

Signature of Subject/ Guardian
Date:

Continuation Sheet (Number each sheet consecutively)

Principal Investigator: Last, first, middle Rahman Motiur

Detailed Budget for New Proposal

Project Title: Treatment failure due to ciprofloxacin in gonorrhea; among Bangladeshi female sex workers.

Name of PI: **Motiur Rahman**

Protocol Number: Name of Division: **Laboratory Sciences Division**

Funding Source: **SDC** Amount Funded (direct): 55,550 US$ Total: 63,327 US$ Overhead (%) 14%

Starting Date: July 1999 Closing Date: December 2000

Strategic Plan Priority Code(s) :

Sl. No	Account Description	Salary Support			US $ Amount Requested		
	Personnel	**Position**	**Effort %**	**Salary rate**	**1st Yr** 1/7/99-1/7/2000	**2nd Yr** 1/7-31/12/2000	**Total**
	Principal investigator	Asstt.Scientist	25	9980	2,500		2,500
	Medical officer	NOA	100	7760	7,760	3,600	11,360
	Sr. Res. Officer	GS-6	100	5560	5,560		5,560
	Sr. Interviewer	GS-4	100	3280	3,280		3,280
	Sr. Laboratory Technician	GS-4	100	3280	3,280		3,280
	Sub Total				**22,380**	**3,600**	**25,980**
	Consultants						
	Local Travel				500	250	750
	International Travel					1,500	1,500
	Sub Total				**500**	**1,750**	**2,250**
	Supplies and Materials (Description of Items)						
	1. Transport media, plates and anaerobic jar				2,500	1,500	4,000
	2. Microscope				2,000		2,000
	3. Pipettes and aerosol protective tips.				1,500		1,500
	4. Primer's Reagents, tubes plastic and chemicals,				2,000	1,820	3,820
	5. Reagents and kits for serology				4,000	1,000	5,000
	6. Medicine				2,000		2,000
	Sub Totals				**14,000**	**4,320**	**18,320**

Principal Investigator: Last, first, middle Rahman Motiur

	Other Contractual Services	1st year	2nd year	Total
	Repair and Maintenance			
	Rent, Communications, Utilities	100	100	200
	Training Workshop, Seminars	200		200
	Printing and Publication	300	200	500
	Staff Development	300		300
	Sub Total	**900**	**300**	**1,200**

	Interdepartmental Services	1st Yr	2nd Yr	Total
	Computer Charges	200	100	300
	Pathological Tests			
	Microbiological tests			
	Biochemistry Tests			
	X-Rays			
	Patients Study			
	Research Animals			
	Biochemistry and Nutrition			
	Transport			
	Xerox, Mimeographs etc.			
	Sub Totals	**200**	**100**	**300**
	Other Operating Costs			
	Capital Expenditure **Centrifuge** **Bio Hazard hood**	 **2,500** **5,000**		 **2,500** **5,000**
TOTAL DIRECT COST		**45,480**	**10,070**	**55,550**
Indirect cost @ 14%		**6,367**	**1,410**	**7,777**
Total Project cost		**51,847**	**11,480**	**63,327**

Principal Investigator: Last, first, middle Rahman Motiur

Budget Justifications

Please provide one page statement justifying the budgeted amount for each major item. Justify use of man power, major equipment, and laboratory services.

The budget presented here represents a minimum estimation of the costs.

1. One female physician and one interviewer will be employed for interviewing and collection of samples. A trained research assistant (MSc. Microbiology/Biochemistry) and one Laboratory technician will be recruited.
2. All personnel involved in this study will be trained in the beginning for personal safety material handling, collection transport and other procedures.
3. Equipment and instruments: All equipment and reagents mentioned in the budget will be purchased from the budget code assigned to the study protocol.

Other Support

Describe sources, amount, duration, and grant number of all other research funding currently granted to PI or under consideration. (DO NOT EXCEED ONE PAGE FOR EACH INVESTIGATOR)

USAID – 1800 $ for a pilot study entitled "Prevalence of sexually transmitted infections among female sex workers in Dhaka city".

Principal Investigator: Last, first, middle Rahman Motiur

Check List

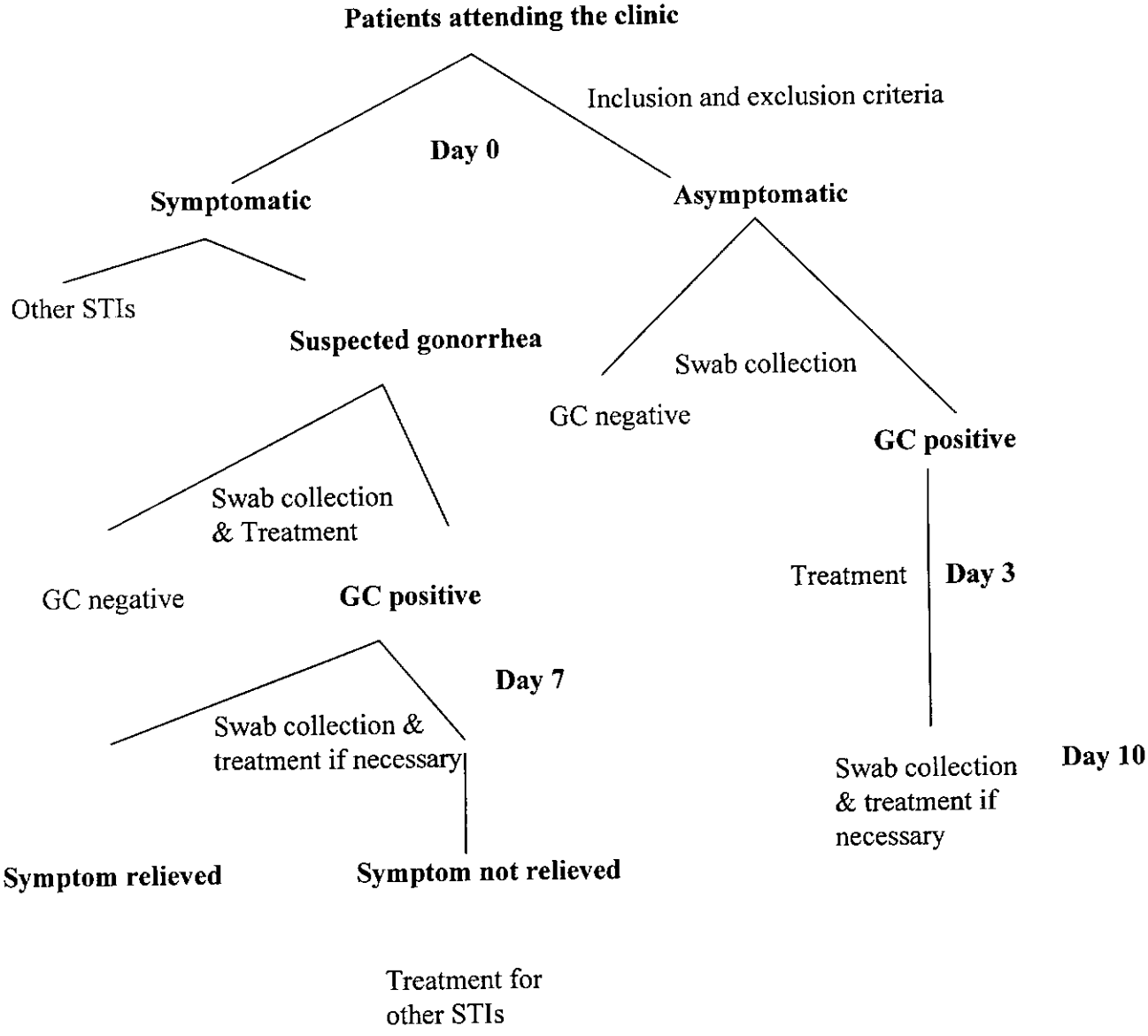
After completing the protocol, please check that the following selected items have been included.

1. Face Sheet Included [X]
2. Approval of the Division Director on Face Sheet [X]
3. Certification and Signature of PI on Face Sheet, #9 and #10 [X]
4. Table on Contents [X]
5. Project Summary [X]
6. Literature Cited [X]
7. Biography of Investigators [X]
8. Ethical Assurance [X]
9. Consent Forms [X]

Detailed Budget [X]

Annex 1

Project Name: Treatment failure due to ciprofloxacin in gonorrhea; among Bangladeshi female sex workers.
P. I. Motiur Rahman



Annex 2

Project Name:Treatment failure due to ciprofloxacin in gonorrhea; among Bangladeshi female sex workers.
P. I. Motiur Rahman

Task	0-1 month	1-2 month	2-3 month	3-5 month	5-7 month	7-9 month	9-11 month	11-12 month
1. Recruitment								
2. Planning								
3. Training								
4. Sample collection								
5. Evaluation								
6. Data analysis								
7. Dissemination								

Principal Investigator: Last, first, middle Rahman Motiur _____

Annex 3

Title of the Research Project: Treatment failure due ciprofloxacin in gonorrhea among Bangladeshi female sex workers.

Voluntary Consent Form (Symptomatic patients)

You are suffering from a disease, which we suspect to be gonorrhea. The disease is caused by infection due to a germ called *Nesseria gonorrhoeae*. Treatment of gonorrhea requires the use of an antibiotic drug that kills the germs. Oral administration of a single, 500-mg dose of ciprofloxacin only once comprises a simple but effective treatment of gonorrhea. However, we have recently observed that a significant proportion of the germs in Bangladesh are resistant to this drug, which means that the drug may not be effective in the treatment of gonorrhea when the infections are caused by such germs. A single, 125-mg intramuscular injection of another antibiotic drug, ceftriaxone, is also effective in the treatment of gonorrhea.

We are conducting a study to compare the effectiveness of ciprofloxacin and ceftriaxone in the treatment of gonorrhea. Results of this study will help us determine which of these two drugs should be used in the treatment of gonorrhea in Bangladesh. You may help us in our efforts by participating in the study. If you agree to participate in our study:

1. We will ask you some questions regarding your health, and a trained female doctor will perform your physical examination including a vaginal examination.
2. Using a cotton-tipped stick, we will collect specimen from your vagina for diagnosing the cause of your problem and also for other special tests for the research. The procedure is painless, and will not cause any harm to you.
3. If we suspect that you may have gonorrhea, we will treat you with either a single 500mg oral dose of ciprofloxacin only once, or a single 125-mg intramuscular injection of ceftriaxone. We will not treat you for other STIs at this moment, but we will treat you for other STIs when laboratory results are available.
4. We will ask you to return to this clinic after 7 later to reassess your condition. Results of the laboratory tests done during your first visits will be available by this time, and we would be able to tell you whether or not you had gonorrhea, and also if you problems other than gonorrhea. If you did not have gonorrhea but have persistence of symptoms, we will treat you according to the standard guidelines. If you had gonorrhea, we will again collect specimen from your vagina to perform tests, which will tell us if you are free from the germs.
5. You will be directly benefited from participation in this study since we will diagnose your problem and provide you free treatment. This will also prevent transmission of the disease to others. Additionally, the results of this study will benefit the society.
6. There is no physical risks involved in this study.
7. If you do not participate in this study, you will receive the standard treatment of this clinic. You would also be able to withdraw your consent at any time during the study without causing any penalty to you and without affecting your further treatment at this clinic.
8. All of your medical information including the results of the laboratory tests will be kept confidential, and no body other than the investigators of this study and the Ethical Review Committee that overseas protection of human rights would be able to see them.
9. We will be happy to answer to your questions, now or a later time.

If you agree to participate in this study, please indicate that by putting your signature or left thumb impression on the specified space below.

Thank you for your cooperation.

Signature of the client	Signature of the Investigator	Signature of the witness
Date: _____	Date: _____	Date: _____

• Principal Investigator: Last, first, middle Rahman Motiur _____

Annex 4

Title of the Research Project: Treatment failure due ciprofloxacin in gonorrhea among Bangladeshi female sex workers.
P.I. Motiur Rahman

Voluntary Consent Form (Asymptomatic patients)

In our previous study we found that 40% of the FSWs in Bangladesh are suffering from gonorrhea which could be symptomatic or asymptomatic. As you are involved in the occupation we suspect that you may be suffering from asymptomatic gonorrhea. The disease is caused by infection due to a germ called *Neisseria gonorrhoeae*. Treatment of gonorrhea requires the use of an antibiotic drug that kills the germs. Oral administration of a single, 500-mg dose of ciprofloxacin only once comprises a simple but effective treatment of gonorrhea. However, we have recently observed that a significant proportion of the germs in Bangladesh are resistant to this drug, which means that the drug may not be effective in the treatment of gonorrhea when the infections are caused by such germs. A single, 125-mg intramuscular injection of another antibiotic drug, ceftriaxone, is also effective in the treatment of gonorrhea.

We are conducting a study to compare the effectiveness of ciprofloxacin and ceftriaxone in the treatment of gonorrhea. Results of this study will help us determine which of these two drugs should be used in the treatment of gonorrhea in Bangladesh. You may help us in our efforts by participating in the study. If you agree to participate in our study:

10. We will ask you some questions regarding your health, and a trained female doctor will perform your physical examination including a vaginal examination.
11. Using a cotton-tipped stick, we will collect specimen from your vagina for diagnosing the cause of your problem and also for other special tests for the research. The procedure is painless, and will not cause any harm to you.
12. We will ask you to return to this clinic after 3 days. Results of the laboratory tests will be available by this time, and we would be able to tell you whether or not you had gonorrhea. If we found that you have gonorrhea, we will treat you with either a single 500mg oral dose of ciprofloxacin only once, or a single 125-mg intramuscular injection of ceftriaxone.
13. We will ask you to return to this clinic after 7 later to reassess your condition. We will again collect specimen from your vagina to perform tests, which will tell us if you are free from the germs.
14. You will be directly benefited from participation in this study since we will diagnose your problem and provide you free treatment. This will also prevent transmission of the disease to others. Additionally, the results of this study will benefit the society.
15. There is no physical risks involved in this study.
16. If you do not participate in this study, you will receive the standard treatment of this clinic. You would also be able to withdraw your consent at any time during the study without causing any penalty to you and without affecting your further treatment at this clinic.
17. All of your medical information including the results of the laboratory tests will be kept confidential, and no body other than the investigators of this study and the Ethical Review Committee that overseas protection of human rights would be able to see them.
18. We will be happy to answer to your questions, now or a later time.

If you agree to participate in this study, please indicate that by putting your signature or left thumb impression on the specified space below.

Thank you for your cooperation.

_____	_____	_____
Signature of the client	Signature of the Investigator	Signature of the witness
Date: _____	Date: _____	Date: _____

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র
মহাখালী, ঢাকা-১২১২

স্বেচ্ছা সম্মতি পত্র (উপসর্গযুক্ত রোগীর জন্য)

আপনার রোগ লক্ষণ হতে আমরা ধারণা করছি যে, আপনি 'গণোরিয়া' রোগে আক্রান্ত। রোগটি নাইসেরিয়া গণোরিয়া নামক একটি জীবাণু দ্বারা সংক্রমিত এবং এই রোগের চিকিৎসার জন্য এমন একটি এ্যান্টিবায়োটিক প্রয়োজন, যা জীবাণুটিকে মারতে সক্ষম। সিপ্রোফ্লোক্সাসিন-৫০০ মিগ্রা মুখে একবার সেবন করেই রোগটির কার্যকরী চিকিৎসা সম্ভব। সম্প্রতি এটি প্রতীয়মান হয়েছে যে, জীবাণুটির একটি উল্লেখযোগ্য অংশ এই এ্যান্টিবায়োটিকে অকার্যকরীঃ অর্থাৎ এই এ্যান্টিবায়োটিক অকার্যকরী জীবাণু দ্বারা সংক্রমিত গণোরিয়া রোগের চিকিৎসায় উল্লেখিত এ্যান্টিবায়োটিকটি কার্যকরী নাও হতে পারে। সেক্ষেত্রে সেফট্রায়েক্সন - ১২৫ মিগ্রা মাংসে ইনজেকশন দিয়েও গণোরিয়া রোগের কার্যকরী চিকিৎসা সম্ভব।

আমরা গণোরিয়া চিকিৎসার এই সিপ্রোফ্লোক্সাসিন এবং সেফট্রায়েক্সন এর কার্যকারিতা তুলনা করার জন্য একটি জরিপ পরিচালনা করছি। এই দুটি এ্যান্টিবায়োটিকের মধ্যে কোনটি বাংলাদেশে গণোরিয়া চিকিৎসায় অধিক উপযোগী এবং ব্যবহার করা উচিত এই গবেষণা তা বের করতে আমাদের সাহায্য করবে। আপনি এই গবেষণায় অংশগ্রহণ করে আমাদের সাহায্য করতে পারেন। আপনি যদি এই গবেষণায় অংশগ্রহণ করতে চান তাহলে ঃ

১। আমরা আপনার স্বাস্থ্য সম্পর্কে কিছু প্রশ্ন করবো এবং একজন ট্রেনিংপ্রাপ্ত মহিলা চিকিৎসক আপনার শারীরিক পরীক্ষা করবেন। যার মধ্যে আপনার যৌনাঙ্গ পরীক্ষাও অন্তর্ভুক্ত থাকবে।

২। অগ্রভাবে তুলা লাগানো একটি কাঠির সাহায্যে আপনার যৌনাঙ্গ হতে 'স্পেসিমেন' সংগ্রহ করে বিভিন্ন পরীক্ষার মাধ্যমে আপনার সমস্যা/ সমস্যা সমূহের কারণ নির্ণয় করা হবে। এতে আপনি কোন ব্যাথা অনুভব করবেন না এবং আপনার কোন ক্ষতির সম্ভাবনা নেই।

৩। আমাদের ধারণায় যদি স্পষ্ট প্রতীয়মান হয় যে, আপনি গণোরিয়া রোগে আক্রান্ত, তবে আপনাকে সিপ্রোফ্লোক্সাসিন-৫০০ মুখে একবার অথবা সেফট্রায়েক্সন - ১২৫ মিগ্রাঃ একবার মাংসে ইনজেকশনের মাধ্যমে চিকিৎসা করা হবে।

৪। এর ৭ দিন পর আবার আপনার পরীক্ষা করা হবে। ইতিমধ্যে আপনার থেকে নেওয়া স্পেসিমেন এর ল্যাবরেটরী পরীক্ষার ফল পাওয়া যাবে। আপনি গণোরিয়া রোগে সত্যিই আক্রান্ত কিনা অথবা আপনার সমস্যা অন্য কোন কারণে কি না তা আমরা জানতে সক্ষম হবো। যদি আপনি গণোরিয়া রোগে আক্রান্ত না হন এবং আপনার সমস্যা সমূহ বর্তমান থাকে তাহলে প্রচলিত চিকিৎসা বিধান অনুযায়ী আপনার চিকিৎসা করা হবে। যদি আপনি গণোরিয়া রোগে আক্রান্ত হন, আপনার যৌনাঙ্গ হতে আমরা আরেকটি স্পেসিমেন সংগ্রহ করবো, যা দিয়ে আবার ল্যাবরেটরীতে পরীক্ষা করা হবে এবং আপনি রোগমুক্ত হয়েছেন কি না তা নির্ণয় করা হবে।

৫। আমাদের এই গবেষণা হতে আপনি সরাসরি উপকৃত হবেন, কারণ আমরা আপনার রোগের কারণ নির্ণয় করে আপনাকে বিনামূল্যে চিকিৎসা প্রদান করছি। এই ব্যবস্থা আপনার রোগটি অন্যদের মধ্যে ছড়াতে প্রতিরোধ করবে। উপরন্তু, এই গবেষণার ফল সমাজকে ভীষণভাবে উপকৃত করবে।

৬। এই গবেষণায় অংশগ্রহণ করলে কোনরূপ শারীরিক ঝুঁকির সম্ভাবনা নেই।

৭। আপনি যদি এই গবেষণায় অংশগ্রহণ নাও করেন তাহলেও এই ক্লিনিকের প্রচলিত ব্যবস্থা অনুযায়ী আপনি চিকিৎসা পাবেন। অন্যদিকে অংশগ্রহণ করেও যে কোন সময় কোনরূপ ক্ষতিপূরণ ছাড়াই আপনি আপনার সম্মতি প্রত্যাহার করতে পারবেন। এমনকি এই ক্লিনিক হতে প্রাপ্ত আপনার পরবর্তী চিকিৎসা ব্যবস্থারও কোনরূপ পরিবর্তন হবে না।

৮। ল্যাবরেটরী পরীক্ষার ফলাফল ও আপনার যাবতীয় তথ্য সম্পর্কে গোপনীয়তা রক্ষা করা হবে। এই গবেষণায় অংশগ্রহণকারী, গবেষকগণ এবং মানবিক অধিকার রক্ষার ইথিক্যাল কমিটি ছাড়া সেসব তথ্য অন্য কেউ জানতে পারবে না।

৯। আমরা যে কোন সময় আপনার যে কোন প্রশ্নের উত্তর দিতে আনন্দবোধ করবো।

আপনি যদি এই গবেষণায় অংশগ্রহণে ইচ্ছুক হন, তাহলে অনুগ্রহ করে নিচে প্রদত্ত নির্দিষ্ট স্থানে স্বাক্ষর অথবা টিপসহি দিন।

আপনার সহযোগিতার জন্য ধন্যবাদ।

গবেষণায় অংশগ্রহণকারীর স্বাক্ষর/টিপসহি
তারিখঃ

পরীক্ষকের স্বাক্ষর
তারিখঃ

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র
মহাখালী, ঢাকা-১২১২

স্বেচ্ছা সম্মতি পত্র (উপসর্গহীন রোগীর জন্য)

আমাদের পূর্ববর্তী গবেষণায় দেখা গেছে যে, বাংলাদেশে ৪০% যৌনকর্মী গণোরিয়া রোগে আক্রান্ত, যাদের মধ্যে উপসর্গসহ এবং উপসর্গহীন উভয় শ্রেণীই রয়েছে। যেহেতু আপনি এই পেশায় নিয়োজিত আছেন, আমরা আশংকা করছি যে, আপনি উপসর্গহীন গণোরিয়া রোগে আক্রান্ত থাকতে পারেন। রোগটি 'নাইসেরিয়া গণোরিয়া' নামক এক প্রকার জীবাণু দ্বারা সংক্রমিত হয়। গণোরিয়া চিকিৎসায় এমন এ্যান্টিবায়োটিক প্রয়োজন হয় যা জীবাণুটিকে ধ্বংস করতে সক্ষম। সিপ্রোফ্লোক্সাসিন-৫০০ মিগ্রা (মুখে ব্যবহারযোগ্য) একবার সেব্য এমন একটি এ্যান্টিবায়োটিক যা গণোরিয়া চিকিৎসায় কার্যকরী। আমাদের সাম্প্রতিক গবেষণায় দেখা গেছে যে, গণোরিয়া জীবাণু সমূহের একটি উল্লেখযোগ্য অংশ এই এ্যান্টিবায়োটিককে অকার্যকর/প্রতিরোধ করতে সক্ষম, অর্থাৎ এ্যান্টিবায়োটিকটি এই রকম প্রতিরোধী জীবাণু দ্বারা সংক্রমিত গণোরিয়া রোগের চিকিৎসায় কার্যকরী নাও হতে পারে। সেক্ষেত্রে সেফট্রায়েক্সন - ১২৫ মিগ্রা একক মাত্রায় মাংসে ইনজেকশনযোগ্য অন্য একটি এ্যান্টিবায়োটিক যা গণোরিয়া রোগের চিকিৎসায় কার্যকরী হতে পারে।

আমরা গণোরিয়া চিকিৎসার এই দুটি এ্যান্টিবায়োটিক অর্থাৎ সিপ্রোফ্লোক্সাসিন এবং সেফট্রায়েক্সন এর কার্যকারিতা তুলনা করার জন্য একটি গবেষণা করছি। এর ফলাফল থেকে বাংলাদেশে গণোরিয়া চিকিৎসায় এই দুটি এ্যান্টিবায়োটিকের কোনটি ব্যবহার করা উচিত তা আমরা নির্ণয় করতে পারবো। আপনি এই গবেষণায় অংশগ্রহণ করে আমাদের সাহায্য করতে পারেন। আপনি যদি এই গবেষণায় অংশগ্রহণ করতে চান ঃ

১। আমরা আপনার স্বাস্থ্য সম্পর্কে কিছু প্রশ্ন করবো এবং একজন ট্রেনিংপ্রাপ্ত মহিলা চিকিৎসক আপনার শারীরিক পরীক্ষা করবেন। যার মধ্যে আপনার যৌনাঙ্গ পরীক্ষাও অন্তর্ভুক্ত থাকবে।

২। অগ্রভাবে তুলা লাগানো একটি কাঠির সাহায্যে আপনার যৌনাঙ্গ হতে 'স্পেসিমেন' সংগ্রহ করে রোগ নির্ণয়ের জন্য গবেষণাগারে পরীক্ষা করা হবে। এতে কোন ব্যাথা অনুভব করবেন না এবং আপনার কোন ক্ষতির সম্ভাবনা নেই।

৩। ৩ দিন পর আপনাকে এই ক্লিনিকে আবার আসতে হবে, তখন ল্যাবরেটরী পরীক্ষার ফলাফল থেকে আপনি গণোরিয়া রোগে আক্রান্ত কিনা জানানো সম্ভব হবে। যদি আপনি গণোরিয়া রোগে আক্রান্ত হন, তবে এর চিকিৎসার জন্য আপনাকে ৫০০ মিগ্রাঃ সিপ্রোফ্লোক্সাসিন একটি মাত্রায় মুখে খেতে দেওয়া হবে বা সেফট্রায়েক্সন ১২৫ মিঃ গ্রাঃ একক মাত্রায় মাংসে ইনজেকশন দেওয়া হবে।

৪। আবার ৭ দিন পর আপনাকে এই ক্লিনিকে আসতে হবে, যখন আপনার যৌনাঙ্গ হতে পুনরায় স্পেসিমেন সংগ্রহ করে ল্যাবরেটরীতে পরীক্ষা করা হবে। এই পরীক্ষা থেকে আপনি জীবাণুমুক্ত হয়েছেন কি না তা আমরা জানতে পারবো।

৫। আপনি এই গবেষণায় অংশগহণ করে সরাসরি উপকৃত হবেন। কারণ এর থেকে আপনার রোগ আছে কি না নির্ণীত হবে এবং বিনামূল্যে নির্ণীত রোগের চিকিৎসা পাওয়া যাবে। এইভাবে অন্যদের মধ্যে এই রোগের বিস্তারও রোধ করা যাবে। উপরন্তু এই গবেষণার ফলাফল থেকে সমাজ উপকৃত হবে।

৬। এই গবেষণায় অংশগ্রহণ থেকে কোনরূপ শারীরিক ঝুঁকির সম্ভাবনা নেই।

৭। আপনি যদি এই গবেষণায় অংশগ্রহণ নাও করেন তাহলেও এই ক্লিনিকের প্রচলিত ব্যবস্থা অনুযায়ী আপনি চিকিৎসা পাবেন। অন্যদিকে অংশগ্রহণ করেও যে কোন সময় কোনরূপ ক্ষতিপূরণ ছাড়াই আপনি আপনার সম্মতি প্রত্যাহার করতে পারবেন। এমনকি এই ক্লিনিক হতে প্রাপ্ত আপনার পরবর্তী চিকিৎসা ব্যবস্থারও কোনরূপ পরিবর্তন হবে না।

৮। ল্যাবরেটরী পরীক্ষার ফলাফল ও আপনার যাবতীয় তথ্য সম্পর্কে গোপনীয়তা রক্ষা করা হবে। এই গবেষণায় অংশগ্রহণকারী, গবেষকগণ এবং মানবিক অধিকার রক্ষার ইথিক্যাল কমিটি ছাড়া সেসব তথ্য অন্য কেউ জানতে পারবে না।

৯। আমরা যে কোন সময় আপনার যে কোন প্রশ্নের উত্তর দিতে আনন্দবোধ করবো।

আপনি যদি এই গবেষণায় অংশগ্রহণে ইচ্ছুক হন, তাহলে অনুগ্রহ করে নিচে প্রদত্ত নির্দ্দিষ্ট স্থানে স্বাক্ষর অথবা টিপসহি দিন। আপনার সহযোগিতার জন্য ধন্যবাদ।

গবেষণায় অংশগ্রহণকারীর স্বাক্ষর/টিপসহি
তারিখঃ

পরীক্ষকের স্বাক্ষর
তারিখঃ

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
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CENTRE
FOR HEALTH AND
POPULATION RESEARCH

09 August 1999

Memorandum

To : Dr. Motiur Rahman
Laboratory Sciences Division

From : Professor Mahmudur Rahman
Chairman, Ethical Review Committee

Sub : Protocol # 99-013

The Ethical Review Committee met on 4th August 1999 and considered your prptocol # 99-013 entitled "Treatment failure due to ciprofloxacin in gonorrhoea among Bangladeshi female sex workers". After a thorough review and discussion, the Committee made the following observations to be addressed in your protocol:

a) on the Face Sheet, item # 2(a) should be marked 'Yes'

b) the objectives and hypotheses should be clearly written.

c) the title of the protocol should be revised to reflect the methodology.

d) the flow-chart should be revised to make it more reflective and representative of the study.

You are requested to modify the protocol incorporating the above observations, in consultation with Dr. Halida A. Akhtar. The revised copy should be submitted to the Chair for necessary action.

Thank you.

Copy:- Division Director
Laboratory Sciences Division

International Centre for Diarrhoeal Disease Research, Bangladesh
CENTRE FOR HEALTH AND POPULATION RESEARCH

INTERIM/FINAL ✓

SUMMARY COMPLETION FORM FOR PROTOCOLS

Title : Prevention of treatment failure due to ciprofloxacin and ceftriazone in gonorrhoea among Bangladeshi female sex workers.

Investigator(s) : Dr. Motiur Rahman, LSD

Protocol No. : 99-013 Budget Code : 207451

Findings (Abstract) :

The study was conducted between July 1999 to Dec 2000. Between September 1999 to August 2000 a total of 527 subjects were enrolled for the study. Of the 527 enrolled subject 513 were eligible for sample collection. Among these 513 patient 186 (36%) were culture positive for *N. gonorrhoeae*. Out of these 186 patients 150 were randomized to treatment (Tab. Ciprofloxacin or Inj. Ceftriaxone). Of these 150 subjects 80 were treated with tab. Ciprofloxacin and 70 were treated with Inj. Ceftriaxone. After one week 123 (82%) subject were available for a follow up sampling.

Among the patients treated with ciprofloxacin 34. 3% (24/70) were cured compared to 98.1% (52/53) treated with ceftriaxone. Of this population, 250 (48.7%) had cervical infection with either *N.gonorrhoeae* and /or *C. trachomatis*. Dual infection with both gonorrhea and chlamydia was found in 10.3% (53/513) of the subjects. The overall prevalence of gonorrhea and chlamydia was 36% (186/513) and 23% (117/507) respectively. The prevalence of vaginal infection trichomoniasis and Bacterial vaginosis was 32% (148/459) and 79% (387/489) respectively. Sero-prevalence for syphilis was 26% (134/513).

Policy Implications:

The finding of this indicates that the current treatment guideline for gonorrhea needs to be changes in Bangladesh. High prevalence of STD among floating sex workers indicates the need for targeted intervention.

Dissemination plans:

The study finding has been presented as abstract in International conference of Antimicrobial Agent and Chemotherapy. The data has been presented in forums of Skin and Venereal Diseases specialists in Dhaka. We are planning to publish this data in international journals.

4/6/2001

Motiur Rahman

Signature of the P.I.