



Research Article

Assessment of knowledge on breast self-examination among female adolescent: a cross-sectional study

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Summary

Background: Breast self-examination is the most important screening method for early detection and diagnosis of Breast cancer. Females assess their breasts regularly to detect any abnormalities to seek instant medical attention.

Objectives: The main objective of the study was to assess the knowledge on breast selfexamination among female adolescents of Nepal.

Method: A cross-sectional study was conducted using self-structured questionnaires among female adolescents of Model Multiple College, Dhanusha. The sample size was 120 participants. Probability proportionate stratified sampling technique was used to collect the data from October 28th to November 12th, 2013. Data were processed through Statistical Package for Social Sciences version 16 and analyzed using descriptive statistics.

Results: Out of 120 participants 67.5% participants had knowledge about breast cancer and 40% had knowledge of breast self-examination (BSE). Most of them (94.2%) had a poor knowledge of BSE followed by 5.8% of participants with a moderate level of knowledge of BSE. The mean knowledge score was 18.7 ± 3.5. The majority (66.7%) of participants were from science faculties. More than half (51.7%) of participants stated source of information on BSE was health personnel. Only 25% of the respondent had a family history of breast cancer.

Conclusion: The study revealed that most (94.2%) of the participants had poor knowledge of breast self-examination. There is further need for awareness and health education on breast self-examination.

More Information

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Keywords: Adolescent female; Breast cancer; Breast self-examination; Cancer screening; Knowledge





Introduction

Globally, the female death rate due to breast cancer is high as it accounts for the fifth rank among cancer mortality and second rank among cancer disorders [1-4]. The incidence of breast cancer reached 2.1 million people worldwide in the year 2018 [1]. Though cervical cancer is still occupying the first place, breast cancer is the next common malignancy among Nepalese women [5,6]. Most of the tumors of the mammary gland are self-discovered [11] and more than 90% of them can be cured if detected early [7-9]. The five years survival rate is high i.e. more than 85% among early-stage detection of breast cancer than the late stage [10]. Inadequate treatment facilities and lack of knowledge on early detection of malignancy are key to low survival rates in Asian countries like Nepal.

Recommended screening approaches of breast cancer include breast self-examination (BSE), clinical breast examination (CBE), and mammography [11]. The BSE is very useful in low-income countries, where routine health checkup is uncommon and screening services like a mammogram is expensive and scary. By the time 85% of patients visit specialized care the tumor is more than 5 cm, while BSE can detect the tumor at the size of 1cm, so information, education, and communication (IEC) play a vital role in the recognition of abnormal breast condition [13]. BSE focuses on the importance



of self-awareness that aids in early detection as BSE can detect tumors even the size of 1 cm [5,13].

The death rate from breast cancer is high in developing countries in comparison to other developed countries [14]. Most of the cases in developing countries are diagnosed at the advanced stage resulting poor survival rate [15]. In adolescent age i.e. 15-20 years almost all the reproductive organs are developed as an adult so every female adolescent should have the knowledge about breast self-examination [14]. Health education and screening programs on breast selfexamination are the essential elements to detect cancer in the early stage and reduce the morbidity and mortality rate in Nepal. A breast self-examination creates awareness as well it helps adolescents to understand the normal look and feel their breast by themselves. The key importance of breast selfexamination is that it improves drastically the outcomes of treatment modalities of breast cancer. It is one of the cheapest non-invasive procedures and can be done with the least domestic tools like a towel, mirror, and pillows. The breast self-examination is the best way to increase breast health awareness and allow for timely detection of anomalies [16].

The study aims to identify the knowledge level of Nepalese adolescent girls about breast self-examination. The results of the present study are salient to notify the future attempt on reduction of morbidity and mortality regarding breast cancer.

Methods and materials

The study employed with quantitative approach, a cross-sectional descriptive design among female adolescents of Model Multiple College of Dhanusha District of Nepal, from October 28th to November 12th, 2013. A probability proportionate stratified sampling technique was used to select the sample meeting criteria. People who were willing to participate and available at the time of data collection were included in the study. Out of 597, 20% of students from each stratum were selected using a simple random technique. After a random selection of students, 17 students from class 11 and 23 from class 12 in commerce faculty and 47 from class 11 and 33 from class 12 were selected from science faculty. Altogether 120 students were selected for the study.

A self-structured questionnaire was developed in English. The questionnaire was divided into two parts i.e. first part questions were related to bio-demographic data and the second part questions were related to knowledge on breast self-examination. The total questions were 18 and the maximum score was 32 for knowledge. The correct answer was assigned as 1 point, there was no negative marking for a wrong answer. To interpret the level of knowledge, the score was distributed as a) > 75%: adequate knowledge b) 50% - 75%: moderate knowledge c) < 50%: Poor knowledge. The validity of the instrument was maintained by consultation with the supervisor, subject expertise, and statistician and by reviewing maximum literature. The pretesting of the

instrument was done on a 10% sample size i.e. 12 subjects and necessary correction and modification was done on the basis of the feedback.

The study protocol and procedure were approved by the Institutional review board of Pokhara University before the formal survey. Formal permission and approval sheet to conduct the study was taken from the college of the participants. The objectives of the study were clearly expressed to the participants as well as verbal informal consent of participants was taken before data collection. Statistical Package for Social Sciences (SPSS) version 16 was used for data processing. Analysis and interpretation were done by descriptive statistics like frequency distribution and percentage distribution.

Results

Demographic characteristics

Out of 120 participants, the mean age of participants was 16.7 ± 0.922 years. In response to demographic characteristics, more than half of the participants were Chhetri in ethnicity. Participants selected from commerce faculty in class 11 were 17 (14.2%), class 12 were 23 (19.2%) and science faculty 47 (39.2%) were in class 11 and 33 (27.5%) were in class 12. One-quarte of subjects i.e. 30 (25%) had a family history of breast cancer among them 37% of participants had a maternal family history and 13% had a paternal family history of breast cancer. Half of the participants stated health personnel, 18.3% stated mass media and only 15.8% stated relatives as a source of information regarding cancer and breast self-examination (Table 1).

Knowledge of breast cancer

67.5% of participants knew that breast cancer is an abnormal growth that begins in the tissue of the breast. The majority of participants i.e. 87 (73.1%) stated clinical breast examination is the only identification method of breast cancer whereas 48 (40.30%) had heard about mammography. Regarding breast self-examination, nearly half of the participants i.e. 57 (47.9%) reported as early identification method of breast cancer. Considering abnormal breasts 43 (35.8%) of participants had the correct answer and 63 (52.5%) stated different sizes and shapes of breasts, 58 (48.3%) as abnormal discharge from the nipple, and 63 (52.5%) stated enlargement of lymph nodes to breast and related area. Higher the participants i.e. 80 (66.7%) answered that early identification of breast cancer is important to prevent complications and mortality rate. Half of the participants 70 (58.3%) believed early identification can cure cancer and 40 (33.3%) believed early identification is needed to initiate the timely treatment. Women's quality of life can be improved by early detection of breast abnormality was stated by 32 (11.7%) of participants. When the participants asked what will be their reaction if they get abnormalities in their breast,



	Socio-demographic characteristics of respondents.

Table 1: Socio-demographic characteristic		
Characteristics	Frequency (<i>n</i> = 120)	Percentage %
Age		
15 years	11	09.10
16 years	38	31.70
17 years	50	41.70
> 18 years	21	17.50
Mean ± SD	16.7 ± 0.922	16.7 ± 0.922
Ethnicity		
Brahmin	09	07.50
Chhetri	67	55.80
Dalit	03	02.50
Others	41	34.20
Educational faculties		
Science	80	66.70
Commerce	40	33.30
Class		
11	64	53.30
12	56	46.70
History of breast cancer in the family $(n = 120)$		
No	90	75.00
Yes	30	25.00
Relation with a family member with breast cancer (n = 30)		
The maternal side of the family	11	36.66
Paternal side of the family	04	13.33
Siblings	02	06.66
Others	13	43.33
Source of information		
Peer group	10	08.30
Relatives	19	15.80
Health personal	62	51.70
Mass media	22	18.30
Others	07	05.80

'Others relation with family members with breast cancer' includes sister-in-law's, cousins, close friends, and family friends.

the majority of participants i.e. 91 (75.8%) reaction was to consult with a family member, and 28 (23. were was ready to consult a doctor or other health care personnel. The aggregate responses were summarized in Table 2.

Knowledge on breast self-examination

The majority of the participants that is 113 (94.2%) had poor knowledge and the rest of the 7 (5.8%) participants had a moderate knowledge score. The mean knowledge score was 18.7 ± 3.5 (Table 5). Among total participants, 48 (40%) participants knew the correct meaning of breast selfexamination (BSE) while 59 (49.2%) of participants had an idea about the main purpose of BSE. Regarding the time to start BSE, 74 (61.7%) participants responded correctly which is after menarche. Only 39 (32.5%) participants knew the correct period of BSE, but the majority of the participants 88 (73.3%) knew that BSE should be examined once a month. With regards to the technique of BSE (Table 3), most of the participants knew about articles required for breast selfexamination such as mirror 67 (55.8%), towel/pillow 29 (24.2%), and own hand 103 (85.8%). The participants who started correct shape and size of both breasts was 45%, color and texture of breast and accessory organs was 23%, any

Table 2: Meaning, Abnormality, and Identification Method of Breast Cancer.

Decemention	Response	
Description	Frequency (<i>n</i> = 120)	Percentage
Meaning of breast cancer		
A cancerous growth	81	67.5
Ulcer in breast	28	23.3
Pain on breast	11	9.2
Identification method*		
Breast self-examination	57	47.90
Clinical breast examination	87	73.10
Mammography	48	40.30
Laboratory investigations	37	31.10
Abnormal breast*		
Different size and shape	63	52.50
Abnormal discharges	58	48.30
Enlargement of the lymph nodes	63	52.50
Any of the above conditions with or without pain	43	35.80
Importance of early identification of Breast Cancer*		
To cure	70	58.30
To prevent	80	66.70
To initiate timely treatment	40	33.30
To improve quality of life	32	11.70
The reaction of respondents towards breast cancer		
Go to doctor	28	23.30
Can't tell anyone	1	00.80
Consult with a family member	91	75.80
Multiple response*.		

Table 3: Knowledge regarding breast self-examination.

Description	Response	
	Frequency (<i>n</i> = 120)	Percentage %
Meaning		
Screening method	48	40.00
Treatment of breast cancer	23	19.20
Surgical procedure	37	30.80
Advance therapy	12	10.00
Purpose *		
To obtain structural information	59	49.20
To identify early changes in breast	55	45.80
To identify the early stage of breast cancer	74	61.70
To control mortality and morbidity	57	47.50
To be cost-effective	03	02.50
Time to start breast self-examination		
After menarche	74	•
After marriage	06	05.00
After being pregnant	29	24.20
After menopause	11	09.20
Period of performing breast self- examination		
7-10 days of menstruation cycle	39	32.50
During menstruation	18	15.00
Before menstruation	07	05.80
Any time you want	56	46.70
Frequency of performing breast self- examination		
Once a month	88	73.30
Once a year	15	12.50
Every 3 years	2	01.70
Multiple response*		



Table 4: Technique of breast self-examination. Responses Description Frequency *n* = 120 Percentage % Observable part* 45.00 Shape and size of both breasts. Color and texture of breast and accessory 28 23.30 organs Any abnormal discharge from the breast, 93 77 50 dimplina 59 49.20 Painful or painless lumps Process of palpation * 40.00 Use finger pads of three middle fingers 48 31 70 Use left hand to palpate the right-sided breast 38 Palpate in a circular motion in a clockwise 74 61.70 direction from inner to outside Palpate lightly, medium pressure, deeper 56.70 68 pressure Direction of palpation' Circular motion from the outer edge 80 66.70 Vertical strip or lines the from forearm 29.20 24.20 Horizontal stripes or lines 29 Clockwise direction 73 60.80 Articles required for breast selfexamination* 67 55.80 24 20 Towel/pillow 29 Your own hand 103 85.80 Multiple Response*

Table 5: Respondent's knowledge score.				
Knowledge level Frequency	(n = 120)	Percentage %		
Poor knowledge (< 60%)	113	94.20		
Moderate knowledge (< 79%)	007	05.80		
Mean ± SD	18.7 ± 3.5			

abnormal discharge from breast and dimpling on the breast was 77% and painful or painless lumps was 49%. The majority of the participants 74 (61.7%) participants responded that the breast should be palpated in a circular motion in a clockwise direction from inner to outside and 68 (56.7%) of participants stated that the breast should be palpated lightly, medium pressure, and followed by deeper pressure. About 40% of participants knew about using finger pads of three middle fingers to palpate the breast, 38 (31.7%) knew that the left hand should be used to palpate the right breast. Concerning direction of palpation, 80 (66.7%) participants responded to perform palpation in a circular motion from the outer edge, 35 (29.2%) participants responded to perform palpation as vertical strip or lines from the forearm, 29 (24.2%) participants responded as horizontal strip or lines and 73 (60.8%) participants responded to palpate breast in a clockwise direction (Table 4). Cumulatively, we found only 5% of participants had an average level of knowledge, and the majority of participants had a deficient level of knowledge regarding breast self-examination.

Discussion

The knowledge towards a specific illness can be influenced by the seriousness of the illness, the spread of the disease, fatality rate, and methods for sharing and distribution of knowledge. The current study aimed to assess the level of knowledge on breast self-examination among female adolescents of Nepal.

The findings of the background characteristics show that 41.7% of participants were of 17 years of age and the mean age of 16.7 years with a standard deviation of 0.922. More than half (55.8%) of the participants were of Chhetri ethnicity. The majority (66.7%) of the participants were students of science faculties and 53.3% of the students were from class 11. More than half (51.7%) of the source of information about breast self-examination were health personnel. A similar study done in Ahmadabad, India supports that Health professionals (34.4%) were the main source of information on the knowledge about BSE [17].

In our study, 25% of the participants had a family history of breast cancer, among them only 9.2% had a positive for maternal family history. Similar findings were seen in a study done in Malaysia where about 20% of the participants had a family history of breast cancer [18]. In this study 67.5% of participants had knowledge about breast cancer and 40% had knowledge of breast self-examination. Another supporting data was similar to a study conducted in North West Ethiopia, subjects had a family history of breast cancer and were directly associated with breast self-examination practices [16]. This finding is in contrast with a related study done at Abuja, Nigeria where 56% of participants had knowledge of breast cancer, while 75.6 had the knowledge of breast self-examination [19]. The reason for contradictory result could be due to difference in the knowledge level of respondents of both studies as this study is done among the participants of the higher secondary school students and the study of Nigeria is done on the participants who were secondary level students, and also because the main source of information in this study is health personnel and in Abuja, it is the mass media.

The result of the study showed that 27.8% of participants stated enlargement of the lymph nodes is abnormal breast as the breast cancer can spread to lymph nodes. This study also revealed that according to 29.8% of the participants the purpose of breast self-examination is to identify the early stage of breast cancer. This finding is also supported by the study done at Oyo State, Nigeria resulted as only 22% understood breast self-examination helps in early detection [20]. In this study 54.7% of participants answered that breast cancer is curable and preventable if diagnosed in the early stage of life. Regular breast self-examination is important to improve the quality of life was believed by 11.7% of the participants. Nearly half of the participants strongly supported that women should perform monthly breast self-examination to detect early changes in the breast that help to reduce mortality and morbidity of females.

The finding of the study showed that the majority of participants (61.7%) answered that the breast self-examination should be started after menarche, 32.5% stated



that 7 to 10 days of the menstrual cycle is the timing for the breast self-examination and 73.3% answered that the frequency of breast self-examination is once a month. Our study contradicts a similar study done at Oyo State, Nigeria as the study showed that only 16% knew the age of starting BSE, only 20% stated the correct timing and 12% knew the accurate frequency of breast self-examination [20]. The variance result of the study may be due to the difference in the source of information or educational level of the participants.

The majority of participants (39.7%) responded that any abnormal discharge, dimpling, and scaling of the breast should be observed during breast self-examination. This finding is supported by the study done at Bhimad, Nepal as 69.23% stated that any abnormal discharge, scaling, or dimpling should be observed [17]. In our study majority of participants (66.7%) answered that palpation of the breast in a circular motion from the outer edge is the best method. The finding is inconsistent with a similar study done at Bhimad, Nepal as 32.5% of respondents answered circular motion from the outer edge is a correct method of breast palpation [21]. Our finding revealed that nearly half of the respondents (43.5%) had a clear idea regarding the article's requirement for breast self-examination. The majority of the participants (75.8%) responded that they will consult with a family doctor or nurse if they get any changes in their breasts.

The study revealed that most of the participants (94.2%) had poor knowledge, and 5.8% of the respondent had moderate knowledge on breast self-examination. The mean knowledge score on breast self-examination was 18.7 ± 3.5 . The finding of the study was inconsistent with a similar study conducted at Bhimad, Nepal as the majority of participants (65.38%) had poor knowledge level, 32.69% had average and minority (1.93%) had good knowledge on breast selfexamination [22]. Likewise another study was done in Abuja, Nigeria also supported the findings as 56.8% of participants had poor knowledge of breast cancer, while 75.6% had poor knowledge of BSE [19]. Next similar study conducted again in Akure, Nigeria among adolescent girls supported our finding as the study revealed that there was a significant difference among the student's pre and post-knowledge scores and had poor attitudes and practices regarding breast self-examination [22].

Finally, our study findings may be utilitarian to healthcare professionals, policymakers, health interventions, awareness-raising, and health education programs. Our finding suggests that health education and information should be provided to the high-risk population such as to adolescent girls, women, and women at menopause period. The potential limitation of the study includes its small sample size that might not be enough to represent the total population of our country.

Conclusion

Most of the participants had poor knowledge of breast

self-examination. The majority of participants were unaware and confused regarding how to perform BSE. To fulfill their need breast self-examination should be included in the course curriculum of higher secondary schools as well community-level general awareness programs should be initiated.

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References

- Freddie B, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018; 68: 394-424.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/30207593/
- Althuis MD, Dozier JM, Anderson WF, Devesa SS, Brinton LA. Global trends in breast cancer incidence and mortality 1973-1997. Int J Epidemiol. 2005; 34: 405-412.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/15737977/
- Shibuya K, Mathers CD, Boschi-Pinto C, Lopez AD, Murray CJL. Global and regional estimates of cancer mortality and incidence by site: II. Results for the global burden of disease 2000. BMC Cancer. 2002; 37.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/12502432/
- Hortobagyi GN, Salazar JDL, Pritchard K, Amadori D, Haidinger R, et al. The global breast cancer burden: variations in epidemiology and survival. Clin Breast Cancer. 2005; 6: 391-401.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/16381622/
- Singh YP, Sayami P. Management of breast cancer in Nepal. J Nepal Med Assoc. 2009; 48: 252-257.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/20795469/
- Pun CB, Pradhananga KK, Siwakoti B, Subedi K, Moore MA. Malignant Neoplasm Burden in Nepal – Data from the Seven Major Cancer Service Hospitals for 2012. Asian Pacific J Cancer Prevent. 2014; 16: 8659-8663.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/26745133/
- Pham T, Bui L, Kim G, Hoang D, Tran T, et al. Cancers in Vietnamburden and control efforts: a narrative scoping review. Cancer Control. 2019; 26. PubMed: https://pubmed.ncbi.nlm.nih.gov/31319695/
- Ersin F, Gozukara F, Polat P, Ercetin G, Bozkurt ME. Determining the health beliefs and breast cancer fear levels of women regarding mammography. Turk J Med Sci. 2014; 45: 775-781.
 PubMed: https://pubmed.ncbi.nlm.nih.gov/26422845/
- Beacham AO, Carpenter JS, Andrykowski MA. Impact of benign breast biopsy upon breast self-examination. Prevent Med. 2004; 38: 723-731.
 PubMed: https://pubmed.ncbi.nlm.nih.gov/15193892/
- Smith EM, Francis Am, Polissar L. The effect of breast self exam practices and physician examinations on extent of disease at diagnosis. Prev Med. 1980; 9: 409-417.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/7208448/
- Hallal JC. The relationship of health beliefs, health locus of control, and self concept to the practice of breast self examination in adult women. Nur Res. 1982: 31: 137-142.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/6918918/
- Humphrey LL, Helfand M, Chan BKS, Woolf SH. Breast cancer screening: a summary of the evidence for the U.S. preventive services task force. Ann Intern Med. 2002; 137: 347-360.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/12204020/



- Mazzini CB. Knowledge and practice of the breast self exam on students from a public university in Lima. Arch Cancer Res. 2016; 4: 3.
 PubMed: https://pubmed.ncbi.nlm.nih.gov/34007246/
- 14. Ghimire BR. Nepali women in the worst condition of breast cancer. 2010. www.ekantipur.com/kathmandu
- American cancer Society, Breast cancer risk and life style. 2009. http://www.cancer.org
- Dange AH, Ayele AD, Assefa EM. Assessment of breast selfexamination practice and associated factors among female workers in Debre Tabor Town public health facilities, North West Ethiopia, 2018: Cross-sectional study. PLOS ONE. 2019.
 PubMed: https://pubmed.ncbi.nlm.nih.gov/31437209/
- Bala DV, Gemeti H. An Educational Intervention Study of Breast Self-Examination (BSE) in 250 women beneficiaries of urban health centers of west Zone of Ahmedabad. Health line. 2011; 2: 46-49.
- Naggar Al RA, Bobryshev YV, Al-Jashamy K. Practice of breast selfexaminationamongwomeninMalaysia.CommunityMedicalDepartment. International Medical School, Management and Science University

- (MSU), Malasia. Asian Pac J Cancer Prev. 2012; 13: 3829-3833. PubMed: https://pubmed.ncbi.nlm.nih.gov/23098479/
- Isara AR, CI.OiedokunKnowledge of breast cancer and practice of breast self examination amongfemale senior secondary school students in Abuja, Nigeria.Department of Community Health, College of Medical Sciences, University of Benin, Benin City, Nigeria. J Prev Med Hyg. 2011; 52: 186-190.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/22442923/
- Faronbi JO, Abolade J. Breast self examination practices among female secondary school teachers in a rural community in Oyo State, Nigeria. Open J Nur. 2012; 2: 111-115.
- Sherestha K. Knowledge of Breast Self Examination on Reproductive Age Group Females. Tribhuvan University. 2012; 32.
- 22. Ibitoye OF, Thupayegale-Tshwenegae G. The impact of Education on knowledge attitude and practice of Breast self-examination among adolescents girls at the Fiwasaye Girls Grammar School Akure, Nigeria. J Cancer Educ. 2021; 36; 39-46.
 - PubMed: https://pubmed.ncbi.nlm.nih.gov/31377988/