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Editorial

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Accreditation, Quality, Challenges, and Making Hospital Care Better

Healthcare system has witnessed marked social, economic and technological change in the past few years and has undergone transformation from physician centered approach to patient centered approach. Demand for quality in healthcare services has risen due to various forces such as medical tourism, insurance, corporate growth and competition.[1,2] Such changes are expected to continue for foreseeable future because of restructured economic and social policies, globalization of markets and enhanced worldwide communication. National health systems are coming under increasing scrutiny with a view to cost containment and quality improvement.[1] Many of the health systems in India have neglected evaluation of the quality of individual and systematic institutional care, giving rise to an unnecessary increase in costs, poor patient care, negligence, and inadequate resources with inefficient facilities, lack of information and unwanted medical interventions, complications and patient morbidity.

Such being the case, assuring quality in healthcare services becomes a mandate and receiving an accreditation is the only answer to it. It is the single most approach for improving the current standards of the hospitals.

Accreditation is a process of review that allows healthcare organizations to demonstrate their ability to meet regulatory requirements and standards established by a recognized accreditation organization. It assesses the quality and operational systems in place within the facility. To further define, it is a "self-assessment and external peer assessment process used by health care organizations to accurately assess their level of performance in relation to established standards and to implement ways to continuously improve".[3] The various standards of accreditation are based on the principles of quality assurance, evidence based practice, medical ethics and prevention of medical error.The various objectives of accreditation are[3]:

1. Enhanced health systems: integrating and involving hospitals as an active component of the health care network.
2. Continuous quality improvement: using the accreditation process to bring about changes in practice that will improve the quality of care for patients.
3. Informed decision-making: providing data on the quality of health care that various stakeholders, policy-makers, managers, clinicians and the public can use to guide their decisions.
4. Improved accountability and regulation: making health care organizations accountable to statutory or other agencies, such as professional bodies, government, patient groups and society at large

Health care accreditation can be done both by national and international agencies.[3]

International Healthcare Accreditation Bodies:

1. **ISQua (International Society for Quality in Health Care):** an umbrella organization for organizations seeking international healthcare accreditation ISQua is a small non-profit limited company withmembers in over 70 countries. India becomes 12th nation to join ISQua.

2. **ISO (International Organization for Standardization) 9001 – 2015(applicable to healthcare organizations):** It does not prescribe any standards ofits own. The organizations having an effective quality management system and infrastructurefor providing quality services as well as for continuous quality improvement, are issued ISOcertification.

3. **Joint Commission on Accreditation of Healthcare Organizations (JCAHO):** It is the oldest and pioneer organization who started the hospital accreditation program in USA.

4. **Joint Commission International (JCI):** JCI accreditation of hospitals was started by JCAHO in the year 2002 with the purpose of accreditation of hospitals across the globe.

Healthcare Accreditation Bodies in India:

1. **CRISIL RATING of Hospitals / Nursing Homes (Credit Rating Information Services of India Ltd.):** provides ratings, research and risk and policy advisory services. It's grading of healthcare institutions is an opinion on the relative quality of healthcare delivered by the institutions to its patients. The grading scale has two components –The Hospital classification and the hospital's service quality grading within that classification on a four-point scale (Grade A – Good quality, Grade B – Good but lower than Grade A quality, Grade C – Average quality, Grade D – Poor quality).

2. **ICHA (Indian Confederation for Healthcare Accreditation)** is the mechanism created in 2002 and established as a not for profit organization of the companies act in 2004. ICHA is an autonomous body, globally recognized most optimal and credible platform.

3. **Quality Council of India, an autonomous body, and its constituent National Accreditation Board for Hospitals and Healthcare providers (NABH)** is the leading accreditation body in India. QCI works under the guidance of Ministry of Commerce. NABH as a constituent of QCI was established in 2006.[4] NABH is an institutional member of the ISQua and the approval of ISQua authenticates that NABH standards are in consonance with the global benchmarks set by ISQua. The first edition of standards was released in 2006 and after that the standards has been revised every 3 years. Currently the 4th edition of NABH standards, released in December 2015 is in use.[5] Regardless of ownership, legal status, size and degree of independence it provides accreditation to hospitals in a non-discriminatory manner. The applicant facility must have conducted internal audit against NABH standards after implementing for at least 3 months.[4]

NABH is structured such that:

1. It catersto much desired needs of the consumers and to set benchmarks for progress of health industry.
2. To be apex national healthcare accreditation and quality improvement body, functioning at par with global benchmarks.
3. To operate accreditation and allied programs in collaboration with stakeholders focusing on patient safety and quality of healthcare based up on national/international standards, through process of self and external evaluation.

National Accreditation Board for Testing & Calibration Laboratories (NABL)

Similar to the hospitals, laboratories, blood banks/ blood centers are an integral part of health care system. NABL is an accreditation body for Laboratories in India working under the parent body of Quality Council of India to recognize, provide technical skills and reference material so as to have uniform International standards. In the field of Medical Testing laboratories accreditation is granted in Clinical Biochemistry, Clinical Pathology, Haematology & Immunohaematology, Microbiology & Serology, Histopathology, Cytopathology, Genetics, Nuclear Medicine (In-vitro tests only) disciplines.[6] Accreditation of Blood banks/ Blood centres and Blood Transfusion services through NABH strives to improve the quality and safety of collecting, processing, testing, transfusion and distribution of blood and blood products including guidelines set by National AIDS Control Organization (NACO)[4].

Ensuring quality is a critical component of high-performing health systems. Having access to health care is not enough: patients who enter the health care system—whether a clinic, a hospital, or another venue need to be confident that they will receive care that is safe, effective, and consistent with the latest clinical evidence. The primary goal of the accreditation is to ensure that the hospitals not only perform evidence based practices but also give importance to access, affordability, efficiency, quality and effectiveness of healthcare.[7] Accreditation fills the gaps or removes the areas of deficiency and ultimately establishes optimum standards, professional accountability and clinical excellence. Even the Government has acknowledged that accreditation should be performed by a way of independent assessment programmes and with incentives both for secondary and tertiary level of hospitals to ensure patient safety and quality of care. Variety of benefits can be availed by the healthcare organization on being certified by NABH. The biggest beneficiaries are the patients, since it ensures that the accredited healthcare organization practices and delivers continuous quality services by the credential medical staff and also functions in the best interests of all patient's. As accreditation ensures continuous learning, leadership, good working environment and ownership of clinical process, the hospital staff feels more satisfied and contented at work. It provides an opportunity to get empanelled by various insurance

companies and other third parties. Lastly, it provides access to reliable and certified information on facilities, infrastructure and level of care.

Over the past few decades, accreditation has been gaining traction around the world. As global health care leaders increasingly focus on improving quality of health systems, accreditation has been considered a valuable tool. However, implementation of accreditation country-wide in India has not been possible. It is quite evident that many regulations made by the government are not followed in most states and hence the quality of healthcare remains poor and unattended.[8]

Challenges in Implementing Hospital Accreditation:

A. Program Challenges: related to outside of a healthcare organization

i. Need for a legal framework regarding accreditation bodies - Since accreditation is voluntary, it challenges the medical regulations laid down by the government both at state and central level.

ii. financial cost of sustainable accreditation programs

iii. need of health care professional

B. Organizational Challenges: related inside healthcare organization

I. **Human Resource:** Management and Organization, Knowledge, skills and commitment of hospital managers. Institutionalizing improved quality of care through accreditation requires more than a technical approach Failure to change the behavior and attitudes of people and organizations is the commonest cause of ineffective quality initiatives.

II. **Financial and Facilities Resources**
Sustained improvements often require a change in attitude and acquisition of a sense of ownership with regard to the quality of services

Conclusion

Accreditation is essential in transforming the healthcare scenario and helps healthcare organizations to establish objective systems aimed at patient safety and quality care. It is a transparent system of control over the accredited hospital which assures that the hospital will constantly fulfill the accreditation criteria. The on-site survey of the hospital and staff by the experienced accreditation assessment team encourages them to establish educational and performance improvement goals. The best part is that it gives the opportunity to the patients to give a feedback on the services they availed during their stay in the hospital and also to complain if they were dissatisfied. Finally it ensures that hospitals, whether public or private, national or expatriate, play there expected roles in national health system. Establishment and implementation of accreditation programs need empowerment of hospitalsin terms of resources and knowledge along with development and growth in determinants ofquality in terms of structure, process and outcome of the services.

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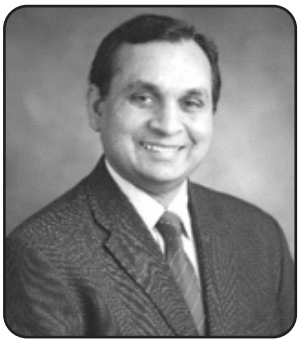
" Do the best you can until you know better.
Then when you know better, do better. "
Maya Angelou

Shri R J Kinarivala Research Oration Award, Year - 2018



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Targeting Pancreatic Tumor Microenvironment for Effective Pancreatic Cancer Treatment

Pancreatic cancer (PanCa) management is exceptionally difficult due to the extremely poor response to available therapeutic modalities and lack of effective therapeutic strategies. Highly desmoplastic (excessive fibrosis and extracellular matrix deposition) microenvironment in pancreatic tumor causes suboptimal drug delivery and increases chemo-resistance. In addition to tumor cells, presence of stromal components such as tumor associated fibroblasts (TAFs), pancreatic stellate cells (PSCs), cancer stem cells (CSCs) and tumor associated macrophages (TAMs) also play a pivotal role in induction, progression and metastasis of PanCa. At the onset of cancer induction and progression various oncogenic signaling molecules such as Mucin 13 (MUC13), KRas, NF-κB, and Sonic Hedgehog (SHH) play critical roles. In response to aberrant expression of these oncogenic molecules, cancer cells and stromal cells secrete various growth factors which are involved in reciprocal cross-talk in between tumor and stromal cells. This creates desmoplastic tumor microenvironment (TME) to facilitate PanCaprogression and metastasis. Thus, targeting components of TME along with oncogenic signaling pathways by non-toxic agents/ drugs will be effective therapeutic approach to combat this lethal disease.

In this talk, we will discuss how components of pancreatic TME and oncogenic signaling pathways play an important role in PanCa progression and metastasis. We will also discuss new strategy and molecular mechanisms to suppress components of pancreatic TME by non-toxic nutraceuticals. Our lab has identified novel nutraceuticals (curcumin, α-Mangostin, and plumbagin) which inhibit expression of fibroblast cells marker (α-SMA, and CYGB) and oncogenic CXCL12/CXCR4/Shh signaling pathways in human TAFs and PanCa cells. Moreover, we have developed novel nano-formulations of these nutraceuticals which show high significant therapeutic and chemosensitization potential in orthotopic xenograft mouse model involving co-injection of PanCa cells along with TAFs. In, addition these agents also inhibit the growth of pancreatic CSCs via targeting CSCs marker (Nanog and CD44). These nutraceuticals could be a potential therapeutic modality in near future for the prevention and treatment of human PanCa.

" Persistence, perseverance, and continuous improvement are the ingredients for forming a successful person. "

Debasish Mridha

Clinical Significance of Wnt Acyltransferase - Porcupine in Breast Cancer

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Summary

Porcupine (Porcn) protein plays a crucial role for secretion and function of Wnt signaling molecules and thereby in Wnt-induced cell signaling, which further stimulates the expression of diverse cancer-related genes resulting in development of various cancers, including breast cancer. Hence, the present study aimed to investigate the expression of Porcn protein in patients with primary breast carcinoma and explore their relation with clinico-pathological parameters as well as the prognostic significance. The study comprised of 160 breast cancer patients who underwent surgery as the primary treatment. The protein expression of Porcn was detected by immunohistochemical staining and analyzed using H-score method. Statistical analysis was carried out using SPSS and $p \leq 0.05$ were considered significant. Porcn protein was detected in 96% (153/160) of breast cancer patients with an over expression observed in 46% (73/160) of breast cancer patients. The correlation of Porcn protein with traditional clinico-pathological parameters of breast cancer revealed that the expression was significantly higher in Her2 negative patients (54%, 49/91) as compared to Her2 positive patients (35%, 24/69; $\chi^2=5.749$, r=-0.190, p=0.016); while a trend of higher incidence was observed in patients with T1+T2 tumor size (48%, 65/134) as compared to those with T3+T4 tumor size (31%, 8/26; $\chi^2=2.762$, r=-0.131, p=0.098). However, no other significant associations were observed with rest of the breast cancer characteristics. In addition, Porcn protein failed to emerge as a significant prognosticator in breast cancer patients. Porcn protein was detected in substantial number of breast cancer patients indicating its role in malignant development. However, further studies in more number of patients are warranted for a conclusive finding.

Keywords: Wnt signaling, immunohistochemistry, breast cancer

Introduction

Secreted Wnt proteins activate signal transduction pathways which are crucial in regulating a multitude of developmental and homeostatic processes in embryos and in adults.[1,2] Wnt proteins signal through both β-catenin dependent and β-catenin independent pathways. Aberrant activation of Wnt signaling is proposed to be causal in a subset of cancers due to over expression in either upstream or downstream components.[3, 4] Thus, Wnt driven cancers can be targeted at several steps in the pathway.[5,6] One approach is to target the secretion of all Wnts by inhibiting the enzymatic activity of a multi-pass integral membrane-bound O-acyl transferase (MBOAT) Porcupine (Porcn). Porcn is essential for post-translational modification of all Wnt proteins to enable their transport, secretion and activity.[7]

Porcn catalyzes the acylation of the serine residue of Wnt required for its anchoring function in cellular membranes by inserting into the lipid bilayer. Secondly, Porcn also catalyzes palmitoylation of cysteine residue of Wnts necessary for ability of Wnts to interact with Fzd or other receptors.[7,8] Thus the post-translational lipid-modification is essentially required for trafficking through the intracellular secretory pathway, release from cell membranes and the extracellular transport.[9] Moreover, the dual lipidation of Wnts by Porcn contribute to its hydrophobic nature and could be addressed as lipidation for signaling activity.[10,11] Hence, Porcn is required for the secretion of functional Wnt in diverse organisms.

However, data regarding Porcn activity is conflicting. In vivo studies have shown that inhibition of Porcn leads to developmental disorders, most notably Goltz Syndrome which causes focal dermal hypoplasia.[12] Conversely, overactive Porcn results in cancerous cell growth.[13] Further, inhibition of Porcn has been found to be an effective strategy for broadly suppressing Wnt signaling and thus hold potential in regenerative medicine and anticancer applications.[14] Moreover, apart from Porcn mRNA studies, there is a single study by Bonne et al that has reported Porcn protein expression by immunohistochemistry (IHC) in ovarian cancer patients.[15] Hence, little is known with regard to Porcn protein expression by IHC in human cancers including breast cancer. Moreover, as Wnt-induced cell signaling stimulates the expression of various cancer-related genes, some gene expressions might also be regulated by the level of Porcn.[16] Therefore, to investigate the significance of Porcn in human breast cancer, current study examined the Porcn protein expression, correlated it with traditional clinico-pathological variables and analyzed its prognostic role in breast cancer patients.

Materials and Method

Patients:

A total of 160 untreated histologically confirmed breast cancer patients with Invasive Ductal Carcinoma (IDC) type registered at Gujarat Cancer & Research Institute from March 2014 to December 2015 were enrolled. The study was approved by the

Table 1: Clinico-pathological characteristics of Breast Cancer patients (N=160)

Variables	N (%)
Total patients	160 (100)
Age (years)	≤
≤50	81 (51)
>50	79 (49)
Menopausal status	
Pre-menopause	56 (35)
Post-menopause	104 (65)
Tumour size	
T1 (≤20 mm)	21 (13)
T2 (20-50 mm)	113 (71)
T3 (>50 mm)	17 (11)
T4 (Extension to chest wall and/or skin)	09 (05)
Nodal status	
Negative	65 (41)
Positive	95 (59)
TNM stage	
I	12 (08)
II	86 (54)
III	61 (38)
IV	1 (6)
Tumor grade	
Grade 1	13 (8)
Grade 2	103 (64)
Grade 3	44 (28)
ER	
Negative	72 (45)
Positive	88 (55)
PR	
Negative	100 (62)
Positive	60 (38)
Her2	
Negative	91 (57)
Positive	69 (43)
Molecular subtype	
Luminal A	52 (33)
Luminal B	36 (22)
Her2-positive	35 (22)
TNBC	37 (23)
Treatment administered	
S	11 (7)
S+CT	45 (28)
S+CT+RT	27 (17)
S+CT+HT	35 (22)
S+CT+RT+HT	42 (26)

S=Surgery; CT=Chemotherapy; RT= Radiotherapy; HT= Hormonal therapy

Institute's Ethics Committee Board and written consent forms were obtained from all the patients prior to treatment administration. Detailed clinical and pathological history of the patients [age, tumor-node-metastasis (TNM) stage, histopathological findings, ER, PR, Her2 status, treatment given, etc.] was obtained from the case files maintained at the Medical Record Department of our institute. All patients underwent surgery and adjuvant treatment decision based on molecular subtypes of breast cancer patients was done by clinicians of the institute. The clinico-pathological characteristics of the enrolled patients are enlisted in Table 1. Complete follow-up details of 69% (111/160) patients were obtained, who were included in overall survival (OS) analysis. Amongst these, 3% (2/111) patients had persistent disease and hence only 68% (109/160) patients were included for the analysis of relapse free survival (RFS).

Immunohistochemistry:

Porcn protein expression was studied immunohistochemically using formalin-fixed paraffin embedded tissue blocks retrieved from the tissue repository of our institute's Pathology Department. The blocks were cut into 4 μm sections and mounted on 3-amino propyl triethoxy silane (APES)-coated slides. The staining was performed using HRP/DAB (ABC) Detection IHC kit (Abcam, Cambridge, UK) according to manufacturer's protocol. Briefly, antigen retrieval treatment was given by heating the sections in 10 mM sodium citrate buffer (pH-6.0) in a pressure cooker. Then after, sections were incubated overnight at 40 C with rabbit polyclonal primary antibodiy for Porcn procured commercially (HPA049215, Sigma-Aldrich, USA) at a dilution of 1:100. The stained sections were mounted with DPX and observed under the light microscope. Sections with intense staining for Porcn were used as positive control, whereas negative control was obtained by omission of primary antibody.

Assessment of Porcn expression:

The stained sections were evaluated independently by semi-quantitative histoscore (H-score) method on the basis of staining intensity and percentage of positive cells. The staining intensity was scored on a scale of 0-3 where 0 indicated no staining obtained, 1+ for weakly stained cells, 2+ for moderately stained cells and 3+ for strong intense staining of the cells. The extent of staining was expressed by percentage of positive cells (0-100%) by 10% intervals. The final H-score was calculated by multiplying the staining positivity score with the staining intensity score of each section, ranging from 0 to 300. The mean H-score value of Porcn was 105 (range of 0 to 255) and this was used as a cut-off value to subgroup the patients into low (≤105 H-score) and high (>105 H-score) expression groups, respectively.

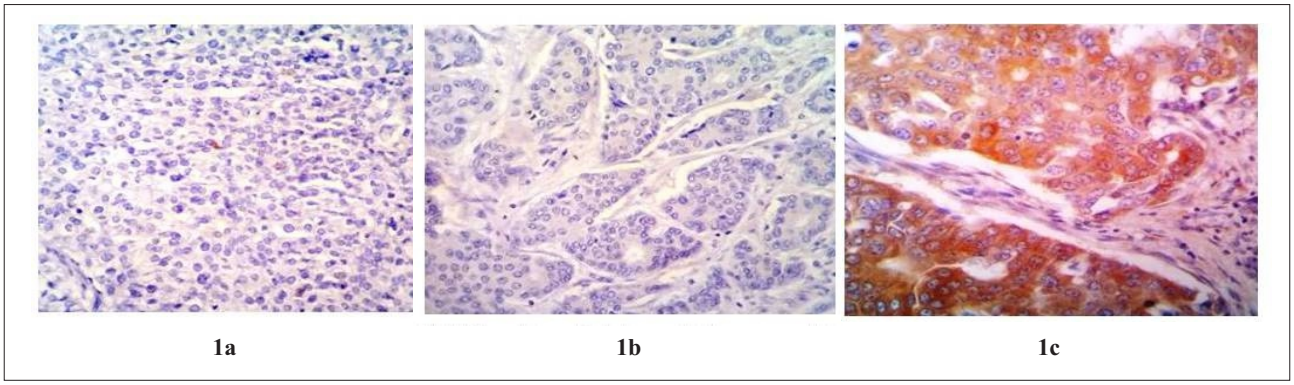

Figure 1: Representative immunohistochemical staining pattern of Porcn in Breast Cancer patients **Figure 1a:** Negative control for Porcn staining **Figure 1b:** Negative staining of Porcn protein **Figure 1c:** Cytoplasmic staining of Porcn protein in breast tumors

Statistical Analysis:

The data was analyzed statistically using SPSS Inc. version 23 software. The correlation between the expression of Porcn protein and various clinico-pathological characteristics of breast cancer patients was determined by two-tailed chi square test ($\chi 2$) and spearman's correlation. Survival analysis was performed using Kaplan-Meier survival function and the differences in survival were tested for statistical significance using log-rank statistic. $p \leq 0.05$ was considered to be statistically significant.

Results

Incidence of Porcupine protein expression in breast cancer patients

Porcn protein was detected solely in the cytoplasm of tumor cells in 96% (153/160) of breast cancer patients. Figure 1 shows the representative photomicrographs for Porcn staining. The staining intensity of 1+, 2+ and 3+ was noted in 26% (41/160), 38% (61/160) and 32% (51/160), respectively. According to the cut-off value as described previously, 54% (87/160) of patients exhibited low Porcn expression and 46% (73/160) patients exhibited high Porcn expression.

Correlation of Porcn protein with clinico-pathological features of breast cancer patients

The correlation of Porcn protein with various clinico-pathological parameters of breast cancer patients such as age, menopausal status, tumor size, nodal status, TNM stage, BR score, lymphatic permeation, vascular permeation, perineural extension and perinodal extension showed no significant association of Porcn protein expression with any of the mentioned parameters. However, when the patients were subgrouped on the basis of tumor size as T1+T2 and T3+T4, a trend of higher Porcn expression was observed in patients with T1+T2 tumor size (48%, 65/134) as compared to those with T3+T4 tumor size (31%, 8/26; χ^2=2.762, r=-0.131, p=0.098) (Table 2).

Table 2: Correlation of Porcn expression with clinico-pathological features

Characteristics	N	Porcn protein expression		χ2	R	p
		Low N (%)	High N (%)			
Age (years)						
≤50	81	41(51)	40(49)	0.934	-0.076	0.337
>50	79	46(58)	33(42)			
Menopausal status						
Pre-menopausal	56	29(52)	27(48)	0.233	-0.038	0.632
Post-menopausal	104	58(56)	46(44)			
Tumor size						
T1	21	12(57)	9(43)			
T2	113	57(50)	56(50)	4.120	2.762	-0.072
T3	17	13(76)	4(24)			
T4	09	5(56)	4(44)			
T1 + T2	134	69(52)	65(48)	-0.131	0.364	0.098
T3 + T4	26	18(69)	08(31)			
Nodal status						
Negative	65	34(52)	31(48)	0.189	-0.034	0.660
Positive	95	53(56)	42(44)			
TNM stage						
I	12	5(42)	7(58)			
II	86	45(52)	41(48)	2.296	-0.101	0.203
III	62	37(60)	25(40)			
IV	01	1(100)	00(00)			
Early (I+II)	99	51(52)	48(48)	0.856	-0.073	0.358
Advanced (III+IV)	61	36(59)	25(41)			
BR score						
Low (BR3-BR5)	13	5(38)	8(62)			
Intermediate (BR6-BR7)	103	56(54)	47(46)	1.721	-0.088	0.270
High (BR8-BR9)	44	26(59)	18(41)			
Low+Intermediate	116	61(53)	55(47)	0.544	-0.058	0.464
High	44	26(59)	18(41)			
Lymphatic permeation						
Absent	84	41(49)	43(51)	2.208	-0.117	0.139
Present	76	46(40)	30(40)			
Vascular permeation						
Absent	140	74(53)	66(47)	1.040	-0.081	0.311
Present	20	13(65)	7(35)			
Perineural invasion						
Absent	147	80(54)	67(46)	0.002	+0.003	0.968
Present	13	7(54)	6(46)			
Perinodal extension						
Absent	94	50(53)	44(47)	0.129	-0.028	0.722
Present	66	37(56)	29(44)			

Table 3: Correlation of Porcn expression with ER, PR, Her2 expression and molecular subtypes

Characteristics	N	Porcn protein expression		χ2	R	p
		Low N (%)	High N (%)			
ER						
Negative	72	43(60)	29(40)	1.509	+0.097	0.222
Positive	88	44(50)	44(50)			
PR						
Negative	100	56(56)	44(44)	0.284	+0.042	0.597
Positive	60	31(52)	29(48)			
Her2						
Negative	91	42(46)	49(54)	5.749	-0.190	0.016
Positive	69	45(65)	24(35)			
Molecular subtypes						
Luminal A	52	21(40)	31(13)	8.396	-0.117	0.140
Luminal B	36	23(64)	36(60)			
Her2 positive	35	24(69)	11(31)			
TNBC	37	19(51)	18(49)			

Table 4: Univariate survival analysis for RFS and OS in relation to Porcn protein expression in breast cancer patients

Porcn protein expression	RFS (N=109)			OS (N=111)		
	N	No recurrence N (%)	Recurrence N (%)	N	Alive N (%)	Dead N (%)
Low	64	49(77)	15(23)	65	50(77)	15(23)
High	45	35(78)	10(22)	46	40(87)	06(13)
	Log rank= 0.049, df= 1, p= 0.825			Log rank= 1.748, df=1, p= 0.186		

Correlation of Porcn protein expression with ER, PR, Her2 expression and molecular subtypes of breast cancer patients

As shown in Table 3, a significant preponderance of Porcn expression was found in Her2 negative patients (54%, 49/91) as compared to Her2 positive patients (35%, 24/69; χ^2=5.749, r=-0.190, p=0.016). However, no significant association of Porcn expression was observed with ER or PR status. In addition, the patients were subcategorized according to molecular subtypes based on ER, PR and Her2 status, where the incidence of Porcn expression was higher in Luminal A (60%, 31/52), followed by TNBC (49%, 18/37), Luminal B (36%, 13/36) and Her2 positive (31%, 11/35), although the difference was not statistically significant (χ^2=8.396, r=-0.117, p=0.140).

Survival outcome of breast cancer patients in relation to Porcn protein expression

In total patients with breast carcinoma, univariate analysis showed that Porcn protein failed to predict RFS and OS (RFS: Log rank= 0.049, df= 1, p= 0.825; OS: Log-rank = 1.748, df = 1, p= 0.186). Further, survival analysis was performed in patient's subgroups according to lymph node status, disease stage and BR score. However, Porcn protein expression did not emerge as a significant prognosticator in any of the patient subgroups (data not shown).

Discussion

An altered regulation of the proteins involved in Wnt signaling pathway is linked to the development of a wide range of human cancers, in particular breast carcinoma.[17,18] Increased activity of the Wnt/β-catenin pathway can result from upregulation at different steps in the signaling pathway: overexpression of the cell surface receptors LRP5, LRP6, and Frizzled or increased activity of the Wnt target genes survivin, cyclin D1, Axin2, and c-myc.[19-21] The endoplasmic reticulum-resident Ô-acyltransferase Porcupine is one such putative enzyme that catalyzes the lipid modification of Wnt proteins. This acylation is necessary for the Wnt secretion via Golgi as well as it contributes to the binding of Wnt to its surface receptors and, therefore, Wnt-induced cell signaling.[22-25] Hence, Porcn is a crucial component necessary for Wnt ligand transport, secretion and activity and has been identified as a potential target to inhibit Wnt/β-catenin signaling.[26] Moreover, studies by Chen et al and Mo et al have reported the role of Porcn mRNA over expression in human lung and gastric cancer, respectively.[27,28] Therefore, current study investigated Porcn protein expression, correlated it with traditional clinico-pathological variables and evaluated its prognostic role in breast cancer patients using IHC technique.

In present study, protein expression of Porcn was found to be localized in the cytoplasm of breast tumor cells. Similarly, Bonne et al also observed cytoplasmic Porcn expression in ovarian cancer samples.[15] In addition, Porcn immunoreactivity in present study was observed in 96% of patients; and on the basis of mean H-score value as cut-off, high expression of Porcn was found in 46% patients. Elevated levels of PPN/MG61 (orthologue of Porcn) mRNA expression are reported in human lung cancer cell lines as well as in human primary lung cancer tissue samples (22 out of 24), when compared to their matched normal lung tissues.[27] Similarly, the mRNA levels are reported to be over expressed in 62.5% of gastric cancer tissue samples compared with adjacent normal tissue samples. The authors also showed significant overexpression in gastric cancer cell line compared to normal tissues, implying the importance of PPN in gastric cancer.[28] Also, the mRNA expression of Porcn is found to be present in several breast cancer cell lines;[29] suggesting the potential clinical implications of Porcn in cancer cells, whereby it may promote post-translational modification of the oncogenic Wnt molecules and contributes to aberrant activation of the Wnt signaling pathway in cancer development.

Moreover, current study observed a trend of higher Porcn protein expression in patients with smaller tumor size (T1+T2) as compared to those with larger tumor size (T3+T4). However, Covey et al (2012) has shown a critical role of Porcn in cell proliferation in xenografts, where the knockdown of Porcn leads to decrease in Wnt activity and thereby development of significantly smaller and lighter tumors in mice. Additionally, high Porcn was significantly associated with Her2 negative status of the patients enrolled in present study. Moreover, no other significant associations of Porcn protein expression was observed with rest of the parameters of breast cancer patients. Further, survival analysis also showed no significant correlation of Porcn expression with RFS and OS in total patients or in any of their subgroups. However, Porcn protein is also involved in an alternative function, which is independent of acyltransferase activity and is rate-limiting for the cell proliferation and growth of transformed epithelial cells. Hence, moonlighting of Porcn performs additional Wnt-independent functions alongside their catalytic roles that promotes cancer cell proliferation and regulates expression profiles of a distinct set of genes other than Wnt pathway using the same protein domain.[29]

Moreover, there are small molecule inhibitors of Porcn being developed that are highly effective in preventing Wnt secretion and thereby therapeutically target Wnt-dependent cancer cells.[30] However, downstream activation of Wnt/β-catenin signaling is often due to APC or β-catenin mutations, which might render them insensitive to Porcn inhibition.[31] Hence, the above observations and literature survey suggests that Porcn may be a novel marker for cancer, especially human lung cancer and that post-translational modification of the Wnt signal molecules by Porcn may be important for the function of Wnt pathway in lung cancer and gastric cancer. [27,28]

Conclusion

The present study has detected the presence of Porcn protein in breast tumor cells immunohistochemically. Moreover, the protein is over expressed in substantial number of patients with a significant high expression in Her2 negative patients. Although, the association of Porcn protein with survival outcome failed to reach the level of significance, further studies are required to evaluate the prognostic role of Porcn protein expression in large number of breast cancer patients.

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" When you reach the top, keep ascending,
otherwise you start descending. "
Lincoln Patz

Clinical Relevance of JAK2V617F Mutation with Lactate Dehydrogenase Activity in Patients with Myeloproliferative Diseases

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Summary

Clinical significance of the JAK2V617F mutation in patients with a myeloproliferative disease has been the target of intensive research in recent years. There is a need for development of newer molecular parameters for detection of myeloproliferative diseases. Therefore, aim of the present study was to identify the effect of JAK2V617F mutation on clinical phenotypes in patients with myeloproliferative diseases. Eighty eight patients with myeloproliferative diseases were included in the present study. Blood samples were collected by venipuncture from the subjects and DNA isolation was carried out. Real-Time Polymerase Chain Reaction (RT-PCR) method was carried out for analysis of JAK2V617F mutation status. Lactate Dehydrogenase (LDH) and routine hematological parameters were analyzed by autoanalyser. Statistical analysis was carried out using SPSS statistical software (version 15). JAK2V617F mutation was detected in 45.5% of patients with myeloproliferative diseases. In which 64.3%, 50.0% and 68.0% positivity of JAK2V617F mutation showed in polycythemia (PV), essential thrombocythemia (ET) and primary myelofibrosis(PMF) respectively. Present study was observed that mean LDH activity were higher in patients with PMF compared to ET and PV. Furthermore, it was also noted that patients with JAK2V617F mutation had higher mean LDH activity as compared to patients without JAK2V617F mutation. Concluding remarks from present study is that the integration of laboratory testing for JAK2V617F mutation and LDH activity is necessary to improve the diagnosis and screening of the myeloproliferative diseases. In Furtherance, isoforms of LDH activity would provide better understanding for correlation of JAK2V617F mutation with LDH activity in myeloproliferative diseases.

Keywords: Essential Thrombocythemia, JAK2V617F Mutation, Lactate Dehydrogenase, Myeloproliferative Diseases, Polycythemia Vera, Primary Myelofibrosis

Introduction

Myeloproliferative diseases (MPDs) are clonal disorders characterized by excessive production of mature blood cells.[1] in the most recent World Health Organization (WHO) classification of hematologic malignancies, this group of diseases was renamed from "myeloproliferative diseases" to "myeloproliferative neoplasms". This reflects the underlying clonal genetic changes that are a salient feature of this group of disease.[2] All myeloproliferative neoplasm (MPNs) are clonal disorders with an initial hit in the HSCs resulting in an excessive production of blood cells in some combination in the bone marrow, peripheral blood, and body tissues because of hypersensitivity or independence from normal cytokine regulation.[3] In 1951, the hematologist William Dameshek was first introduced concept of myeloproliferative diseases and also described four different diseases with clinical and biologic similarities: polycythemia vera (PV), essential thrombocythemia (ET), primary myelofibrosis (PMF).[3] Some MPNs are the result of a genetic event leading to the constitutive activation of a tyrosine kinase that mimics the intracellular signalling pathways induced by hematopoietic growth factors. The risk of thrombosis is increased in some types of MPN. [3,5-6]

The most commonly recognized mutation in the remainder of the Philadelphia chromosome-negative MPNs is Janus kinas 2 (JAK2V617F), which is located on chromosome 9p24.[7] This mutation substitutes phenylalanine for valine at position 617 in the JH2 domain (Val617Phe, V617F) of exon 14, leading to constitutive activation of the JAK-STAT and other pathways resulting in uncontrolled cell growth. In the western population, this mutation is found in almost all PV cases and nearly half of PMF and ET cases.[8] various studies have recommended that analysis of JAK2V617F allelic burden is useful for discriminating between the different MPNs subtypes.[9]

Characterization of a malignant disease by molecular marker is expected to improve understanding of variations in the clinical course of individual patient and help to estimate their prognosis. Moreover, molecular marker that is linked to malignant transformation may provide a non-surgical therapeutic approach by targeting these molecules. The body of literature on molecular markers of malignancy in general is huge, but there is fewer reports have been shown association of JAK2V617F mutation with LDH activity in myeloproliferative diseases. Therefore, the aim of the study was to

Table 1: Clinical characteristics of patients with myeloproliferative diseases

Characteristics	No. of Patients
Gender	
Male	44
Female	44
Age (year)	
Range	17-87
Median	38
Diagnosis N	
PV	14
ET	22
PMF	25

Table 2: Frequency of JAK2V617F mutation in different types of myeloproliferative diseases

	JAK2V617F negative patients N (%)	JAK2V617F positive patients (%)
PMF	8(32.0)	17 (68.0)
ET	11 (50.0)	11 (50.0)
PV	5 (35.7)	9 (64.3)

Table 3: Correlation of hematological parameter with JAK2V617F mutation status in myeloproliferation diseases

	Negative JAK2V617F Mutation Status (Mean Values)	Positive JAK2V617F Mutation Status (Mean Values)
WBC count (×103/cmm)	19.42	35.79*
Hemoglobin (gm/dl)	11.09	11.26
Platelet count (×103/cmm)	454.71	558.71

*p=0.001 compared with negative status of JAK2V617F mutation

correlate JAK2V617F mutation with LDH activity and haematological parameters in myeloproliferative diseases.

Materials and Methods

The study was conducted in The Gujarat Cancer & Research Institute and prior consent was obtained from all the subjects to participate in the study. A total of eighty eight patients with myeloproliferative diseases were enrolled in the study, in which, fourteen cases were diagnosed with PV, twenty two cases as ET and twenty five cases as PMF. The patient group represented a median age of 38 years with an age range of 17 to 87 years (Table 1). Blood samples were collected for JAK2V617F mutation analysis. Genomic DNA from peripheral blood was extracted using QIAamp DNA blood Kit (Qiagen, Germany) as per manufacturer instructions.

Figure 1: Frequency of JAK2V617F mutatioNin myeloproliretaive diseases patients

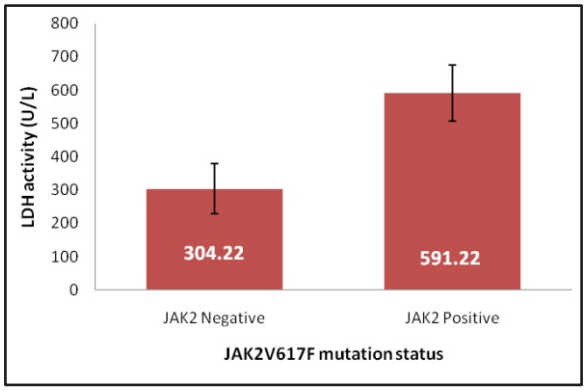

Figure 2: Correlation of mean LDH activity with JAK2V617F mutations status in myloproliferative patients

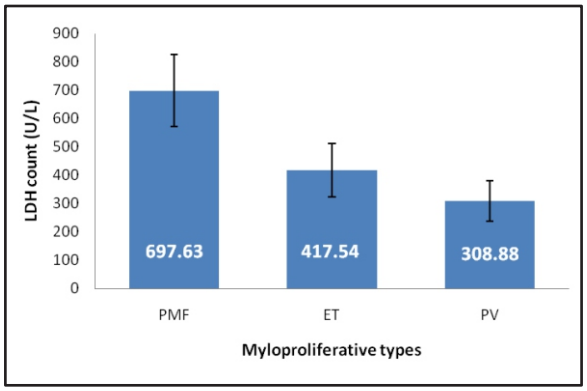

Figure 2: Correlation of mean LDH activity with JAK2V617F mutations status in myloproliferative patients

Further, JAK2V617F mutation were analysed from genomic DNA by real time PCR method. Routine haematological parameters and LDH activity were carried out by auto analyzer. Statistical analysis was performed using SPSS software version 15. Student's independent't' test was performed to analyze the significance between different groups.

Results:

JAK2V617F mutation status in patients with myeloproliferative diseases

PV, ET and PMF are different types of myeloproliferative diseases. Therefore, present study evaluates overall status of JAK2V617F mutations in myeloporlierative diseases. Figure 1 shows JAK2V617F mutation status in patients with myeloproliferative disease. Among these patients, 45.5% were JAK2V617F positive and 54.5% were JAK2V617F negative. It is clear from results that there was no difference in JAK2V617F mutation status of myloprolierative diseases. Present study also evaluated JAK2V617F mutation in myeloprolierative disease like PMF, ET and PV. Table 2 depicts the positivity and negativity of JAK2V617F mutation in PMF, ET and PV. It was observed that JAK2V617F allele burden was higher in PMF (68.0%) and PV (64.3%) patients as compared to the ET (50.0%).

Association of JAK2V617F status with hematological parameters in myeloproliferative diseases

Present study also observed association of hemoglobin, WBC and platelet counts with JAK2V617F mutations in myloproliferative diseases (Table 3). JAK2V617F positive patients with myeloproliferative diseases had significantly higher WBC counts as compared to JAK2V617F negative patients with myeloproliferative diseases. But there was no statically significant correlation of JAK2V617F mutation status with hemoglobin and platelet count in myeloproliferative diseases.

Correlation of JAK2V617F mutation status with LDH activity in myeloproliferative diseases

In present study, correlation of JAK2V617F mutation status with LDH activity in myeloproliferative diseases was also analysed. Figure 2 depicts correlation of JAK2V617F mutation status with LDH activity in myeloproliferative patients. Mean LDH activities in patients with positive and negative JAK2V617F mutation were 591.06 and 304.22 U/L, respectively. LDH activity was lower in patients with no JAK2V617F mutations as compared to patients with JAK2V617F mutations. Figure 3 depicts that LDH activity was higher in PMF patients as compared to patients with ET and PV. However, it was not statistically significant. Mean value of LDH activity in PMF, ET and PV were 139.90, 731.18 and 440.75 IU/L, respectively.

Discussion

Myeloproliferative diseases are currently increasing in general population and the incidence per year is approximately 0.55%. The annual incidence rate per 100,000 populations was 2-2.53% for PV and ET.10 The JAK2V617F mutation has a prevalence of 0.1-0.2% in the general population, but its clinical implications are still unknown for those individuals who are harboring the mutation without overt signs of a myeloproliferative disease.[11] The hallmark of myeloproliferative disease is over production of mature blood cells which initiate myeloproliferative diseases.[12] The impact of JAK2V617F mutation burden on a number of clinical parameters such as WBC counts, hemoglobin concentration, platelet counts and thrombosis especially for thrombotic events had been demonstrated in patients with myeloproliferative diseases.[13] In present study, JAK2V617F mutation was observed in 45.5% of myeloproliferative diseases. Similar results were also observed by Baxter et al[14] It was also observed that among all myeloproliferative diseases, 26.6% patients were PV, 36% patients were ET and 33.3% patients were PMF.[14]

It has been previously suggested that the JAK2V617F mutation in PV patients can be detected approximately in 95% of patients.[15] The JAK2V617F allele burden was significantly different among patients with PV and ET. Moreover the burden of JAK2V617F was highest in primary myelofibrosis (63.64%). In patients with PV, 50% of the patients showed JAK2V617F positive mutation. JAK2V617F mutation is found in approximately 55% of patients with ET, and these represents by World Health Organization diagnostic criterion. In present study, it was observed that about 50% patients with ET showed JAK2V617F positivity. Similar results were found in Chinese patients suggested by Zhao et al[16] Currently, JAK2V617F mutation is considered as a genetic diagnostic criterion for myeloproliferative diseases.

Numerous studies indicate that the JAK2V617F allele has been variably associated with higher indices of erythropoiesis, decreased platelet count, older age, and longer duration of disease in PMF.[17-18] Present study observed that platelet count was decreased in PMF patients than the patients with ET and PV. The platelet count was significantly higher in patients with ET and PV. Additionally, patients with WBC count had higher proportion of JAK2V617F mutation positive patient's burden than negative.

A number of studies suggested leukocytosis as a novel marker for vascular risk.[19-20] In present study, neither WBC counts nor JAK2V617F mutation burden appeared to be a risk factor for thrombosis in patients with PV, ET and PMF patients. V617F allele burden progressively increases alongside changes in phenotype, with lower allele burden inducing isolated thrombocytosis and higher levels being accompanied by increases in hemoglobin level, leukocytosis, and spleenomegaly. As expected, erythrocyte volume fraction increased during follow up in individuals with a myeloproliferative disease. Lower JAK2V617F allele burden has been reported in women with MPN compared with men. Several

studies reported that JAK2V617F allele burden was higher in PV than that in ET. [21]

In a study by Zhao et al., it was observed that PV patients with leukocytes had higher JAK2V617F allele burden and in ET with high hemoglobin level, the mean JAK2V617F mutation burden was more than those without elevated hemoglobin level.16 Controversial results were found in our study that higher leukocytes counts were found in PMF. LDH activity exceeded control level among individuals diagnosed with essential thrombocythemia; but present study had observed higher LDH activity in PMF patients. However, difference was observed in JAK2V617F mutation positive and negative patients. But present study also observed higher LDH activity in patients with myeloporlierative disease with positive JAK2V617F mutation as compared to patients with negative JAK2V617F mutation status. These results indicated significant association of LDH activity with frequency of JAK2V617F mutation in patients with myeloproliferative disease. It was indicated from present study that association of isoforms of LDH enzymes with JAK2V617F mutation would give better understanding for higher LDH activity in myeloproliferative diseases.

It can be concluded from the present study is that the detection of JAK2V617F allele burden is a simple and easily accepted in clinical set up. It was also observed that the clinical and hematological phenotypes of myeloproliferative diseases were associated with JAK2V617F mutation. JAK2V617F mutation was also associated with LDH activity. Therefore, the integration of laboratory testing for JAK2V617F mutation with LDH activity is necessary to improve the diagnosis and screening of myeloproliferative diseases In Furtherance, isoforms of LDH enzymes with JAK2V617F mutation would give better understanding of role of LDH activity in different types of myeloproliferative diseases.

Conflict of Interest: Nil

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" Practice the philosophy of continuous improvement.
Get a little bit better every single day. "
Brian Tracy

Effect of Palliative Care Interventions on Symptom Profile in Head Neck Cancers: A Prospective Observational Trial

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Summary

Head and Neck cancer patients often present with diversity of distressing physical and psychological symptoms, which significantly affect quality of their life. This study aims to assess effectiveness of palliative care interventions on symptom profile in Head and Neck cancer patients. This single centre prospective observational study was done on 173, adult patients with Head and Neck cancer, referred to Palliative Medicine outpatient department at a tertiary cancer hospital in India. Patients were regularly assessed as a part of routine protocol. Symptoms were assessed and compared by Edmonton symptoms assessment system at baseline which was considered day zero and at day seven. Palliative care was given in the form of symptomatic management and nursing care. Out of 173 patients, from 20 to 75 years of age with mean age of 48.15years, 130 were male and 43 were female. Most common symptoms as mean ± standard deviation on Edmonton symptoms assessment scale were pain(5.86±2.30), fatigue(4.42±2.45), loss of appetite (4.54±2.69) and insomnia(3.54±3.03) on day zero. After seven days with palliative intervention, greater number of patients experienced improvement in their symptom profile like pain(1.50±1.61) ($P<0.0001$), fatigue(2.34±1.97)($P < 0.0001$), loss of appetite(1.86±1.83)($P<0.0001$) and insomnia(1.24±2.02)($P< 0.0001$). Feeling of well being had statistically very significant improvement ($P<0.0001$). All other symptoms were having mild to moderate scores on ESAS scale. Patients with advanced Head and Neck cancer have a significant burden of symptom. A palliative care intervention significantly reduces the symptoms burden and thereby improve the quality of life of patients and care givers.

Key words: Head and neck cancer, Symptoms burden, Palliative care intervention

Introduction

Head and neck cancer (HNC) is the most prevalent and the most common cancer found in Indian population.[1] Standard treatment measures include surgery, radiotherapy and chemotherapy. Patients with HNC often present with spectrum of symptoms ranging from physical to spiritual issues.[2] Mixed type (Nociceptive and neuropathic) pain is seen in more than two third of patients. Changes in body images and involvement of nerves are responsible for severe pain and distress in such patients. This dramatically affects their physical, psychosocial functioning and thus quality of life. Previous studies showed positive effect of palliative care interventions in patients suffering from advanced cancers.[3] Hence, we decided to conduct an observational trial to see the effect of palliative care interventions on symptom profile in HNC patients at a tertiary cancer centre.

Material and Method

This single-institutional, prospective, questionnaire-based study was conducted after Institutional Review Board approval. Consecutive patients who were referred to palliative medicine outpatient department (OPD) over a period of three months from first April to thirty first June 2018 were enrolled in this study. Inclusion criteria for study were, age between 20 to 75 years, able to understand Hindi or Gujarati language, clinical diagnosis of advanced head and neck cancer (stage III or IV) and consenting to participate in study. Patients with any psychiatric illnessor refusing to participate were excluded from study.

Patients were assessed for their symptoms using Edmonton Symptom Assessment System (ESAS) at baseline which was considered day zero and at day seven of starting Palliative care intervention.

Palliative care was given in the form of Symptomatic management, counselling to develop copping skill with psychological support, generalised nursing care and diet counselling regarding semi solid or liquid diet and nasogastric tube feeding.

Pain treatment was given according to WHO step ladder guideline. Generalised nursing care was taught to patient and care giver, e.g. dressing of wound, nasogastric tube feeding and oral hygiene.

The ESAS tool

The ESAS is a ten-items symptom assessment questionnaire, where patients rate their symptoms from zero to ten on a visual analogue scale.[4] This questionnaire can be completed by the patient alone or with the assistance of a proxy. Although the reliability of the use of a proxy is questionable as many times the result is an assessment that underestimates patients' Quality of life (QOL). The assessed ESAS symptoms, that patient may be

experiencing include pain, fatigue, nausea, depression, anxiety, drowsiness, breathlessness, appetite, insomnia, and other problems. A score of zero corresponds to the absence of the symptom, and ten corresponds to the symptom being of the worst possible severity. Feeling of well being is more at score zero and worst at score ten.

Table 1: Demographic data

Characteristic	No of Patients
Study Duration	1st April to 31st July 2018
Total No of Patients	173
Age (Mean) years	48.152 (Range 20-75) <60 years – 136 >/=60 years – 37
Sex (M:F)	130:43
Education level <10th grade >10th grade	 150 23
Socioeconomic status Poor Middle Upper	 121 34 18

Table 2: Diagnosis of 173 patients

Diagnosis	No of Patients and Percentage (%)
Ca Tongue	59 (34.10)
Ca Buccal Mucosa	42 (24.27)
CaAlvelous	9 (5.20)
Ca Larynx	5 (2.89)
Ca Lip	3 (1.73)
CaMaxila	7 (4.04)
Ca Retro Molar Trigone	5 (2.89)
Ca Pyriform Fossa	9 (5.20)
Muo Neck	9 (5.20)
Ca Post Cricoid	5(2.89)
Tonsil	3(1.73)
Ca Parotid	6 (3.46)
Carcinoma with Unknown Primary	5(2.89)
Ca Hard Palate	4 (2.31)

Statistical Analysis

Demographic information was summarized through descriptive statistics. Mean scores were compared at day zero and at day seven using paired t test. p value of <0.05 was considered as statistically significant. Statistical analysis was done using Graph Pad Quick Calcs online calculator.

Results

A total of 173 patients with head and neck cancer were enrolled during period of three months. All patients filled ESAS at baseline day zero and at follow up on day seven. Range of patients' age was from 20 to 75 years with mean age of 48.15years. 130 patients were male and 43 were female.(table1). Majority of them were from poor socio-economical class and were nongraduated (Table 1)

Primary sites of cancer were, tongue (59),buccal mucosa (42), retromolar trigone (5),larynx (5), parotid (6), post cricoid (9),maxilla (5), pyriform fossa (9), tonsil (3), MUO Neck (9), alveolus

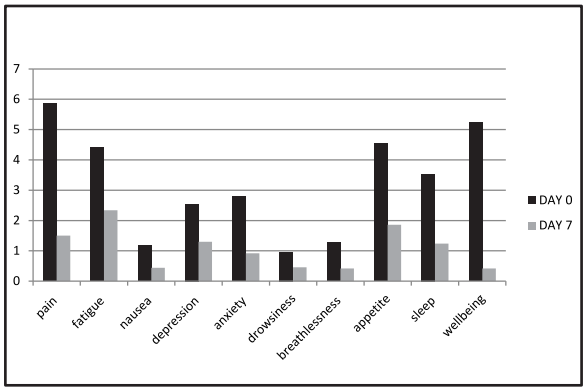

Figure 1: Graphical presentation of Mean values of different parameter according to ESAS, on day zero and on day seven after palliative intervention

Table 3: Symptoms – Mean values ± standard deviation and P value of different parameter according to ESAS, on day zero and on day seven after palliative intervention

Symptoms	No of patients having moderate to severe symptoms	Day 0	Day 7	P value
Pain	142	5.86±2.30	1.50±1.61	0.0001
Fatigue	68	4.42±2.45	2.34±1.97	0.0001
Nausea	21	1.18±2.48	0.44±1.30	0.645
Depression	38	2.54±2.62	1.30±1.88	0.0077
Anxiety	31	2.80±5.17	0.92±1.41	0.0148
Drowsiness	13	0.96±1.87	0.46±1.05	0.1032
Breathlessness	22	1.28±2.16	0.42±1.30	0.0175
Anorexia	87	4.54±2.69	1.86±1.83	0.0001
Other (sleep disturbance)	65	3.54±3.03	1.24±2.02	0.0001
Feeling of Wellbeing	113	5.24±2.25	0.42±0.91	0.0001

(9), lip (3) carcinoma of unknown primary (5) (Table2) at baseline, most prominent symptoms were pain and fatigue. Mean scores for these symptoms were 5.86±2.30 and 4.42±2.45 respectively on day zero and 1.50±1.61 (P <0.0001) and 2.34±1.97 (P <0.0001) on day seven after palliative interventions. Most of the patients complained about mixed type of pain, i.e., both nociceptive and neuropathic pain. Other symptoms those relatively scored high on ESAS were sleep disturbances, loss of appetite, depression and anxiety with a mean score of 3.54±3.03, 4.54±2.69, 2.54±2.62 and 2.80±5.17 respectively on day zero, and those also had significant improvement on day seven,i.e. 1.24±2.02 (P<0.0001), 1.86±1.83 (P<0.0001), 1.30±1.88 (P<0.0077) and 0.92±1.41 (P<0.0148).As there were good symptom control, feeling of wellbeing had statistically very significant improvement (P<0.0001).All other symptoms were having mild to moderate scores on ESAS scale(Table 3).

Four symptoms and feeling of wellbeing demonstrated statistically significant improvement at day seven. Some of the symptoms showed mild to moderate improvement. (Figure 1)

Discussion

The National Cancer Institute defines head and neck cancer as "cancer that arises in the head or neck region (in the nasal cavity, sinuses, lips, mouth, salivary glands, throat or larynx)". Most head and neck cancers are squamous cell carcinomas.[5] Globally it is ninth most common cancer and cause of cancer mortality.[6] and remains a potentially disfiguring disease.[7] Head and neck cancers are the most common cancers in developing countries.[1] Gujarat is one of the most affected states in India.[8] In our study Head and neck cancers are more common in males compared to females and same results have been given by Mohammad ShadabAlam and team in their study 'Epidemiological profile of head and neck cancer patients in Western Uttar Pradesh and analysis of distributions of risk factors in relation to site of tumor.[9]

This is mainly attributed to tobacco, areca nut, alcohol, etc. Poverty, illiteracy, presentation at advanced stage, lack of access to health care and poor treatment infrastructures are the major challenges in management of head and neck cancers.[9] Level of education is directly related to consumption of tobacco and related products. Use of tobacco is more popular in the developing countries.[10] It is more prevalent among men, rural population, illiterates, poor, and vulnerable section of the society.[11] Patients with advanced HNC often presents with numerous symptoms which include variety of physical symptoms and psychological issues and social problems. Common symptoms and signs observed in such patients are pain, oral mucositis, insomnia, fatigue, fungating wound, oral dryness, dysphasia, weight loss, communication difficulties, feeding difficulties, halitosis, loss of appetite and fatigue.[2] According to WHO, palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.[12] Palliative care takes a holistic approach. Treatment modalities which may be appropriate to palliative care include oncological and surgical approaches, drug management, psychological support, and complementary therapies. It is important to make effective decision in palliative care setting. Patient and family should have adequate information about disease status and prognosis. The team should not convey any unrealistic hope simply because the goal is not indefinite survival. Hope can be maintained accordingly to the patient's own goals whether they are physical (symptom relief), psychological (distress, fear of bleeding and unbearable pain in end of life) or social (desire to witness a family event).[13]

Pain is the most common symptom according to our study. Gellrich et al reported that 54% of oral cancer patients had "some type of pain".[14] the head and neck area is highly sensitive to pain due to rich nervous supply and the confinement of many anatomical structures to a small space. HNC is the most common cause of neuropathic pain. It has been suggested that the etiology of pain in head and neck cancer patients is multifactorial, and that pain can be due to a direct tumor effect or as a result of cancer treatment or may be factors unrelated to cancer like age, gender, ethnicity, smoking or drinking . Structural alteration and chronic pain among post treatment survivors of head and neck cancer is very common.[15] Due to advanced cancer treatment modalities, the numbers of cancer survivors are increasing but their Quality of life would be affected at the same time if pain is not properly assessed and treated. Therefore, screening programs for timely and early identification of pain are necessary. Epstein et al., who pointed out that orofacial pain improves following treatment and, in many cases, does not return to its baseline value.[16] Clinicians must use a screening tool like Questionnaires for assessing and treating cancer pain at an early stage of the treatment and assessment must include the presence of 'total pain' i.e. physical, spiritual, psychological and social issues. WHO pain ladder should be used to treat pain and for refractory pain specialized pain management services should be considered early in pain palliation. In our study VAS was 8-9 in many of the patients but after effective pain management VAS comes down to 2-3 in same population of patients.

Insomnia increases cancer symptom burden and impairs quality of life. It is common complaint in head and neck cancer patients with an incidence reported ranging from 30% to 75% and it includes early awakening, excessive day time sleep, difficulty falling asleep, poor sleep efficacy, difficulty in maintaining sleep. It affects quality of life, decrease work attentively, decrease mental health, and serve as a consequence of other complications.[17] Insomnia is correlated with pain, fatigue, anti-cancer treatment and depression in most of the patients. The correlation between pain and insomnia in head and neck cancer patients has been previously demonstrated by Rogers LQ, Courneya KS, Robbins KT, et al.in their study 'Factors associated with fatigue, sleep, and cognitive function among patients with head and neck cancer'.[18] Management includes Systematic screening, Pharmacological and Non-pharmacologic therapies like cognitive behavioural therapy. Management of associated symptoms like fatigue, pain, and hot flashes with appropriate symptom-specific agents is important.[19] Successful management have shown a significant positive impact on global quality of life in our study.

Fatigue or cancer related fatigue [CRF] is defined by The National Comprehensive Cancer Network (NCCN) as "a distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning".[20] It is more common in patients on chemotherapy and radiotherapy.[21] Fatigue affects the patient's physical and psychosocial well being and ability to work. Assessment of fatigue includes 1-laboratory studies ,2-disease status and treatment given and 3-fatigue characteristics like severity, onset, duration, exacerbating and alleviating factors and impact on quality of life. Psychosocial interventions and Pharmacological treatments help in patients with fatigue.

Loss of appetite or anorexia may be simply defined as either loss of appetite or reduced caloric intake. It is always associated with weight loss. It is a common concerning symptom among patients with cancer, particularly those with advanced-stage disease and may result from disease itself, chemotherapy, radiation or a variety of other causes, including physical and psychological causes. Reduced calorie intake, alterations in basal energy expenditure, alterations in nutrient metabolism and emotional stress may be the cause of weight loss. Management of Cancer-related anorexia and weight loss includes appetite stimulants, anti-catabolic agents and addressing the psychological issues.[22] As the patient has already experienced a lot of complex issues throughout the trajectory of the disease, an individualized, comprehensive, and interdisciplinary approach is needed to reduce patient suffering and ensure appropriate symptom management and support from the time of diagnosis to end of life. Patients provided with early palliative care can experience relief of symptoms and improvements in quality of life, mood, satisfaction, resource use, and advanced care planning.[3] For an effective palliative care, it is important for oncologists to be familiar with the principles of primary palliative care and interdisciplinary team-based approaches to palliative care. Palliative care is a key component of oncologic care, and we highly recommend that it should be integrated into the plan of care for patients with advanced cancer.[23] A number of trials indicates that early palliative care interventions in patients of incurable cancer, who is suffering physically and psychologically have shown more improvements in QOL and symptom intensity than among those given standard cancer care.[24]

Conclusion

Palliative care takes a holistic approach addressing physical, psychological, social and spiritual needs of the patient, their care givers and family. Head and neck cancer patients present with many physical and psychological symptoms. In our study we found that with intervention of palliative care greater number of patients experienced significant improvement in pain, fatigue, anorexia and insomnia. They also had improvement in depression, anxiety and overall welling.

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" Great things are done by a series of small things brought together. "

Vincent Van Gough

Marginal Zone Lymphoma of Bilateral Buccal Mucosa: A Case Report

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Summary

Non-Hodgkin's lymphoma (NHL) of the mucosa-associated lymphoid tissue (MALT) is characterized by their mucosal and glandular tissue localization. Non-Hodgkin's Lymphoma (NHL) involving only buccal mucosa is a very rare presentation. The etiological factor is unknown but lots of risk factors have been associated such as infection with Helicobacter pylori, Epstein Barr virus and immunodeficiency. Symptoms are very non-specific leading to delay in diagnosis and may be confused with otolaryngologic benign diseases. We hereby present a case of NHL of buccal mucosa, with a history of slowly developing white and red patches in bilateral buccal mucosa and increasing trismus over a year. Biopsy and immunohistochemistry (IHC) lead to the final diagnosis of NHL. Other radiological investigations, including PET-CT was suggestive of isolated buccal mucosal involvement. In view of localised involvement, we treated him with single modality i.e. radiotherapy with complete remission post treatment.

Keywords: NHL, MALT, Buccal Mucosa, Involved-field Radiotherapy

Introduction

Lymphomas are malignant neoplasm of the lymphocyte cell lines, mainly classified as Hodgkin's and Non-Hodgkin's Lymphoma (NHL) based on a characteristic morphologic pattern, immunophenotypic pattern and distinctive chromosomal aberrations. NHL includes a spectrum of behavior. NHL of the mucosa-associated lymphoid tissue (MALT) are rare, represent only 0.2-0.3% of all NHL. Local growth is usual, whereas dissemination occurs late in course of the disease. Extra nodal presentation in NHL is seen in 20-30% of all with usual sites being stomach, bowel, tonsil.[1] Primary lymphomas of oral cavity are uncommon consisting of approximately 2% of all extra nodal lymphomas but isolated buccal mucosal involvement is very rare.[2,3] NHL are more likely to develop in immunosuppressed people or in elderly, especially over 6th decade of life. In some cases, they have been related with auto-immune based disease, such as Hashimoto's thyroiditis and Sjogren's syndrome. Correlation with Helicobacter pylori-induced gastritis has also been hypothesized. We hereby present a case of marginal zone lymphoma of bilateral buccal mucosa which is very rare presentation.

Case Report

A 49 years male with no medical co-morbidities, presented in surgical oncology OPD with complain of ulcer in right cheek and restricted mouth opening since 1 year, resistant to NSAIDs and antibiotic therapy. Personal history revealed addiction of tobacco and betel nut chewing, beedi smoking since past 20 years. On intraoral examination, mouth opening was 3 cm, bilateral buccal mucosa showed leukoplakic patches and fibrosis. Small erythematous, indurated area was present over right buccal mucosa which measured about 2.5 cm in longest dimension (antero-posteriorly). Lesion did not extend to upper or lower gingiva-buccal sulcus or other surroundings and no clinical evidence of lymphadenopathy. Clinical diagnosis which seemed possible in presence of non-infectious lesion and the rate of growth was a benign lesion. Laboratory study showed normal hematological counts and biochemical profile. Serology for human immunodeficiency virus (HIV) was negative. Biopsy from both side buccal mucosa was taken. Histopathology was suggestive of low grade NHL. Immunohistochemistry was suggestive of NHL, low grade B cell marginal zone type. With CD5, CD20, CD43, CD79a, BCL2 positivity, MIB1 10% and cytokeratin negative. CT scan of PNS and Neck was suggestive of heterogeneously enhancing soft tissue thickening involving anterior aspect of both buccal space, maximum thickness of 9 mm on right side and few subcentimetric nodes in bilateral level IB. Based on this report, an exhaustive systemic study including, bone marrow biopsy was performed which reported normocellular bone marrow uninvolved by disease infiltration. PET – CT was also performed which revealed absence of hypermetabolic lymphadenopathy on both sides of diaphragm and any other extra lymphatic site to suggest disease infiltration. Case was discussed in tumour board. In view of solitary lesion, it was concluded that this was a case of stage IE oral primary marginal zone lymphoma and patient was planned for involved field curative radiotherapy in our department. Patient was taken for simulation after preparing customised thermoplastic mask with extended neck position. On

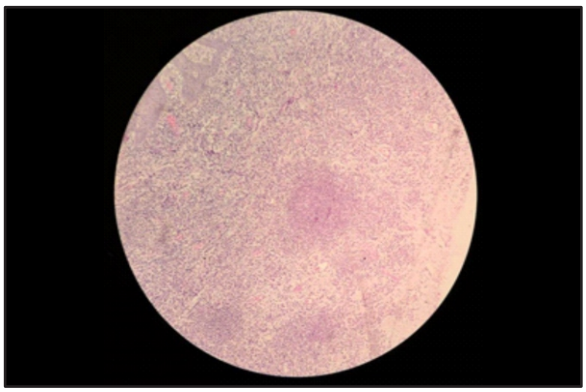

Figure 1: Histologic microphotograph of biopsy specimen

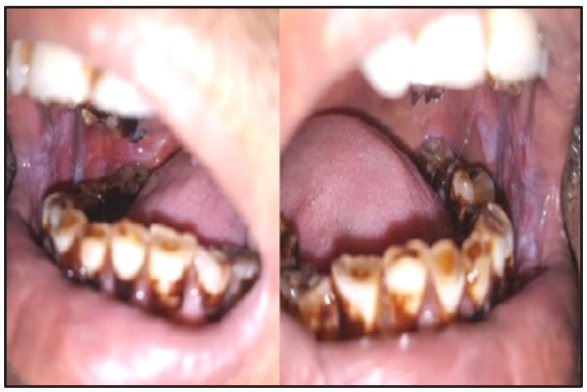

Figure 2: Clinical picture before treatment

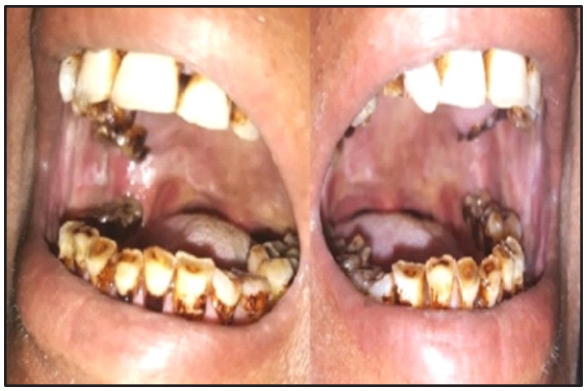

Figure 3: Clinical picture 3 months post-radiotherapy

X-ray simulator, radiotherapy portal was marked with upper border at infra-orbital margin (at the level of base skull) and lower border at the level of clavicle and laterally include 2/3rd of medial part of clavicle. 40 Gy in 20 fractions, 200cGy per fraction, 5 days a week for 4 weeks was delivered on linear accelerator with 6 MV photons with anterior-posterior and posterior-anterior fields. During treatment, patient developed RTOG grade 3 mucositis. Trismus increased, measuring 1.5 cm between the two incisors. After the treatment, patient was followed up. On 15th day post-RT follow up, patient had resolving mucositis. On 3rd month, patient had complete resolution of lesion, clinically and radiologically. Patches of leukoplakia also resolved. With continuous physiotherapy and mouth opening exercises, trismus also improved. A year after diagnosis, patient is disease free and doing well.

Discussion

NHL of MALT is characterized by the mucosal and glandular tissue localization. The case described here falls into the European–American classification of a low-grade B-cell lymphoma of MALT type, with intra-oral lesion.[4] Extragastric MALT lymphomas are very infrequent and little information exists on them. Added to this fact, when a lesion is observed in the buccal mucosa, other pathologies may seem more probable, further hindering correct diagnosis.[7] Oral cavity lymphoma most commonly presents with a persisting ulcer and other symptoms may include pain, foetor, paraesthesia, anaesthesia, or mucosal discolouration. Flow cytometry analysis distinguishes lymphomas from chronic inflammation through the detection of clonality based on surface of Ig light chain expression studies, which is restricted to either kappa or lambda in lymphomas, whereas inflammatory processes reveal a mixed expression of kappa and lambda light chains. One of the characteristics of NHL of MALT is their tendency to remain localized for long period in the originating mucosa, although an exhaustive systemic study should be made to exclude its presence in other tissues. Several factors are known to increase NHL risk including the Epstein-Barr virus and immune deficiency.[5, 6] the prognosis differs between HIV positive and HIV negative patients, and depends on clinical stage. After establishing the correct diagnosis, several aspects have to be considered prior to institution of therapy, as treatment options largely depend on pathological as well as clinical criteria. There is tendency for disease to remain localized for long time, local treatment is often indicated. They respond well to most treatments (surgery, radiotherapy and or chemotherapy), for which reason the least aggressive methods should be used. However local recurrence is frequent, including several years after first diagnosis, and long term follow up is necessary.

Conclusion

With this rare presentation, the possibility of lymphoma being a differential diagnosis for buccal mucosa lesions has to be kept in mind. An accurate clinical examination, a cytohistological and immunohistological diagnosis and flow cytometry have become fundamental steps to decide a proper therapeutic protocol. Treatment needs to be tailored according to the risk-benefit ratio for the patient. In our case, radiotherapy has proved to be an effective

treatment with preservation of function and better cosmesis. However long term follow-up and close observation is needed.

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" Continuous improvement is better than delayed perfection. "

Mark Twain

Nutraceuticals and Stress

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"Give your stress wings and let it fly away."

Terri Guillemets

Can be well said but, It's not that easy. Stress has become a pervading feature of people's life in modern world. The modern world which is said to be a world of achievements in science and technology, along with remarkable growth of economy and sources of luxury still remains a world of "**Stress**". Stress is in fact a vital part of our physiological make-up and an ancient response to any sort of threat to our existence.1 A feeling of emotional or physical tension that people have when they are overloaded and struggling to cope with demands. It can come from any event or thought that makes a person feel frustrated, angry, or nervous. It is your body's reaction to a challenge or demand. These demands can be related to finances, work, relationships, and other situations, but anything that poses a real or perceived challenge or threat to a person's well-being can cause stress.

On one hand "**Stress**"- can be a motivator and can be essential to survival. The "fight-or-flight" mechanism can tell us when and how to respond to danger. However on the other hand, if this mechanism is triggered too easily, or when there are too many stressors at one time, it can undermine a person's mental and physical health and become harmful. Thus, although in acute situations or in short bursts, stress can be positive, and can help avoid danger or meet a deadline; when it lasts for a long time and becomes chronic, it may harm one's health.

In order to understand how stress affects the body and what the biological effects of this response might be, it is necessary to look at the various stages of stress. **Coriander Stone**, a functional medicine-trained Nutritional Therapist, has well mentioned in an article about the three main stages of stress.[1]

Stage I is the Alarm State (fight or flight): When a threat occurs, the brain sends a message to the sympathetic nervous system (SNS) giving instructions to prepare the body for fight or flight. This increases heart rate and blood flow to the liver and dilates the lungs for increased oxygen flow. The SNS then alerts the adrenals to produce adrenaline and noradrenaline to increase oxygen and blood to the heart, brain and skeletal muscles for energy supply so that the body can either fight or run from the threat. Blood pressure and heart rate are raised so as to provide sufficient blood to vital organs during the necessary exercise and blood lipids as well as glucose levels rise to provide the fuel needed. The digestive and reproductive systems are also suppressed to conserve energy for vital organs and survival responses. All of these emergency systems are in place to prepare us for fight or flight.

Stage II is the Resistance State: It lasts longer than the alarm state, different hormones replace adrenaline leading to damage. In this stage, messages are sent from the hypothalamus to the adrenal glands to release cortisol. Cortisol releases glucose and fatty acids into the bloodstream and breaks proteins down into amino acids. These are then used either for energy or to repair damaged cells. It also leaches calcium from bones to aid clotting in case of injury and affects the area of the brain involved in memory, causing a flash back type memory in order to avoid future danger of the same kind. Human growth hormone (hGH) is also released to further stimulate fatty acid and glucose release for energy and thyroid stimulating hormone is released which combines with hGH to supply cell energy factors. All the resistance state factors work towards providing additional energy for our bodies so that we are able to continue to fight or run until the threat is combated. However, the resistance state eventually leads to stage III.

Stage III, the Exhaustion State, which is a long term stress damage state The body's resources are depleted and it can no longer maintain the second stage. Exhaustion often leads to the inability to even get out of bed in the mornings. This is where long term physical and physiological damage occurs.

Although the stress response is natural and crucial to the survival of any living organism, the threat is quickly resolved and thus the response is normally short lived. Stress hormones are not supposed to circulate for long periods of time, yet modern day stress is hugely different from that of early man's. While much of modern stress is unavoidable, there is quite a lot we can do to protect our bodies against the detrimental effects of this constant response.

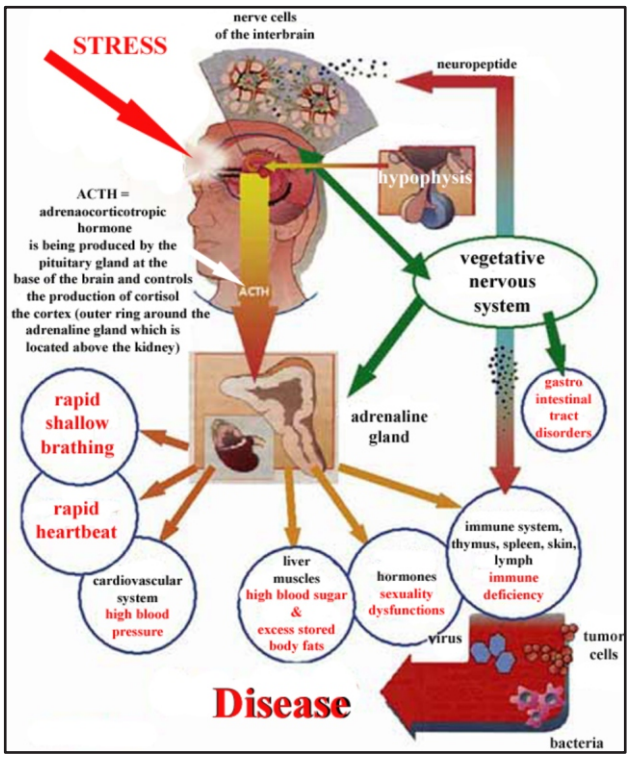

Figure 1: Biological effect of Stress

Adapted from - http://silvecorarostenadrenaline.weebly.com/effect.html

But then again, today a person has to perform a variety of roles, and while performing them, he/she is likely to accomplish only some responsibilities. However he/she must execute all the roles since our work life and personal life are interconnected and interdependent. The conflict arises when the burdens, obligations and responsibilities of work or the family roles become incompatible. As age advances, the increasing responsibilities on the personal front can also create stress on personal and professional fronts. Tension in the workplace to meet the challenges has an alarming spike in the incidence of reported stress among employees in recent years and its impact on the bottom line and also at home. And this repetitive exposure of the stress response on our body is proven to lead to long lasting psychological and physical health issues; these include cardiovascular disease, diabetes, **anxiety** and **depression**. Ultimately, when one gets to the point of no longer **being able to cope**, they are "burned out," like a candle. This is where stress management can offer tools, and help people avoid the unpleasant experience.

Stress and its Management

Stress can be effectively managed in many different ways. The following 7 tips are adapted from The American Psychological Association ("Check Out the Stress Tip Sheet," 2018) to support individuals with a stress management plan:

- Understand your stress
- Identify your stress sources
- Recognize your stress strategies
- Learn to recognize stress signals
- Implement healthy stress management strategies
- Make self-care a priority
- Ask for support when needed

But again everyone has a unique response to stress; there is no "one size fits all" solution to managing it. Therefore, when deciding which option to choose, it's helpful to think of the **four A's: Avoid, Alter, Adapt or Accept.**

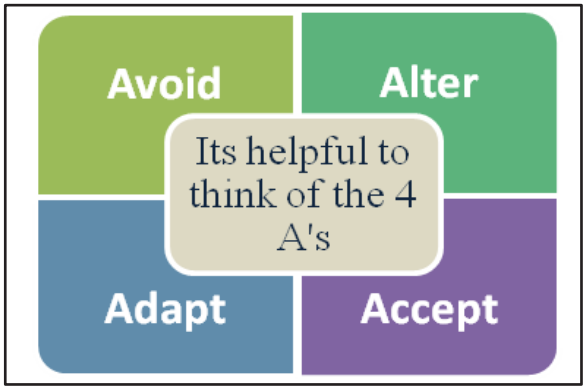

Figure 2: Four A's – basic primary ways to cope with stress

Adapted from: https://www.helpguide.org/articles/stress/stress-management.html

Taken together, stress wreaks havoc on your emotional equilibrium, immune system and ultimately your physical health. It narrows your ability to think clearly, function effectively, and enjoy life. To combat that it's important to **implement healthy stress management strategies**. Hence, it is very rightly said that - take care of your body and mind and they will take due care of all types of traumas you face throughout your existence. That is, control stress by adopting a healthful lifestyle which includes eating well, exercising, meditation, yoga, sleeping adequately and enjoying your free time. Likewise, awareness of herbal remedies is growing, people are more open to trying herbs to help reduce the feelings or physical manifestations of stress. The current scenario also has therefore shifted towards organic food and ingredients (nutraceutical substances) which seems to play an important role in prevention and cure of disease burden.

The term "nutraceuticals" was first coined by Dr. Stephen DeFelice, MD in 1989. Who defined it as "a substance that is a food or a part of food and provides medical and health benefits, including prevention and treatment of disease." Moreover, the term "nutraceutics" comprises of "nutrient" (a

nourishing food component) and "pharmaceutical" (a medical drug) which refers to extracts of foods claimed to have a medicinal effect on human health.

In Eastern philosophy, it is mentioned that "Nasti moolam an aushadham" **नास्ति मूलं अनौषधं**: no plant created by the God is without medicinal values; however, one has to know how to use these and for which disease.

Now a day, nutraceuticals have received considerable interest due to potential nutritional, safety and therapeutic effects.[2]

The natural bioactive compounds called adaptogens have shown to help against stress related cellular damages. They exert to normalize and provide balancing action for stress and intellectual strength. Thus they gradually increase emotional performance that promotes recovery from stressful situations. Herbal nutraceuticals like aswagandha, rhodiola, L-theanine, ginseng are affective adaptogens that activate the production of stress suppressing heat-shock protein 70 (HSP-70). They also stabilize physiologic process, promote homeostasis, increase resistence to environmental stress, reduce moderate to severe anxiety, improve sleep, reduce depression and improve secondary memory.[3]

Thus, the newest trend is moved towards 'nutraceuticals' yet a new era of medicine and health. It is still in its stage of formative years in India. But in this hype period we must say "let food be your medicine" and "appropriate nutraceuticals daily can keep the medicine away."[4]

Today, Nutraceuticals have received a noteworthy keenness for their expected safety, impending nutritive and therapeutic effects. These are being used as alternative to modern medicines that promote quality of health, increase nutritive value of the diet and prolong life expectancy. Major constituents of the nutraceuticals are herbals, various nutrients and dietary supplements involved in preventing different diseases and minimizing pathophysiology of the disease too. It also acts as immune boosting, natural antioxidant, anticancer, anti-inflammatory, antidiabetic, cardioprotective, organoprotective agent in addition with different health promoting effects.

Nutraceuticals detoxify our body, restoring our healthy digestion and dietary habits also. They can be classified based on the source of foods, mechanism of action and their chemical properties.[5] The food sources used as nutraceuticals are all natural and they are dietary fiber, probiotics, prebiotics, PUFA, antioxidant vitamins, polyphenols etc.[6] Nutraceuticals with various bioactivities towards human body are being widely examined for their ability to provide health benefits.[7]

Several nutraceuticals reported till date having free radicals scavenging capacity. Studies show that onion, garlic, grapes, rosemary, broccoli, spinach, turmeric, parsley possess considerable antioxidant activities.[8] Mitochondria targeted nutraceuticals (MTNs) too have antioxidant effects at the molecular level and boost mitochondrial bioenergetics.[9]

Herbal nutraceuticals like probiotics play a unique role for healthy digestive function. It may stimulate the growth of healthy gut microflora, slow down harmful bacterium and reinforce the body's natural gut defense mechanisms. It can reduce lactose intolerance and prevent GI tract disorders.[10]

Specific nutraceuticals like magnesium citrate, pine bark of pycnogenol, pygeum, potassium citrate, IP6, lutein, lycopene, xeaxanthin play a significant role at our excretory system that includes promotion of healthy urinary oxalate excretion, provide protective activity on kidneys, improve healthy urinary bladder health and sphincter tone, help to balance calcium accumulation, formation of calcium and oxalate crystals, maintain normal microbial flora in the bladder and urinary tract.[11,12]

Certain nutraceuticals produce significant effects on stem cell growth and proliferation and show significant role in healing and tissue regeneration by stimulating and recruiting endogenous stem cell at the site of injury. Blueberries, green tea, catechins, carnosine, vitamin D3, PUFA and essential amino acids strengthen our immune system.[11,12]

Nutraceuticals present in citrus fruits and soybean have effects on epigenetic modifications, autophagy and necrosis.[13,14] Researches have shown that spermidine and its derivatives confer lifespan extension in humans by enhancing autophagy. Caffeic acid and Rosmarinic acid present in fruits, vegetables and herbs are also anti carcinogenic, antioxidant, anti-rheumatic and anti- microbial. They can prolong the healthy life span extension.[10]

The scope of nutraceutical field is plenty both in terms of type and the varieties. Nutraceuticals industry in India is one of the rapid growing markets. Higher and upper middle class consumers are perceiving nutraceuticals as alternative to prescribed drugs and exclusively for their beneficial properties without any side effects. Ultimately, they ensure better quality of life.

Finally concluding, the natural properties of nutraceuticals for boosting energy and improving physical endurance and mental alertness, can be very beneficial and one of the best approach to cope with modern day stress.

Lastly, Happiness is a choice. You can choose to be happy. There's going to be stress in life, but it's your choice whether you let it affect you or not. - Valerie Bertinelli

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" Do the best you can until you know better.

Then when you know better, do better. "

Maya Angelou

Presentations at the Clinical Meetings

(January 2019 to June 2019)

Sr. No.	Date	Speaker/Department	Title
1	12.01.2019	Rachh Swati Nuclear Medicine	Clinical Utility of Gallium-68 PSMA PET/CT Scan for Prostate Cancer
		Saini Simran Gynecology oncology Unit-2	A Comarison i=of Sentinel Lymph Node Biopsy to Lymphadenectomy for Endometrial cancer Staging (FIRES Trial): A Multicentre, Prospective, Cohort Study
2	09.03.2019	Patel Kinjal Molecular Oncology Lab	Assessment of Blood Tumor Mutational Burden as a Potential Biomarker for Immunotherapy in Patients with Non-Small Cell Lung Cancer with Use of a Next-Generation Sequencing Cancer Gene Panel
3	13.04.2019	Sanghavi Priti Pain and Palliative Medicine	Choosing Wisely India: Ten Low Values or Harmful Practices that should be avoided in Cancer Care
		Chauhan Bhavya Radiology Department	LI-RADS V2017 for Liver Nodules: How we Read and Report
4	22.04.2019	Patel Hitesh Consultant Intensivist	Guest Lecture on " USG: Point of Care and Fluid Management"
5	11.05.2019	Kusumgar Rima Blood Bank Pathology	Advantages of type and screen policy: Perspective from a developing country!
		Modi Nikhil Neuro Oncology	Evolution of Surgical Techniques in the Management of Vertebral Body Tumors and the Current Status
6	08.06.2019	Trupti Trivedi Clinical Carcinogenesis Lab	The Utility of "Liquid Biopsy" in central Nervous System Malignancies
		Sadhwani Manish	Sentinel Lymph Node Biopsy for early stage Tongue Cancer –A 14 Year Single-Centre Experience

" Continuous improvement requires systematic evaluation.
Continuous improvement requires unfiltered evaluation. "
Anonymous

Panel Discussion at the Clinical Meetings

(January 2019 to June 2019)

Sr. No.	Date	Moderator/ Department	Panelist/ Department	Title
1	26.01.2019	Warikoo VikasSurgical Oncology	Tadaiya Mahavir GI & HPB-I Rachh Swati Nuclear Medicine Jetly Dhaval Pathology	Management of Neuroendocrine Tumors
2	23.02.2019	Parikh Sonia Medical Oncology Unit-3	Vora Hemangini Cancer Biology Garg Akanksha Medical Oncology Yadav Rajan Radiotherapy Joshi Nitin Medical Oncology	Management of Leukemias: Current Status and Scope for Advancement
3	23.03.2019	Poddar Jyoti Radiotherapy	Tahiliani Nahush Medical Oncology Warikoo Vikas Surgical Oncology Shah Ashini Pathology Parikh Ankita Radiotherapy	Preoperative Long Course CT-RT Vs. Short Course Only RT in Ca. Rectum
4	22.06.2019	Rachh Swati Nuclear Medicine	Patel Trupti Pathology Soni Himanshu Radiodiagnosis Tiwari Rasna Nuclear Medicine Puj Ketul Surgical Oncology Roy Parag Radiotherapy	Challenges in the Management of Differentiated Thyroid Carcinoma: Tailoring Treatment to Fit the Risk
5	25.05.2019	Vadhiya Rupal Radiology	Jain Abhishek Surgical Oncology Soni Himanshu Radiodiagnosis Patel Sapna Radiology	Introduction to Digital Mammography

Case Presentations for Morbidity, Mortality at Clinical Meetings

(January 2019 to June 2019)

Sr. No.	Date	Presenter / Department	Case Presentation
1	26.01.2019	Dr Dushyant Vaidya Anaesthesiology	Morbidity and Mortality Data presentation of Surgical and Medical Departments
2	23.02.2019	Dr Jinesha Chauhan Anaesthesiology	Morbidity and Mortality Data presentation of Surgical and Medical Departments
3	23.03.2019	Dr Jinesha Chauhan Anaesthesiology	Morbidity and Mortality Data presentation of Surgical and Medical Departments
4	27.04.2019	Dr Dushyant Vaidya Anaesthesiology	Morbidity and Mortality Data presentation of Surgical and Medical Departments
5	25.05.2019	Dr Dushyant Vaidya Anaesthesiology	Morbidity and Mortality Data presentation of Surgical and Medical Departments
6	22.06.2019	Dr Jinesha Chauhan Anaesthesiology	Morbidity and Mortality Data presentation of Surgical and Medical Departments

" Practice the philosophy of continuous improvement.
Get a little bit better every single day. "
Brian Tracy

About the Journal and Instructions to Authors

About the Journal

Gujarat Cancer Society Research Journal is a biannually (April and October) peer-reviewed journal published by the Gujarat Cancer Society (formerly published as GCS Research Bulletin). The journal's full text is available online at http://www.cancerindia.org

Scope of the Journal

The Journal intents to cover basic, clinical, clinico-basic research and medical education carried out by the staff of the Gujarat Cancer Society and Gujarat Cancer and Research Institute related to human well being including ethical and social issues in the field of Oncology. The Journal gives preferences to original scientific papers, case reports, anecdotal reports and mini reviews. It may comprise invited review articles, publish oration speeches and work presented in the clinical meetings and the journal clubs. Hence it will continue to serve as an academic-research bridge between the basic sciences and the applied sciences, viz. various disciplines of medicine within and outside GCS-GCRI.

Authorship Criteria

Authorship credit should be based only on contributions any of the three components mentioned below:

1. Concept and design of study or acquisition of data or analysis and interpretation of data;
2. Drafting the article or revising it critically for important intellectual content; and
3. Final approval of the version to be published. Each contributor should have participated sufficiently in the work to take public responsibility for appropriate portions of the content of the manuscript. The order of contributors should be based on the extent of contribution towards the study and writing the manuscript.

Review Process

The submitted manuscripts not meeting with the Instructions to Authors would be returned to the authors for technical correction, before they undergo editorial / peer-review process. The editors will review all submitted manuscripts initially for suitability for formal review. Manuscripts with insufficient originality, serious scientific or technical flaws, or lack of a significant message will be rejected before proceeding for formal peer-review. Manuscripts that are unlikely to be of interest to the Gujarat Cancer Society Research Journal readers are also liable to be rejected at this stage itself. Manuscripts that are found suitable for publication in Gujarat Cancer Society Research Journal are sent to expert reviewer/s.

The journal follows a double-blind review process, therein the reviewer/s and authors are unaware of each other's identity. Every manuscript is also assigned to a member of the editorial team, who based on the comments from the reviewer/s takes a final decision on the manuscript.

The comments and suggestions (acceptance/ rejection/ amendments in manuscript) received from reviewer/s are conveyed to the corresponding author. If requisite, the author is requested to provide a point by point response to reviewers' comments in a separate sheet and submit a revised version of the manuscript with the changes duly highlighted in different color. This process is repeated till reviewers and editors are satisfied with the manuscript. Manuscripts accepted for publication are copy edited for grammar, punctuation, print style, and format. Page proofs are sent to the corresponding author. The corresponding author is expected to return the corrected proofs within two days.

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Ethics

Do not use names and initials of patient or hospitals numbers, especially in illustrative material. When informed consent for the same has been taken from the patient, it should be mentioned in the manuscript. Any report of experimental investigation on human subjects must contain evidence of informed consents by the subjects and of approval by the institutional ethics committee.

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Avoid abbreviations in the title and abstract. All unusual abbreviations should be fully explained at their first occurrence in the text. All measurements must be in metric units, preferably with corresponding SI units in parentheses. No periods, no plural form (eg. '10 cm' not '10 cms.').

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Use only generic names of drugs. In case trade names (Proprietary drugs) are used, the manufacture should be identified clearly.

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Manuscript submitted using Microsoft Word, Font Times Roman, Paper size A4, Margin 2.5 cm from all four sides for Windows is preferred. Images should be submitted as JPEG file.

Manuscripts reporting clinical studies should, where appropriate, contain a statement that they have been carried out with ethical committee approval.

All manuscripts should include the following sections, in order. All sections are mandatory unless designated "optional":

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- Contributions (optional)
- Competing interests
- References
- Tables
- Figures

Types & size of manuscripts

1. **Original article:** The text of original articles amounting to up to 3000 words (excluding Abstract, references and Tables) should be divided into sections with the headings Abstract (unstructured - max. 200 words), Key-words, Introduction, Material and Methods, Results, Discussion, Conclusion, References (max. up to 25), Tables and Figure legends.

2. **Case report:** It should have maximum limit up to 1000 words (excluding Abstract and references) and should have the following headings: Abstract (unstructured - max. 200 words), Keywords, Introduction, Case report, Discussion, Reference (max. up to 10), Table and Figure legends.

3. **Review article:** It should have abstract (max. 200 words), Introduction/Historical Background, Discussion, Conclusion, References, Tables and Figure Legends.

4. **Short communication:** The length of it should not exceed 1000 words and References 10.

Note: Discussion and conclusion can be combined in one section. Please do not add numbers before subtitles. Write subtitles and headings in sentence case.

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Include in the title page the manuscript title, author's name(s), affiliations, and corresponding author's phone/fax number and/or email. The name of the department(s) and institution(s) to which the work should be attributed

Title: Use sentence format; only the first word and proper nouns should be capitalized.

Authors: The list of authors and contributors should conform to the guidelines set out by the International Committee of Medical Journal Editors. Provide full names of all authors. Eg: **Write surname** before **the first name** and initials of middle name (Patel Rajesh K) with institutional affiliation.

Language and grammar

- Uniformly American English
- Abbreviations spelt out in full for the first time
- Numerals from 1 to 10 spelt out
- Numerals at the beginning of the sentence spelt out

Abstract: A structured abstract must be included with each original scientific manuscript with 4 clearly identifiable elements of content: rationale (goals of the investigation), methods (description of study subjects, experiments, and observational and analytic techniques), results (major findings), and conclusions. Except for the rationale, these sections should be preceded by headings (i.e., Methods, Results, and Conclusion). **Abstract** should not contain citations to references, any images or math equations.

Keywords: Submit 5 keywords with the abstract.

Research manuscript sections (Font size: 12):This should comprise of Introduction (comprising of Aims and Objectives), Materials and Methods, Results,Discussion with Conclusions. Cite every Reference, Figures and Tables mentioned in the text in Arabic numerals (e.g. 1,2,3).

Introduction/Aims and Objective

Briefly place the study in a broad context and highlight why it is important. Define the purpose of the

study or observation and its significance, including specific hypotheses being tested. Review carefully current state of the study research field citing key publications. Finally, briefly mention the main aim of the work and highlight the main conclusions.

Materials and Methods

Describe precisely your selection of the observational or experimental subjects (patients, including controls). Identify the methods, apparatus (including manufacturer's name and address in parenthesis), and procedures in sufficient detail to allow others to reproduce the method. New methods and protocols should be described in detail while well-established methods can be briefly described and appropriately cited. Identify precisely all drugs and chemicals used, including their generic names, their manufacturer's name, city and country in parenthesis, doses, and routes of administration.

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Provide a concise and precise description of the only important observations of experimental results, their interpretation as well as the conclusions that can be drawn. Do not repeat in the text all the data in the Tables, and Figures. Restrict Tables and Figures to those needed to explain the argument of the paper and to assess its support. Avoid duplication and repetition of data in Figures and Tables. Specify the statistical methods used to analyze the data.

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Authors should discuss the results and how they can be interpreted in perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible and limitations of the work highlighted. Future research directions may also be mentioned. This section may be combined with Results.

Conclusions

This section is not mandatory, but can be added to the discussion.

Tables (Font size: 12)

Type each Table double-spaced on a separate sheet .Number Tables consecutively in Arabic numerals (e.g. 1, 2, 3) in the order of their first citation in the text and supply a brief title, which should be shown at the top of each table.

Figures and Legends (Font size: 12)

All Figures must be submitted on separate sheet, in JPEG finished format that is ready for reproduction. Figures should be numbered consecutively in Arabic numerals (e.g. Figure 1, 2, 3) according to the order in which they have been first cited in the text. If photographs of persons are used, the subjects or patients must not be identifiable.

Legends (Font size: 12)

Present the legends for Figures on separate sheet (Font size: 12) using double-spacing with Arabic numerals corresponding to the Figures.

Acknowledgements (Font size: 9)

State contributions that need to be acknowledged.

References (Font size: 12):

References on separate sheet and must be numbered in order of appearance in the text Identify references in the text in numerals in superscript and parenthesis. Omit month and issue number. List all authors, but if the number is six or more, list first three followed by et al. The references should be cited according to the Vancouver agreement (International Committee of Medical Journal Editors). Authors must check and ensure the accuracy of all references cited. Abbreviations of titles of medical periodicals should conform to the latest edition of Index Medicus. Some examples are shown below:

Standard Journal

You CH, Lee KY, Chey RY et al: Electrogastrographic study of patients with unexplained nausea, bloating, and vomiting. Gastroenterology 1980; 79:311-314

Online journal article

Miyamoto O, Auer RN: Hypoxia, hyperoxia, ischemia and brain necrosis. Neurology [serial online] 2000; 54:362-71. Available at: www.neurology.org. Accessed February 23, 2000.

Chapter in a book

Weinstein L, Swartz MN: Pathogenic properties of invading microorganisms. In: Sodeman WA Jr, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease.Philadelphia: Saunders, 1974: 457-472

Online book or website

Garrow A, Weinhouse GL: Anoxic brain injury: assessment and prognosis. In: Up To Date Cardiovascular Medicine [online] Available at: www.UpToDateInc.com/card. Accessed February 22, 2000.

In press

Lillywhite HB, Donald JA: Pulmonary blood flow regulation in an aquatic snake. Science. In press.

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2. We surrender the rights to the corresponding author to make necessary changes as per the request of the journal, do the rest of the correspondence on our behalf and he/she will act as the guarantor for the manuscript on our behalf.

3. The manuscript is original work or compilation, without fabrication, plagiarism and fraud.

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(Up to 4 contributors for case report/ short communication / review)

5 _____	_____	_____
6 _____	_____	_____

(Up to 6 contributors for original studies)

Corresponding author: _____
Mailing address: _____

_____

Phone: _____ Email: _____

Cancer Centers in State

GCRI is instrumental in the development of Cancer Centers in the state. GCRI has developed (1) Siddhpur Cancer Center and (2) The Saurashtra Cancer Care & Research Centre at Rajkot.

(1) Siddhpur Cancer Centre

Sharma Ayushi,
Assistant Hospital Administrative
Siddhpur
ayushi.sharma@gcriindia.org

Regional Cancer Care Center & Cancer Hospital Siddhpur, under the umbrella of The Gujarat Cancer & Research Institute, Civil Hospital Campus, Ahmedabad. Siddhpur cancer care center was established on September 2012 and is providing free cancer patient care.

At present the institute is well equipped to provide the following facilities:

1. Registration Counter
2. OPD Services.
   (a) Radiation Oncology
   (b) Medical Oncology
   (c) Gynec Oncology
   (d) Surgery Oncology
3. Radiotherapy
4. Brachy Therapy
5. Chemotherapy Ward.
6. Indoor Ward
7. X-ray.
8. CT Scan (Only for planning of radiotherapy patient)
9. Basic Laboratory Services
10. Pharmacy Services
11. Sanjeevani Rath (For Cancer Screening with Mammography & PAP Test)

As the center is not fully developed yet, some supporting services are being provided by General Hospital Siddhpur.

(1) Blood Bank
(2) Ambulance

Other Referral services

(1) SurgeryOncology
(2) Gynec Oncology etc.

Services in Pipeline

(1) Surgical Oncology (Operation Theatre, Surgical ward, CSSD etc.)
(2) Ayushman Bharat Yojana will start soon.

Other Facilities For The Patient

These two foundation provide food to patients at free of cost

(1) Snehanjali Foundation Food
(2) Ramji Mandir Trust Food

Patient Data 2014-2018

Year	Gynec	Surgical	Total RT OPD	RT Treatment Total	Chemo	Day Care	CVS	ICRT	CT	PAP	Memo	Indoor	Lab
2018	42	647	16264	17243	3261	1553	17	28	575	21	82	1744	4541
2017	77	918	18532	18513	4274	2541	32	58	438	22	127	2549	3375
2016	142	566	15422	20708	4154	1049	66	63	526	75	95	589	537
2015	134	404	7007	15705	1750	-	-	-	40	39	122	-	-
2014	51	560	1804	4564	-	-	-	-	-	43	50	-	-

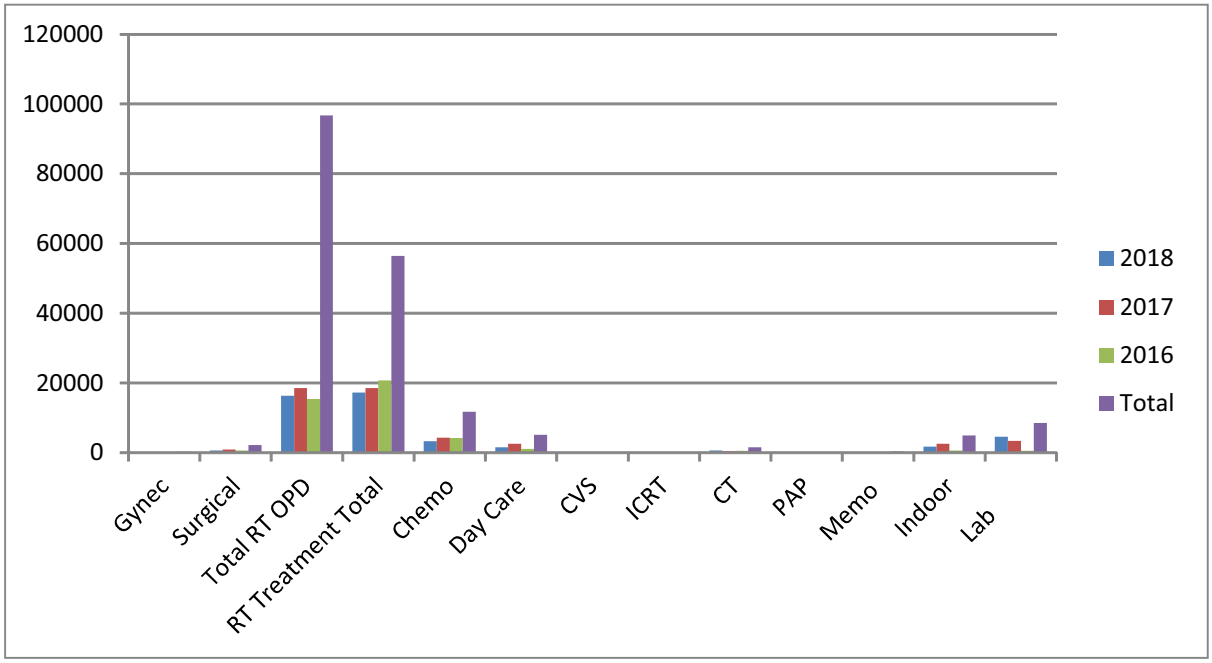

Figure 1: Yearly patient detail

" Perfection is not attainable.
But if we chase perfection, we can catch excellence. "
Vince Lombardi

(2) The Saurashtra Cancer Care & Research Institute

Mehta Nupur
Assistant Hospital Administrative
Rajkot
nupur.mehta@gcriindia.org

"Cancer may have started the fight, but we will finish it. Together we will beat cancer".

Cancer is the leading cause of death across the globe. For years now, researchers have led meticulous studies focused on how to stop this deadly disease in its tracks. How close are we to finding more effective treatments?
Currently, the most common types of cancer treatment are Surgery, Radiotherapy and Chemotherapy — and in some cancer cases targeted therapy, hormonal therapy etc.

The Saurashtra Cancer Care & Research Institute situated at University Road, Rajkot (Managed by The Gujarat Cancer & Research Institute, Regional Cancer Center, Ahmadabad) established in September 2017, takes pride in providing free care to all of its cancer patients.

At present the institute is well equipped to provide the following facilities:

1. Registration Counter
2. OPD Services.
   (A) Radiation Oncology
   (B) Medical Oncology
   (C) Gynec Oncology
   (D) Surgery Oncology
   (E) ENT Oncology
3. Chemotherapy Ward.
4. Ultrasonography.
5. Blood Sample Collection
6. Pharmacy Services
7. Ambulance Services
8. Sanjeevani Rath (For Cancer Screening with Mammography & PAP Test- The only one in Saurashtra region)

As the center is not fully developed yet, all the supporting services are being provided by P.D.U. Hospital, at free of cost and P.D.U Hospital will continue it's services till the center is fully developed.

Supporting services provided free of cost at P.D.U Hospital

(1) All kinds of Onco-surgical work done by our Surgical Oncologist utilizing OT theatre of P.D.U. Hospital, Rajkot by our Oncologist.
(2) Laboratory investigation
(3) Blood Bank
(4) CT & MRI (free for BPL Patients)
(5) X-Ray
(6) Other Referral services
   (A) Surgery
   (B) Medicine
   (C) Gynec
   (D) ENT etc.

Services in Pipeline

⇨• Radiation Oncolog
⇨Linear Accelerator, C.T Simulator, HDR Brachythearphy machines purchase order has been placed..
- Pathology
- Radiology
- Surgical Oncology (Operation Theatre, Surgical ward, CSSD etc.)

Monthly Statistics

Month (Since GCRI taken over)	OPD			IPD		
	New Patients	Follow Up Patients	Total	New Patients	Follow Up Patients	Total
Jun-18	80	444	524	25	54	79
Jul-18	75	517	592	30	180	210
Aug-18	100	424	524	34	159	193
Sep-18	100	447	547	45	186	231
Oct-18	95	536	631	30	283	313
Nov-18	100	444	544	37	275	312
Dec-18	145	593	738	54	254	308
Jan-19	147	608	755	50	307	357

Month (Since GCRI taken over)	OPD			IPD		
	New Patients	Follow Up Patients	Total	New Patients	Follow Up Patients	Total
Jan-19	147	608	755	50	307	357
Feb-19	151	566	717	44	243	287
Mar-19	142	644	786	45	322	367
Apr-19	130	642	772	44	306	350
May-19	149	600	749	55	304	359
Jun-19	117	700	817	37	364	401
Jul-19	166	911	1077	45	404	449
Aug-19	157	855	1012	73	469	542
Total	**1854**	**8931**	**10785**	**648**	**4110**	**4758**

SCCRI Cancer Patients Data																
Dingnosis	**Months**															
	Jun 18	Jul 18	Aug 18	Sep 18	Oct 18	Nov 18	Dec 18	Jan 19	Feb 19	Mar 19	Apr 19	May 19	Jun 19	Jul 19	Aug 19	Total
Head and Neck	148	167	145	142	170	173	248	246	249	279	282	273	297	315	340	3474
Breast	218	193	230	269	323	275	379	382	327	410	363	360	357	366	400	4852
Cervix	10	15	28	28	51	32	50	74	67	64	81	81	28	32	18	659
Others	311	427	314	339	400	376	369	410	361	400	396	394	382	602	566	6047
Total	687	802	717	778	944	856	1046	1112	1004	1153	1122	1108	1064	1315	1324	15032

No. of camps conducted by GCRI using Rajkot Sanjeevani Rath	**June 2018 - May 2019**
Number of camps	06
Number of beneficiaries	254
Mammography	51
Pap Test	122

•Total surgeries performed since GCRI taken over is 106 till August 2019

" When you reach the top, keep ascending,
otherwise you start descending. "
Lincoln Patz

THE GUJARAT CANCER SOCIETY
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2018 - 19
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	Dr. Trupti Patel	Dr. Franky Shah

Siddhpur Cancer Centre

Hospital Building

Registration Counter

OPD Waiting area

Chemotherapy Ward

X-Ray Service

Indoor Ward

Radiotherapy

CT Scan Room

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The Saurashtra Cancer Care & Research Institute

Hospital Building

Registration Counter

OPD

Indoor Ward

Ultrasound Room

Chemotherapy Ward

Pharmacy Service

Ambulance Service

All Donations are exempted from Income Tax Under IT Act 35(i)(ii)(175%), 35AC(100%) & 80G(50%) Donations in Foreign Currencies Accepted approval vide Reg. No.041910257 Dated 22-03-2001. Visit Us at on http://gcriindia.org E-mail:gcriad1@bsnl.in

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