

AUTHOR'S REPLY

Dear Sir,

I am replying to the queries raised⁽¹⁾ on our paper entitled, "Lifestyle, reproductive factors and risk of gallbladder cancer".⁽²⁾ The cases and controls were prospectively identified over a period from 1999 to 2003. It is not a prospective case-control study; rather it should be labelled as a "prospectively-identified case-control study".

When the study is on matched cases and controls, the association cannot be shown. To find the disease association with age, a base population is required, which is impractical in our hospital context. The researchers have no base population because it is not the only hospital providing healthcare services to the catchment population. The main aim of the present study was to assess whether the lifestyle and reproductive factors of the study population were a risk factor for gallbladder cancer; and thus the variables of age and gender were matched between the cases and controls, and other variables such as religion, education and per capita income, were presented as the characteristics of the participants and tested for statistical difference between the cases and controls, as these characteristics affect the food habits and environmental conditions and may have an influence on gallbladder cancer.

The authors have not mentioned a Hindu preponderance of cases (only), as the study participants of both cases and controls were from a community comprising mainly Hindus.

The title of Table II is absolutely correct. The raw data included every variable by individual cases and controls. The table provides the duration and dosage which are presented in the form of summary statistics. The authors do not think it is essential to provide the detailed classification; the summary statistics can validate the results. The duration of tobacco consumption either via chewing or smoking showed no significant difference between the cases and controls, in contrast to the dose, which the results show the possibility of dosage being a risk factor. A detailed analysis could be carried out by various categories of dose and duration, but it may give a spurious result for such a small sample size; a larger data set and logistic regression analysis are recommended. In addition, dosage may not always be the product of quantity and duration, as smoking one cigarette per day for 40 years and smoking ten cigarettes per day for four years may have a dissimilar effect.

As people here consume tobacco in different forms, tobacco use in any form was first analysed to explore the possibility of tobacco being a risk factor for gallbladder cancer, then it was segregated according to the individual form. However, this required an advanced statistical approach, which was not possible with a small data set and having several categories of the variables. This analysis had only explored the conditions required for further scientific study on a larger sample size. The odds ratios (OR) were provided generally for the consumption of tobacco in any form, and specifically for chewing tobacco.

The authors agree that for smokers, the patient's increased risk of carcinoma mentioned is not correct based on the confidence interval. However, the lower limit of the confidence interval was more than 0.95 and upper limit was 13.82; this may be due to the small sample size. The authors would like to point out that many studies used the same basis where the lower limit of the confidence interval was more than 0.90. The statement that the risk of carcinoma "was particularly more in patients who started smoking lately" is not correct.

Table IV clearly presented the means and standard deviation as the summary statistics, and these were not tested for statistical differences. These could be used for further analysis using the *t*-test to identify the risk factors. The OR was calculated on the variables, and the reference categories were also listed. The confidence limits of the OR were calculated via Woolf's method,⁽³⁾ which is now commonly applied by statisticians to calculate the confidence limits of the OR. The logistic regression was not done because the sample size was too small and the variables too many to obtain robust risk factors. The analysis was carried out for menstruating and menopausal women separately, and hence, two ORs were indicated. However, the numbers presented in the table are incorrectly presented. The cases and controls were age- and gender-matched; but when only women were considered, they differed for their age. For the menstruating women category, the reference category to calculate OR and its confidence limit was < 25 years of menstruating duration, and for those in the menopausal category, it was < 5 years of menopausal duration. Obviously, age would be a confounder in this situation; therefore, the correct table and age-adjusted OR following Mantel-Haenszel's method,⁽³⁾ along with its confidence limit should be as follows:

Menstrual status / duration (years)	No. of cases	No. of controls	Odds ratio (95% confidence interval)
Menstruating			0.36 (0.11–0.76)
< 25	2	6	
≥ 25	8	9	
Total	10	15	
Menopausal			
< 5	30	14	5.44 (2.70–15.16)
≥ 5	8	28	
Total	38	43	

Yours sincerely,

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