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Indian Study of Women with Cervical Lesions called Unethical

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Doctors in India are questioning the ethics of a study which observed the natural course of precancerous uterine cervical lesions without treatment in women who had not given written consent to take part. In at least nine women the lesions progressed to invasive cancer, and 62 women developed carcinoma in situ of the cervix before they were treated.

In an attempt to study rates of progression of uterine cervical dysplasias to malignancy, the Indian Council of Medical Research during 1976-88 allocated 1158 women with varying degrees of cervical dysplasias to long term follow up. The development of carcinoma in situ was defined as the end point for treatment.

The investigators, from the Institute of Cytology and Preventive Oncology in New Delhi, said that they did not obtain written consent on the grounds that most of the women in the study were illiterate and that written consent was not mandatory when the study was launched. The study has helped India evolve screening guidelines for the national cancer control programme.

A gynaecologist has alleged that the investigators had neither informed the women that their lesions were known to progress to cancer nor offered them treatment at the outset. "The crucial information that dysplasias were suspected precancerous lesions was withheld and no immediate treatment options offered," said Dr Puneet Bedi, a consultant gynaecologist in New Delhi.

The institute of cytology has denied the allegations and said that the women had given verbal consent after they were informed "in simple language" about the implications of their lesions and the aim of the study and that they were assured of timely treatment. However, the absence of documented consent has sparked a debate in medical circles on the need for genuine informed consent in the country.

Ethics experts reject the argument that written consent was considered unnecessary because the women were illiterate. "Illiteracy is not stupidity," said Dr Sunil Pandya, a neurologist at the King Edward Memorial Hospital in Bombay and chairperson of the Forum for Medical Ethics, a non-government

society organised by doctors. "The ethical process demands evidence that the women volunteered after understanding the risks involved and after rejecting available treatment," said Dr Pandya.

Some doctors are also questioning the decision to observe severe dysplasias every three months without treatment until a diagnosis of carcinoma in situ. Forty women with severe dysplasias developed malignancies within the first three months. The researchers followed up at least 21 women with persistent severe dysplasias for periods ranging from six months to two years. Ten women with severe dysplasias were lost to follow up. Women with mild and moderate dysplasias at the beginning of the study who developed severe dysplasias were also observed until the lesions regressed or progressed to carcinoma in situ. By the close of the study 71 women had developed malignancies.

Until colposcopic examinations became mandatory in 1982 most lesions were studied on the basis of cytology. Some doctors have described this as a major flaw in the study because a diagnosis of mild dysplasia on cytological examination sometimes hides any degree of dysplasia, carcinoma in situ, or even invasive cancer.

The institute of cytology says that doctors in the participating hospitals reviewed individual patients, and women who needed treatment were "managed according to prevailing clinical practice" and excluded from the study. They argue that the study should be viewed in the context of diagnostic and treatment facilities available at the time.

"The issue is, why were persistent severe dysplasias followed up without therapy," argues Dr Bedi. The institute maintains that there was "no conclusive evidence" that all severe dysplasias progress to cancer. But gynaecologists have expressed doubts about whether a similar study could have been conducted in countries with more advanced clinical services and greater patient awareness dm in India. "Even in 1976, world opinion was to the effect that severe dysplasias advanced to cancer so often that treatment was indicated," said Joseph Jordan, medical director at the Birmingham Women's Hospital in the UK.

"The study should have been terminated as soon as the first malignancies were detected," says Samiran Nundy, former editor of the National Medical Journal of India. "Patients in India are not treated very well. It is time researchers here begin to honestly believe that unethical research is worse than no research."

In the late 1980s them was a similar scandal surrounding a study carried out at the National Women's Hospital in Auckland, New Zealand (BMJ 1988;297:533-8). An inquiry headed by Judge Silvia Cartwright was set up to investigate

allegations that a research programme had been undertaken to study the natural course of carcinoma in situ of the cervix by withholding conventional treatment from some patients. The women in the trial had not been asked to give consent. Judge Cartwright found that the research programme, which started in the 1960s, had resulted in the failure to treat adequately several women with carcinoma in situ. For a minority of women their management had resulted in persistent disease, the development of invasive cancer, and, in some cases, death. Judge Cartwright concluded that the research should not have been approved; that consent should have been sought; that the study was not monitored adequately; and that the concerns of other doctors were not acted on.