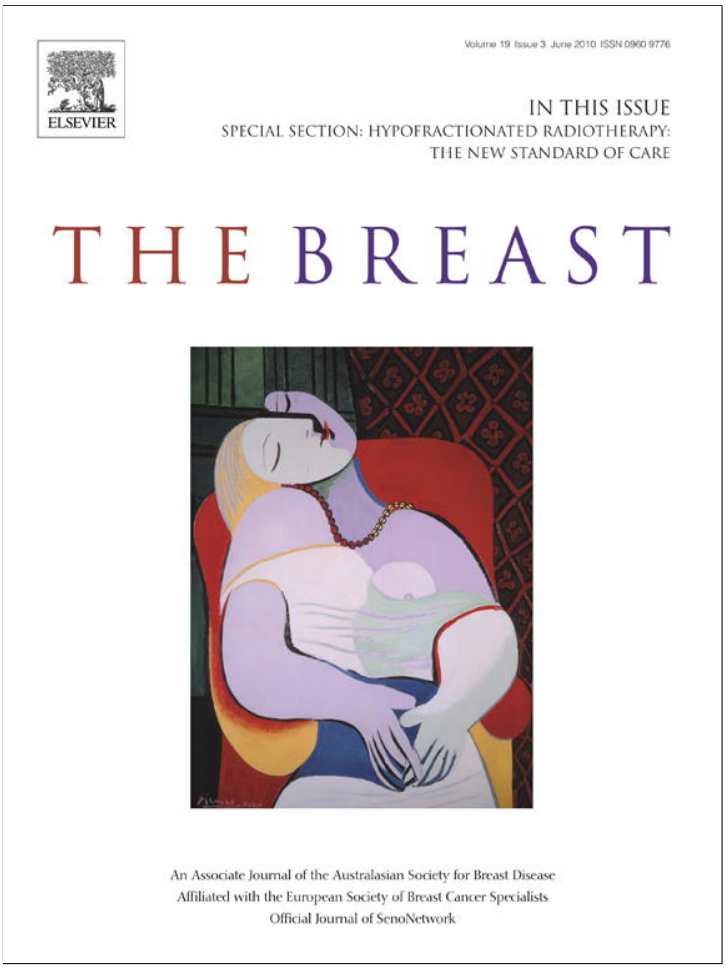
Provided for non-commercial research and education use.
Not for reproduction, distribution or commercial use.




This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:

http://www.elsevier.com/copyright

Author's personal copy

The Breast 19 (2010) 238–242

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

# Visual analogue scale for assessing breast nodularity in non-discrete lumpy breasts: The Lucknow – Cardiff breast nodularity scale

Sandeep Kumar [a,*], Ruchi Rai [a], Vinita Das [b], Surender Kumar [a], Varsha Dwivedi [a], G.G. Agrawal [c]

[a] Department of Surgery, King George's Medical University, Lucknow 226 003, UP, India
[b] Department of Obstetrics and Gynecology, KG Medical University, Lucknow, India
[c] Department of Statistics, Lucknow University, Lucknow, India

ARTICLE INFO

*Article history:*
Received 27 July 2009
Received in revised form
6 October 2009
Accepted 4 February 2010
Available online 11 March 2010

*Keywords:*
Benign breast disorders
Breast nodularity
Objective assessment
Mastalgia

ABSTRACT

*Background:* Objective measurement of benign non-discrete lumpy breasts is not performed routinely that would lead to disease measurement, inter-physician communication, therapeutic response assessment and a normative function of reducing unnecessary biopsies. A schematic 5-point ordinal visual analogue scale was developed.

*Methods:* Two blinded experienced clinicians graded breast nodularity on a pre-determined *five point* analogue scale (grades 0–4) to determine its inter-observer reliability after its face validity that excluded inflammatory, nipple, areola and discrete lump problems.

*Results:* 784 Women (hospital 384; community 400) aged between 20 and 70 years (mean 31.9) underwent physical breast examination by 2 experienced clinicians. Inter-observer matched nodularity grading in women attending hospital were Grade 0 in 123 (32.03%), grade 1 in 67 (17.44%), grade 2 in 54 (14.06%), grade 3 in 52 (13.54%) and grade 4 in 23 (5.99%) and in community it was grade 0 in 172 (43%), grade 1 in 88 (22%), grade 2 in 60 (15%), grade 3 in 28 (7%) and grade 4 in 14 (3.5%) women. There was very good agreement (kappa = 0.7798) across all grades in hospital subjects and excellent agreement (kappa = 0.8659) in community subjects. Both estimates of kappa coefficients were highly significant from population kappa coefficient of zero ($p < 0.001$). Overall, 1/3rd normal women have absolutely smooth textured breasts.

*Conclusion:* User-friendly tool developed for objective evaluation of non-discrete lumpy breasts showed excellent reliability and validity. This tool should be useful for clinical drug trials in benign breast disorders and for wide routine clinical recording of patients.

© 2010 Elsevier Ltd. All rights reserved.

## Introduction

Benign breast disorders that present as pain, inflammation, nipple areola problems, discrete lump and nodularity are common. Pain and nodularity in the breast is the single most common reason for which women seek medical advice about their breasts.[1] This was the presenting symptom in 45–85% of women with breast problems.[2] The problem of benign breast diseases has so far received scant attention in India but it is expected to increase due to lifestyle changes, dietary modifications, early menarche, delayed first child birth and exogenous hormone administration. An apparent increase is occurring on account of increasing awareness. Estimates regarding breast pain as the presenting feature and the underlying causes of breast pain in the Indian population remain speculative because of lack of population-based studies and lack of uniformity in terminology.[3,4] Breast nodularity with or without pain of the breast is a symptom that deserves full attention and careful evaluation. This condition has been described in literature for the past 2 decades as ANDI or Aberration of Normal Development and Involution.[5] There are no consistent radiological and histopathological changes in the breast tissue that can be ascribed to breast pain and nodularity. Breast pain and nodularity per se causes undue worries on account of rampant poor first hand management of this condition. One reason for this is lack of a popular objective instrument to evaluate benign breast nodularity and its serial assessment during mastalgia treatment trials. A popular yardstick to measure an aberration in breast and a bookish mandamus will perpetuate a useful clinical practice of providers of primary breast care and should also restrain unnecessary biopsies, hitherto very common in general hospitals. A robust objective scale to evaluate breast nodularity in non-discrete

* Corresponding author. Tel.: +91 522 225 7388 (office), 232 2577 (home), 9335 240 880 (mobile); fax: +91 522 225 7674.
*E-mail address:* k_sandeep@hotmail.com (S. Kumar).

0960-9776/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.breast.2010.02.002

Author's personal copy



lumpy breasts with universal external validity like Glasgow Coma Scale was therefore conceptualized. The internal validity of this scale was tested in hospital and community based settings.

## Patients and methods

A tool to evaluate breast nodularity was evolved as an ordinal scale from the construct of two decades of experience of working in breast clinics in India and abroad. The original first hand figure (scale) drawn by the author (SK) – a visual schematic linear analogue scale (VAS) for measuring breast nodularity is shown in Fig. 1 and named as The Lucknow – Cardiff Breast Nodularity Scale. This figure has been used by the author across several breast clinics and focus groups with good face validity and global applicability. The aim of this study was to evolve a robust tool with high internal consistency in the absence of a gold standard to measure breast nodularity.

The above breast nodularity scale is a 5-point ordinal scale depicting increasing order of nodularity shown schematically in upper outer quadrants of the breasts. Clinically breast nodularity is especially and most commonly noticeable in the upper outer quadrant of the breast that has the maximum amount of breast tissue hence the depiction in the above scheme is mostly shown in the upper outer quadrants of the breasts. An extrapolation can be charted for other quadrants of the breast in the index picture. Grade – 0 depicts a smooth textured breast with extreme extent of normalcy and grade – 4 the maximum nodularity. In the present scale, the five figures are cue for the examining doctor to chart the nodularity in the index breast. The examining clinician or nurse is taught to make a holistic interpretation of breast nodularity as a sum of area or quadrants involved and the coarseness of nodularity.

Face validity and wide applicability of the above instrument was tested and confirmed in a focus group of 20 senior and resident level doctors working in the breast clinics across the country. An excellent inter-observer reliability was observed in this workshop. Test retest intra-observer reliability was also tested in 40 subjects along with participant inter-observer reliability in a pilot study.

This study was duly approved by the institutional ethical committee. In the first part, consecutive women (aged between 20 and 70 years,) presenting at the outpatient Departments of Surgery and Gynecology at King George Medical University, Lucknow from May 2005 to December 2007 were included for the hospital based study. A second part of the study of the same pre-determined sample size was conducted in the community so that the scale may be tested in a low prevalence population. Women not soliciting advice for any breast related symptom from the community were randomly selected from different women organizations. After an informed consent proforma directed details were recorded. Subjects were physically examined by authors 1 and 2 blinded to each other. The maximum nodularity in each breast was charted in the index breast on each side.

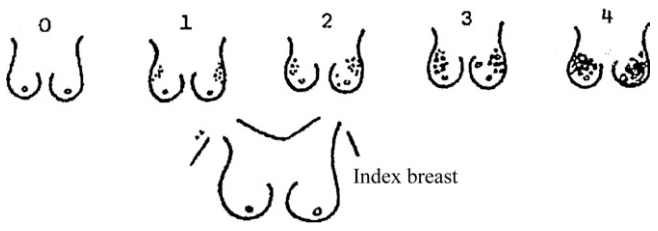



**Fig. 1.** Lucknow – Cardiff breast nodularity scale.

### Sample size

A proportion of 50% was assumed to have significant nodularity of grade 2, 3 and 4 that led to the most conservative sample size. Assuming probability of type I error equal to 0.05 and expecting the absolute precision equal to 95%, a sample size of 384 was reached using the following formula:

$$n = \frac{Z^2_{1-\alpha/2} \cdot p(1-p)}{e^2}$$

where $p$ = proportion of subjects with nodularity, $\alpha$ = probability of type I error, $Z_{1-\alpha/2}$ is the upper 100 percentile of standard normal distribution, $e$ = precision (half width of confidence).

### Analysis

Breast nodularity is considered an abstract physical finding by some clinicians. Breast nodularity in the absence of a discrete breast lump has no clinical, bio-chemical or pathological gold standard. Thus, face validity and high level of agreement between two and more than 2 observers were taken as the gold standard. Two experts could be agreeing just by chance alone. *Kappa* is a statistic that tells us the extent of agreement between observers above and beyond chance alone.[6]

$$Kappa = \text{proportion of observed agreement} - \text{proportion of agreement by chance } 1 - \text{proportion of agreement by chance}$$

If the two observers agreed as expected by chance only, *Kappa* would be 0; if the two observers are in perfect agreement, *Kappa* would be 1. Similarly, *Kappa* value of $<0.5$ is poor agreement, 0.5–0.6 is fair agreement, 0.6–0.7 is good agreement, 0.7–0.8 is very good agreement, $>0.8$ is an excellent agreement.

## Results

The overall nodularity perceived from mild to high grades was in 2/3rd of the subjects and only a minority 1/3rd women were declared having overall smooth breasts. The nodularity grades were marginally higher in the hospital as compared to community-based study (Table 1)

### *Hospital based study*

Three hundred and ninety consecutive patients from the breast clinics of the Departments of Surgery and Obstetrics and Gynaecology were independently examined and recorded when both the observers were present. Six patients with non-discrete lump were found to have malignancy and excluded from the analysis. The percentage of agreement level (Table 2) for grade 0 was 123/123 (100%), grade 1 was 67/82 (81.71%), grade 2 was 54/78 (69.23%), grade 3 was 52/70 (74.29%) and grade 4 was 23/31(74.19%). Sample *Kappa* across all grades was 0.760 and standard error was 0.025. This represented a very good agreement between the two clinicians that was highly significant from population kappa coefficient ($p = 0.001$, CI = 0.7318–0.8278). Nodularity was maximally seen in the reproductive age group, i.e., 21–40 years of age (74.3%) it was least common in the post menopausal women (Table 4). Breast nodularity grade 2–4 was more common in higher socio-economic class (Table 5). The most common presenting complaint amongst this set of women was a lump in breast in 124 (32.29%), breast pain in 102 (26.56%) and lumpiness in 60 (15.63%) women.

Author's personal copy



**Table 1**
Distribution of benign breast nodularity grades in hospital and community.

| Subjects | Grade 0 | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Agreement level (Kappa κ) | Std. error | *p* Value |
|---|---|---|---|---|---|---|---|---|
| Hospital study ($n = 384$) | 123 (32.03%) | 82 (21.35%) | 78 (20.31%) | 70 (18.23%) | 31 (8.07%) | 0.760 | 0.025 | 0.000 |
| Community study ($n = 400$) | 172 (43.00%) | 97 (24.25%) | 80 (20.00%) | 34 (8.5%) | 17 (4.25%) | 0.861 | 0.020 | 0.000 |
| Total subjects ($n = 784$) | 295 (37.62%) | 179 (22.83%) | 158 (20.15%) | 104 (13.26%) | 48 (6.12%) | 0.836 | 0.016 | 0.000 |

*Community based study*

Similarly, a total of 400 community women not having any breast related complaints were also examined blindly by 2 independent experts with all details noted as per proforma. The agreement level (Table 3) for grade 0 was 172/172 (100%), grade 1 was 88/97 (90.72%), grade 2 was 60/80 (75.0%), grade 3 was 28/34 (87.5%) and grade 4 was 14/17 (82.35%). Sample *Kappa* across all grades was then calculated which came out to be 0.8659 and standard error was 0.020. This represented an excellent agreement between the two clinicians that was highly significant from population kappa coefficient ($p = 0.001$, CI = 0.8267–0.9051). Nodularity was maximally (68.8%) seen in the reproductive age group, i.e., 31–50 years of age (Table 4). It was mostly seen in lower socioeconomic class 271 (67.8%) women (Table 5).

## Discussion

Several attempts have been made to comparatively and longitudinally measure breast nodularity at the time of conducting drug trials for mastalgia and breast nodularity. A scale to measure female breast *nodularity* that is generally not abnormal, after thorough testing of its reliability and validity has not been described. Breast nodularity assessment per se, may not be important in the countries where mammographic screening for breast cancer is a routine, however, it is still relevant for majority of the countries as population based mammographic breast screening is unlikely to start in India in the next 2 or 3 decades.

In 2 randomised trials[7,8] of a dopamine agonistic agent – bromocriptine, in painful nodular benign breast disease (BBD) simple scales were used for mastalgia as: absent, mild, moderate or severe. And for nodularity the scale used was as follows:

Grade 0 absent
Grade 1 single
Grade 2 few
Grade 3 many
Grade 4 diffuse

These scales though made a headway towards calibrating and comparing breast nodularity are over simplistic and nondescript. These scales were used in such studies without any prior validation of their tool. Vitamin E and caffeine withdrawal in the treatment of breast nodularity in a randomized control clinical trial were studied. In both these studies a five point ordinal scale was used to objectively assess breast nodularity.[9,10]

**Table 2**
Breast nodularity agreement between two clinicians, hospital-based study ($n = 384$).

| Observer I | Observer II | | | | |
|---|---|---|---|---|---|
| | Grade 0 | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
| Grade 0 | 123 | 4 | 2 | | |
| Grade 1 | | 67 | 16 | 4 | 2 |
| Grade 2 | | 10 | 54 | 5 | 1 |
| Grade 3 | | 1 | 6 | 52 | 5 |
| Grade 4 | | | | 9 | 23 |

The examining physician recorded findings for each quadrant of both breasts on a scale of 0–4, where: 0 = soft fatty tissue only with no nodularity, 1 = slight/fine nodularity, 2 = moderate nodularity, 3 = firm, irregular nodularity or confluent firm dysplasia, 4 = hard nodularity or confluent hard dysplasia. A total of 8 quadrants in both breasts gave a highest possible total score of 32 in each patient. These authors however, have not described the scale in detail neither have they tested the reliability and validity of such a measurement. Giving a scoring system to stratified ordinal data has the setback of providing a euphemistic interval data that in true sense does not qualify for a parametric statistical test. Secondly, it takes away the simplicity and clarity of a 0–4 grading system in clinical practice. Having no schematic/visual cue it is difficult to learn by beginners and require observer participant in the breast clinics to make a reliable and valid assessment of the nodularity.

Haagensen suggested recording breast nodularity with a sketch of nodularity in the so called breast quadrants .[11] The pictorial 5-point ordinal visual analogue scale described in the present study, no attempt is made by the examining physician to categorically commit upon breast nodularity in individual breast quadrants. Instead, a pictorial scheme allows the examining physician to make a holistic assessment of the entire breast nodularity. As such, the nodularity is commonest in the upper outer quadrant of the breast. Thus in our opinion, a simpler and less complicated instrument has evolved which is more user friendly in clinics of busy general practitioners, gynecologists and surgeons.

In a more recent study by Goodson's group[12,13] an effort was made to evaluate breast nodularity and durity (from Latin *duritia* meaning "hardness"). A sample of 371 consecutive women attending breast clinic and not found to have breast cancer and 386 women detected with breast cancers of any stage underwent a breast examination. Overall characteristics of clinical breast examination (CBE) were recorded at the initial consultation. Two separate ordinal scales for nodularity and durity were used.

*The durity scale*

Overall breast "durity" was recorded as the inverse of whether rib edges could be felt through breast tissue in the most dur (firm to hard) part of the breast, usually the upper outer quadrant adjacent to the areolar.

a ribs easily felt through breast tissue less dur
b ribs felt through breast tissue with difficulty

**Table 3**
Breast nodularity agreement between two clinicians, community-based study ($n = 400$).

| Observer I | Observer II | | | | |
|---|---|---|---|---|---|
| | Grade 0 | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
| Grade 0 | 172 | | | | |
| Grade 1 | | 88 | 9 | 2 | 1 |
| Grade 2 | | 7 | 60 | 3 | 2 |
| Grade 3 | | 2 | 9 | 28 | |
| Grade 4 | | | 2 | 1 | 14 |

Author's personal copy



**Table 4**
Overall benign breast nodularity frequency.

| Age | Nodularity grade 2–4 ($n = 384$) | Percent |
|---|---|---|
| *Hospital subjects* | | |
| ≤20 | 27 | 07.3 |
| 21–30 | 155 | 40.4 |
| 31–40 | 130 | 33.9 |
| 41–50 | 56 | 14.6 |
| 51–60 | 13 | 3.4 |
| 61–70 | 3 | 0.8 |
| Age | Nodularity Grade 2–4 ($n = 400$) | Percent |
| *Community subjects* | | |
| ≤20 | 72 | 18.8 |
| 21–30 | 1 | 0.3 |
| 31–40 | 148 | 37.0 |
| 41–50 | 127 | 31.8 |
| 51–60 | 39 | 9.8 |
| 61–70 | 12 | 3.0 |

c ribs cannot be felt through breast tissue
d ribs cannot be felt and tissue cannot be deformed more dur

*The nodularity scale*

Nodularity was recorded in this same area by means of an ordinal scale ranging from the "surface is smooth" to "coarse nodularity".

A no nodules at all
B fine nodules "***rice***"
C prominent nodularity but not coarse "***peas***"
D coarse, prominent nodularity "***beans***"

The above study demonstrated that the scale for the prominence of nodularity is reproducible (test-retest reliability) when the same patients are examined after an interval of 2–24 h. Inter-observer reliability was not performed. These authors used the names of edible items as descriptors. Nodularity scores can probably be understood as ranging from "no nodules at all" through sequential similarities to rice, peas and beans. Durity and nodularity were reported to be having a highly significant inverse relationship. In order to further simplify their data the authors dichotomized a 4-point ordinal scale. This renders the above scale as mere nominal scale having less and more "*dur*"/"*nodular*" properties. Furthermore, nodularity and durity were examined as independent predictor variables for delay in detection of breast cancer. Over all physician related breast cancer detection was delayed in 9.1% subjects. Delay was least common for less *dur* and less nodular breasts (RR 1.0) and most common (13.5%) for less *dur* and more nodular breasts (RR 6.23; 95% CI 3.58–10.22). This study concluded that neither clinical breast nodularity alone nor *durity* correlated with delay in the diagnosis of breast cancer.

**Table 5**
Overall benign breast nodularity frequency – socio-economic distribution.

| Socio-economic status | Nodularity grade 2–4 ($n = 384$) | Percent |
|---|---|---|
| *Hospital subjects* | | |
| Lower | 77 | 20.05 |
| Lower middle | 59 | 15.36 |
| Upper middle | 149 | 38.80 |
| Upper | 99 | 25.78 |
| Socio-economic status | Nodularity grade 2–4 ($n = 400$) | Percent |
| *Community subjects* | | |
| Lower | 271 | 67.8 |
| Lower middle | 80 | 20.0 |
| Upper middle | 34 | 8.5 |
| Upper | 15 | 3.8 |

Thus the main preoccupation of the authors in the above study was to examine whether the textural properties of breasts affect breast cancer detection by examining physicians.[12] Ironically, clinicians have always felt the need but have used *make-shift* designs for measuring breast nodularity in drug trials for BBD.[7–10] A universally acceptable visual analogue scale has not been used for sequential measurement of breast pain in these trials, however. The main objective of the present tool is not to exclude cancer but to create a modality for valid and longitudinal measurement of breast nodularity after cancer has been excluded by routine clinical practices.

Epidemiological studies on BBD reported have not confirmed to this new understanding of disease classification of BBD.[1–5] No study so far has reported the degree of breast nodularity in female population. The present study additionally provides a data for its prevalence in community and hospital settings. A natural history study has shown that such nodularity tends to stay till menopause.[14]

With the majority subjects having significant breast nodularity in 3rd–5th decades of life, the present study included women between 20 and 70 years of age. The overall nodularity perceived from mild to high grades was in 2/3rd of the subjects and only a minority 1/3rd women had overall smooth breasts. The nodularity grades were marginally higher in the hospital as compared to community-based study. There were fewer younger subjects in the community study due to more non-responders in this group. In non-discrete lumpy breasts, it still remains to be explored if nodularity will impose a greater risk for cancer. These patients may form an interesting cohort that may be maintained, rescaled, graded and followed up for development of cancer. One could perhaps carry out studies for hormonal markers and genetic polymorphism in such patients in future. Up scaled nodular subjects can be submitted to rigorous (e.g., MRS) work up for risk factor determination.

To test for a relationship between clinical breast examination and histopathology, Goodson used the above described 4-point scales of clinical durity and nodularity and validated these patients by repeat examination after 4 or more months apart in 199 separate breasts (the scale was the same or within one point on repeat examination in 87% for durity and 90% for nodularity).[15] Durity and nodularity were compared to histopathology of breast tissue at the margins of resected specimens of 60 women undergoing breast conserving treatment for primary breast carcinoma. As expected various degree of clinical nodularity and durity showed no special histopathological patterns. Similarly, during this study it was considered unnecessary to conduct cyto or histo morphological correlations with the grade of nodularity.

Lucknow – Cardiff breast nodularity scale in our opinion is superior. Its efficacy has been demonstrated by the present study. Its effectiveness and user friendliness will be determined once this is put into the public domain. Breast cancer presents either as a mammographic abnormality before it becomes palpable or as a palpable discrete lump. Breast cancer rarely presents as a part of firm breast nodularity. Indeed the problem of breast pain and nodularity is not uncommon and women not uncommonly demand treatment for breast pain and nodularity despite reassurance. There is no single drug that is effective and devoid of side effects. Two decades ago it was considered as good clinical practice to obtain a biopsy from women presenting with firm, tender and nodular breast and allay the anxiety after affixing with a *quasi* morphological featured benign histopathology report.[16] With true and apparent increase in women soliciting opinion for breast related problems, it is important to measure the clinical morbidity of breast nodularity. An accurate morbidity indicator is important to allow inter-physician communication and assess the response to treatment of breast pain and nodularity. This indicator may shift and assume a normative role[17] to become an object of capacity building the general practitioners, gynecologists and surgeons to be more discrete in prescribing subsequent tests.

Author's personal copy



## Conflict of interest statement

None. There are no disclosures to make except that this work was carried out purely as a research project and the author no. 2 (RR) and 5 (VD) worked as research fellows funded from governmental research agency – Indian Council of Medical Research – ICMR, New Delhi without any encumbrances.

## Funding source

The above work was supported by an ad-hoc research scheme funded by the Indian Council of Medical Research – ICMR, New Delhi vide grant no. 5/7/37/02 – RHN.

## Ethical approval

Approved by Institutional Ethical Committee, CSM (King Georges) Medical University (www.kgmcindia.edu) vide letter no. 3441/GA dated 3/2/2003.

## Acknowledgements

We gratefully acknowledge that the above work was supported by an ad-hoc research scheme funded by Indian Council of Medical Research – ICMR, New Delhi vide grant no. 5/7/37/02 – RHN. I thank Prof RE Mansel, Department of Surgery, University of Wales for the insight he has provided in this subject.

## References

1. Nichols S, Waters WE, Wheeler MJ. Management of female breast disease by Southampton general practitioners. *Br J Surg* 1980;**281**:1450–3.
2. Roberts MM, Elton RA, Robinson SE, French K. Consultations for breast disease in general practice and hospital referral patterns. *Br J Surg* 1987;**74**:1020–2.
3. Shukla HS, Kumar S. Benign breast disorders in non-western population part II benign breast disorders in India. *World J Surg* 1989;**13**:746–9.
4. Rangabashyam N, Ganaprakasam D, Krishnaraj DB, Manohar V, Vijayalakshmi SR. Spectrum of benign lesions in Madras. *J Roy Coll Surg Edin* 1983;**28**:369.
5. Hughes LE. Benign breast disorders–introduction. fibrocystic disease? non-disease? or ANDI? *World J Surg* 1989;**13**:667–8.
6. Smoller SW. *Biostatistics and epidemiology: a primer for health professionals*. In: second ed. p. 33–4.
7. Mansel RE, Preece PE, Huges LE. A double blind trial of the prolactin inhibitor bromocriptine in painful benign breast disease. *Br J Surg* 1978; **65**:724–7.
8. Parlatti E, Polinari U, Salvi G. Bromocriptine for the treatment of benign breast disease. A double blind clinical trial versus placebo. *Acta Obstet Gynecol Scand* 1987;**66**:483–8.
9. Ernster VL, Goodson III WH, Hunt TK, Petrakis NL, Sickles EA, Miike R. Vitamin E and benign breast "disease": a double blind, randomized clinical trial. *Surgery* 1985;**97**:490–4.
10. Ernster VL, Mason L, Goodson III WH. Effects of caffeine free diet on benign breast disease: a randomized trial. *Surgery* 1982;**91**:263–7.
11. Haagensen CD. *Diseases of the breast*. Revised reprint. 2nd ed. Philadelphia, Pa: WB Saunders Co; 1971.
12. Goodson WH, Moore DH. Overall clinical breast examination as a factor in delayed diagnosis of breast cancer. *Arch Surg* 2002;**137**:1152–6.
13. Goodson WH, Moore DH. Causes of physician delay in the diagnosis of breast cancer. *Arch Intern Med* 2002;**162**. 1343–1148.
14. Wisbey JR, Kumar S, Mansel RE, Preece PE, Pye JK, Hughes LE. Natural history of breast pain. *Lancet* 1983;**ii**:672–4.
15. Goodson WH, Miller TR, Sickle EA, Upton RA. Lack of correlation of clinical breast examination with high risk histopathology. *Am J Med* 1990;**89**:752–6.
16. Foote FW, Stewart FW. Comparative studies of cancerous versus non-cancerous breasts. *Ann Surg* 1945;**6**:121.
17. Murray CJL, Lopez AD. *The global burden of disease. Pub: the Harvard school of public health*, vol. 1. WHO & World Bank, Harvard University Press; 1996. p. 1–5.