

# Atypical Lesions of the Breast and Lobular Carcinoma in Situ in Pregnancy – Surgeons' Practice

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## ABSTRACT

**Objective:** Approach to precancerous and high-risk breast lesions occurring in pregnancy has received little attention in the literature. We carried out a study to investigate the practice of surgeons in the management of these cases.

**Materials and Methods:** A short survey was sent to surgeons, including a multiple-choice questionnaire about their practice for atypical hyperplasia or lobular carcinoma in situ presenting in each trimester of pregnancy or at time of breastfeeding. Answer options included observation, immediate vacuum biopsy, immediate surgery, surgery in next trimester, surgery after delivery, and surgery after end of breastfeeding; based on the time of presentation.

**Results:** Out of the 671 practitioners invited, 97(14.5 %) responded to the survey. Participants were from 23 countries. Answers showed that management of gestational Atypical Ductal Hyperplasia (ADH) and Lobular Neoplasia (LN) was readily postponed by surgeons in favor of fetus safety while being cautious about risks of conservative management alone.

**Conclusion:** Various methods of treatment are selected by surgeons for managing high-risk breast lesions during pregnancy. In the absence of relevant literature, decision making in a multidisciplinary team would be the best approach in these cases.

**Keywords:** Atypical ductal hyperplasia, lobular carcinoma in situ, pregnancy, lactation, survey

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## Introduction

Some benign breast lesions are unique to the gestational period, and some others undergo alterations due to elevated levels of sex hormones during pregnancy (1, 2). Pregnancy associated breast cancer (PABC) may also occur, embracing many diagnostic and treatment challenges (3-5). All these have been thoroughly described, and many studies have covered, and are still investigating, different aspects of care of these diseases.

Conversely, issues concerning precancerous and high-risk breast lesions occurring in pregnancy have seldom been contemplated in the literature. There are several plausible reasons for this: overall low incidence, occurrence in ages higher than usual age of pregnancy, presentation as non-mass, non-palpability, and image-dependent detection. It might be that these lesions have been less studied in non-pregnancy periods as well.

Nonetheless, ultrasonography (US) of the gravid breast might be carried out for the follow-up of previous breast lesions, or for assessment of a new clinical finding. With the advent of highly accurate US which allows for detailed assessment, many structural deformities, microcalcifications, or other abnormalities of breast tissue are discovered; many of which would expectedly undergo biopsy, and histologic evaluation of the specimen. In this setting, reports of atypical hyperplasia (AH) or lobular carcinoma in situ (LCIS) by the pathologist create a therapeutic dilemma in the prenatal period.

The approach to atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), and LCIS in the general woman has undergone continuous modifications since they were first described, till recent times (6-8). Recommended treatment has extended from most invasive procedures such as bilateral mastectomy to plain observation (9, 10). Because of the lack of recorded evidence, physicians would presumably rely on that literature and their common sense for making therapeutic decisions when facing such diagnoses in the gestational period.

We carried out the following study in order to find out what the practice of surgeons would be in management of such cases.

### Materials and Methods

A short survey involving a brief account of the purpose of the investigation, a short description of the cases, three optional blanks for the surgeon email address, specialty/subspecialty, and country where they practice, followed by a multiple choice questionnaire (Figure 1), was designed. The questionnaire included two parallel sets of questions. The first set described a pregnant or lactating patient whose supposed lesion was a mass, and the second consisted of a non-mass lesion. In

both sets, surgeons were asked to determine their approach for each trimester of pregnancy and during breastfeeding individually. ADH, ALH, and LCIS were considered separately in the questions.

Participants could choose for the first and second trimester among following variables: observation, immediate vacuum biopsy, immediate surgery, surgery in next trimester, and surgery after delivery.

For the third trimester, participants could choose among following variables: observation, immediate vacuum biopsy, immediate surgery, and surgery after delivery.

**High-Risk Breast Lesions in Pregnancy**

When atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), or lobular carcinoma in situ (LCIS) is seen in a specimen of core needle biopsy of the breast, the routine practice is to excise the specimen. Depending on several factors like previous history or other known breast cancer risk factors of the patient, type of breast abnormality, accompanying lesions, size of biopsy specimen... this may be substituted by other practice such as simple observation or risk-reducing options.

Only two sets of questions are asked in the following text to see how you would manage one of the above breast lesions when detected on core needle biopsy during pregnancy, supposing that you and your patient have access to any equipment or facility that may be needed.

Please write your email:

Specialty/Subspecialty:

Country where you practice:

**Q1: Core needle biopsy of a breast MASS LESION, palpable or not, in following trimesters of pregnancy or during lactation in a woman less than 45 years old with no other risk factor for breast cancer:**

1st Trimester: ADH  ALH  LCIS

2nd Trimester: ADH  ALH  LCIS

3rd Trimester: ADH  ALH  LCIS

Lactation: ADH  ALH  LCIS

Please add any comment you wish:

**Q2: Core needle biopsy of a breast NON-MASS LESION, in following trimesters of pregnancy or during lactation in a woman less than 45 years old with no other risk factor for breast cancer:**

1st Trimester: ADH  ALH

2nd Trimester: ADH  ALH

3rd Trimester: ADH  ALH

Lactation: ADH  ALH  LCIS

Please add any comment you wish:

Observation

Immediate vacuum biopsy

Immediate surgery

Surgery after Lactation

Submit

**Figure 1.** Multiple choice questionnaire for survey of surgeons' choice regarding management of AH and LCIS in pregnant and lactating women

For the lactation period, the variables included: observation, immediate vacuum biopsy, immediate surgery, and surgery after end of breastfeeding.

The survey was sent to general, breast, and oncologic surgeons, as well as gynecologists who were known to practice breast surgery. Methods of contacting practitioners consisted of sending the link with an invitation to take part in the survey and a brief description of the work through emails, LinkedIn network, Short Message Service (SMS) and WhatsApp mobile application. Furthermore, members of the International Network on Cancer, Infertility and Pregnancy (INCIP) ([www.cancerinpregnancy.org](http://www.cancerinpregnancy.org)) were both contacted by email and invited to the survey personally via printed questionnaires handed out in an INCIP meeting.

The ethics committee approval was not needed for this study and participation in this study was volunteer.

**Table 1. Countries of practice of the participants**

Country	Number of participants	Country	Number of participants
Belgium	1	Malaysia	2
Bosnia and Herzegovina	1	Pakistan	5
Brazil	1	Panama	1
Bulgaria	1	Peru	1
Egypt	2	Poland	1
France	1	Russia	1
Germany	1	Saudi Arabia	1
Greece	3	UAE	3
India	3	UK	5
Iran	35	USA	10
Italy	6	Venezuela	2
Jordan	2		
Total : 97			

Statistical analysis was performed using Statistical Package for Social Sciences software version 18 (SPSS Inc.; Chicago, IL, USA). Categorical variables were summarized as N (%). Categorical variables were compared using the chi-square test or Fisher exact test, when appropriate.

**Results**

Overall, we offered the survey to 671 practitioners. Seven of them proposed to send the link to their colleagues, and we do not have the number of these invited doctors. Of all queried surgeons, 24 (3.5 %) answered that they did not practice breast diseases anymore and so would not participate in the survey. One surgeon replied that he was displeased with the work and believed the question was incorrect, around 550 (82%) of the directly invited surgeons did not answer at all, and 97 (14.5 %) took part in the survey.

The country where they practiced had been marked by 97 of the participants and is demonstrated in Table 1. Also, 88 participants wrote their specialty or subspecialty; this is shown in Table 2. Answers of participants to questions regarding their practice in different trimesters of pregnancy and in breastfeeding time is presented in Tables 3, 4 and 5 respectively. Colored cells show the highest values in each row, and p-values in last columns show the significance of different attitudes toward mass and non-mass presentations.

**Discussion and Conclusion**

Results of this study disclosed that surgeons were mostly inclined toward extraction of ADH histology, either by vacuum-assisted biopsy

**Table 2. Specialty or subspecialty of the participants**

Specialty/subspecialty	Number (%)
Breast/Breast Oncology Surgeon	51 (52.6)
General /Plastic surgeon	12 (12.4)
Gynecologist/Gynecologic Oncologist	4 (4.1)
Oncological Surgeon	21 (21.6)
Unknown	9 (9.3)

**Table 3. Practice of surgeons in ADH presenting during pregnancy or breastfeeding**

Period	Presentation	Observation	Im VAB	Im Sx	Sx next T	Sx after	p*
T1	Mass	21 (21.6)	31 (32)	11 (11.3)	23 (23.7)	8 (8.2)	0.08
	Non-mass	30 (30.9)	38 (39.2)	7 (7.2)	12 (12.4)	10 (10.3)	
T2	Mass	15 (15.5)	28 (28.9)	36 (37.1)	3 (3.1)	15 (15.5)	0.05
	Non-mass	28 (28.9)	34 (28.9)	20 (20.6)	2 (2.1)	13 (13.4)	
T3	Mass	16 (16.5)	26 (26.8)	22 (22.7)	-	33 (34)	0.07
	Non-mass	27 (27.8)	33 (34)	15 (15.5)	-	22 (22.7)	
Lactation	Mass	12 (12.4)	25 (25.8)	37 (38.1)	1 (1)	22 (22.7)	0.77
	Non-mass	16 (16.5)	29 (29.9)	29 (29.9)	1 (1)	22 (22.7)	

ADH: Atypical Ductal Hyperplasia; Im: immediate; VAB: Vacuum assisted biopsy; Sx: surgery; T: trimester; after: after delivery/end of breastfeeding  
Data are presented as number with percentage in parenthesis

Table 4. Practice of surgeons in ALH presenting during pregnancy or breastfeeding

Period	Presentation	Observation	Im VAB	Im Sx	Sx next T	Sx after	p
T1	Mass	41 (42.3)	30 (30.9)	6 (6.2)	6 (6.2)	14 (14.4)	0.50
	Non-mass	48 (49.5)	32 (33)	4 (4.1)	6 (6.2)	7 (7.2)	
T2	Mass	32 (33)	25 (25.8)	26 (26.8)	2 (2.1)	11 (11.3)	0.07
	Non-mass	46 (47.4)	28 (28.9)	13 (13.4)	0 (0)	10 (10.3)	
T3	Mass	16 (16.5)	26 (26.8)	21 (21.6)	-	34 (35.1)	<0.001
	Non-mass	45 (46.4)	27 (27.8)	8 (8.2)	-	17 (17.5)	
Lactation	Mass	24 (24.7)	25 (25.8)	28 (28.9)	-	20 (20.6)	0.32
	Non-mass	35 (36.1)	25 (25.8)	21 (21.6)	-	16 (16.5)	

ALH: Atypical Lobular Hyperplasia; Im: immediate; VAB: Vacuum assisted biopsy; Sx: surgery; T: trimester; after: after delivery/end of breastfeeding  
Data are presented as number with percentage in parenthesis

Table 5. Practice of surgeons in LCIS presenting during pregnancy or breastfeeding

Period	Presentation	Observation	Im VAB	Im Sx	Sx next T	Sx after	p
T1	Mass	31 (32)	34 (35.1)	9 (9.3)	16 (16.5)	7 (7.2)	0.09
	Non-mass	45 (46.4)	32 (33)	2 (2.1)	11 (11.3)	7 (7.2)	
T2	Mass	14 (14.4)	30 (30.9)	37 (38.1)	1 (1)	15 (15.5)	<0.001
	Non-mass	40 (41.2)	30 (30.9)	17 (17.5)	0 (0)	10 (10.3)	
T3	Mass	15 (15.5)	27 (27.8)	21 (21.6)	-	34 (35.1)	<0.001
	Non-mass	41 (42.3)	25 (25.8)	9 (9.3)	-	22 (22.7)	
Lactation	Mass	24 (24.7)	18 (18.6)	35 (36.1)	-	20 (20.6)	0.40
	Non-mass	33 (34)	20 (20.6)	26 (26.8)	-	18 (18.6)	

LCIS: Lobular Carcinoma in Situ; Im: immediate; VAB: Vacuum assisted biopsy; Sx: surgery; T: trimester; after: after delivery/end of breastfeeding  
Data are presented as number with percentage in parenthesis

(VAB) or surgery. The approach was more invasive where it presented a mass, and more conservative with other findings. This could be anticipated because ADH usually does not present as a mass. This also shows that surgeons are highly concerned about the rate of upgrade of ADH and prefer to make sure the lesion is only high risk benign one or not malignant because when it has ADH in core biopsy, it is not a really benign one. However, in the third trimester, most of the surgeons chose to operate on the patient after delivery in case of mass lesions, and to perform VAC for non-mass lesions. In addition, among the 4 suggested treatment options, the “immediate surgery” ranks third for mass lesions, and fourth (15.5%) for non-mass lesions in the practice of participating surgeons. This is interesting considering that part of literature claims that ADH can be managed with no surgical excision at all. The approach of most surgeons to ALH was conservative. The only situations which pushed physicians toward surgical excision were lumps harboring ALH detected in the last trimester, with the decision to operate the patient after delivery; or found during breastfeeding. These results, however, might be interpreted as a tendency to excise unusual presentations of biopsy-detected ALH (lumps) as soon as the gestational state is safe enough. This also might be related to the small percentage of respondents to the survey, which brings in mind the possibility that surgeons who are more determined to extract borderline lesions during gestation might have answered the survey more frequently than others.

In LCIS, surgeons observed non-mass cases, while mass lesions were chosen to be excised; either by VAB or surgery. This complies with protocols that suggest excision of pathologic-radiologic non-concordant lesions, and observation of others. Time and method of excising the lesion depended on the gestational stage and was in accord with rules of mother and fetus safety.

All aspects of breast tissue atypia and LCIS including histologic definition, incidence, risks, and management have been discussed in the literature for non-pregnant women. ADH is defined as a borderline lesion which carries some of the histologic features of Ductal Carcinoma in Situ (DCIS), but not all of them (6, 7). Lobular neoplasia (LN) is proliferation of atypical epithelial cells within the terminal duct lobular units and comprises ALH and LCIS, which are very similar except for quantitative difference in abnormal and atypical characteristics. These are infrequent lesions that have been diagnosed more frequently since mammographic screening has taken place. ADH is seen in 0.5 to 17% of biopsied breast specimens with benign results (8-13). The incidence of LN is very different in various studies, from 0.1% for ALH alone, to 0.5% -7.8% for LCIS with or without ALH. ADH is more frequently diagnosed around 45- 46 years of age (12), and LN between 40 and 55 years (12-14). The most frequent mode of presentation is through mammographically-detected microcalcifications, nonetheless it may very occasionally present as a palpable or an US-

detected mass (6, 12, 15-18). LN is usually not associated with any image finding, but may infrequently cause a “shadowing, avascular, irregular, hypoechoic mass” on US (14).

There are two major concerns about AH and LCIS. The first consists of the probability to upgrading to malignancy when excised, this is due to the presence of adjacent cancer. The second concern is future risk of malignancy in the breast. When ADH is diagnosed by core needle biopsy, the rate of upgrade to DCIS or invasive disease has been reported from 0% to as high as 65% (6-8, 10, 19, 20). Rate of upgrade for biopsy-detected LN has been from 9% to 33% (8, 21). For subsequent risk of cancer in AH, figures up to 3- to 4-fold increase in risk have been detected, mostly in same but also in opposite breasts, more frequent in younger ages, and more frequently invasive than in situ (9, 22-24). The risk of future cancer in ALH is around 4- to 5- fold, and 8- to 10-fold in LCIS. In both lesions, the cancer might be ductal or lobular invasive, and in same or opposite breast, with a predilection for the same breast (11-13, 18, 22).

Management of ADH detected on image-guided biopsy has been subject to various suggestions. At present, because of the high rate of upgrading, excision of the lesion is mostly recommended (6, 7, 9, 10, 16-18, 20, 25-27), except for very small microcalcifications which have excised by VAB (8, 18, 26, 27). For LN found in core needle biopsy specimens, the optimal therapeutic approach is still debated. The most recent approach is to keep lesions under observation whenever the radiologic and pathologic results are concordant; if not, excision is advised (9, 13, 18, 20, 21, 23, 27). Counseling for risk-reduction with tamoxifen should also be considered in AH and LCIS (14, 18, 23, 27, 28).

Issues regarding incidence, risks, and management of these lesions during pregnancy have not been considered in the literature. Whether the same approach as non-pregnant women should be undertaken, or should physicians avoid any treatment because of low risks of malignancy and indolent nature of lesions; and whether the highly modified hormonal milieu of pregnancy would affect the course of the disease are not known. Our study scanned the practice of surgeons in various countries of the world in regard to these matters.

Overall and in contrast with PABC which infers immediate action, management of gestational ADH and LN was easily deferred by surgeons because of their relative benignity; in favor of fetus safety. Nevertheless, most surgeons stood vigilant toward these borderline lesions in selecting type of management.

This study also revealed some supplementary points. For example, the diversity of answers and heterogeneity in practice of surgeons was very interesting. One surgeon who believed the survey was inappropriate wrote: “No one in their right mind will operate on a pregnant patient with ADH, ALH, or LCIS”, and stated that ABS and ASCO guidelines have clearly defined the suitable management. Nonetheless the survey shows that many skilled and experienced surgeons chose to operate on the patient, which should not be considered incongruous for a high-risk lesion, where there is no specific guideline or consensus over the subject.

Our study shows that in the lack of specific evidence and absence of guidelines, decision-making varies significantly among practitioners. Yet, guidelines do not cover rare instances, and cases in the survey are probably rare enough not to deserve being discussed in an international consensus. The best approach to these cases is to have the disorder managed by a multidisciplinary team comprising related specialty or subspecialties.

Our study had some limitations. Because we planned to design a concise survey that would take a short time to complete, we did not ask participants about their years of expertise, their statistics about yearly number of breast surgeries or management of pregnant cases with breast complaints; and also if they worked in a referral center, or if they had ever managed cases similar to our questions. In addition, around one third of the participants were from Iran, because we knew who worked on breast diseases in our country, and we also called them and asked to participate. However they were from different centers, and different cities, where practices are not based on same guidelines.

In conclusion, in the absence of relevant literature and guidelines, approach of surgeons to high-risk lesions of the breast that could occur in pregnancy differs to some extent; but follows those common scientific bases that concern safety of pregnant mothers and their fetuses. Decision-making in a multidisciplinary team would be the best option in these cases.

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