Dear Editor,
Many authors have tried to find out about risk factors for breast cancer in India. The most special thing in cancer of the breast is that it many a times metastasizes before it spread in the primary tissue. This puts the dual responsibility on the shoulders of the experts in public health to discover accurate risk factors of breast cancer and their appropriate quantity to cause the disease.

During the course of this review we came across many studies on breast cancer in India. One remarkable study done at Udupi on risk factors of breast cancer among patients attending the Tertiary Care Hospital in Udupi District of Karnataka has been taken for explanation of the young readers. They assessed the factors associate with breast cancer.

CONFUSING ASSOCIATION WITH RISK/CAUSATION

One of the study results states that more than 7-12 years of education was found to be a significant risk factor and nonvegetarian diet was also observed as an important risk factor for breast cancer in women. This worried me a bit as education brings a positive change in life, better jobs, and thus better health and self-care needs are being felt. I believe that education is a protective factor instead of calling it a risk factor since common sense says that frequency of visits to a doctor for complaints are more among educated and hence there are more likely chances of detecting breast cancer at early stages among educated people. To authenticate that fact let me quote a study done by Mashelkar et al. on risk factors of breast cancer among women in Goa and found that risk of breast cancer was found to decrease as the level of education increased. These two are extremely opposite findings. In fact I would say that education directly or indirectly plays a role, can be an associated factor, but labeling it as a risk factor is not right in any way. In the conclusion section, the Udupi study states that breast cancer occurs a decade earlier in Indian women as compared with the women of developed countries and is a leading cause of mortality in developing countries like India so raising the awareness regarding screening procedures and treatment regarding breast cancer can help reduce mortality. My submission here is that Is awareness not generated by going to school for long time? This contradicts earlier statement. Let the authors should make this point very clear to the readers since the new readers might interpret that education is risk but awareness is a protective factor.

CLINICAL SIGNIFICANCE AND STATISTICAL SIGNIFICANCE

Latter in the discussion the authors of the Udupi study state that because nonvegetarians consume more fat than vegetarians and the diet with animal fat intake has been shown to increase the risk of breast cancer, nonvegetarians are more at risk. To refute this fact let me state another study done by Harrison et al. on risk factors for breast cancer among women attending a Tertiary Care Hospital in Southern India and found that nonvegetarian diet showed an association, however dietary factor was not found to be significant statistically. Let me categorically point out that association and risk are two different entities and need to be understood in context accordingly. Furthermore, statistically significant result need not be clinically significant and can we really conclude that nonvegetarian diet is a risk factor for breast cancer? Mashelkar et al. (referred earlier) found that women who reported red meat intake were 2.22 times more risk of breast cancer compared to those not consuming red meat. Let me categorically point out to the fresh readers that consumption of excess amounts of oil or ghee and dietary pattern of being vegetarian and nonvegetarian are two entirely different concepts and may not be confused please. In fact we cannot come to the conclusion that vegetarians or nonvegetarians consume more saturated fats. The amount of energy needed to digest nonvegetarian food is more as compared to the vegetarian food. The current cooking practices have changed among nonvegetarians as compared to the yester years. They roast or steam the food. Hence, such direct conclusions appear baseless. Nonvegetarian foods like fish are rich in essential fatty acids such as eicosapentaenoic acid and docosahexaenoic acid which are much vitally needed by the body. By communicating the message that vegetarians are comparatively less at risk of breast cancer as compared to nonvegetarians it may sound good but may give a false image to the readers most of who are fresh Public health postgraduate students in their respective Medical Colleges.
or Institutes of Public Health. Thus, I feel that we need to be finding clinical significance before even having a thought of statistical significance in our observational studies.

**INCORRECT SELECTION OF CASES AND CONTROLS**

This is the basic need of any case control study. There are some innate errors in case and control choice as well as statistical analysis with the Udupi study. Patients other than breast cancer were chosen as controls. First degree relatives of cases, controls having personal history of breast disease, pregnant women, and women with gynecological problems were excluded from the study. We know patients with prior biopsy are more at risk of breast cancer so excluding them would not be right. Patients with fibro adenoma should have been chosen as controls. Why pregnant women were excluded from the control group needs a special mention by the authors. Why a lady whose hysterectomy or ovariecctomy was done was not related to breast cancer were excluded from the study. This I have concluded since the authors of Udupi study have mentioned that the women with gynecological problems were excluded from the study. What outcome change was expected since it was a case control study and data was collected by history taking in a retrospective manner using a structured questionnaire. It was in no way an interventional study.

**DISCUSSING IMPORTANT KNOWN RISK FACTORS**

Gajalakshmi *et al.* did a multi-centric case control study to assess the breastfeeding and breast cancer risk in India. They have also included a lady whose hysterectomy or ovariecctomy was done not related to breast cancer. In fact such a case was classified as postmenopausal by them, and they have stratified the data according to the menopausal status. That study mentions that cases with in-situ carcinoma or with sarcoma of the breast were excluded from the study. In fact the authors have concluded since the study this would unnecessarily invite a nonresponse bias in the study. Gajalakshmi *et al.* have sincerely mentioned that their nonresponse rate was 10% in both cases and controls. Refusal was the reason for nonparticipation. This type of honest statement deserves appreciation.

**RESPONSE RATE**

Again there is no mention of the response rate in the study done by Udupi study and the readers are left with only one option that it to guess that it might have been close to 100%. In fact the authors have mentioned that those who were not willing to participate were excluded from the study this would unnecessarily invite a nonresponse bias in the study. The mean age of cases was 45.64 and controls were 44.9 years. Only 7 out of 188 participants used OC pills that too only one control. How can we apply statistics like Chi-square test to such data as we know that Chi-square test should not be used when even 1 value is ≤1 or >25% of the values are ≤5. Here, only 1 lady among controls and six ladies among cases were using OC pills. I do not know how they have concluded that OC pill is not a risk factor for development of breast cancer wherein appropriate chance has not been given for the variable to really make interplay. If the study subjects are not exposed to the risk factor, then how come the authors can conclude that there is no association. The question of applying Odds ratio (OR) also does not arise since odds shows the strength of association for that we should prove proper association among the variables by giving them appropriate chance by including substantial group of ladies of a specific age group who consume OC pills. Similarly, we cannot apply this test even to variable like abortion, family history of breast cancer in Udupi study. Thus, the conclusion that ladies with induced abortions or with family history of breast cancer are at more risk.
of breast cancer sounds meaningless if concluded only from the study.

Interpreting crude odds ratios without considering potential confounders

The authors need to pay attention to the confidence intervals (CIs) and not the odds ratio only. For example in the variable Age at the first child birth, although OR is 1.88 for 21-30 years, the CI ranges from 0.93 to 3.80. The number 0.93 indicates that it is protective and we cannot blatantly make the statement that from this study it was proved that the age at first childbirth is risk for breast cancer as made by Udupi study. We already know that induced abortions are significant risk factors for breast cancer through literature.[8]

On reading news daily we found this statement made by Brind - “With only 94 cases and 94 controls, the study was way too small for a significant risk of the order of 1.5-fold to even show up,” explained Professor Joel Brind (Baruch College, City University of New York). “Yet induced abortion did show up as the strongest risk factor (and right on the border of statistical significance) because the risk increase was so high at 6.38-fold.” Brind J further states that “It’s indisputable that abortion contributes to delayed first full term pregnancies; and in some cases, women remain childless forever, which is also an accepted risk factor.”[7] We already know that OC pills are significant risk factors for breast cancer through the literature.[8]

Obesity has not been taken as risk factor at all by the Udupi study. There is no mention of Waist Hip ratio or body mass index (BMI) by Udupi study. I appreciate the statement made by Harrison et al.[9] that interestingly, age at menarche <11 years and a BMI >25 were found to have a protective effect contrary to what is reported in the literature.[9]

Pan chewing, tobacco chewing, areca nut chewing, and snuffs use were not significantly associated with breast cancer risk but in the discussion section the author states that no cases or controls reported the habits of smoking and drinking. If the study subjects are not exposed to the risk factor, then how come the authors concluded that there is no association. In fact the literature states that smoking and alcohol consumption are the risk factor for all cancers.[8]

Instead of income socioeconomic status should have been taken. Gajalakshmi et al. in their study derived an indicator of socioeconomic status by summing up scores given to home ownership, number of the rooms and number of people living in the house, availability of toilet, and running water as well as comfort and luxury items owned by the study subject.[10] This states that lot of hard work was done by Gajalakshmi et al. just to calculate one variable. Furthermore, since it was a multicentric study its results are more authentic as compared to the Udupi study.

Tiwari et al. did a study on changing trends in breast cancer awareness in young females of north India: A pilot study from rural cancer hospital in north India and found that owing to improved education levels and awareness, the young rural females are more informed of the breast-related symptoms and are seeking proper care for the same.[11] This does not go hand in glove with the Udupi study which states exactly the opposite.

Thus, the conclusion by Udupi study that the study results are in accordance with the results of previous investigations on risk factors of breast cancer appear to be baseless and alarming to the scientific community. There are many statements which have to be understood by the readers by reading in between lines where likely chances of error are optimized. Hence, I would rate that this published matter by read with a pinch of salt in future and not taken for face value at least by young and inexperienced readers. The positive point in Udupi study was that it was a case — control design which is best suited study design in determining risk factors.

This boils down to the statement what are the risk factors of breast cancer finally which are available in our Preventive and Social Medicine textbooks.[9] We need systematic reviews.

Let me quote this from a very famous book written by an Indian author[12] Susan Sontag once said “Illness is a night-side of life, a more onerous citizenship. Everyone who is born holds a dual citizenship, in the kingdom of well and in the kingdom of sick. Although we all prefer to
use only a good passport, sooner or later each one of us is obliged, at least for a spell, to identify ourselves as citizens of that other place.” For 3000 years or more, the disease of cancer is known to the medical profession. Moreover, for 3000 years and more, humanity has been knocking at the door of the medical profession for a cure. Now it is cancer’s turn to be the disease that does not knock before it enters.

Financial support and sponsorship
Nil

Conflicts of interest
There are no conflicts of interest.

Sagar Borker
Department of Community Medicine, KVG Sullia Medical College, Sullia, Dakshina Kannada, Karnataka, India
E-mail: sagarborker@gmail.com

REFERENCES

1. Kamath R, Mahajan K, Ashok L, Sanal T. A study on risk factors of breast cancer among patients attending the tertiary care hospital, in Udupi district. Indian J Community Med 2013;38:95-9.
2. Mashelkar U, Ferreira A, Kulkarni M, Vaz F, Perni S, Kamat U. Risk factors for breast cancer among women in Goa, India: A case control study. Asian J Med Clin Sci 2013;2:68-71.
3. Harrison P, Srinivasan K, Binu V, Vidyasagar M, Nair S. Risk factors for breast cancer among women attending a tertiary care hospital in South India. Int J Collab Res Intern Med Public Health 2010;2:109-16.
4. Gajalakshmi V, Mathew A, Brennan P, Rajan B, Kanimozhi VC, Mathews A, et al. Breastfeeding and breast cancer risk in India: A multicenter case-control study. Int J Cancer 2009;125:662-5.
5. Dixit JV. Tests of significance. In: Principles and Practice of Biostatistics. 2nd ed., Vol. 7. Jabalpur: Banarasidas Bhonath Publishers; 2005. p. 120.
6. White E, Malone KE, Weiss NS, Daling JR. Breast cancer among young U.S. women in relation to oral contraceptive use. J Natl Cancer Inst 1994;86:505-14.
7. Malec K. Study: Abortion Ups Breast Cancer Risk Six-Fold, Millions of Women Have Died. Life News, Washington, DC; 7th January 2013.
8. Daling JR, Malone KE, Voigt LF, White E, Weiss NS. Risk of breast cancer among young women: Relationship to induced abortion. J Natl Cancer Inst 1994;86:1584-92.
9. Park J, Park K. Parks Textbook of Preventive and Social Medicine. 22nd ed. Jabalpur: Banarasidas Bhonath Publishers PSM; 2011. p. 359-60.
10. Rai M, Pandey R, Singh M, Rai A, Shukla H. Assessment of epidemiological factors associated with breast cancer. Indian J Prev Soc Med 2008;39:71-6.
11. Tiwari V, Shukla P, Gupta G. Changing trends of breast cancer awareness in young females of north India: A pilot study from a rural cancer hospital. Int J Med Public Health 2014;4:62-5.
12. Mukherjee S. Emperor of all Maladies-A Biography of Cancer. Thomson Press India Ltd.; 2011.

How to cite this article: Borker S. Common mistakes done by authors in conduct and reporting risk factor (observational) studies. J Mid-life Health 2015;8:137-40.