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April 2018

Healthy Babies to Healthy Mothers

ESTD 1989
ISPAT

talkBACK

Newsletter of the Indian Society for Prenatal Diagnosis and Therapy

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editor's DESK

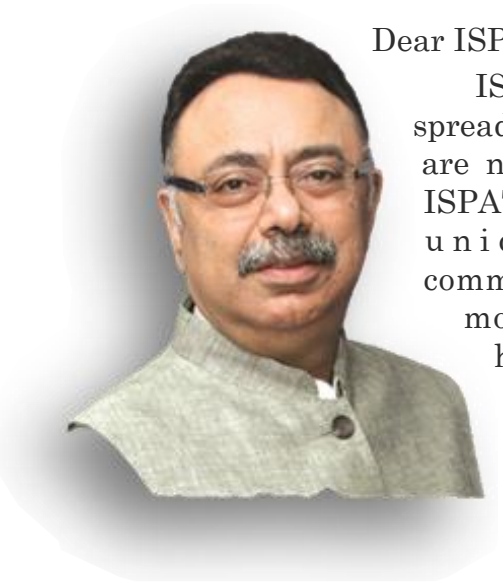
Dear ISPATIAN friends,

Greetings! After enjoying colorful Holi festival, we all have entered into the "Women Empowerment" era in March, 2018 and there is nothing more gracious than to select the topic related exclusively to women cancer, especially the Breast Cancer for this issue.

The emergence of cancer screening program has no doubt reduced the burden of breast cancer showing descending trend in mortality as well in developed countries. The well-planned breast screening program, education & awareness has contributed to this significant reduction. in the incidence. However, the screening in Indian women for breast, cervical or ovarian cancer is a distant dream! Nevertheless, we as health & medical professionals need to take a responsibility of awareness & early detection of this second most burden of the most common cancer in Indian rural & semi-urban women who are deprived of the diagnostic facilities & infrastructure for therapy follow-up. This issue is therefore dedicated to the current Indian scenario of breast cancer & the simple tips for its early detection, management & recent molecular genetic approaches for care of breast cancer. It is hoped that one of our objectives of teaching & training is achieved through this effort & this simplified knowledge can be applicable in your practice. We urge that the message is disseminated down the line by imparting Breast Cancer Genetic information to health workers working in the community & in rural areas to achieve the better control over this devastating women cancer.

As usual the upcoming events like interesting national and international conferences, a few pictures of past ISPAT events about the happenings & scientific break-through news are captured. Of

president **MALHOTRA**



Dear ISPATIANS

ISPAT wings are spreading, our collegues are now knowing what ISPAT is. We are a unique society committed to safe motherhood, safe healthy fetus and healthy neonate.

We have this year been busy with holding "Protein Summit" with the makers of Horlicks and several Genetic conferences and CME's. Lots of our members have been very active.

The International Academy of Perinatology will be meeting in Bucharest, Romania and I have been invited as Associate fellow to attend and give talk on F.G.R. Dr. Jaideep the incoming ISPAT president and current FOGSI president will also be addressing on the unique initiative "ADBHUT MATRATVA" ISPAT should join hands with FOGSI to take this initiative of ANC to new levels. We have also promised the Prime Minister of India that 9th of every month we will give our services free to Pregnant women even at our Private clinics.

We are looking forward to the GENETIC & FETAL MEDICINE Conference in Patna in June.

Yours in ISPAT

Dr. Narendra Malhotra
President

Continued from **Pg1**

course, the Quiz will have some exercise to your brain!

As the Editors of this E-Newsletter, we would be more than happy if you come forward and share your experiences in the form of an interesting case, any article review or any innovative work or simply a genetic healthcare activity taken place in your area.

Wishing you all a happy reading,

Yours truly,

Dr. Usha Dave

Dr. Seema Pandey

membership **UPDATE**

TOTAL

860

Become an ISPATian

https://goo.gl/ExJQvv

What's in **NEWS** these days

Analysis of cell-free DNA in maternal blood in screening for aneuploidies: updated meta-analysis.
www.ncbi.nlm.nih.gov/pubmed/28397325

Multicenter screening for pre-eclampsia by maternal factors and biomarkers at 11-13 weeks' gestation: comparison with NICE guidelines and ACOG recommendations.
https://www.ncbi.nlm.nih.gov/pubmed/28295782

some **PAST EVENTS**

Adbhut matrutva TOT project

Self Experience by Neharika Malhotra

"Adbhut matrutva" - In an easy word to explain means "incredible motherhood". The concept behind this is to give a divine spiritual experience to our mothers to be able to understand Garbh-Sanskar and good antenatal care. it is traditionally believed that child's mental and behavioral development starts as soon as he/she is conceived and now we do have scientific reasons for that .we all know the fetal origin of adult diseases. Any mother to give birth to a healthy child should be in a state of mental and physical calmness which is also related to food habits and many other factors. adding music throughout your pregnancy gives a positive effect to the baby. some mantras like samveda mantras gives positive energies within the womb. The mother can shape up the child's impression by doing yoga, thinking positive and eating right. it's now our duty as doctors also to provide this concept to all our pregnant patients to have healthier and happier future generations. Sister Shivani tells us importance of creating positive vibrations during pregnancy.

To attain this objective FOGSI in association with Brahmkumaris had organized a training program for gynecologists from all over India in Manesar on 17-18 March 2018. Views were exchanged and evidences were shared regarding acceptance of 'mind' by scientists and fetal origin of diseases and how could we prevent it by an early but simple interventions.

Adbhut Matrutva was something which made me learn many new things about myself.

- Adbhut Matrutva taught me how to bring simple small changes for a happier me.
- Adbhut Matrutva made me understand pregnancy and my patients in a spiritual aspect.
- Adbhut Matrutva taught me the simple art of meditation and healing.
- Adbhut Matrutva taught me the strength of prayer.
- Adbhut Matrutva taught me the strength of yoga.
- Adbhut Matrutva also made see the importance of positive vibrations.
- Adbhut Matrutva made me learn team work is the best way forward.
- Adbhut Matrutva made me see the light within.

quiz of the MONTH

by Dr. Bela Bhatt

1) The Best test for screeing for preeclampsia is
A: Ut A PI at 11-13 wks
B: Ut A PI & PAPP-A at 11-13 wks
C: Ut A PI at 18-20 wks scan
D: none of the above

2) If only 1 scan is allowed by patient during pregnancy that would be:
A: Dating scan in first trimester
B: Nuchal Scan
C: Anomaly scan at 18-20wks
D: Growth scan at 28-30 wks

3) NIPT replaces Combined Test(Nuchal Scan + Double marker)
A: True
B: False

4)Which of the following helps to decide timing for termination of pregnancy in IUGR
A: <5 centile Growth
B: Uterine A Doppler
C: Umbilical A & MCA Doppler
D: none of the above

5) Which of the following is NOT a soft marker for aneuploidies
A: Nuchal Translucency
B: Nasal Bone
C: Ductus Venosus flow
D: Uterine A PI

Answers: Last Page

upcoming **EVENTS**

FOGSI – ISPAT GFMCON

Date : 16/06/2018 - 17/06/2018

Venue : Patna, Bihar

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Genetics of Breast Cancer- Every Woman Must Know !

by Swarna Mandva, Purvi Mohanty & Usha Dave

Breast cancer is one of the most fearful invasive cancer in women & 2nd most common in the rural areas after cervical cancer as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women. The recent global statistical analysis of breast cancer also offers age related risk (Table-1). India is facing challenging situation due to 11.54% increases in incidence and 13.82% increase in mortality during 2008–2012. The main reason for this observed hike in mortality is due to lack of inadequate breast cancer screening, diagnosis of the disease at an advanced stage and unavailability of appropriate medical facilities.

Every woman should be well aware of simple steps of self-breast examination as explained here. The observation of any one of the symptoms shown in Table-2 should be quickly prompted by a visit to the family physician. If in doubt, it should be followed by the breast cancer screening tests, e.g. mammography & USG. The clinical signs & symptoms highlighted here is a precautionary from the point of early detection & further management of breast cancer to avoid mortality & morbidity.

Understanding of Breast Cancer :

Any cancer is the uncontrolled growth of abnormal cells in the body and develops when the body's normal control mechanism stops working. Old cells do not die and instead grow out of control, forming new, abnormal cells. Same is true for breast cancer.

Breast cancer is the most complex disease associated with both genetic and environmental risk factors. The various causative factors are well described in the literature as shown in Fig. 2. However, regular breast self-examination is the effective way of early detection of breast cancer as shown in Fig.1. Increasing urbanization and Westernization associated with changing lifestyle

Table 1. Estimated New Female Breast Cancer Cases and Deaths by Age, US, 2017

	In Situ Cases		Invasive Cases		Deaths	
Age	Number	%	Number	%	Number	%
<40	1,610	3%	11,160	4%	990	2%
40-49	12,440	20%	36,920	15%	3,480	9%
50-59	17,680	28%	58,620	23%	7,590	19%
60-69	17,550	28%	68,070	27%	9,420	23%
70-79	10,370	16%	47,860	19%	8,220	20%
80+	3,760	6%	30,080	12%	10,910	27%
All ages	**63,410**		**252,710**		**40,610**	

Estimates are rounded to the nearest 10. Percentages may not sum to 100 due to rounding.

Table-2 Clinical Symptoms of Breast Cancer

Lump, swelling or hard tissue formation in either breast.
Breast Pain/ clear or bloody discharge from breast other than breast milk
Change in shape and size of one or both breasts.
Dimpling on the skin of the breast or change in the appearance of the breast
Rash around nipple /nipple sunken in the breast

and food habits has lead breast cancer to attain top position.

Breast Cancer is divided stage wise (0 to IV & TNM system) based on four characteristics such as the size of the cancer, invasive or non-invasive, presence in the lymph nodes or whether the cancer has spread to other parts of the body beyond the breast.

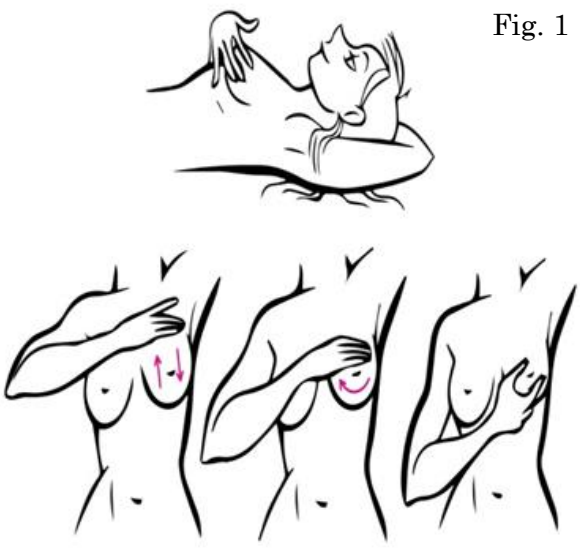
The primary subtypes of breast cancer are according to its associated estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2(Her-2). Further, the gene-expression subtypes are as following: luminal A, luminal B, Her2-enriched, and basal-like. The luminal subtypes are relate to expression of estrogen and progesterone receptors (ER and PR) and differentiated luminal epithelial cell markers. Among them, triple negative (Basal-like) breast cancer whose estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 are all negative possess the greatest number of mutations.

Diagnosis of breast cancer can be done using Breast exam., Mammogram, Breast ultrasound, removing a sample of breast cells (biopsy) for histology or molecular genetic testing and breast MRI. In rural areas, cancer patients are diagnosed at late or advanced stages of disease with a higher proportion of them having widespread metastasis suggesting for need of more attention in terms of awareness, treatment and facilities for early diagnosis. Lack of organized breast cancer screening program, paucity of diagnostic aids, and general indifference toward the health of females in the predominantly patriarchal Indian society are also the drawbacks leading to increased breast cancer incidence. According to various studies, majority

How to do Breast Self Examination (BSE) ?

Do your BSE at the end of your monthly period.
If you are pregnant, no longer have periods or your period is irregular, choose a specific day each month.
This should not be performed in the shower or with lotion on your skin or fingers.
If you find a lump or notice other unusual changes, don't panic. About 80% of lumps found are not cancerous. See your doctor promptly for further evaluation.

Fig. 1



of carcinoma breast cases in the West report in stages I and II of disease, whereas in India 45.7% report in advanced stages. Factors as marital status, location (urban/rural), BMI, breast feeding, waist to hip ratio, low parity, obesity, alcohol consumption, tobacco chewing, smoking, lack of exercise, diet & environmental factors were reported as major risk factors in India leading to increasing incidence of breast cancer; however, the reason for high incidence of breast cancer in younger women are yet not well known.

The relevant treatment can only be suggested once a breast cancer has been identified appropriately with confirmed diagnosis and its degree is properly analysed. Based on the degree & onset, further options can be offered to the patient such as surgery, radiotherapy, chemotherapy or hormone therapy.

Genetics and Breast Cancer:

Human breast cancer is caused due to genetic alterations in somatic cells of breast & individual genetic susceptibility plays a significant role in hereditary breast cancer. About 5 to 10 percent of all breast cancers are hereditary in nature. The well-known chromosomes harboring genes are Chr 17 & 13 as shown in Fig 3. However, other genes on Chr1p, 3p, 11p, 13q, 16q & some more are also involved in causing breast cancer.

The best-known genes linked to breast cancer are BRCA1 (location: 17q21) & BRCA2 (location : 13q12) gene inherited from parents. Offspring of an individual with a BRCA1 or BRCA2 germline pathogenic variant have a 50% chance of inheriting the variant. It is important to note that everyone has these genes but mutations in these genes play a major role in promoting breast cancer. Other gene mutations like ATM, TP53, CHEK2, PTEN, CDH11 and STK11 are also associated with breast cancer. The frequency of BRCA1/2 genetic mutations was reported in many studies to range from 2.9% to 24.0% among Indian familial breast cancer patients. Notably, the occurrence rates of BRCA2 mutations were lower than those of BRCA1 in India.

Advanced Genetic Diagnostic technology

DNA microarrays used for whole genome screening have the potential to assess the thousands of genes simultaneously. Recent preliminary researches indicate that gene expression profiling based on DNA microarray can offer potential and independent prognostic information in patients with newly diagnosed breast cancer. The potential application of Tandem mass spectrometry (MS) based proteomics in investigation of human breast milk as a biomarker signature for early detection of BC and monitoring its treatment is currently on the frontiers of research-based services. Using human breast milk samples from both healthy controls and BC suffering individuals, several alterations in protein expression are identified by research scientists such as lower expression, overexpression, or post translational modification of some proteins which might be associated with BC risk.

Genetic Counseling

While many women are diagnosed with breast cancer each year, please note that only a small percentage of breast cancer is caused by an inherited genetic mutation. The families most appropriate for genetic counseling have-

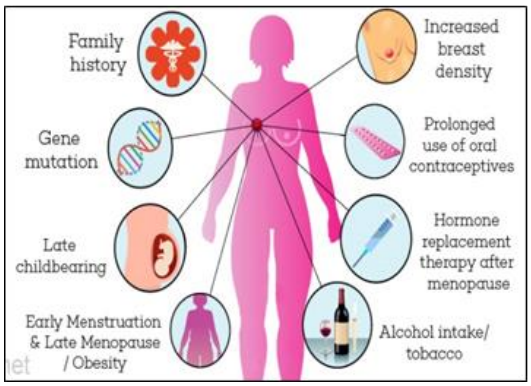


Fig. 2

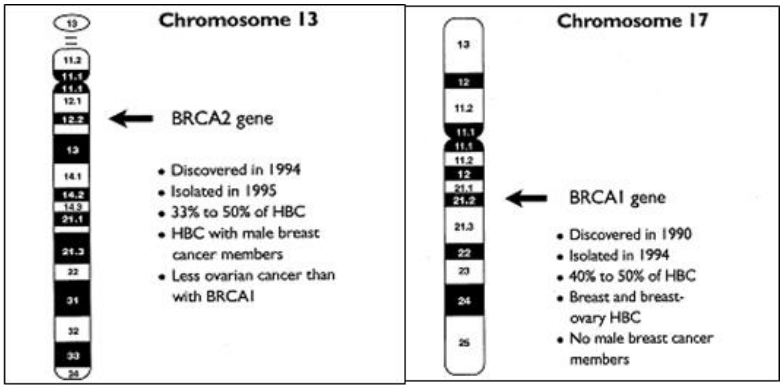


Fig. 3

1) High numbers of family members with cancer diagnoses (especially breast and ovarian) throughout several generations, either maternal or paternal,
2) Family member diagnosed with cancer before age 50,
3) Family members who have been diagnosed with multiple cancers (for example, breast and ovarian) &
4) Male breast cancers (Remember even males can have breast cancer).

Hence, it is important for every woman to understand her individual risk because genetic testing may not be the right option for everyone. During Genetic Counseling (GC), individuals are explained basic cancer genetics with an accurate assessment of their personal risk for developing breast cancer and it offers a plan for follow-up and preventive care. The GC includes a complete family & a personal health history including an explanation of an assessment of cancer risk with a discussion of genetic testing options.

The specific mutational diagnosis is generally done using laboratory genetic testing. Prenatal diagnosis is possible for pregnancies at increased risk if the cancer-predisposing genetic variant in the family is known. However, requests for prenatal diagnosis of adult-onset diseases are uncommon and require careful genetic counseling. With advent of Next Generation Sequencing (NGS) technology, Non-invasive Prenatal Screening (NIPS) test for fetal aneuploidies by scanning cell-free fetal DNA in maternal plasma is rapidly becoming a major prenatal genetic test. The many research studies have revealed presymptomatic detection of tumors in pregnant women undergoing routine NIPT. This is possible because similar to placental DNA, tumor DNA can be detected in the plasma & analysis of cell-free tumor DNA can be used to characterize and monitor cancers in gynecologic care & surgical options.

In conclusion, the challenge lies in making best use of breast cancer knowledge that has been gained using lower-resolution chromosomal methods on thousands of cases to direct the NGS studies to have the greatest impact on clinical management of the highly heterogeneous disease associated with diverse outcome. A multidisciplinary team approach to breast cancer including awareness programs, preventive measure, screening programs for early detection and availability of treatment facilities are vital for reducing both incidence and mortality of breast cancer in Indian women.

Finally, it is the responsibility of each one of us to disseminate the updated genetic information on early detection & prevention of breast cancer, to our patients & community at large to achieve a favourable and positive clinical picture in the country.

Answers (April 2018): 1. B, 2. C, 3. B, 4. C, 5. D