Research Article

Prevalence of breast cancer and comparative analysis of invasive ductal carcinoma, invasive lobular carcinoma and mucinous carcinoma in Punjab (Faisalabad)

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Abstract

Cancer incidence and mortality rates are increasing rapidly in Asian region. Breast cancer is the most common malignancy throughout the world and might be related to various social, cultural, environmental life style related habits along with many other factors. There is plenty of research work on medical side of this cancer in Pakistan but it is deficient on epidemiological studies. 468 patients were analyzed for all types of breast disease. 129 patients (27.56 %) out of 468 were found for lump case and 37 patients (28.6%) out of 129 were found for all other types of cancer. Invasive ductal carcinoma (breast cancer antigen NY-BR-49, protein 1), invasive lobular carcinoma (E-cadherin, protein 2), and mucinous carcinoma (heregulin, a specific activator, protein 3) were analyzed for sequential comparison. Protparam, SOPMA, REP, protein colourer and Compute PI/MW tools were used to analyze breast cancer types, invasive ductal carcinoma, invasive lobular carcinoma and mucinous carcinoma. Structure of band forming between one amino acid and other further along the chain, phi and psi angles of each residue in a random coil were found to be independent of phi, psi torsion angles of every other residue. Only tryptophan

and tyrosine amino acids, to a lesser extent cysteine contribute significantly to peptide at 280 nm absorbance, phenylalanine absorbs only at lower wavelengths (240 nm to 265 nm). The instability index was found to be lower than 40 only for E-cadherin. REP showed that all three proteins had their own characteristics and repeated fragments hence different functions. Mucinous carcinoma was found to be the rare type of cancer.

Keyword: Breast cancer; types; prevalence; comparative analysis

Introduction

Breast cancer is the most common malignant neoplasm among women worldwide, with approximately 1.7 million new cases diagnosed in 2012. This corresponds to about 12% of all new-fangled cancer cases. It was also found that 25% of all types of cancers in women are hormone related. The reported breast cancer cases were 124.6 per 100,000 women per year and deaths were 22.2 per 100,000 women per year [1]. This high rate of cancer incidence and deaths were found to be age-adjusted based on 2007-2011 reports in United States. In 2011, there were an estimated 2,899,726 women living with breast cancer in the U.S. and 1.7 million new cases diagnosed in 2012 [2]. Invasive ductal carcinoma (IDC), occasionally called infiltrating ductal carcinoma, was found to be the most prevalent breast cancer in the world and approximately 80% of all breast cancers are IDCs [3]. Currently it is accepted unanimously two pathways of multi-step breast cancer progression. One of them is well-differentiated DC In-Situ, progressing to grade I IDC, and other one is poorly-differentiated DC In-Situ progressing to 3rd grade IDC. High grade (poorly-differentiated) DC In-Situ is associated with cellular proliferation, apoptosis and necrosis [4]. Alterations in the molecular pattern of DC In-Situ lesions may direct collapsing the myoepithelium, invade the surrounding stroma forming an invasive carcinoma and escape of ductal structure [4, 5].

IDC might not indicate any type of symptom and often recognized as an anomalous area which turns up on screening mammograms,

guiding further testing for verifications. In several cases, first sign of IDC is a new lump or tissue mass in the female breast that patient or her doctor can feel [6]. Invasive lobular carcinoma (ILC), occasionally called infiltrating lobular carcinoma (ILC), is found to be the second most widespread type of breast cancer after IDC [7]. Most often radiation therapy is suggested after surgeries that preserve healthy breast tissue, such as partial mastectomy and lumpectomy radiation therapy may be recommended after mastectomy. Such treatments also reduce the risk of recurrence [8]. An attempt has been made for epidemiological studies of breast cancers and molecular analysis of its various types by using useful bioinformatics tools as Protparam, SOPMA, REP, protein colourer and Compute PI/MW. The present study will provide baseline data for the development of the disease databases and need for the use of recent technology or preventive measures.

Materials and Methods

Data for this study was obtained from the Punjab Institute of Nuclear Medicine (PINUM). 468 patients of all breast diseases like fibro adenomas, Proliferate changes, abscess, micro calcifications, Galactoceles, cyst, lump, pain and discharge. Lump were checked by mammography, FNA and true cut biopsy, and the different diseases like fibro adenomas, Proliferative changes, abscess, micro calcifications, Galactoceles, cyst and carcinoma were diagnosed at different stages in lump cases.

For comparative study of breast cancer and its types invasive ductal carcinoma (breast cancer antigen NY-BR-49, protein 1),

invasive lobular carcinoma (E-cadherin, protein 2), and mucinous carcinoma (heregulin, a specific activator, protein 3), sequences were retrieved from NCBI. Five different bioinformatics tools were used to study different aspects of proteins related to these cancers. PROTPARAM tool was used to study the physiological properties e.g. composition of amino acids, molecular weight, molecular formula, half life of each protein, stability index, gravity index. These were used to measure to detect the degree of stability of the proteins. Compute PI/MW tool was used for the computation of the theoretical pI (Isoelectric point) and Mw (molecular weight). SOPMA tool was used to study α -helix, Beta turn, random coils, and extended strands etc. Protein colourer was used to simply color the protein sequence and REP tool to examine the repeated fragments in sequences.

Results

A total of 468 patients were studied for all breast disease. 129 patients (27.56 %) out of 468 were found for lump case and 37 patients (28.6%) out of 129 were found for other types of cancer (Fig. 1). SOPMA tool was used to study α -helix, B turn, random coils, and extended strands. A helix is spring like coil of polypeptide that forms itself of a rigid cylinder of great regularity shown by the protein 1 followed by the protein 2 and 1 respectively. Structure of band forming between one amino acid and other further along the chain, phi and psi angles of each residue in a random coil were found to be independent of phi, psi torsional angles of every other residue. These bands were used to compare the each protein (Fig. 2; Table 1).

PROTPARAM was used to study the physiological properties of the sequences e.g. composition of amino acids, molecular weight, molecular formula, half life of each protein, stability index, and gravity. Protein PI was calculated by using PK values of

amino acids which were delineated by examining the poly-peptide migration between pH 4.5 and 7.3 in an immobilized pH gradient. Only the amino acids tryptophan and tyrosine and to a lesser extent cysteine contribute significantly to peptide or protein absorbance at 280 nm, Phenylalanine absorbs only at lower wavelengths (240 nm to 265 nm). The instability index is a measure of a particular protein, whether it will be stable in a test tube or not. If the index is less than 40 then it is probably stable in the test tube as shown by the protein 2 (Table 2). Aliphatic index is defined as the relative volume of a protein occupied by aliphatic side chains (alanine, valine, leucine and isoleucine) and the positive factor indicating the increase of thermo-stability of these globular proteins. PI/MW from Compute PI tool, amino acids colour from colourer and repeated fragments in sequences from REP showed that all three proteins had their own characteristics hence different functions (Fig. 2).

Discussion

Breast cancer is the most common malignant neoplasm among women in United States and the state of North Carolina. There are different types of breast cancer and this study includes the prevalence of invasive ductal carcinoma, invasive lobular carcinoma, and mucinous carcinoma and their protein molecular comparison. Invasive ductal carcinoma (IDL) was found to be the most frequently occurring breast cancer among women. About 80% of all cancers were invasive ductal carcinomas which refer to cancer that has broken through the wall of milk duct and began to invade the tissue of breast. In this type one of the proteins which were found to be involved was serologically defined breast cancer antigen NY-BR-49. This reacts with serum IgG from breast cancer patients. This antigen was found to be over expressed in breast cancer patients [9]. The second most common type of breast

Fig. 1. Classification of 129 (Lump) patients on the basis of disease category

Table 1. Results from SOPMA

Structure parameters	Signs	Protein 1		Protein 2		Protein 3	
Alpha Helix	(Hh)	120	4.09%	127	14.40%	129	20.16%
Extended Strand	(Ee)	45	2.78%	242	7.44%	100	15.62%
Beta Turn	(Tt)	33	9.38%	45	5.10%	19	2.97%
Random Coil	(Cc)	154	3.75%	468	3.06%	392	61.25%

Protein 1; breast cancer antigen NY-BR-49, Protein 2; E-cadherin, Protein 3; heregulin (a specific activator)

Table 2. Results from Protparam

Parameters	Protein 1	Protein 2	Protein 3
No. of Amino acids	352	882	640
Molecular weight	37874.5 <i>amu</i>	97456.1 <i>amu</i>	70391.8 <i>amu</i>
Theoretical PI	8.78	4.58	9.00
Formula	C ₁₆₂₀ H ₂₆₅₂ N ₅₁₄ O ₅₁₆ S ₉	C ₄₃₂₇ H ₆₇₄₉ N ₁₁₅₁ O ₁₃₇₄ S ₁	C ₃₀₀₉ H ₄₈₄₇ N ₉₀₅ O ₉₈₅ S ₂₉
Total no. of Atoms	5311	13619	9775
Extinction Coefficients*	23865/23490	94240/93740	29630/28880
Estimated Half life**	3.5 hours	30 hours	30 hours
Instability Index	54.59	35.43	56.55
Aliphatic Index	82.10	84.54	59.58
GRAVY	-0.508	-0.351	-0.780

*Extinction coefficient refers to several different measures of the absorption of light in a medium measured at 280 nm, ** mammalian reticulocytes in-vitro, Protein 1; breast cancer antigen NY-BR-49, Protein 2; E-cadherin, Protein 3; heregulin (a specific activator).

Protein 1. Breast cancer antigen NY-BR-49

Protein 2. E-cadherin

Protein 3. Heregulin (a specific activator)

Fig. 2. Bands showed that blue color is helix, red color is sheets, green are turns and others are extended strands. Peaks showed that concentration of helix, sheet, beta turns and random coils (Window width: 17, Similarity threshold: 8, Number of states: 4)

cancer was found to be invasive lobular carcinoma about 10% of all cancers. Invasive lobular carcinoma refers to cancer that is broken through the wall of lobule. The protein involved in invasive lobular carcinoma is cadherins which were major cell-cell adhesion molecules both in tumor and normal tissues. Another study by Ito, (1990) also showed higher levels of serum soluble E-cadherin in the cancer patients when compared to healthy volunteers [10]. Mucinous carcinoma was found to be the rare type of cancer. The mucinous contains breast cancer cells could be easily distinguished from normal cells under microscope. One of protein involve in this type is heregulin, a specific activator. The proto-oncogene elected as erbB2 or HER2 encode an enzyme protein of 185-kilodalton known as transmembrane tyrosine kinase, over expression of which has been allied with a poor prognosis in numerous human malignancies [11]. Protein PI calculations were also found to be in concordance with other studies [12]. In Pakistan there is dire need to divert the research towards early diagnosis, the most common types of cancers and causes, development of databases for the records of the patients for their cancer types so that the recovery rate from particular disease be improved.

Conclusion

Breast cancer is very common in Pakistan and about 80% of all cancers were invasive ductal carcinomas indicating strong correlation among various types of cancer. Sequential and molecular study of proteins involved in various types of cancer showed that they are closely related to each other on the basis of structural indices and the need is to find the societal causes of the cancers. The study will be useful for knowing the taxonomy and evolution of proteins participating in neurodegenerative diseases.

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