INTRODUCTION

Breast diseases are generally found to be common in females (99.3%) compared to man (0.7%) [1]. In developing countries like Nepal, females are unaware of breast pathologies because of social taboo and are hesitant to reveal, hence it is detected usually in advanced stages. Some of the common pathologies of breast are various benign breast lesions e.g fibroadenomas, cyst, abscess, galactoceude, duct actasia, enlarged lymph nodes and different malignancies.

Among them breast malignancies is most common cause of cancer death in women and overall fifth common cause of cancer deaths in the world[2]. It is the second most common malignancy among women in Nepal. It is a heterogeneous disease with no single cause. Delay in the detection causes malignancy to progress in advanced stage which comprises of inoperable masses, metastasis (bone, brain, lung) and is a significant cause of morbidity and mortality worldwide[3,4]. Breast lesions at ultrasound have a number of characteristics which allows classification as malignant and benign. The differentiation between malignant and benign lesions, screening of younger age group women, identifying lesions in a fatty breast, identifying recurrence lesion, monitoring tumor response to therapy, etc. are some of the vital clinical issues to be addressed. Still, large numbers of breast lesions cases remain unreported due to lack of awareness, education and lack of facilities in people residing in rural areas. Early diagnosis and treatment are important to decrease the morbidity and mortality. Benign breast diseases need early detection and management because of its high prevalence and its cancerous potential (3-5%). Thus, early detection, diagnosis, and screening of breast lesions have a significant impact on patient management like treatment outcome and survival.

Imaging is required for the diagnosis, appropriate treatment decision and proper follow up. Treatment modality depends upon the extent of the disease and tumor biology. However, there is a strong need for standard guidelines for the proper management of breast cancer in Nepal so that surgery, chemotherapy, hormone therapy and radiotherapy are standardized in the country. Palliative care has been initiated to provide to some patients with metastatic breast cancer recently. The diagnosis of breast lesion is generally based on physical examination, X-ray mammography, USG and FNAC. X-Ray mammography is the first line of technique used for primary detection and screening of breast cancer with sensitivity between 69% and 90% but with variable specificity in many countries [5]. However, it is reported that this technique has false negative rate (misses lesion) around 10% to 25% in detecting breast cancers in dense breast [6]. In addition, mammogram limitation includes exposure to ionizing radiation. Fine needle aspiration cytology (FNAC) is considered the gold standard method, cost effective and useful for mass lesions [7,8,9]. It has a sensitivity and specificity of > 90% and > 65%, respectively. The positive predictive value was reported to be > 99.5%10 depending on the skill of person performing the aspiration and expertise of the cytopathologist [11]. Sometimes the problematic cells are missed, resulting in a false negative result. Further, FNAC cannot reliably predict invasion of tumor [12], additionally there is difficulty in assessing deep seated lump within the breast and it is an invasive procedure as well. Thus, breast Ultrasonography (USG) has evolved as an indispensable problem solving tool in patients with dense breasts, post-radiation breasts, and women less than 35 years of age, pregnant and lactating patients [13]. It is an important technique adjacent to mammography and clinical examination in assessing impalpable breast abnormalities and mammographically occult lesions [14,15]. It differentiates cystic from solid lesions; benign and malignant breast neoplasm in women when mammography is less sensitive due to dense breasts. The sensitivity of detecting cancer is reported as 65% and 92%[16]. Keeping these vital clinical issues in apprehension we decided to conduct this study in the Nepalese group of women.

Objectives

1. To evaluate the sonographic features of different breast lumps and analyze the feasibility of ultrasonic diagnosis.
2. To assess the reliability of USG features of malignancy and
developed by triple assessment that comprises of clinical history and
physical examination, radiology (ultrasonography), and pathology (fine
needle aspiration cytology) evaluation. A total of 47 patients were
recruited for the study. Of the 47, statistical analysis was carried out on
44 patients. Three of them were excluded due to unavailability of the
cytology report because of the inadequate sample. Out of 44, thirty
four were with benign breast pathology (mean ± SD age, 31.8 ± 9.7
years, range; 16 - 61 years); nine cases (mean ± SD age, 45.3 ± 10.2
years, range; 25 - 75 years) were diagnosed as malignant and one (38
year) was diagnosed as intermediate in USG the clinical details of these
patients are given in Table 1. Clinical evaluation of lumps was
performed in all the cases which include history regarding appearance of
the lumps, pain, discharge, duration of symptoms, presence of other
conditions, etc. The entire patients underwent USG examination with
using a high resolution frequency (7.5MHz) linear array transducer
(Aloka 1300 machine). USG features were documented prior to
subjecting the patient for FNAC. After USG examination and diagnosis,
FNAC was performed under USG guidance by the radiologist and
pathologist from department of pathology.

Table 1: categorization of breast lump based on USG diagnosis Ultrasonography Diagnosis.

<table>
<thead>
<tr>
<th>Age gr. Pt (in years)</th>
<th>Fibroaedenoma</th>
<th>Cyst</th>
<th>Intermediate</th>
<th>Malignancy</th>
<th>infective</th>
<th>Total no cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-20</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>21-30</td>
<td>16</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>31-40</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>41-50</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>51- above</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>2</td>
<td>1</td>
<td>9</td>
<td>3</td>
<td>44</td>
</tr>
</tbody>
</table>

Method for USG guided FNAC

After the lump was located under guidance of USG, it was fixed in
position with one hand. Under aseptic precaution a 20 ml syringe fitted
with 18 to 22 gauge needle was used to puncture the lesions. Vacuum
was applied to the syringe by pulling the plunger and the needle was
moved back and forth a few times within the lesion under USG.

Table 2: The 2 by 2 table showing sensitivity, specificity, Negative
predictive value, Positive predictive value and accuracy in n=43
cases.

<table>
<thead>
<tr>
<th>Cases</th>
<th>Benign</th>
<th>Malignant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive USG Diagnosis</td>
<td>8 (TP)</td>
<td>1 (FP)</td>
<td>9</td>
</tr>
<tr>
<td>Negative USG Diagnosis</td>
<td>1 (FN)</td>
<td>33 (TN)</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>34</td>
<td>43</td>
</tr>
</tbody>
</table>

Statistics

Finally, both the diagnosis was compared. All the statistical analysis was
carried out in SPSS 16.0. Patient’s age (in each group) was calculated
using parametric one way ANOVA test. The predictive values (sensitivity, specificity, positive predictive value, negative predictive
value and accuracy) of USG between benign and malignant groups of
breast lesion were calculated using 2 by 2 table. A P<0.05 was
considered to be statistically significant.

Results

The results presented here are based on the observation of each
characteristic feature of breast lesions detected in USG and finally
correlating them with FNAC diagnosis. All the cases of breast lump
were diagnosed with USG were subjected to fine needle aspiration for
cytology (FNAC). Finally, A total of 44 the findings of USG were
compared with the findings of FNAC.

The mean age of the patient was 32.84 ± 13.71 (16-75) Years. Based on
age all patients were divided into 5 groups, age group 1 represent 16-20
yrs which is 14% of total patients; group 2 represents 21-30 yrs, 45%
patients; group 3 represents 31-40 yrs, 16% patients; group 4 represents
41-50 yrs, 14% patients and the latest group represents 51 yrs and above,
11% patients (see Figure 1). Patient’s age in each group was found to be
statistically significant (P<0.001) using Parametric one way ANOVA
test.
While, in cases of sonological homogenous echotexture, USG had diagnosed 27 cases as benign while FNAC had diagnosed 28 cases as benign. Similarly, 1 case had been diagnosed as malignant in USG but no case was found to be malignant in FNAC [Figure 2 (B)]. In total 28 cases with homogenous echotexture, 27 cases (96.42%) of USG diagnosis matched exactly with the FNAC diagnosis.

The Figure 2 (C) shows among 30 cases with sonologically well-defined margins, USG diagnosis was 29 benign lesions and 1 malignant lesion while FNAC diagnosed all the 30 cases to be benign. One case diagnosed as malignant in USG and no case was found to be malignant in FNAC. In total 30 cases with well-defined margin, 29 cases (96.67%) of USG diagnosis matched exactly with the FNAC diagnosis. One case turned out to be benign in FNAC which was diagnosed as malignant in USG.

As is evident in Figure 2 (D) among 14 cases with sonologically ill-defined margins, USG diagnosis was 6 benign lesions and 7 malignant lesions whereas; FNAC diagnosed 6 cases as benign lesions and 8 malignant lesions. One case was diagnosed as indeterminate in USG. In total 14 cases with ill-defined margin, all the 6 cases of USG diagnosis matched exactly with the FNAC diagnosis for benign lesions while 1 case was under diagnosed in USG compared to FNAC. One case turned out to be benign in FNAC which was diagnosed as indeterminate in USG.

Comparison of USG and FNAC diagnosis of the lesions based on sonologically detected shapes

Among 37 cases with sonologically oval, round and ellipsoid shape, USG diagnosis was 33 benign lesions and 3 malignant lesions while FNAC diagnosed as 36 benign and 1 malignant lesions. One case was diagnosed as indeterminate in USG as shown in Figure 3 (A). In total 37 cases with round, oval and ellipsoid shape, 33 cases (91.67%) of USG diagnosis matched exactly with the FNAC diagnosis for benign lesions while 3 cases diagnosed as malignant in USG, only one case was diagnosed as malignant in FNAC diagnosis, i.e., 33.33% matched.

Figure 3 shows among 7 cases with sonologically pleomorphic shape, USG diagnosis was 1 benign lesion and 6 malignant lesions while FNAC diagnosed as all the 7 cases to be malignant. Hence, 6 cases (85.71%) matched with FNAC diagnosis of malignancy.

Comparison of USG and FNAC diagnosis based on sonologically detected calcified and non-calcified lesions

Among 5 cases with sonologically calcified foci, USG diagnosis was 1 infective which is considered as benign for shake of convenience which matched exactly that of FNAC diagnosis and 4 were diagnosed as malignant in USG which also matched with the FNAC diagnosis [see Figure 4 (A)].

The Figure 4 (B) depicts that among 39 cases with sonologically noncalcified lesion, USG diagnosis were 33 benign and 5 malignant. One case was diagnosed as indeterminate in USG. However, FNAC showed 35 cases to be benign and 4 cases to be malignant. So, 94.29%
benign USG diagnosis matched with FNAC; 80% of malignant USG diagnosis matched with FNAC.

Comparison of USG and FNAC diagnosis based on halo sign present, posterior shadowing and posterior enhancement lesions present or absent

The Figure 5 (a) shows, among 5 cases with halo sign noted on USG, no cases were diagnosed as benign in USG as well as FNAC while 5 cases were diagnosed as malignant in USG matched exactly with the FNAC diagnosis. Hence, 100% diagnosis matched in benign as well as malignant lesions.

Among 7 cases with posterior shadowing noted on USG, 1 case was diagnosed as benign in USG and no case was diagnosed as benign in FNAC while 6 cases were diagnosed as malignant in USG and 7 cases were diagnosed as malignant in FNAC as evident in Figure 5 (B). 85.71% of malignant diagnosis in USG matched with FNAC diagnosis.

The Figure 5 (C) reflects that among 2 cases with posterior enhancement noted on USG, both cases were diagnosed as benign in USG as well as in FNAC. No case was found malignant in USG as well as in FNAC. Hence, 100% of diagnosis in USG matched with FNAC diagnosis.

Among 35 cases with posterior shadowing absent noted on USG, 31 cases were diagnosed as benign and 3 as malignant in USG whereas FNAC showed 34 cases as benign and 1 as malignant. One was diagnosed indeterminate in USG [see Figure 5 (D)]. Hence, 91.17% diagnosis of benign cases matched with that of FNAC, and 33% diagnosis of malignant cases in USG matched with that of FNAC.

Comparison of USG and FNAC diagnosis based on AP and transverse dimensions detected lesions on USG

All the benign lesions diagnosed by USG, mean AP diameter (3.16 cm) is less than mean transverse diameter (3.97 cm) while in malignant lesion mean AP diameter (4.01 cm) is more than mean transverse diameter (3.87 cm)

Comparison of USG and FNAC diagnosis based on lymphadenopathy detected on USG

In all cases of lymph node enlargement, the USG diagnosis was malignant which matched exactly with FNAC diagnosis.

The sensitivity, specificity, negative predictive value, positive predictive value and accuracy of USG in (n=43) cases was calculated using 2 x 2 table. The result shows sensitivity of 88.89% with of specificity: 97.06%. The negative predictive value was 97.06% while, positive predictive value was 88.89% and the accuracy was found to be 97.67% (see Table 2).

DISCUSSIONS

The manifestation of any lump in the breast is a highly significant and warrants a comprehensive investigation. Ultrasound has potential of visualizing and detecting differences in the appearance of different breast lesions. It is highly accurate in the benign/ malignant differentiation of breast masses [14,17] and is useful in predicting the invasive extent of breast cancers in many cases [18]. The present study was conducted to study the precision of ultrasonography in the diagnosis of palpable breast lumps. The result showed US features that most reliably characterize lesion as benign were a round or oval shape were (91.67%); with well circumscribed margins (96.67%); absent of halo sign (100%), posterior enhancement (100%) in cases of cyst; posterior shadowing and lymph node enlargement absent (91.17%). Also a mean anteroposterior
USG out of which 4 (80%) turned to malignant in FNAC; present of halo sign (100%); posterior shadowing noted (85.71%); lymphadenopathy (100%). Further, a mean anteroposterior diameter 4.01 cm is more than mean transverse diameter.

In a similar study by Rabhar et al. [19] to evaluate the role of USG and FNAC in differentiation of breast lesion, reported the reliable parameters to characterize lesion as benign were round or oval shape (94%) which was similar to our results; well circumscribed margins of 91% in their study also agree with our results. While, the posterior enhancement in their study was found in 78% of the cases whereas we observed in one cystic lesion. While the features that characterize lesion as malignant reported in their literature was 61% irregular shape which was found to be higher (85.71%) in our study. Further, they reported ill defined margins in 47% of the total cases only. This finding doesn’t comply with our results which may be due to various reasons as USG being operator dependent. They have not commented on the other parameters like absent or calcified nodule, presence or absence of halo sign, lymphadenopathy which are considered as important parameters during differentiation of the breast lesions.

In another similar study by Pande et al. [20] observed round or oval shape in 94%; well circumscribed margins in 90% of the benign cases which was comparable to our findings. While the features like irregular shape and ill defined margins were 100% each, respectively in malignant cases also similar to our results. 100% result reported in cases of irregular margin was same as observed in our study.

In 2005, Watermann et al. [21] published data on the ultrasound features of breast cancer. They found that an irregular shape, indistinct margins and posterior acoustic shadowing were described significantly more often in malignant than in other tumor types (88% versus 67%, *p* < 0.001; 95% versus 76%, *p* = 0.001; 84% versus 58%, *p* = 0.001, respectively). These findings highly comply with our results as we found alike observations in our study as well.

In sonological homogenous echotexture of 29 cases, 96.55% of USG diagnosis matched exactly with the FNAC diagnosis. One case turned out to be benign in FNAC which was diagnosed as malignant in USG. Same result was reported by Rabhar et al. [19] while in heterogeneous echo texture, USG has diagnosed 6 cases as benign while FNAC has diagnosed 7 cases. Similarly, 8 cases have been diagnosed as malignant in USG and these 8 cases were found to be malignant in FNAC as well. One case was diagnosed as indeterminate in USG. In total 15 cases with heterogeneous echo texture, 14 cases (93%) of USG diagnosis matched exactly with the FNAC diagnosis. One case which did not match the FNAC diagnosis was diagnosed as indeterminate in USG. We found no variables that influence the distribution of echogenicity. Our results comply with reports in the literature that also found no significant difference in the groups [22,23].

Further, we also reported in all benign lesions diagnosed by USG, mean AP diameter (3.16 cm) is less than mean transverse diameter (3.97 cm)
When we calculated predictive values of USG after comparing with FNAC in the diagnosis of malignancy in breast mass, both the specificity and negative predictive value was found to be 97.06%. Thus the ability of USG to detect positive cases correctly (malignant report) can be considered confirmatory and further treatment decision can be made solely on this report without any further additional diagnostic investigation. A sensitivity result of USG of 88.89% in our study suggests that a negative (benign) result of USG does not completely rule out the possibility of malignant nature of the mass. Hence, in the event of a negative result (benign report) physician should seek for additional investigations to rule out malignancy should utilize his clinical skill and experience to assume malignant nature of the lump. In this circumstance of USG findings 11.11% cases having malignant lesion was missed if USG was solely used for evaluation of breast lump. Similarly a specificity of 97.14% of USG means that a positive (malignant) result of USG does not completely rule out the possibility of benign nature of the lesion. However, the percentage of indeterminate result was also found in USG (1 out of 44) compared to FNAC. In addition three breast masses could not be characterized. One case of indeterminate USG result was correctly diagnosed as malignant by FNAC. Thus, both the diagnostic tools should be considered complementary and the physician should use the basis of his clinical findings and experience in choosing either one of or both the tools in diagnosing is of paramount importance.

In a similar study by Reinikainen et al. (1999) [40] to evaluate the role of USG and FNAC in the diagnosis of palpable solid breast lesions, they retrospectively reviewed the mammograms and ultrasound images of 84 palpable breast lesions and the cytologic reports of 57 lesions. Results were compared to the final histopathological diagnoses. 81 of the 84 lesions (96%) were observed as a local abnormality at USG thereby missing three lesions. Also, the sensitivity and specificity of FNAC were reported as 92 and 98%, respectively. There were no false-negative malignancies in the three modalities (USG, mammography and FNAC) combined. They concluded that active and critical use of various modalities could cut down the number of surgical biopsies of benign breast lesions [40].

CONCLUSION

Breast USG not only helps in differentiating solid from the cystic lesion but also plays important role in characterizing breast lesion. USG features suggestive of malignancy include spiculations, hypoechochogenicity, microlobulations, internal calcifications, shadowing, taller than wider, angular margins among others. USG features suggestive of benignity include round or oval shape, well defined margins with thin echogenic capsule, hyperchochogenicity, absent of posterior shadowing and non-calcified nodule. Thus, the ability to characterize lesion on USG help to determine the next step in patient care. Ultrasound is valuable in evaluating the breast lesions in patients with benign and malignant diseases. However a definite diagnosis is still dependent on histopathology.

The result of the study in terms of both high specificity and negative predictive value revealed sonography can be used to accurately classify some solid lesions as benign, allowing imaging follow-up rather than biopsy substitute. USG is an ideal imaging modality due to its cost effectiveness and non ionizing radiation potential. Thus, this correlative study of USG findings with fine needle aspiration for cytology describes reliable, frequent and reproducible features for differentiating benign from malignant breast masses. It is hoped that the outcome of this research would be useful for early diagnosis and management of breast lump in perspective of Nepal. Cancer edification, screening and early detection are the essential elements to influence the diagnosis, treatment and prognosis of breast cancer in Nepal. Breast cancer alertness and clinical breast examination are key tools for early detection in our resource of narrow context. The diseases can be cured in majority of the cases if diagnosed in early stages. However, diagnoses of two breast masses were missed by USG which were correctly diagnosed by FNAC. Thus both the diagnostic tools should be considered complementary on the basis of clinical findings and based on experience one should choose either one of or both the tools. Sonography can be used to accurately assess and classify some solid lesions as benign, allowing imaging follow-up rather than cytology/biopsy surrogate.