¹⁸F-FDG PET-CT SCAN VERSUS BONE MARROW BIOPSY IN PEDIATRIC HL - A QUANTITATIVE ASSESSMENT OF MARROW UPTAKE AND NOVEL INSIGHT INTO CLINICAL IMPLICATION OF MARROW INVOLVEMENT: SHOULD BONE MARROW BIOPSY BE PERFORMED IN ALL THE HL CASES?

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Purpose/Objective: To evaluate whether positron emission tomography/computed tomography using Flourine-18 fluro-deoxyglucose [¹⁸F-FDG PET-CT] scan predicts bone marrow involvement[BMI] by Hodgkin's Lymphoma[HL] in pediatric population with sufficient accuracy to supplant routine staging iliac bone marrow biopsy[BMB].

Material/Methods: Retrospectively pediatric HL patients between July 2010 and June 2015 who underwent staging ¹⁸F-FDG PET-CT scan and BMB were analyzed. The FDG uptake pattern in those with BMI was assessed visually and quantitatively. BMI indicated positive BMB and/or foci of marrow uptake on ¹⁸F-FDG PET-CT that behaved concomitantly with other sites of lymphomatous involvement on post-treatment scans. Standardized Uptake value [SUV_{max}] of marrow uptake sites was recorded. Progression free survival [PFS] and overall survival [OS] was calculated and statistically evaluated among stage IV cases with and without BMI [PET+ BMB-, PET+ BMB+ and PET- BMB-].

Results: Total of 784, 653 [83.3%] males and 131 [16.7%] females were included. Age range: 2-18 years [mean 10.3 years]. Overall 13.3% had BMI. BMB and ¹⁸F-FDG PET-CT scan had concordant BM findings in 728 [93%]; with positive concordance in 54 and negative concordance in 674. Out of disconcordant cases [n=56, 7%], four were upstaged by BMB with normal ¹⁸F-FDG PET-CT scans, while 46 with negative BMB were upstaged by increased focal marrow FDG uptake that normalized after treatment. The remaining six had diffuse increased uptake with negative BMB. For BMI, ¹⁸F-FDG PET-CT scan had a sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 96%, 99%, 94%, 99% and 98.7% respectively versus 56%, 100%, 99.6%, 93.7% and 94% for BMB. On a quantitative assessment, mean BM-SUV_{max} of bilateral iliac crests was significantly higher in those with BMI [p<0.05]. For survival analysis results, please refer to table shown at the bottom.

Conclusion: ¹⁸F-FDG PET-CT scan was more sensitive than BMB in newly diagnosed pediatric HL with potential upstaging in 6%. BMB should be limited to those with normal marrow uptake on ¹⁸F-FDG PET-CT scan in the presence of poor risk factors or those with diffuse increased uptake even in the absence of poor risk features to differentiate between marrow disease and paraneoplastic marrow activation.

DIFFERENT PATTERNS OF CORONARY ARTERY VARIATION IN ADULT PAKISTANI POPULATION- SINGLE CENTER EXPERIENCE USING 64-SLICE COMPUTED TOMOGRAPHY.

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Purpose/Objective: The knowledge of the variant coronary arterial anatomy is essential in the assessment of cardiac CT examination. Although most of the variations are benign, however, few might have clinical significance such as malignant inter-arterial course of RCA arising from left aortic sinus, which can be potential cause of sudden death in young individuals. Moreover, pre-operative knowledge of the aberrant/anomalous coronary circulation can be handy for cardiac interventionist to avoid potential inadvertent morbidity/mortality.

Material/Methods: The study was aimed to determine different pattern of coronary arteries variations in the Pakistani population.

Material and Methods: Hospital electronic record was retrospectively reviewed of 1000 patient who had CT Angiography from 2006 to 2016. On CT angiography, the coronary artery variations/anomalies were observed and analyzed in SPSS 20.

Results: The overall prevalence of coronary arterial variations in sample population of 1000 patients was around 5.4%. The most frequently observed variation was myocardial bridging. The rare type of coronary anomaly such as RCA arising from the left aortic sinus and coursing between aortic root and right ventricular outflow tact was also seen in three patients (0.3%). Other patterns observed in our study population briefly include anomalous origin of LCX from RCA, fusiform aneurysm of RCA, hypo plastic RCA and absent Left main trunk etc.

Conclusion: Cardiovascular CT is valuable non-invasive imaging technique to assess variation in coronary arterial anatomy. The reporting radiologist and cardiologist should be aware of different patterns of coronary arterial variations/ anomalies to better evaluate the cardiac CT examination and prevent possible complications during cardiac intervention.

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Purpose/Objective: Image-guided transcatheter hepatic chemoembolization (TACE) is accepted worldwide as an effective treatment for patients with unresectable hepatocellular carcinoma (HCC) and for adequate preservation of liver function. Although considered relatively safe, TACE has been associated with several complications. The aim of this study was to determine the the complications associated with TACE therapy and to identify the risk factors associated with adverse events.

Material/Methods: Approval from IRB was sought. Electronic records were retrospectively reviewed for patients, who had TACE from 1st November,2009 – 31st August,2016. Baseline imaging, multidisciplinary team(MDT) and clinical notes, pathology labs, TACE angiograms and follow up imaging were reviewed. Procedure complications were reviewed and analyzed in SPSS version 19.

Results: Total of 171 patients had TACE for HCC. 58 patients had chemo related side effects which included post embolization syndrome. 79 had transient liver failure, 2 had hepatorenal syndrome and access site hematoma in 3 patients. Post procedural paraparesis was noted in 1 patient. There was dissection of segmental branch of hepatic artery in 1 patient, tumor perforation in 1 patient and death in 1 patient.

Conclusion: TACE is relatively safe procedure with low complication rate.

ROLE OF COMPUTED TOMOGRAPHY IN EARLY DETECTION OF FUNGAL INFECTION IN IMMUNOCOMPROMISED PEDIATRIC CANCER PATIENTS

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Purpose/Objective: Fungal infections in immunocompromised children have high morbidity and mortality despite development of newer antifungal agents. It is essential to diagnose at the earliest possible stage. In early stages chest radiograph is usually normal. CT findings in children include segmental and multilobar consolidation, peripheral infiltrates, multiple small nodules, and peripheral nodular masses. We conducted a study to look for CT sensitivity to detect fungal infection and common patterns in early stages in immunocompromised pediatric cancer patients.

Methods/Materials: Electronic records were retrospectively reviewed for immunocompromised pediatric cancer patients who had CT thorax from 01-05-2015 to 30-04-2016 with clinical suspicion of fungal infection. Number of patients, gender, CT thorax findings and histopathology reports were observed and analyzed in SPSS 20.

Results: Total 126 pediatric cancer patients had clinical suspicion of fungal infection in 1 year and CT thorax was performed. All children had age 15 years and below. Out of the total only 46 children showing various patterns of nodules and multiple small consolidations raising fungal infection possibility radiologically were reported as suspicious and underwent biopsy/bronchoalveolar lavage to confirm fungal infection by histopathology. Out of these 43% (20) were female and 57% (26) were male children. 53% were positive and 47% were negative on histopathology. The most common presentation on CT was solid nodules with ground glass haze in 26% (12) patients followed by peripheral solid nodules with consolidation and cavitatory lesions each in 6 patients.

Conclusion: CT is quite sensitive in detecting early fungal infection in immunocompromised pediatric cancer population as an initial investigation.

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POST ESOPHAGECTOMY ANASTOMOTIC LEAKAGE- EARLY RADIOLOGICAL DETECTION AND OUTCOMES

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Purpose/Objective: Esophagectomy is the common method of esophageal carcinoma treatment with many surgical technique options. Many early and late complications are noted in post esophagectomy patients. Regarding early complications anastomotic leakage is most frequently seen which may change outcome of the procedure and affects prognosis. Fluoroscopic examination is first radiological investigation to look for leakage which can be complemented by immediate CT if necessary. It's not uncommon to witness some degree of aspiration in patients performing swallow contrast studies. We performed a study to look for frequency of anastomotic leak and check sensitivity of radiological procedures in early postoperative period.

Material/Methods: We retrospectively reviewed the electronic records of patients over a period of 6 months from 01 January 2016 to 30 June 2016 who underwent various types of esophagectomy procedures and had radiological evaluation during first post-operative week. Frequency of anastomotic leakage and radiological sensitivity to detect were observed and data was analyzed on SPSS 20.

Results: Out of total 108 patients 68(63%) were female and 40(37%) were male. Age range was between 35 to 72 years. All these patients underwent post esophagectomy imaging during 1st postoperative week to rule out anastomotic leakage. Total 13(12%) patients out of 108 showed evidence of anastomotic leakage on contrast swallow study. 3(2.7%) patients had contrast leakage picked on CT only and was missed on swallow procedure. 6(5.5%) patients had frank aspiration during swallow.

Conclusion: Anastomotic leaks can be detected confidently during early postoperative esophagogastrectomy period radiologically helping surgical peers in active management.

SIGNIFICANCE OF CT UROGRAPHY INVESTIGATION IN DETECTING UROLOGICAL MALIGNANCY

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Purpose/Objective: CT urography has become the modality of choice for imaging the urinary tract. The reasoning for using ct urography to investigate hematuria is based on its high diagnostic accuracy for urothelial cell carcinoma (UCC) and favorable comparison with other imaging techniques. The optimum diagnostic imaging strategy for patients with hematuria at high-risk for ucc involves the use of ct urography as a replacement for other imaging tests (ultrasonography, intravenous urography, or retrograde ureteropyelography) and as a triage test for cystoscopy, resulting in earlier diagnosis and improved prognosis of bladder cancer, uut-ucc, renal cell cancer and stones. Ct urography is recommended as the initial imaging test for hematuria in patients at high-risk for ucc. The study is designed with following objective. Significance of CT haematuria protocol among all other standard protocol investigation with emphasis on the diagnosis of urological malignancy using subjective and objective approach.

Material/Methods:

Data were prospectively collected on haematuria referrals to Radiology department of Shaukat Khanum Memorial Cancer Hospital. The standard protocol of investigation included flexible cystoscopy, urine cytology and culture, upper tract imaging, consisting of a renal tract ultrasound scan and a radiograph of kidney-ureterbladder (KUB), proceeding to an intravenous urogram (IVU) and CT haematuria protocol in selected patients.

Results:

209 patients were examined; 67% (n = 141) had microscopic haematuria and 33% (n = 68) had frank haematuria. No malignancy was found in patients with microscopic haematuria below 50 years of age. The findings of malignancy were not associated with either the sex or duration of symptoms in either groups. No association between the presence of symptoms and the finding of malignancy was observed in the microscopic haematuria group. 28% of patients presenting with frank haematuria had malignancy compared with 3.9% of patients with microscopic haematuria (p < 0.0001). Of patients under 70 years with frank haematuria, males were more likely than females to have malignancy. Urine cytology had a poor predictive value for detection of malignancy with a sensitivity of only 25%. Almost 70% of urological malignancy is detected on CT haematuria protocol. In this data 58% of urological malignancy is of bladder, 42% of kidneys and ureters. These results showed that Ct haematuria protocol scan is a good modality for detecting the urological malignancy.

Conclusion:

Full investigation of all patients with frank haematuria and those with microscopic haematuria above 50 years of age, is well justified. Patients under 50 years with microscopic haematuria should have a lower priority for investigation. Out of all standard protocol of investigations CT haematuria is the best for detecting the urological malignancy.

07_O

SHEARWAVE ELASTOGRAPHY PATTERN OF PRESENTATION OF BREAST LUMPS- A NOVEL SCORING SYSTEM

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Purpose/Objective: Shearwave elastography (SWE) is a recent imaging technology being used for assessment of breast lumps. There is a default setting to measure tissue stiffness of the lesion in order to determine its biological nature. The technique showed superiority in determining malignancy in breast lumps however this still lacks definition of characteristics of malignant lesions on shearwave. This prospective study was conducted to:

(i) Define characteristics of malignancy on SWE and analyze if there is any influence of age over the qualitative or quantitative measurements. (ii) Analyze combination of quantitative and qualitative parameters to assess diagnostic accuracy

Material/Methods: All patients over 15 years of age presented with breast lumps were included. They were grouped into three categories according to age <40, 40-60 and >60 years. Shearwave elastography was done by using Aixplorer Ultrasound System Multiwave version 8.2.0 (Supersonic Imagine S.A., Aix-en-Provence, France) with Superlinear TM (SL15-4* 50 mm Super Linear Array) probe. Qualitative assessment was done on color code (ie blue, yellow, orange, red and dark red) and presence of signal void dark area. Quantitative assessment was taken in kilopascals (KPA), where mean KPA was taken from the darkest area. All patients underwent tru-cut biopsy to confirm histopathology. Each parameter was individually correlated with histopathological diagnosis; broadly categorized into benign and malignant lesions. Finally the parameters were combined to see if combination further improves diagnostic accuracy. The data was analyzed by using SPSS (18.0) and comparison was done by using chi-square test.

Results: There were 109 patients with breast lumps. Summary of the results is given in table 1 and 2. Following the results of the individual correlation a combine score was determined into three categories: Score1= Color: blue, yellow, orange, signal void area: absent, Mean KPA; <200, Score 2= Color: Red, dark red, signal void area: ±, Mean KPA: 200-250, Score 3= Color: Dark red, punched out lesion: present, Mean KPA: >250.

Conclusion: Shearwave elastography show different characteristics of benign and malignant lesions. However on individual parameters there is a little overlap, while combining these parameters score 1 & 3 accurately define benign and malignant lesions. The diagnostic accuracy for malignant lesion is highest for women >60 years.

BONE SCINTIGRAPHY IN GASTROINTESTINAL MALIGNANCIES - INSTITUTIONAL EXPERIENCE

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Purpose/Objective: The aim of the study is to review Tc99mMDP bone scans performed in patients with known gastrointestinal malignancy and the utility of SPECT/CT in characterization of bone lesions.

Material/Methods: Retrospective review of bone scans done between June 2014 to June 2016 in patients with known gastrointestinal malignancy, using electronic Hospital Information System (HIS).

Results: A total of 71 patients (34 males, 37 females; age range: 22 - 84 years) had bone scan over 24 months period. The commonest indications for referral was musculoskeletal pain (n=30) followed by suspected bone metastasis on other imaging [CT (n=23), PET/CT (n=3)], pathological fracture (n=1), neurological symptoms (n=1), hypercalcemia (n=1) or others (n=12). Metastatic lesions were identified in 21 (30%) patients while 50 (70%) patients had benign lesions or normal bone scans. Amongst 21 patients with osseous metastasis unifocal lesion (19%) were identified in 4: axial skeleton (n=1) appendicular skeleton (n=3). Seventeen (81%) patient had multifocal lesions; axial skeleton (n=3), appendicular skeleton (n=4) and both axial + appendicular (n=10, 59%). Only 3 (14%) patients had concurrent visceral metastasis along with osseous metastasis. In our cohort, based on the location of primary tumor the frequencies of osseous metastasis were; esophagus 31% (11 out of 35), gastric 36 %(4 out of 11), gastroesophageal junction 1.5% (1 out of 8) and colorectal 29% (5 out of 17). SPECT/CT was acquired in 15 out of 71 patients, which characterized lytic (n=4), osteoblastic (n=2) lesions and degenerative changes (n=5). Additional lesions were seen in 3 cases (metastasis 1, benign 2). Overall, bone scan upstaged disease in 30% and down staged 11% patients.

Conclusion: Bone metastases in GI malignancies, though uncommon, show an aggressive pattern, with axial and appendicular involvement, and can be readily identified with bone scintigraphy in symptomatic patients.

HIGH PREVALENCE AND PREDOMINANCE OF BRCA1 GERMLINE MUTATIONS IN PAKISTANI TRIPLE-NEGATIVE BREAST CANCER PATIENTS

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Purpose/Objective: Women harboring BRCA1/2 germline mutations have high lifetime risk of developing breast/ovarian cancer. The identification of women carrying mutations in these genes is clinically important and has a significant socio-cultural impact. The recommendation to pursue BRCA1/2 testing is based on patient's family history of breast/ovarian cancer, age of disease-onset and/or pathologic parameters of breast tumors. Here, we investigated if diagnosis of triple-negative breast cancer (TNBC) independently increases risk of carrying a BRCA1/2 mutation in Pakistan.

Material/Methods: Five hundred and twenty-three breast cancer patients including 237 diagnosed ≤30 years of age and 286 with a family history of breast/ovarian cancer were screened for BRCA1/2 small-range mutations and large genomic rearrangements. Immunohistochemical analyses were performed at one center. Univariate and multiple logistic regression models were used to investigate possible differences in prevalence of BRCA1/2 mutations according to patient and tumor characteristics.

Results: Thirty-seven percent of patients presented with TNBC. The prevalence of BRCA1 mutations was higher in patients with TNBC than non-TNBC (37% vs. 10%, P < 0.0001). 1% of TNBC patients were observed to have BRCA2 mutations. Subgroup analyses revealed a larger proportion of BRCA1 mutations in TNBC than non-TNBC among patients 1) diagnosed at early-age with no family history of breast/ovarian cancer (14% vs. 5%, P = 0.03), 2) diagnosed at early-age irrespective of family history (28% vs. 11%, P = 0.0003), 3) had a family history of breast cancer (49% vs. 12%, P < 0.0001), and 4) those with family history of breast and ovarian cancer (81% vs. 28%, P = 0.0005). TNBC patients harboring BRCA1 mutations were diagnosed at a later age than non-carriers (median age at diagnosis: 30 years (range 22–53) vs. 28 years (range 18–67), P = 0.002). The association between TNBC status and presence of BRCA1 mutations was independent of the simultaneous consideration of family phenotype, tumor histology and grade in a multiple logistic regression model (Ratio of the probability of carrying BRCA1/2 mutations for TNBC vs. non-TNBC 4.23; 95% CI 2.50–7.14; P < 0.0001).

Conclusion: Genetic BRCA1 testing should be considered for Pakistani women diagnosed with TNBC.

ABSENCE OF THE FANCM C.5101C>T MUTATION IN BRCA1/2-NEGATIVE TRIPLE-NEGATIVE BREAST CANCER PATIENTS FROM PAKISTAN

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Purpose/Objective: Breast cancer (BC) is the most common cancer among women worldwide. Approximately 5– 10% of BCs are hereditary caused by monoallelic germ line mutations in BC susceptibility genes such as BRCA1, BRCA2, PALB2, BRIP1, and genes of the RAD51 family. BC susceptibility is connected with the Fanconi anemia (FA) pathway, since biallelic mutations in at least four genes, BRCA2 (FANCD1), PALB2 (FANCN), BRIP1 (FANCJ) and RAD51C (FANCO) have been shown to also cause FA. Recently, a nonsense mutation, c.5101C>T in FA gene FANCM has been reported in BRCA1/2-negative triple-negative breast cancer (TNBC) patients from Finland. Given that deleterious mutations in other FA genes including FANCD1 (BRCA2) and FANCO (RAD51C) have previously been identified among TNBC patients from Pakistan, we investigated whether the FANCM c.5101C>T mutation is associated with BRCA1/2-negative TNBC patients in Pakistan.

Material/Methods: Constitutional genomic DNA from 117 BRCA1/2-negative TNBC patients and 188 controls from Pakistan were screened for FANCM c.5101C>T mutation using denaturing high-performance liquid chromatography analyses followed by direct DNA sequence analysis of variant fragments.

Results: The FANCM c.5101C>T mutation was absent in the 117 TNBC cases and 188 controls implying that this mutation does not or rarely contributes to TNBC in this population. However, two other FANCM missense mutations in exon 20 were identified. A mutation, c.4931G>A (p.R1644Q) was found in two unrelated early-onset TNBC patients of Persian ethnicity from families with no history of any cancer. It was absent among the 188 controls suggesting that it may be disease causative. The overall frequency of this mutation among early-onset TNBC patients was 2.7% (2/75). The other novel, in silico predicted to be likely disease causative mutation, c.4936G>C (p.A1646P), was found in a 39-year-old control of Punjabi ethnicity with no family history of breast/ovarian cancer. Her son and a nephew were diagnosed with leukemia at age 4 and 6, respectively. Both patients were deceased before initiating this study hampering co-segregation analysis of the mutation with the disease.

Conclusion: FANCM c.5101C>T mutation is absent in Pakistani TNBC patients. Whole gene screening studies are warranted to clarify the role of FANCM gene in TNBC predisposition in Pakistan.

DIAGNOSTIC UTILITY OF P120 (DELTA-CATENIN) IN DIFFERENTIATING INVASIVE LOBULAR CARCINOMA FROM INVASIVE DUCTAL CARCINOMA OF BREAST

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Purpose/Objective: To determine the diagnostic accuracy of p120 in differentiating invasive lobular carcinoma from invasive ductal carcinomas of breast by taking histopathology as gold standard.

Material/Methods: This study was conducted at Fatima Memorial Hospital, Lahore. A total of 200 cases of ILC and IDC found suitable by inclusion criteria were included in this study. The cases were stained with Hematoxylin and Eosin to see the morphology and to establish the diagnosis. IHC staining for p120 was performed according to the specifications given by the manufacturer including appropriate positive and negative controls. Demographic details and p120 IHC staining results were recorded on the proforma. Cytoplasmic p120 staining was taken as positive and only membranous or absent p120 staining was taken as negative.

Results: Out of 200 cases, 38.5% (n=77) were between 20-40 years of age while 61.5% (n=143) had age 40 years or more. Mean age + SD was calculated as 43.94+7.45 years. Regarding the type of carcinoma, 86.5% (n=173) were IDCs while 13.5% (n=27) were ILCs. The diagnostic accuracy of p120 in differentiating invasive lobular carcinoma from invasive ductal carcinomas of breast was calculated as 81.48%, 88.44%, 52.38%, 96.84% and 87.5% for sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate respectively.

Conclusion: We concluded that p120 has good diagnostic utility in differentiating invasive lobular carcinoma from invasive ductal carcinomas of breast and may be used as a useful breast cancer marker for ILC. **Keywords:** p120, Invasive Lobular Carcinoma, Invasive Ductal Carcinomas

POTENTIAL OF SUBSTANCE P/NK-1R AS A DIGNOSTIC MARKER IN BREAST CARCINOMA PATIENTS

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Purpose/Objective: Breast carcinoma (BC) is the most frequent type of cancer in females. Aims: Aim of the present study was to evaluate the expression and distribution of Substance P (SP) in different grades of BC and the potential of SP/ Neurokinin-1 Receptor (NK-1R) as a diagnostic marker.

Material/Methods: 34 BC biopsies were immunohistochemically analyzed by using SP antibody and NK-1R in few core biopsies. 3 cases were well differentiated, 8 were moderately differentiated and 23 were poorly differentiated. HE, ER, PR, HER2 and Ki-67 staining was performed.

Results: Maximum cases fall in the age range of 30-50 years. Mean age of patients was 46.65 years. 68% of cases were SP positive. 30% moderately differentiated, 61% poorly differentiated and 8% of well differentiated carcinoma cases were positive for SP. SP expression intensity was maximum (+3) in poorly differentiated and moderately differentiated cases.

Conclusion: SP is over expressed in BC and there is significant association between grade of tumor and SP over expression. SP can be considered as a cheap and effective marker for the diagnosis of BC. We also suggest SP /NK-1R system as a potential therapeutic strategy to inhibit and manage BC. Its expression can be used as a predictor for BC prognosis.

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LKB1- A POTENTIAL NOVEL THERAPEUTIC MARKER AND CLINICAL SIGNIFICANCE IN BREAST CANCER

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Purpose/Objective: The role of liver kinase B1 (LKB1), a serine/threonine kinase, has been described in the development of Peutz Jagher's syndrome, where a large proportion (45%) of patients have been reported to develop breast cancer in their life time. Cell line studies have also shown a link of LKB1 with the action of oestrogen, metformin and diabetes. This study aimed to investigate the intracellular molecular relationships of LKB1 in older women with early operable primary breast cancer and its correlation with clinical outcome.

Material/Methods: Between 1973-2010,a consecutive series of 1,758 older (≥70 years) women with T0-2N0-1M0 breast carcinoma were managed in a dedicated facility. Of these 813 patients underwent primary surgery and 575 had good quality tumour samples available for tissue microarray construction. LKB1 was assessed by indirect immunohistochemistry using Ley37D/G6-ab15095/Abcam(primary antibody) and Envision method (secondary antibody). Tumours having 30% of cells with cytoplasmic LKB1 expression were considered positive. LKB1 expression was compared with a number of pathological factors and biomarkers, and also correlated with the long-term clinical outcome.

Results: Positive LKB1 expression was seen in 318 (78.1%) patients, significantly associated with high tumourgrade (p=0.01), HER2 overexpression (p=0.003), Ki67 (p=0.01), VEGF (p=0.002), HER4 (p=0.001), BRCA2 (p=0.01), MDM2 (p<0.001) and negative expression of CD44 (p=0.03). However there was no significant correlation with tumour size, axillary lymph node status, ER, PgR, p53, basal or luminal cytokeratins, BCL2, Muc1, EGFR, HER3, MDM4, E-cadherin, and BRCA1.

No correlation was found between LKB1 positivity and clinical outcome. However in those patients receiving endocrine therapy LKB1 positivity was significantly associated with better 5-year breast cancer specific survival (93% versus 74%, p=0.03).

Conclusion: While LKB1 positivity shows strong correlations with most biomarkers known to be associated with poor prognosis, it also appears to be associated with better clinical outcome in a selected group of patients treated with adjuvant endocrine therapy. Further research is required to explore its potential role as a therapeutic target.

INVOLVEMENT OF HBA1C WITH BREAST CANCER MORTALITY IN KARACHI, A CROSS-SECTIONAL STUDY

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Purpose/Objective: Breast Cancer is the most common type of cancer among Pakistani females with 45.42% and the studies show the highest incidence of Breast Cancer in Karachi as compare to other regions. Previous studies have shown a relationship of HbA1C among different types of cancers. The purpose of this study is to evaluate the relationship of HbA1C with breast cancer mortality.

Material/Methods: The data were extracted from the Breast cancer unit of tertiary care hospitals and outpatient clinics of Karachi during Nov-2015 to Apr-2016. The systemic data sampling was done and 452 breast cancer patients were recruited for the study (age between 30 to 60 years). The HbA1c, BMI, obesity, menstrual history, socio-economic status, smoking status, disease process, treatment, and any co-morbid status were also included. The mortality status was evaluated from date 1st follow up and diagnosis of the Breast Cancer to date of last follow up. The mortality ratio was analysed with two groups of HbA1C, patients whose HbA1C was less than 7% and greater than 7%. The association of HbA1C with other variables were analysed by chi-square. The mortality ratio was obtained and compared with HbA1C level.

Results: The higher ratio of mortality is being seen in patients with higher levels of BMI, obese women, postmenopausal women, low socio-economical status especially rural areas of Karachi, and with prolonged Diabetes. The association was particularly marked in obese subjects, as compared to non-obese subjects. The mortality status has also shown significant increase in patients having both high levels of HbA1C and BMI. Hence, it has been that diabetes is strongly associated with obesity and it tends to increase the risk of breast Cancer, especially in postmenopausal women. The relationship between mortality and HbA1C level did not show statistically significant increase but the higher mortality is seen in subject having dependently diabetes and in obese women.

Conclusion: It has been seen statistically significant association between HbA1C, obesity and Diabetes, however, there were no significant associations found with mortality.

ROLE OF CISPLATIN AND DOXORUBICIN AS NEOADJUVANT IN LOCALLY ADVANCED TRIPLE NEGATIVE BREAST CANCER

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Purpose/Objective: In Pakistan triple negative breast cancer is getting common. Its aggressive behavior accounts for its detection at advanced stage. Neoadjuvant chemotherapy is very helpful before local surgical treatment. Platin based chemotherapy has proven beneficial for treating patients. Cost of drugs and limited resources are very important factors in treating poor patients. Cisplatin and doxorubicin were used as chemotherapeutic agents to see outcome in patients.

Material/Methods: Patients were enrolled from Sir Ganga Ram Hospital Lahore, Mayo Hospital Lahore and Services hospital Lahore. All patients had biopsy proven locally advanced invasive triple negative breast cancer. There was no evidence of metastatic disease on (CT chest, CT abdomen and bone scan). Patients were planned for treatment with cisplatin (60 mg/m2) and doxorubicin (50 mg/m2) every three weeks for six cycles. Evaluation was done at regular interval after two cycles for response using response evaluation criteria in solid tumors. Patients showing signs of toxicity or progressive disease were excluded and shifted to other chemotherapy. After completion of chemotherapy, local surgical treatment was given followed by loco regional radiation therapy. End point was to access response rate and disease free survival. Complete response, partial response, stable disease and progressive disease were assessed using response evaluation criteria for solid tumors. Patients with recurrent disease were offered further chemotherapy regimen in follow up. Overall survival was also assessed.

Results: A total of 243 patients were enrolled. 10% of the patients progressed during neoadjuvant chemotherapy and were excluded. 230 patients were evaluated for response assessment, disease free interval and overall survival. 28% patients showed complete response, 40% showed partial response and 30% showed stable disease. No acute toxicity was observed during chemotherapy.

Conclusion: Cisplatin and doxorubicin are effective as neoadjuvant chemotherapeutic agents in locally advanced disease. More randomized trial can be carried out to clearly define their efficacy. These drugs can prove helpful in better outcome of breast cancer patients.

PATHOLOGIC COMPLETE RESPONSE IN HER-2 POSITIVE BREAST CANCER PATIENT RECEIVING TRANSTUZUMAB IN NEOADJUVANT SETTING

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Purpose/Objective: Pathological complete response is a predictor of better long term survival. Transtuzumab, a humanized antibody against humanized epidermal growth factor receptor type 2, is effective against HER-2 positive breast cancer patients. We retrospectively compared the PCR in HER-2 positive breast cancer patients getting neoadjuvant chemotherapy with or without transtuzumab.

Material/Methods: HER2-positive, locally advanced with palpable nodes, breast cancer patients who received Neoadjuvant chemotherapy were retrospectively studied. All patients receiving transtuzumab in neoadjuvant setting at shaukat khanum memorial cancer Hospital from 2008 to 2016, fulfilling the inclusion criteria were observed. The comparison group included randomly selected equal number of HER2- positive breast CA patients getting neoadjuvant chemotherapy having same characteristics.

Results: Of 89 patients receiving transtuzumab preoperatively, 66 patients received full dose of transtuzumab alongwith chemotherapy. Equal number of patients were selected by random assortment for the reference group who did not receive transtuzumab before surgery. Pathological complete response (pCR; defined as no residual invasive or in situ residual tumor in breast tissue, or in the lymph nodes) rate of study group was 50%, which was 26.1% higher then the reference group (23.9%) and this difference is statistically significant with a P value of 0.002. The overall pCR was 36.6%.

Conclusion: This study confirms that using transtuzumab with neoadjuvant chemotherapy in HER2 overexpressing breast cancer patients results in much improved pCR rates which in turn can be translated into better patient outcome and disease free survival.

MANAGING THE AXILLA IN EARLY BREAST CANCER. IMPACT OF ACOSOG Z00011 TRIAL IN CHANGING PRACTICES IN A LOW MIDDLE INCOME COUNTRY

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Purpose/Objective: The ACOSOG Z0011 trial has been described as practice-changing. The new guidelines have been adpted at SKMCH since April 2014. The goal of this study was to determine the impact of the trial on surgeon practice patterns at our institution.

Material/Methods: A comparison of patients undergoing surgery for early breast cancer before and after the implementation of the new guidelines was done. We adopted the new guidelines in April 2015. Patients meeting Z0011 inclusion criteria were identified. For group A (Pre Z0011) patients operated between Jan to Dec 2013 were studied. And for Group B (Post Z0011) patients operated between July 2014 to Jun 2015 were included. Clinicopathologic data were compared between the two groups.

Results: There were 318 patients with clinical T1-2 tumors planned for breast conservation. 68% patients had T1 tumor and 32% had T2. 92% of the patients had IDCa. There were 150 patients in the pre-Z0011 group and 168 post-Z0011. 68% of the patients in Group A were ER+ve while 70% in group B. 36 (23.3 %) patients were sentinel lymph node (SLN) positive in the pre-Z0011 group versus 42 (13 %) post-Z0011 (p = 00.06). Before Z0011 100 % (36/36) of SLN-positive patients underwent axillary node dissection (ALND) versus 24 % (10/42) after Z0011 (p < 0.01). Median no of SLNs identified in group A were 1.3 and group B were 1.4. After Z0011, surgeons were more likely to perform ALND on patients with larger tumors (2.8 vs. 1.8 cm, p = 0.01), lobular histology (p = 0.01), presence of LVI (p = 0.04). There was a decrease in median operative times of the two groups (99 vs. 68 min, p < 0.01). There was a significant decrease in the overall hospital stay of sentinel lymph node positive patients in between the two groups (1.8 days vs 1.3 days p value < 0.01).

Conclusion: Surgeons at our institution have implemented Z0011 results with a significant short term advantages. However the real question to be answered is the increased risk of recurrence and decreased overall survival by not doing the axillary dissection in sentinel lymph node positive patients. A question which requires a longer follow up and a bigger population size to be answered adequately. But for now Z0011 guidelines stand implemented because of the apparent short term advantages they offer.

DO WE NEED TO STAGE AXILLA IN CLINICALLY AND RADIOLOGICALLY NODE NEGATIVE BREAST CANCER PATIENTS?

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Purpose/Objective: Lymph node status is one of the most important prognostic factor in breast cancer. Staging the axilla has been a standard procedure for many decades. Recent studies in this area shows that staging the axilla in clinically and radiologically node negative patients is an over treatment and leads to a un-necessary procedure.

Material/Methods: We analyzed the data of 474 patients who underwent staging sentinel lymph node biopsies as their axillary status was clinically and radiologically negative. Patients with breast conserving therapy and mastectomy were included. All patients who had positive axillary node on FNA were excluded. Data was analysed on SPSS 19.

Results: Total of 428 patient's data was analyzed retrospectively. 428 patients underwent staging sentinel lymph node biopsy. 138 patients had N1 disease and 13 patients had N2 disease while 277 patients were node negative. They all underwent chemotherapy to down stage their disease. 151 node positive patients were subjected to axillary node dissection. Out of 138 patients with N1 disease on staging, only 25 patients were found to had positive lymph nodes while 113 were pathologically node negative. In N2 group only 03 patients stayed node positive while 10 patients became node negative.

Conclusion: This study shows that staging the axilla before chemotherapy in clinically and radiologically node negative patients is a un-necessary procedure and leads to loss of resources.

FREQUENCY OF HPV INFECTION IN HEAD AND NECK SQUAMOUS CELL CARCINOMA- DEMONSTRATED THROUGH IMMUNOHISTOCHEMICAL DETECTION OF ITS SURROGATE MARKER "P16"

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Purpose/Objective: Cancers of the Head and Neck constitute approximately 4% of all malignant tumors; the most common histological type being squamous cell carcinoma. Human papillomavirus (HPV) type 16 accounts for 90–95% of the HPV associated oropharyngeal squamous cell carcinomas. The aim of this study is to find out the prevalence of HPV in head and neck squamous cell carcinomas through p16 IHC immunostaining. P16 is a tumor suppressor gene that regulates cell cycle.

Material/Methods: Paraffin sections of 140 cases of known head and neck squamous cell carcinomas were retrieved from histology section of Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH&RC). All were stained for P16INK4A and the results were evaluated by two pathologists independently. Cervical squamous cell carcinoma was taken as control. It was scored as positive when strong and diffuse nuclear and cytoplasmic staining was observed in more than 50% tumor cells.

Results: The mean age of the patients included in the study was 52 years with 81 males and 59 females. Squamous cell carcinomas from different head and neck sites were included and comprised of 21 cases from pharynx, 18 each from lip, vocal cord and glottis, 19 from tongue, 16 from larynx, 17 from buccal mucosa, 10 from tonsils, and 3 from palate. Out of a total of 140 cases, 49 (35%) were positive for p16 staining and 91 (65%) were negative. 32 out of 49 positive cases (65.3%) showed strong and diffuse nuclear staining. 17 cases (34.7%) showed strong and diffuse nuclear and cytoplasmic staining. HPV 16 was more commonly associated with oropharyngeal, tongue and buccal mucosa SCC than other sites.

Conclusion: HPV 16 has a strong association with causation of head and neck squamous cell carcinomas. p16 proves to be very specific and sensitive surrogate marker for detection of HPV associated head and neck SCC.

METABOLITE PROFILING OF PRENEOPLASTIC AND NEOPLASTIC LESIONS OF ORAL CAVITY TISSUE SAMPLES REVEALED A BIOMARKER PATTERN

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Purpose/Objective: Oral cancer is a major health challenge in the Indian subcontinent and a dreadful form of cancers worldwide. Alarmingly, cancer of oral cavity in Pakistan is second commonest and amongst the highest in the world. This is a globally accepted fact that early detection of cancer greatly increases the chances for successful treatment. It has been strongly proposed that development of effective clinical diagnostic aids and discovery of reliable biomarkers can allow early detection of OSCC or relapse which promises a definitive diagnosis of cancerous and precancerous oral lesions.

Material/Methods: The current study is focused on the identification of distinguished biomarker metabolites of oral cancer tissue samples in comparison with precancerous and control tissue samples using gas chromatography coupled with triple quadrupole tandem mass spectrometry and chemometric analyses.

Samples were collected from Oral and Maxillofacial department of Dr. Ishrat-ul-Ebad Institute of Oral health Sciences, Dow University of Health Sciences, Karachi, consist of 4-6mm punch biopsies of total 51 tissue samples: 15 samples of potentially malignant disorder of oral cavity that is of oral sub-mucous fibrosis (OSF), 21 of diagnosed OSCC patients and 15 from the healthy individuals. GC-MS-based metabolite profiling and chemometric analysis of tissue samples has been performed at H.E.J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi. Metabolites obtained were identified through National Institute of Standards and Technology (NIST) mass spectral (Wiley registry) library. Mass Profiler Professional (MPP) software was used for the alignment and for all the statistical analysis.

Results: 31 compounds out of 735 found distinguishing among oral cancer, precancerous and control group samples using p-value ≤ 0.05 . Partial Least Square Discriminant Analysis (PLSDA) model was generated using statistically significant metabolites gave an overall accuracy of 90.2%. Down-regulated amino acid levels appear to be the result of enhanced energy metabolism or up-regulation of the appropriate biosynthetic pathways, and required cell proliferation in cancer tissues.

Conclusion: In this study, oral cancer and pre-cancerous sample showed a decreased level of amino acids compared to control. Such measurements propose that modulation of amino acid metabolism may represent new potential and novel strategy for the early detection and treatment of premalignant and malignant oral lesions.

RETROSPECTIVE STUDY OF RARE CUTANEOUS MALIGNANT ADNEXAL TUMORS OF HEAD AND NECK IN A TERTIARY CARE CANCER HOSPITAL.

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Purpose/Objective: Skin adnexal tumors are a large and diverse group of benign and malignant neoplasms, which exhibit morphological differentiation towards one of the different types of adnexal epithelium present in normal skin and pose diagnostic challenge. The purpose of this study is to share our experience with these rare but aggressive tumors at a tertiary care cancer hospital in a developing country.

Material/Methods: Retrospective review of 11 patients diagnosed with rare adnexal tumors and its variants from January 2005 to December 2014, treated either surgically or non-surgically, was performed to describe the clinicopathological characteristics and outcome of the disease.

Results: A total of 11 patients were diagnosed with adnexal carcinoma and its variants. Male to female ratio was 1.2:1. The histological variations included sebaceous differentiation (n=3), micro cystic adnexal carcinoma (n=4), trichilemmal carcinoma (n=1), pilomatrix carcinoma (n=1) and hideradenocacinoma (n=1). The mean age at presentation was 49 years (Range 34-75). Primary subsite of involvement was scalp in 9 patients followed by eyelids in 2 patients. Surgery stayed as primary treatment modality in almost all patients while post-operative radiotherapy was offered to 6 patients. Median dose of radiation was 45 Grey to the primary site. Indications for radiotherapy included close margins (n=2), positive margins (n=1), high grade histology (n=3) and multifocal disease (n=1). On follow up, 1 patient (n=1) developed loco-regional recurrence and 2 patients (n=2) developed distant metastasis.

Conclusion: Adnexal carcinomas are rare tumors with diverse histological patterns and a tendency for loco-regional and distant metastasis. Surgery should be the mainstay of treatment reserving radiotherapy for adjuvant, palliative and re-treatment scenarios.

LONG TERM RESULTS OF HYPOFRACTIONATED RADIOTHERAPY IN THE TREATMENT OF EARLY LARYNGEAL CANCER

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Purpose/Objective: Worldwide a range of radiation fractionation policies exist for the treatment of early glottic cancer. The aims of treatment are cure, laryngeal preservation and good voice quality while making effective use of available resources. Radiotherapy is generally the favored treatment in most centers despite comparable cure rates with surgery. In this study we report locoregional control and survival following hypofractionated radiotherapy in T1 early laryngeal cancer treat at Shaukat Khanum Memorial Cancer Hospital and Research Centre.

Material/Methods: Between January 2004 and December 2013, 177 patients with T1 N0 early glottis cancer were treated with hypofractionated Radiotherapy. Radiotherapy dose was 55 Gy in 20 fractions at 2.75 Gy per fraction once daily 5 times per week. All patients were included in the study

Results: Median age was 58 years (range: 21 - 92 years). Male to female Ratio was 12:1. The occurrence of major risk factors for laryngeal cancer smoking and use of smokeless tobacco was seen in 58% and 12% of the patients respectively. Median radiotherapy treatment time was 28 days. At the time of last follow up 6 patients had died of disease, 6 patients were dead of unrelated causes and 4 patients with local failure were successfully salvaged with surgery and are alive and well. The locoregional control rate after primary radiotherapy at 10 years was 84%. The 10 year overall and disease free survival was 86% and 93%.

Conclusion: Hypofractionated radiotherapy 55Gy in 20 fractions provides excellent long term locoregional control and survival with added advantage of optimizing resource usage in early glottis cancer.

OUTCOMES OF HEAD & NECK SQUAMOUS CELL CARCINOMA UNDERGOING SIMULTANEOUS INTEGRATED BOOST INTENSITY MODULATED RADIOTHERAPY (SIB/IMRT) AT SHIFA INTERNATIONAL HOSPITAL (INTERIM ANALYSIS).

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Purpose/Objective: Head & neck cancer can easily be treated with precision radiotherapy. We used simultaneous integrated boost-intensity modulated radiotherapy (SIB-IMRT) in our cohort using the dynamic multileaf collimator (MLC) assembly in linear accelerator, where treatment time for one fraction lasts for ~12-15 minutes on average, and complex IMRT delivery (~15 beams) is completed in approximately 20-25 minutes. The dynamic IMRT ensures limited intra-fractional patient and organ motion, compared to step and shoot IMRT which on the contrary takes >1 hour, and therefore is not a feasible to perform SIB-IMRT, mainly due to time constraints. This trial is the first head & neck SIB/ IMRT study, carried out prospectively in this country. Aims & objectives of the interim analyses are to give preliminary information on clinic-pathological characteristics of patients, acute radiation sequelae, response rates, loco-regional control and disease/ progression free survival till September 30, 2016.

Material/Methods: It is an on-going prospective, cohort study where 50 consecutive patients between September 1st, 2015 to December 31st, 2017 with established diagnosis of head & neck cancer shall be analyzed after being treated with SIB-IMRT + chemotherapy, at Radiation Oncology department, SHIFA International Hospital (SIH), Islamabad. Increasing dose from 1.8 to 2 Gy/ fraction (total 70 Gy) or 2 to 2.2 Gy/ fraction (total dose 66 Gy) to the gross tumor, or the tumor bed will be considered to be associated with a meaningful 15% gain in loco-regional control rates. Consecutive patients undergoing IMRT or 3D-CRT and/or matched patients' who received IMRTor 3D CRT shall act as pre-historic controls in 1:1 or 1:2 manner. The study is approved by Institutional review board & ethics committee of SIH and received a grant from SHIFA Clinical Research, Islamabad. All patients are required to give informed consent. Computerized electronic data from the SIH is being acquired and documented in a questionnaire. Inclusion criteria is: head & neck primary being treated with SIB-IMRT, histology of squamous cell carcinoma, nucopepidermoid carcinoma, adenoid cystic carcinoma, or small round blue cell tumors while the exclusion criteria is, age >70, ECOG PS 3-4, Multiple co-morbid: AKD/ CKD 3-5, GFR <50 ml/ min (when cisplatin is used), decompensated liver disease, poor LVEF (<50%), metastatic disease, dementia, poor charlson comorbidity index, bone sarcoma, lymphoma, melanoma, and benign tumors. RECIST criteria for solid tumors is being used for response evaluation and RTOG/EORT radiation morbidity scoring system and common terminology criteria for adverse events (CTCAE) version 4.0 is used to document all radiation and chemotherapy sequelae.

Results: Interim analyses of enrolled 26 head & neck cancer patients, receiving SIB-IMRT between September 1' 2015 to September 30' 2016, is being presented. The mean age is 58.8 years, (range 43-70 years; excludes a 24 years small sino-nasal round blue cell tumor), median age is 60 years, 14 are males and 12 are females, and the mean time to diagnosis is 7 months (range 15 days-12 months). ECOG PS is 0-1 in 92.3% (24/26) and PS2 7.7% (2/26), 92.3% (24/26) are squamous cell carcinoma, 3.8% each rhabdomyosarcoma and inflammatory myofibroblastic tumour. The primaries locations are; buccal mucosa 23% (6/26), nasopharynx and larynx 19.2% each (5/26), gingiva 7.7% (2/26), and RMT, hard palate, orbit, and maxilla 3.8% each. Tumor grade is Gx 42.3% (11/26), GI 23% (6/26), GII 15.4% (4/26), GIII 19.2% (5/26) and the TNM stage grouping is; Stage I 3.8% (1/26), II 11.5% (3/26), III 19.2% (5/26) and IVa 50% (13/26) & IVb 7.7% (2/26). Resection margins are positive in 36.4% (4/11 patients who underwent surgery) despite frozen section, and the mean tumor size is 4.3 cm (range 1-10 cm). 30.77% (8/26) patients underwent cervical LND with mean number of resected lymph nodes being 31.6 (mean 7-53), mean number of metastatic lymph nodes is 2.6 (range 1-6), and extranodal capsular extension is seen in 11.5% (3/26). 57.7% (15/26) patients received definitive and 42.3% (11/26) adjuvant SIB-IMRT (70/63/56; at 2-1.8-1.6 Gy per fraction x 35 days in 42.3% (11/26) patients, 66/60/54 at 2.2-2-1.8 Gy in 30 days in 50% (13/26) patients, 60/54 at 2-1.8 Gy in 30 fractions and 50/45 at 2-1.8 Gy in 25 fractions in 3.8% each). 69.2% (18/26) received concurrent chemo-radiotherapy (CCRT) (3/18 cetuximab, 13/18 cisplatin, 1 each carboplatin and VAC). 42.3% (11/26) received definitive CCRT, while (27% (7/26) received adjuvant CCRT (4 RM+/ 3 ENE) 23% (6/26) patients have PEG tube insertion prior to commencement of treatment and 3.8% had to undergo tracheostomy, a day before radiotherapy. Mean weight loss is 7.38 kg in 50% patients (13/26) (mean 2-1

The mean high dose region planning tumor volume is 186 cc3 (SD 128 95%CI 130-241) and the range is 31 to 568. The acute radiation + chemotherapy sequelae are; grade 1 face & neck acne like rash 7.7% (2/3) with cetuximab, fatigue, grade I in 46% (12/26), nausea, grade I & II in 42.3% (11/13), vomiting, grade I in 50% (13/26), and renal derangement with cisplatin and grade III vomiting with VAC in 3.8% each. Alopecia in irradiated volumes is seen in 46% (12/26) patients, skin tanning in 77% (20/26), skin grade I in 57.7% (15/26), grade II in 3.8%. Oral mucositis is seen in 57.7% (15/26); grade I in 3.8% (1/26), GII in 38.4% (10/26), and GIII in 15.4% (4/26), with super-added oral candidiasis in 30.77% (8/26) patients despite local measures. Pharyngitis grade II is seen in 38.4% (10/26), grade III seen in 11.5% (4/26), while sinusitis/chest infection is seen in 3.8% receiving VAC. Xerostomia grade II observed in 64.4% (17/26) and taste loss in 57.7% (15/25) patients. Hoarseness grade I 11.5% (3/26), grade II 19.2% (5/26) and SOB 11.5% (3/26), Otitis media grade II 7.7% (2/26), otitis externa grade I is observed in 3.8% each. Most of the acute radiation and chemotherapy associated sequelae are reversed in 3 months.

There is no loco-regional recurrence till filing of this report and all but one patient has persistent regressed disease not amenable to surgery because of contraindication to GA, treated with definitive chemo-irradiation. 19.2% (5/26; 3 nasopharynx, 2 larynx) patients have pathological CR and 77% (20/26) are in clinical and radiological remission. 7.7% (2/26) patients have buccal graft necrosis secondary to chew bite after radiotherapy. 96% (25/26) patients remain disease free till filing of this report (DFS; 8/26 (1-3 months); 7 each (at 3-6 and 6-9 months); and 3 (>12 months) while 3.8% has PFS between 1-3 months.

Conclusion: Majority of these patients (77%) are in advanced stages, and managed in a multidisciplinary team setting, requiring definitive radiotherapy with or without chemotherapy or definitive surgery and reconstruction followed by adjuvant radiotherapy. The mean planning tumor volumes are substantially high and patients' must be counseled for acute side effects, which are anticipated, tolerable, manageable and reversible. Most of the higher grade mucositis occurred in high dose volume. All patients are in remission but one. The follow-up is short and the final outcomes of this ongoing trial shall be available in 2019.

EVALUATION OF TREATMENT PLANS THROUGH DVH TO FIND PTV COVERAGE BY 3DCRT AND IMRT IN LOCALLY ADVANCED NASOPHARANGEAL CANCER PATIENTS.

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Purpose/Objective: Radiation therapy is the mainstay of treatment for nasopharyngeal carcinoma. Moreover its unique location with surrounding critical normal structure and advanced stage at presentation make tumor coverage by radiation a great challenge. Therefore we aim to evaluate our radiation treatment plan through dose volume histogram (DVH) to find planning target volume (PTV) dose coverage and factors affecting it.

Material/Methods: This retrospective study comprised of 45 histologically proven nasopharyngeal cancer patients who were treated with definitive 3D- CRT and chemotherapy between Feb, 2006 to March, 2013 at our institution. DVH was evaluated to find number of shrinking field (phases), PTV volume in different phases and its coverage by the 95% isodose lines along with factors affecting it.

Results: There were 36 male (80%) and 9 female (20%), their ages ranged 12-84 years. Stage IVA (46.7%) was the most common stage followed by stage III (31.1). 86.6% received induction, 95.5% received concurrent and 22.2% received adjuvant chemotherapy. The prescribed median radiation dose was 70Gy to primary, 60Gy to clinically positive neck node and 50 Gy to clinically negative neck. Mean dose to spinal cord was 44.2 Gy. Mean dose to optic chiasma was 52 Gy. 37.8% patients completed their treatment in three phases while 62.2% required four to five phases. Mean volume for PTV3 was 247.8cm3(50-644.3), PTV4 173.8 cm3 (26.5-345.1) and PTV5 119.6 cm3 (18.9-246.1) and PTV volume coverage by 95% isodose line were 74.4%, 85.7% and 100% respectively. Advanced T stage, intracranial extension and tumor volume > 200 cm3 were found to be important factors associated with decrease PTV coverage by 95% isodose line.

Conclusion: 3D CRT results in adequate PTV dose coverage by 95% isodose line. However advanced T stage, intracranial extension and large target volume require more advanced technique like IMRT for appropriate PTV coverage.

SPINDLE CELL CARCINOMA LARYNX: A DISTICNT CLINICO-PATHOLOGICAL ENTITY

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Purpose/Objective: Spindle cell carcinoma (SpCC) is a variant of Squamous cell carcinoma with biphasic components and more aggressive behavior. Its rarity and histopathological pattern poses a diagnostic challenge. Early diagnosis and treatment results in decrease in local and distant metastasis

Material/ Methods: Case presentations: Case 1 is a 71 years old lady presented with Hoarseness of voice and dyspnea for 2 years without any risk factors. FOL revealed smooth polyp hanging from anterior 2/3rd of Left Vocal cord. Micro-laryngoscopic excision revealed Spindle cell carcinoma followed by PORT and is currently alive. Case 2 is a 72 year old male presented with worsening stridor for 2 years post excision of laryngeal nodule and history of smoking and Hookah use for > 20 years. He developed dysphonia after a few months with fixed hard level 3 nodes at right side. Fiber optic laryngoscopy showed a polypoid mass extending from left vocal cord into the supraglottis. FNA of the neck swelling confirmed the diagnosis of spindle cell carcinoma. CT chest/abdomen showed distant metastasis. Palliative RT was given but patient died after 3 months due to loco-regional failure. Case 3 is a 35 year old male presented with history of hoarseness for 3 years with no risk factors. FOL sowed a 1.2 cm polypoid growth on right vocal cord. Total laryngectomy was performed and histopathology showed spindle cell carcinoma. PORT was given and patient is alive without disease with regular follow ups

Conclusion:

Spindle cell Carcinoma (SpCC) is a rare tumor with a tendency for loco-regional recurrence. Surgery should remain the mainstay of treatment followed by Postoperative radiotherapy for a better control.

EVOLUTION OF MANDIBULAR RECONSTRUCTION: SIMPLE TO COMPLEX

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Purpose/Objective: Mandible, the largest and strongest bone of face, is frequently involved in the different pathologies ranging from tumor whether benign or malignant, trauma, and osteoradionecrosis.

The aim of this study is to evaluate the success rate and complications of mandibular reconstruction with different reconstructive options in tumor patients.

Material/Methods: A total of 43 patients who underwent reconstruction of mandibular discontinuity defects between January 2008 to June 2016, at the Jinnah Burn & Reconstructive Surgery Center constituted the study sample. Relevant information was retrieved from the patient's records. This information includes patient's demographics (age and sex) as well as the type of mandibular defect, cause of the defect, source of the vascularized bone graft used and the method of fixation. Morbidity associated with the procedures were assessed by retrieving information on graft failures, length of hospital stays following surgery and associated donor and recipient site complications.

Results: There were 25 males and 18 females with a male: female ratio1.38:1. The age of the patients ranged from 22 to 63 years and for females 25 to 50 years. Jaw defect was caused by resection for tumours (benign or malignant) in all of cases. Reconstruction with vascularized rib graft in 7 cases (16.2%) pectoralis major with sternum 2(4.6%), vascularized iliac crest was used in 05 (11.6%) of the patients and recon plate in 4(9.3%). Free fibula was used in 25(58.1%) cases. Successful reconstruction was recorded in all cases while none failed. Flap reexploration was done in 3 free flap cases and were successfully salvaged. 1 case of recon plate exposure was encountered. Postoperative donor site partial graft loss in 03 patients of free fibula and Wound dehiscence in 1 case of pedicled flaps were the most common complications recorded

Conclusion: The use of vascularized bone graft has best functional and aesthetic outcome and free fibula is the gold standard for the reconstruction of large mandibular defects caused by surgical ablation of benign and malignant conditions. Precise surgical planning and execution, rigid fixation and meticulous postoperative care contributed to the good outcome.

EARLY POST OPERATIVE EXPERIENCE OF WILMS TUMOR SURGERY IN A DEVELOPING COUNTRY.

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Purpose/Objective: To share the experience of the management of patients with Wilms Tumor in a developing country.

Material/Methods: Form Jan 2014 to April 2016 all patients with a diagnosis of Wilms tumor who presented at SKMCH were included in this review. Initial presentation, tumor type, type of surgery offered and early (30 day) surgical outcomes were recorded. Information about complications of surgery and their managements was also retrieved. All data was retrieved from the hospital information system.

Results: A total of 42 patients were operated for Wilms tumor. The most common symptoms were abdominal mass (75%), pain (28%) &fever (19%). Clinical stage at presentation was Stage I in 34%, Stage II in 22%, Stage III in 16% and Stage IV in 27% patients. A total of 48 tumor resections were performed, 45 total nephrectomies and 3 had nephron sparing surgery (NSS). IVC was explored in 6 patients. Seven patients (16%) had a per-operative tumor rupture. Median operative time was 230 mins (±78.7). Median blood loss was 100mls (Range 20-1200mls). Median size of the tumor was 105mm (Range 23-200) and Median Weight of the tumor was 335g (Range 54 to 2016g). Ninety percent patients had a favourable histology. Median time to initiate oral sips were 24 hours and initiation of soft diet was 48 hours. Median high dependency unit (HDU) stay was 1 day (0-6 days) and median hospital stay was 6 days (4-20 days). Complications were observed in 8 patients. 4 patients had persistent vomiting post-operatively requiring prolonged admission. One patient had to undergo exploratory Laparotomy for bowel obstruction due to segmental volvulus of small bowel as a result of adhesive bowel obstruction. One patient developed pneumonia and had to be intubated. Two patients had a wound infection. Thirteen patients had pulmonary metastases, in most patients these resolved after neo adjuvant chemotherapy, 3 had to undergo wedge resections using VATS. One patient had bilateral staged metastatectomy.

Conclusion: Surgery remains a major part of treatment for Wilms tumor. With strictly adhering to the recommended guidelines, multidisciplinary team approach and organized care of individual patients, the outcomes of surgery for can be greatly improved.

SURGICAL EXPERIENCE OF DEALING WITH PEDIATRIC SOFT TISSUE SARCOMAS

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Purpose/Objective: Sarcomas are relatively uncommon type of tumors accounting for less than 15% of pediatric tumors. The accurate diagnosis and expert treatment is pivotal in pediatric sarcomas due to their aggressive nature in most of the cases.

Objectives To evaluate the soft tissue sarcomas in children less than 16 years of age, their anatomical location, type and surgical management

Material/Methods: Case series of soft tissue sarcomas in 26 children aged 16 or less, operated in Plastic surgery department of Patel hospital Karachi. All cases are worked up in children cancer hospital Karachi, discussed in tumor board and sent to Patel hospital Karachi for surgery during 2007 to July 2015 are included in this study. Wide local excisions were performed and reconstruction was done in selected patients.

Results: Rhabdomyosarcoma appeared to be most common type (n: 9) and extremities are most common site (n:18). Wide local excision is most common surgical procedure performed. Primary closure performed in most patients, locoregional and free flaps in 8 patients and skin grafting in 4 patients. All flaps survived. Recurrence was observed in 4 patients.

Conclusion: With early and precise diagnosis, rate of amputation can be reduced in limbs and wide local excision and adjuvant therapy is successful in most of the cases.

RETINOBLASTOMA DISEASE PATTERN SEEN IN A REGIONAL CANCER CENTER IN PAKISTAN.

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Purpose/Objective: Retinoblastoma (RB) is the most common pediatric intra-ocular tumor globally. It is a curable tumor when diagnosed early and treated promptly. In the developed world retinoblastoma accounts for <5% of all pediatric cancers. In the developing world retinoblastoma may comprise of about 10-15% of all diagnosed pediatric cancers according to hospital-based studies in India (Sachdeva et al. Indian J Cancer 2010).

Material/Methods: Medical records at our large regional cancer center were retrospectively reviewed from January 2005 to September 2015 after IRB approval. Data was collected for patients less than 10 years of age at the time of diagnosis with RB.

Results: A total of 255 patients were identified for chart review. There were 160 males and 95 female patients. Out of which 89% (n=242) were diagnosed before the age of 5 years. Positive family history was documented for 7.8% (n=20) of patients. A majority of male patients (n=160) were seen as compared to females (n=95). Total number of bilateral disease was seen in 76 patients as compared 179 unilateral diagnoses. The median age at presentation was 24 months for bilateral disease and 36 months for unilateral disease. Thirty-nine patients abandoned treatment (15.2%).

Conclusion: The median age at presentation shows that there is a significant delay in the establishment of diagnosis for both unilateral and bilateral RB. Compared to data from the U.S. and Europe there was a higher number of male patients seen at the center. Financial stability, access to health care, cultural practices are probable factors leading to delayed presentation and advanced disease sta

OUTCOME OF RENAL TUMORS AMONG CHILDREN AT SINGLE CENTER IN A DEVELOPING COUNTRY

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Purpose/Objective:To determine the outcome of renal tumors among children in our center and compare the results of treatment on the basis of management proposed by the National Wilms tumor study board(NWST) and the Societe international D'oncologie pediatrique (SIOP)

Material/Methods: This study includes 60 children who presented to the Aga Khan University Hospital(AKUH) with renal tumors between 1988 and 2015(aged 0-15 years). The children were divided into those that were diagnosed with wilms tumor and those that had other renal tumors. Wilms tumor patients were further divided according to the treatment strategies they received ie NWST and SIOP and a clinical evaluation was preformed of all patients.

Results: Tumors mostly presented on the right side (65%) and often presented as an asymptomatic abdominal mass in half of the patient population. The diagnostic work up mainly involved CT imaging alone or in combination with an ultrasound abdomen. 39% of the children with Wilms tumor in the SIOP group presented with stage 3 diseases whereas in the NWST group the majority presented with stage 1 disease. Patients with other renal cancers mostly presented with stage 3 disease. In the SIOP group after the treatment 4(14%) patients had disease reoccurrence and 2 patients died due to disease and chemotherapy complications. In the NWST group, 2(9.5%) patients had disease reoccurrence and 1 patient expired. Overall survival of Wilms patients was >80%. In the other tumors group, 1 patient of Rhabdoid tumor expired 2 patients with renal cell carcinoma developed disease complications.

Conclusion: In contrast to nonWilms tumors, Wilms tumors are curable in the majority of the patients even with limited resource as in our country. The NWTS and SIOP treatment approaches are almost equally effective at our center however adherence to a single treatment is mandatory for effective treatments

Keywords:- Renal Tumors, Wilms Tumor, chemotherapy, Societe international D'oncologie pediatrique, National Wilms tumor study board

PAEDIATRIC FEBRILE NEUTROPENIA EMERGENCY MANAGEMENT IN A TERTIARY CANCER CENTER IN PAKISTAN

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Purpose/Objective: Febrile neutropenia (FN) is an emergency in patients with a malignancy. Mortality rates are higher for pediatric patients when compared to older patients (1). Time to antibiotics in patients with fever and neutropenia is an important quality measure for oncology centers. Here we aim to review FN patient data at our institution.

Material/Methods: We retrospectively collected data on a cohort of pediatric patients presenting to the emergency department (ED) over 10-weeks from April to June of 2016. The aim was to determine the time from triage to antibiotic administration and the consequent clinical outcome.

Results: There were 113 patient charts identified with febrile neutropenia. The median time from triage to antibiotic administration was 83 minutes (range: 3 - 319). Most patients did not have a central line. The median length of stay in the hospital was 5 days with no increase seen in patients with delayed antibiotic administration.

Conclusion: Our set-up is of an oncology center with limited resources in a developing country. We do not see increased morbidity or mortality associated with delayed antibiotic administration in the ED. Though as a quality care benchmark we feel that antibiotics should be administered within the first 2-hours of presentation to the ER (2).

ROLE OF BONE MARROW ASPIRATION AND BIOPSY IN DIAGNOSTIC STAGING OF PEDIATRIC EWING SARCOMA

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Purpose/Objective: Ewing sarcoma (ES) is the second most common primary malignant bone tumor in children and adolescents (Esiashvili N et al. J Pediatr Hematol Oncol 2008). ES tumors can occur in bones of the extremities, pelvis, chest wall as well as soft tissue2. Pediatric Ewing sarcoma (ES) treatment protocols at present indicate the need for bilateral bone marrow aspiration and biopsy (BMAB) as part of the initial staging work-up. There are no established recommendations that assist in evaluating the need for BMAB procedure in patients identified as having non-metastatic ES according to conventional imaging (CI). Here we aim to report our institutional experience of positive BMAB findings in patients who were considered non-metastatic on standard imaging studies.

Material/Methods: Medical records at a large regional cancer center were retrospectively reviewed from January 2010 to January 2015 after IRB approval. Data was collected for patients with newly diagnosed non-metastatic ES on imaging studies and less than 20 years of age at the time of diagnosis.

Results:

A total of 139 patients were identified for chart review. Ten patients were excluded from the analysis because BMAB was not done at initial staging. Eleven patients were identified to have bone marrow (BM) disease. Among these 5 (45.5%) had metastatic disease on bone scan (p-002) and 1 (0.09%) had additional pulmonary and bone metastases. Six patients (54.5%) with isolated BM disease were non-metastatic on CI. Two of these patients had primary pelvic disease.

Conclusion: Patients with metastatic disease on bone scan have a higher risk of bone marrow involvement and should get BMAB on initial staging. There can be BM involvement without the presence of metastatic disease. We suggest performing BMAB at the initial staging for all newly diagnosed pediatric patients with ES.

A RETROSPECTIVE ANALYSIS OF PAEDIATRIC PATIENTS WITH WILMS TUMOR FROM A TERTIARY CARE CENTER IN PAKISTAN.

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Purpose/Objective: Wilms Tumor (WT) is common renal malignancy in Paediatrics and requires a team comprised of oncologists, surgeons and radiotherapists. Although outcomes for patients with WT have dramatically improved as a result of this collaboration, in resource poor countries limited treatment centers and delayed treatment initiation cause disparities in overall survival. Our analysis reports time to oncologist among other factors impacting outcome.

Material/Methods: A retrospective analysis was done of Paediatrics patients with WT presenting to cancer hospital from 1/1/2009 to 1/9/2014.

Results: A total of 113 patients with WT were reported (67 male, 46 female). Seventy five percent of patients were <5 years. Time to referring physician after onset of presenting complaint was <4 weeks in 80% of patients. Time to oncologist was <4 weeks (25%), 4-12 weeks (40%) or >12 weeks (35%). Diagnosis was made by Trucut biopsy in 40 patients with a 95% yield and no complications. Twenty-eight patients (25%) had an upfront nephrectomy, of these; recurrent/residual disease was seen in 41 patients (37%). Radiation and pre and post-operative chemotherapy was per SIOP WT-2001. Local stage post-nephrectomy was Stage I (31%), Stage II (18%), Stage III (55%) and Stage IV (2%). Seventy-two percent of WT was favorable-histology and the remainder unfavorable-histology. On last follow up 42% were in complete remission, 8% had progressive disease, 25% succumbed to disease and 24% abandoned treatment.

Conclusion: High rates of metastases and disease recurrence post-nephrectomy are significant contributors to poor survival of children with WT. Our institution accepts patients regardless of ability to pay after diagnoses have been confirmed histopathologically which can be burdensome on families owing to socio-economic constraints, causing delays in treatment initiation. We propose the need for initiatives to broaden awareness within the community, for earlier referral and to prevent inappropriate surgery.

POST INDUCTION MINIMAL RESIDUAL DISEASE ANALYSIS IN CHILDHOOD B LYMPHOBLASTIC LEUKAEMIA

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Purpose/Objective: Presence of post induction minimal residual disease (MRD) in pediatric B Lymphoblastic Leukemia is associated with poor prognosis. This study is aimed to determine the frequency of post induction MRD in pediatric B ALL patients and its relation to gender, age, total leukocyte count (TLC) and CNS involvement at diagnosis.

Material/Methods: This cross sectional study was carried out on pediatric patients presenting at Indus Children Cancer Hospital, conducted at hematology department, Dr. Ziauddin University Hospital from May, 2015 to March, 2016. MRD analysis was performed on 100 post induction bone marrow samples of pediatric B ALL (age 1 to 17 years) by flowcytometer (Becton Dickenson) using Paint-A-Gate software with cut off for MRD positivity of 0.01% blasts.

Results: Post induction MRD was performed on 100 cases (53 male, 47 female) of B ALL and found to be positive in 29 cases (30% male and 28% female). Sixty eight cases were between 1 to 10 years and 32 were >10 years, of which 16 (24%) and 13 (41%) were MRD positive, respectively. At diagnosis CNS was involved in 11 and negative in 89 cases, of which 45% and 27% were positive for MRD, respectively. At diagnosis TLC was >50 x10E9/L in 17 cases and 83 cases had TLC <50 10E9/L, of which 29.4% and 29% were MRD positive, respectively.

Conclusion: MRD positivity was significantly high in CNS involvement and >10 years age, at diagnosis. In contrast, gender and increased TLC had no significant influence on MRD status.

I-131 MIBG SCINTIGRAPHY CURIE VERSUS SIOPEN SCORING: PROGNOSTIC VALUE IN STAGE 4 NEUROBLASTOMA

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Purpose/Objective: I-131 MIBG scan has an established role in staging workup and response evaluation in patients with neuroblastoma. Semi-quantitative analysis with Modified Curie score (osseous and extra-osseous disease) and the International Society of Paediatric Oncology Europe Neuroblastma (SIOPEN) scoring (osseous disease only) systems is helpful in the evaluation of extent of disease and has prognostic impact in stage 4 neuroblastoma.

Material/Methods: Retrospective, cross-sectional analysis of baseline I-131 MIBG scans in 21 patients with stage 4 or 4S neuroblastoma diagnosed between January 2007 and December 2015. All scans were assessed according to Curie and SIOPEN scoring method. Distribution of scores was evaluated for risk factors i.e. age at diagnosis (>18 months) and early relapse (within 12 months). A curie score <2 and SIOPEN score <4 (best defined cutoff *) at diagnosis were correlated for event-free (EFS) and overall (OS) survival. Analyses were performed with IBM SPSS statistics 20. *J clin Oncol.2013, 31:944-951

Results: Data set was comprised of 12(57%) males and 9(43%) females. Nine patients had osteomedullary metastases, while 12 had soft tissue metastases or cytological bone marrow involvement. Patients with age > 18 months (n=9) at diagnosis or tumor relapse within 12 months after diagnosis (n=9) had higher Curie (Mean 5+7.5SD, p=0.004) and SIOPEN (Mean 5.2+10.8SD, p=0.02) scores.

Patients with a Curie score <2 and a SIOPEN score of <4, respectively, had better EFS and OS than patients with higher scores. Curie: 5-year EFS = 79% versus 33% (p 0.03); 5-year OS= 56% versus 36% (p 0.01). SIOPEN: 5-year EFS = 70% versus 17% (p 0.002); 5-year OS= 58% versus 17% (p 0.04). No statistically significant difference was found between the survival predictive value of two scoring systems (Hazard ratio 2.38, 95% confidence interval 0.33-16.9, p = 0.38).

Conclusion: I-131 MIBG Curie and SIOPEN scores have prognostication value in stage 4 neuroblastoma and should be routinely applied. Higher scores predict unfavorable prognosis.

FIVE FRACTIONS STEREOTACTIC RADIOSURGERY (SRS) FOR INTRACRANIAL MENINGIOMAS

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Purpose/Objective:

To describe the efficacy and toxicity of the five fraction stereotactic radiosurgery (SRS) for intracranial meningiomas. History: Effectiveness of conventional adjuvant EBRT, affront Single session gamma knife radiosurgery and moderately hypo fractionated radiotherapy for intracranial meningiomas are wel studied and proven to have good local controls with minimum side effects. Five fractions hypo-fractionated radiotherapy (multisession SRS) was used for relatively large tumors and for those closely lying with critical organs and not suitable for gamma knife single session radiosurgery. This schedule might be of benefit equivalent to single session and the protection of critical organ and toxicity of irradiation to large volumes can be minimized. The reason to choose the five fractions is the evidence of good local control and safety of critical organs.

Material/Methods: From 01.01.10 to 30.06.16, 1220 patients were treated on Synergy-S (Linac based radiosurgery system). 100 patients of intracranial meningiomas (including recurrent) were treated with 5 fractions radiosurgery. 40% were male and 60% were female patients. Mean age was 41.74 years (range: 18-67 years). Patients were followed up at 6 weeks, 3 months and then 6 months till 5 years time. Mean volume (PTV) was 46.87 cc (range: 2.20-90.20cc). Prescription dose 2500 cGy was used in five fractions at 500 cGy/day. Mean prescription Isodose line was 80 % (range: 65-100%). Median Maximum Dose was 3119 cGy(range: 2442- 4284 cGy). Median Mean dose was 3070 cGy (range: 2251-3592 cGy). Median Minimum dose was 2321cGy(range:1909-2950 cGy). Review of literature by using Pubmed, Medscape and Pubmed Central was carried out to establish the safety and efficacy of 5 fractions SRS.

Results: Clinical Improvement was seen in about 90 % of the patients, radiologically most of the tumors were stable around 70 %, 10 % had small residual disease while 10% progressed from original size at about 18 months after SRS.10% patients were lost to follow-up. Treatment was wel tolerated.No acute toxicity was observed, while use of steroids was prolonged in about 10 % of the patients mean duration was 3 months (range 1-6 months).

Conclusion: This retrospective study revealed high local tumor control rate and minimal toxicity of five fractions radiosurgery for intracranial meningiomas. Further larger studies required to establish its future use.

OUTCOME OF HIGH GRADE GLIOMAS: A SINGLE INSTITUTION STUDY

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Purpose/Objective: Evaluation of factors that navigate survival in patients with grade III gliomas.

Material/Methods: Retrospective study on 44 patients with grade III gliomas, aged 18 to 76 years, treated at Shaukat Khanum Memorial Hospital from 2005 till 2010. HIS database was used to extract data for this study.

Results: These gliomas originated from 7 different anatomical locations. 5 year overall survival for gliomas in Cerebellum (2.3%), Suprasellar (2.3%), Brainstem (9.1%), Frontal (40.9%), Parietal (36.4%), Temporal (2.3%), Occipital (2.3%) and Thalamus (4.5%) was 100%, 100%, 74%, 23%, 25%, 0%, 0%, and 0% respectively.

86.4% of the patients underwent surgery with a 5 year overall survival of 25% as compared to 17% for the 13.6% of patients who did not. Among those operated upon, 36.8% underwent optimal debulking, 50% suboptimal debulking and 13.2% only had a biopsy done. 5 year overall survival in respective order was 60%, 22% and 20%.

5 year overall survival of Astrocytomas(76.3%), Oligodendrogliomas(18.4%) and Unspecified gliomas(5.3%) was 26%, 28% and 50% respectively. Patients with less than 20mm (6.8%), 20-40mm(59.1%), 40-60mm(27.3%) and more than 60mm(6.8%) gliomas, had 5 year overall survival of 66%, 30%, 17%, and 0%, respectively, at 5 years. The overall survival was found to be 27% at 5 years and 19% at 10 years.

Chemotherapy was not offered to these patients because of lack of known benefit at that time in addition to affordability issues.

Conclusion: High grade gliomas have a dismal prognosis. Size and adequacy of resection are two important determinants of overall survival. The option of chemotherapy shall be explored to improve outcome.

ROLE OF GAMMA KNIFE RADIOSURGERY IN THE MANAGEMENT OF CAVERNOUS SINUS HEMANGIOMAS.

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Purpose/Objective: Cavernous sinus Hemangiomas (CSHs) are rare vascular tumors. Total resection is difficult because of high vascularity and complex neurovascular structure of cavernous sinus. This is a retrospective study to ascertain the safety and efficacy of gamma Knife Radiosurgery (GKRS) for the treatment of CSHs.

Material/Methods: Nine patients with CSHs underwent GKRS at Neurospinal and Medical Institute, Karachi between May 2008 and January 2016.

There were 5 women and 4 men with mean age of 47.2 years (range 25-77 years). The tumors were located on the right side in 5 cases and on left side in 4 cases. The diagnosis was based on MR images and clinical presentations. The most common symptom was third nerve palsy which occurred in 7 cases. The mean tumor volume was 5.3 c.c. (range 2.6 cc – 14.0cc). The treatment was performed using Leksell Gamma Knife Model 4c. A mean peripheral dose of 13.5 Gy (range 12-16Gy) was delivered at 40 -50% isodose line.

Results: The mean follow up time was 46.5 months (range 6-71 months). In all cases significant shrinkage of the tumors was noted at 3 months. Five patients had complete remission at the last follow up (55%). The four remaining patients had mean shrinkage of 60 % (range 50-80%). In all patients there was swift clinical improvement in 3rd nerve palsy in initial 3 months. No Radiosurgery related complications were found during follow up.

Conclusion: Gamma Knife Radiosurgery is highly effective and safe for CSHs and should be considered in upfront treatment of these lesions.

RANGE OF SPINAL CANAL DOSES THAT ARE DELIVERED TO PATIENTS OF NASOPHARANGEAL CANCERS USING 3DCRT TECHNIQUE

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Purpose/Objective: To report the maximum, minimum, mean and 1% of the total dose that can be delivered to the spinal canal in definitive treatment of patients of Nasopharangeal cancers using 3DCRT Technique.

Material/Methods: A retrospective study is conducted in AKUH in between 2007 to 2013. Total 45 patients of nasopharyngeal cancer were reviewed who were treated with CCRT using 3DCRT technique. The primary target include palpable and visible disease and secondary target include microscopic disease. Total radical doses that are delivered were 66-70 GY. The range of spinal cord doses were analyzed using data extracted from approved physics plans using Dose Volume Histograms. RT Doses delivered to spinal canal during the entire treatment was analyzed at: Maximum Mean & 1% of total dose DVH is a concept used in RT planning. It is the display of dose distribution in the form of isodose curves or surfaces as it shows not only regions of uniform—dose, high dose, or low dose, but also their anatomic location and extent. The purpose of a DVH is to summarize 3D dose distributions in a graphical 2D format. The "volume" referred to in DVH analysis can be a target of radiation treatment, a healthy organ nearby a target, or an arbitrary structure. They are of two types

CUMULATIVE DVH, DIFFERENTIAL DVH. Differential DVH: It represents the percentage or absolute volume (depending on the mode of display) receiving dose in the corresponding dose bin. Cumulative DVH: It represents the percentage or absolute volume receiving greater than or equal to the value in the corresponding dose bin.

Results: A Curative Dose of RT was delivered in these 45 cases via 3DCRT keeping spinal canal doses within acceptable tolerance level.(45Gy)

MAXIMUM DOSE - 46.53Gy MEAN DOSE - 27.38Gy 1% DOSE - 44.74Gy

Conclusion: Precision R.T. Planning Techniques should be considered while planning Radical Courses of R.T. in Head & Neck cancers .This fact gets more important in our setting where we have to treat larger tumors and there is a danger of crossing Spinal Cord tolerance.

MIDLINE CROSSING GRADE I TO GRADE III GLIOMAS: IMPACT OF HIGH DOSE XRT ON SURVIVAL

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Purpose/Objective: Midline crossing gliomas are known to have a dismal prognosis across the globe. There is a paucity of literature on standard radiotherapy regimens for their management. Our study, primarily, aims to evaluate the significance of escalated radiotherapy doses. In addition, the significance of size and enhancement at initial imaging, as prognostic factors of overall survival.

Material/Methods: For our retrospective study , we identified 34 patients with grade I to III midline crossing gliomas, treated at Shaukat Khanum Memorial hospital, from 2005 till 2010. 22 males and 12 females, aged 23 to 59 years, were randomized into four groups, based on the dose of radiotherapy received. They were 60Gy/30#, 56Gy/28#, 48Gy/16# and 30Gy/10#. Their frequencies were 52.9%, 8.8%, 23.9% and 14.7% respectively. The histologies included were Astrocytomas, Oligodendrogliomas and Ependymomas.

With respect to initial tumor size, four groups were identified. Patients with 10-29mm, 30-49mm, 50-69mm and 70-90mm tumors. Their respective frequencies were 14.7%, 41.2%, 17.6% and 26.5%.

55.9% had enhancing tumors and 44.1% had non enhancing tumors.

The outcome compared was 5 years overall survival in the four radiotherapy groups. In addition, difference in overall survival, according to tumor size and enhancement at initial imaging, was evaluated.

Results: The overall survival was found to be 36% at 5 years and 18% at 9 years. At 5 years, the overall survival for patients who received 60Gy/30#, 56Gy/28#, 48Gy/16# and 30Gy/10# was found to be 32%, 62%, 22% and 20% respectively. In summary, the overall survival for patients who received >50Gy was 36% as compared to 20% for patients with <50Gy dosage.

In comparing 5 years overall survival with respect to initial tumor size, the four groups 10-29mm, 30-49mm, 50-69mm and 70-90mm had overall survival of 60%, 32%, 21% and 10% respectively.

5 years overall survival of patients with non enhancing tumors was found to be 42%. It was 20% for patients with enhancing tumors.

Conclusion: The overall survival of patients with midline crossing gliomas is significantly improved with higher radiotherapy doses, while increasing size and enhancement in tumors negatively affect it.

CLASSIFICATION AND MANAGEMENT OF RENAL TUMORS INVOLVING THE INFERIOR VENA CAVA - EXPERIENCE FROM A SPECIALIST ONCOLOGIC CENTRE

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Purpose/Objective: Inferior vena cava (IVC) involvement in renal tumors is a challenging problem to the operating surgeon. Expertise in dissection, isolation and exploration of this large caliber vein is important in management of these tumors. We report our institutional experience in operative management of renal tumors with IVC involvement.

Material/Methods: All adult and pediatric patients with renal tumors and IVC involvement who underwent surgery between 2009 and 2015 were included. Demographic and clinical data, type of tumor, extent of IVC involvement, and operative management strategies were recorded.

Results: Between 2009 and 2015, 14 adult and 4 pediatric (total 18) patients with renal tumors involving the IVC were identified. Twelve patients had renal cell carcinoma, 3 patients had Wilm's tumor, 2 had adrenal tumors, and one patient had clear cell sarcoma of the kidney. Median age was 59 years in adult population and 2 years in pediatric population. Median tumor size was 13 cm (Range 6.8 – 20 cm). Median Hospital Stay was 7 days. Two patients had tumor adherent to IVC which were separated using sharp dissection. Ten patients were managed with IVC thrombectomy. Five patients underwent cavotomy or sleeve resection followed by lateral repair of IVC, while one patient had the tumor densely adherent to IVC which required segmental IVC resection and end-to-end anastomosis.

Conclusion: Management of renal tumors with IVC involvement depends on type of tumor and the extent of IVC involvement but requires expertise in vascular dissection, and reconstruction. We propose a modification to the current classification system of renal tumors involving the IVC which helps in selecting the management strategy in these patients.

SECONDARY HIFU AS SALVAGE TREATMENT AFTER FAILURE OF RADICAL TURP PLUS HIFU: IS IT A VALID THERAPY?

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Purpose/Objective: HIFU (high-intensity focused ultrasound) is a new minimally invasive modality to treat prostate cancer, which demonstrates a 5-year biochemical disease-free survival rate of 80-85%. 15-20% patients have residual tumor when treated by HIFU for localized prostate cancer, and require salvage treatment. HIFU can also be used as salvage therapy in this setting, having good cancer control with much lesser morbidity than traditional therapies (surgery and radiotherapy). There has been little or no literature about this novel use of secondary HIFU. We present our data of using secondary HIFU in the management of residual tumor after primary HIFU, with the aim of determining efficacy and safety of this modality.

Material/Methods: A total of 148 patients underwent HIFU for primary treatment of localized prostate cancer from December 2009 to July 2015. 12 patients were offered HIFU as secondary salvage management. All of these had histologically proven residual/ recurrent prostate cancer after primary HIFU. 8 were given HIFU as the only management, 3 were given hormone therapy with HIFU, and 1 received HIFU, hormone therapy and radiotherapy.

Results: The mean pre-secondary HIFU PSA was 2.28 ng/ml (0.52-4.77). After salvage HIFU, 8 out of 12 patients (66.7%) achieved nadir PSA less than 50% of pre-treatment values. These showed biochemical disease free survival. Mean post-treatment nadir PSA value was 0.39 ng/ml (0.02-0.75). Time to achieve post-treatment PSA nadir was 1.13 months (1-2). The 8 patients had mean post-treatment PSA of 0.78 ng/ml (0.02-1.78) when followed up over a mean period of 11.25 months (1-20), demonstrating biochemical disease free survival.

3 patients (25%) had elevation of PSA, mean 5.6 ng/ml (3.17-7.52), after salvage HIFU. These were registered as failures. One patient was excluded from the study because of negative prostate biopsy, which meant that it could not be ascertained that the disease was localized or metastatic.

The salvage procedure was well tolerated by the patients with minimal side effects. No major complications were found in our patients (rectal injury, fistula, incontinence of urine, epididmyo-orchitis). 1 patient developed urethral stricture and required optical internal urethrotomy/ TURP.

Conclusion: Our early clinical results show the feasibility and good tolerance of salvage HIFU as a management option after primary treatment of prostate cancer with HIFU. Oncological outcomes are satisfactory. No major side effects were noted. Currently there are very few, if any, clinical trials globally, that have studied HIFU as a salvage treatment option after primary HIFU for localized prostate cancer. Larger prospective studies with longer follow-up are needed to confirm our initial results.

DIETHYLSTILBESTROL (DES) IN TREATMENT OF CASTRATION RESISTANT PROSTATE CANCER (CRPC); A LOWER MIDDLE INCOME COUNTRY EXPERIENCE.

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Purpose/Objective: To find out the efficacy and adverse effects of DES when used in castration resistant cases of prostate cancer.

Material/Methods: From Jan 2009 to Dec 2014 all patients with a diagnosis of prostate cancer presenting at Shaukat Khanum Cancer Hospital & Research Centre Lahore were reviewed. Out of these patients who were resistant to the effects of castration were studied. All patients were treated with DES 2.5 initially which in some case increased to 5mg in combination with Aspirin 75mg. The patients were followed clinically as well as with PSA and record was prospectively maintained. The PSA response to treatment, time to disease progression and adverse events were analyzed using SPSS version 20.

Results: A total of 91 patients were studied. Mean age was 66.08 ± 8.48 yrs. Median baseline PSA was 150ng/dl and median Gleason score of 8 was recorded. 90.1% patients had metastatic disease at the time of diagnosis. Hormonal ablation was provided with bilateral orchiectomy in 71 (78.0%) & LHRH analogue in 20 (22.0%). With this treatment median time to PSA progression was 597 days. After DES started 78(87.7%) patients had shown PSA response and median time to progression was 212 days. In 24 (26.4%) patient PSA response was maintained for more than a year. PSA response was quantified as \geq 50% PSA decrease or as partial which was <50%. \geq 50% PSA response was observed in 56 (61.5%) patients with median time to progression of 273 days, partial response in 22 (24.2%) for 109 days while 13 (14.3%) did not respond to DES treatment. The median percent change in PSA was \sim 55.52 (range \sim 99.9 to \sim 4422). Thromboembolic complication observed in 08 (8.7%) patients while 02 patients suffered from liver toxicity.

Conclusion: DES is an effective agent in management of CRPC as more than 75% of the patients responded to this treatment. Addition of aspirin to DES can help take care of the thromboembolic side effects.

DIAGNOSTIC UTILITY OF HNF-1BETA IN DIFFERENTIATING OVARIAN CLEAR CELL AND SEROUS CARCINOMA

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Purpose/Objective: Ovarian cancer is the 5th most common malignancy in developed countries and 2nd most common malignancy in Pakistan (77.6%) after breast carcinoma.Of all the epithelial ovarian neoplasms, clear cell carcinoma of the ovary has the worst prognosis with poor chemo sensitivity. The HNF-1Beta gene(formerly known as TCF2) encodes a POU-domain containing a tissue –specific transcription factor.A study using an oligonucleotide array technique demonstrated that the expression of HNF-1Beta was significantly upregulated in ovarian clear cell carcinoma cell lines, whereas serous carcinoma rarely expressed this protein. The aim of this study is to determine the diagnostic utility of HNF-1beta immunohistochemical stain in differentiating ovarian clear cell carcinoma and serous carcinoma taking histopathology as the gold standard.

Material/Methods: We reviewed sixty specimens ,30 each,of ovarian clear cell and serous carcinoma from the archives of Shaukat Khanum Memorial Cancer Hospital and Research Center(SKMCH and RC). Poorly preserved and previously treated samples were excluded.HNF-1 beta expression was examined immunohistochemically and expression was labeled as negative if <5% cells stained with HNF-1beta and considered positive if ≥ 5% of cells stained with HNF-1beta. Frequency of HNF-1beta immunohistochemical nuclear expression was determined in clear cell and serous carcinoma.

Results: Clear cell carcinomas and serous carcinomas displayed statistically significant differences in HNF-1beta staining. Out of 30 clear cell carcinoma cases,29 (96.6%) showed positive HNF-1beta expression in more than 95% of tumor cells.1 case(3.33%)had<5% cells positive for HNF-1beta. Only 2 cases (6.66%) of serous carcinoma showed HNF-1beta expression in 35-40% of tumor cells.

Conclusion: These results show that HNF-1beta is of diagnostic utility in distinguishing between clear cell and serous carcinoma of ovary .

ROLE OF DIAGNOSTIC OESOPHAGOGASTRODUODENOSCOPY AND COLONOSCOPY IN CARCINOMA OF UNKNOWN PRIMARY

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Purpose/Objective: Carcinoma of unknown primary site (CUP) is one of the common presentations of cancer seen globally, with an incidence of 3–5 % of all malignancies [1]. Presentation is with metastases to various organs without any conclusive primary site of tumour origin [2]. Role of gastrointestinal (GI) diagnostic procedures has not been widely studied in this patient population [3].

objectives: We aimed to study the role of GI procedures, namely oesophagogastroduodenoscopy (OGD) and colonoscopy, in helping to establish a definitive diagnosis (defined as a diagnosis in which primary site of tumour is found) in CUP.

Material/Methods: Data on 115 patients was collected in retrospect, from Jan 2006 to Aug 2016. The patients included were those, who underwent an OGD and a colonoscopy for the diagnosis of a CUP. Data collected included demographics, baseline clinical characteristics, definitive diagnosis, tissue diagnosis and immunohistochemical stains checked. We also looked at patients who achieved a definitive diagnosis via OGD and/or colonoscopy.

Results: 115 patients underwent a diagnostic OGD and a colonoscopy to look for a primary site of malignancy. The procedures were either done by or under the supervision of a consultant gastroenterologist. Of these 115 patients 61% (n=70) were male, whereas 39% (n=45) were female. The mean age was 63 years (Range 22-88, SD \pm 12.6). The most common tissue diagnosis (that was obtained by other means, including liver biopsies, lymph node biopsies/fine needle aspirations, bone marrow biopsies or soft tissue/mass biopsies) observed was adenocarcinoma (62%, n=72), followed by metastatic carcinoma (21.7%, n=25). Abdominal pain comprised the most common presenting complaint, occurring in 53% (n=61). None of the patients reached a definitive diagnosis from OGD and colonoscopy. 75/115 (66%) of OGDs were normal. 17 (14.8%) had gastritis, 8 (6.9%) had changes of portal hypertension whereas 7 (6.1%) showed evidence of extrinsic compression. Similarly in colonoscopy, 84 (73%) were normal, 13 (11.3%) revealed hemorrhoids only, whereas 8 (7%) had polyps histopathology of which showed no evidence of malignancy, 5 (4.3%) of the patients had external colonic compression.

Conclusion: Our data suggests that OGD and colonoscopy when done collectively as diagnostic procedures to look for a primary tumour, has no value in the evaluation of patients with CUP. Retrospective nature is the main limitation of this study and further prospective studies are needed to confirm these findings.

PATTERN OF MICROBIOLOGY CULTURES OF BILIARY STENTS IN PATIENTS UNDERGOING PANCREATICODUODENECTOMY

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Purpose/Objective: To look for stent related complications in patients undergoing Whipples Procedure.

Material/Methods: We selected patients who were operated at Shaukat Khanum Cancer Hospital for periampullary lesions from the period of Dec 2014 to March 16 and who had been stented post ERCP, pre operatively. There were total number of 43 patients who were planned for pancreaticoduodenectomy in this time frame. Most of them were stented outside hospital before presenting at our hospital. We looked at different demographic aspects and were observed for post ERCP complications before undgoing surgery. Tips of stents in whom stent was retrieved intraoperatively was sent for its culture growths and sensitivities. All these patients were observed for any peri operative complication that happened, including mainly surgical site infections and intra abdominal collections. Culture studies of wound swabs were sent and was seen for growth of organisms and sensitivities.

Results: Of 43 patients undergoing Whipples procedure 29 patients had undergone stenting preoperatively. Pattern of culture sensitivities and organisms growth from stent tips

Organism from stent tips	Frequency	Percentage
Ecoli	9	20.9
Enterococcus	3	7
Klebsiella	3	7
Staph epidermidis	2	4.7
Actinobacter	1	2.3
Multiple organism	9	20.9

Post operative complications and management

Type of complication	Frequency	Percentage
SSI	10	23.3
Intra abdominal collection	2	4.7
SSI + intra abdominal collection	8	18.6
Death	1	2.3

SHORT TERM OUTCOME OF PATIENTS AFTER LIVER RESECTION IN A SPECIALIZED HEPATOBILIARY UNIT- OUR EXPERIENCE

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Purpose/Objective: To present the demographics and early outcomes of patients with primary and secondary liver tumours managed at SKMCH.

Material/Methods: Between September 2014 and May 2016, all patients undergoing liver resections were included. Basic demographic, clinical, operative and follow-up data was recorded.

Results: A total of 36 liver resections were performed. Median age was 52 with 20 males and 16 females. The common indications were hepatoblastoma, hepatocellular carcinoma, Gall bladder carcinoma and liver metastasis. Median operative time for the patients were 378 min (165 – 720 min), Median blood loss was 424 mls (Range 30 – 1200 mls). Median ICU stay of the patients was 36 hrs (0-144hrs). Median hospital stay was 8 days (Range 4-10). There were no reoperations or operative mortality.5 patients had pulmonary complications, 3 developed a perihepatic hematoma, 2 patients had an MI, 2 had a surgical site infection and 2 patients developed small for size syndrome.

Conclusion: Surgical outcomes of hepatobiliary malignancies can be significantly improved by following a multidisciplinary approach in addition to advanced diagnostic, therapeutic and technical expertise. A specialist hepatobiliary service can help to improve the overall surgical outcomes of these patients by giving them a better chance to fight their potentially curable disease.

INCIDENCE OF ACUTE KIDNEY INJURY (AKI) IN PATIENTS UNDERGOING TRANS ARTERIAL CHEMO-EMBOLIZATION (TACE) FOR HEPATOCELLULAR CARCINOMA (HCC)

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Purpose/Objective: Hepatocellular carcinoma is the 6th most common malignancy worldwide, with an annual incidence of 600,0001. TACE is an effective first-line therapy for intermediate stage HCC. It involves the direct injection of a chemotherapeutic agent into the artery supplying the tumor under radiological guidance2. During this procedure, significant quantities of intravenous contrast agent are used to opacify the relevant vessels. The use of this contrast, in TACE, is associated with the development of renal dysfunction in as many as 8.6 to 23.8% of the patients3.

Our study aimed to look at the incidence of acute kidney injury4 in our patients diagnosed with HCC who underwent TACE. Only Child's class A patients were included in the study.

Material/Methods: After approval from hospital ethical committee, data on 65 patients was collected retrospectively from Jan 2011 to Sept 2014 on all patients with HCC seen at our cancer centre that underwent TACE. This included demographics, baseline clinical characteristics and presence or absence of risk factors for AKI such as diabetes mellitus, hypertension, ischaemic heart disease or chronic kidney disease.

Results: 65 patients with HCC who underwent TACE were enrolled. The mean age was 59 years (range 36-86). 29 (44.6%) of these were female, whereas 36 (55.4%) were male. The mean baseline levels of bilirubin, albumin and INR were 0.87mg/dl, 3.6mg/dl and 1.1, respectively. Ascites was present in 4 (6.2%) patients. 34 (52.3%) patients had diabetes mellitus, whereas 37 (56.9%) had concomitant hypertension. 11 (17.2%) patient had a history of ischaemic heart disease and/or congestive cardiac failure. None of the patients had a history of chronic kidney disease. According to the AKIN criteria, only 2 (3.1%) patients suffered from AKI in relation to TACE.

Conclusion: TACE appears to be a safe therapeutic modality with respect to AKI, with the incidence at our centre being lower, at 3.1%, than that reported in the literature (8.6 to 23.8%). The limitations of our study included a small sample size and the fact that this was a retrospective analysis. In addition, 23 % of the patients (n=15) did not have follow-up renal function checked within 72 hours of the procedure.

AN EXPERENCE OF ESOPHAGECTOMIES, SERIES OF 178 CASES

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Purpose/Objective: The study was carried out to ascertain the outcome of esophagectomies for malignant esophageal diseases and to determine the morbidity associated with it.

Material/Methods: This is a retrospective study of 178 cases of esophagectomies in five and a half years from Jan 2007 to 2009 and from Jan 2010 to Aug 2013. Patients included were of proven endoscopic histopathologically carcinoma oesophagus with curative intension. On table inoperable carcinoma esophagus were excluded from the study. CT scan staging was employed preoperatively. Approach to oesophagus was dependent on site of lesion. Minimally Access esophagectomy (MIE) and laparoscopic stomach mobilization has been added in the later part of study period.

Results: 108(60.6%) were males and 70(30%) were female patients. 174(98%) had dysphagia to solids in presenting symptoms. Transhiatal esophagectomies were 35(19.6%), thoracophrenic laparotomies were 36(20.2%), and Mckewon esophagectomies were 22 (12.2%). 80 patients had squamous cell carcinoma and 77 patients had adenocarcinoma. In complications 17(10%) patients had anastomotic leakage and 8 (4.49%) patients had recurrent laryngeal nerve injury and 23(13%) had anastomotic stricture which was treated by repeated esophageal dilatations. Orally was started on 4th postoperative day. VATS esophageal mobilization done in 4 patients were part of study along with 3 laparoscopic stomach mobilization.

Conclusion: Voiced concerns regarding the ability to perform a complete esophagectomy can be confidently addressed with the results of our study and as in high volume centers the procedure has acceptable morbidity and addition of MIE(minimally invasive esophagectomy) has added early, smooth recovery and shorter hospital stay.

EFFICACY AND TOXICITY OF CARBOPLATIN/PACLITAXEL BASED CHEMORADIATION FOR LOCALIZED ESOPHAGEAL CANCER.

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Purpose/Objective: To establish the efficacy and safety of Carboplatin/paclitaxel combination for neoadjuvant and radical treatment of localized non-metastatic esophageal cancer in combination with radiation and surgery.

Material/Methods: Data of 200 patients, who got registered at our institute with oesophageal cancer between September 2013 and October 2014, was reviewed retrospectively. Baseline characteristics were studied for those 139 patients who received treatment with carbo/pacli based regimen. For toxicity and efficacy analysis, in the form of radiological response rate, R0 resection rate, Progression free survival (PFS) and overall survival (OS), 102 patients who received radical carbo/pacli based chemoradiation (CRT) were included. Impact of Surgery Vs. no surgery was seen on PFS and OS.

Results: Males and females were 71(51.1%) and 68(48.9%) respectively, with squamous cell carcinoma being the predominant histology (92%). Majority of patient belonged to T3/4 and N1 stage. Grade III/IV thrombocytopenia, neutropenia, anaemia, febrile neutropenia requiring hospitalisation, non-hematologic toxicities were noted in 13(12.8%), 18(17.7%), 18(17.7%), 1(1 %), 1(1 %), patients respectively. Complete Radiological response, partial response, Stable disease, progressive disease were seen in 6(5.9%), 51(50%), 23(22.5%) 8(8.7%), respectively. Resection was done in 29 (28.4%). Complete and partial pathological response were seen 19(65.5%), 10 (34.4%), respectively. PFS at 40 and 80 weeks was 90%, 73%, respectively and OS at 80 weeks was 86%. PFS at 40 and 80 weeks was 100 % and 90.5%, respectively with resection, while it was 86% and 65 %, without resection (P value 0.015). OS at 40 and 80 weeks was 100% (both) with resection, while it was 96% and 79.5 % weeks without resection. (P value 0.034).

Conclusion: Carbo/pacli based CRT is effective with acceptable toxicity profile in treating localised oesophageal cancer as both as Radical CRT and as a part of multimodality therapy. For definitive results long term follow up and prospective analysis are required.

MORBIDITY ANALYSIS IN MINIMALLY INVASIVE ESOPHAGECTOMY FOR ESOPHAGEAL CANCER VERSUS CONVENTIONAL OVER LAST TEN YEARS, A SINGLE INSTITUTION EXPERIENCE.

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Purpose/Objective: There has been an increasing inclination towards minimally invasive esophagectomies MIE at our institute recently for resectable esophageal cancer.

The purpose of present study is to report peri-operative and long term procedure specific outcomes of the two groups and to analyze their changing pattern at our institute.

Material/Methods: All adult patients with a diagnosis of esophageal cancer managed at our institute from September 2005 till September 2015 were included in this retrospective study. All patients demographic, clinical and pathological characteristics were recorded through our hospital information system. The cohort of esophagectomies were allocated into two groups, conventional open esophagectomy OE or total laparoscopic MIE, hybrid esophagectomies were taken as separate group. The short term outcome measures are operative time in minutes, length of hospital and ICU stay in days, post-operative complications and thirty day in-hospital mortality. Complications are graded according to Clavien- Dindo classification system. Long term outcomes are long term procedure related complications over a minimum follow up of 1 year. Trends were analyzed by visually inspecting the graphic plots for mean number of events in each group each year.

Results: Our results showed no difference in mortality, length of hospital and ICU stays and incidence of major complications between three groups on uni and multi-variate analysis(p> 0.05). The operative time was significantly longer in MIE group(OR 1.66,CI 2.4-11.5). The incidence of long term complication was low for MIE(OR -1.0,CI .133-1.017). However, all post-operative surgical outcomes trended to improve in both groups over the course of this study and stayed better for MIE group except for the operative time.

Conclusion: Minimally invasive esophagectomy has overall comparable surgical outcomes to its conventional counterpart. Also the peri-operative outcomes tend to improve in our centre with the maturation of program and experience.

SURGICAL OUTCOME OF PANCREATICODUODENECTOMY- THE LESSONS LEARNT

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Purpose/Objective: Pancreatic cancer is an aggressive malignancy with a very poor prognosis. It is the fourth most common cause of death from cancer. Only around 20% of pancreatic cancers are resectable at the time of diagnosis having an overall five-year survival of 15- 20%. Pancreaticoduodenectomy (PD) is the most commonly used surgical treatment for resection of malignant and benign neoplasms in the periampullary region. Even in centers where pancreaticoduodenectomy is routinely performed postoperative morbidity remains high (30–50 %). In this study we report our experience in the treatment of pancreatic and periampullary neoplasms with emphasis on surgical technique, short term postoperative outcomes and the lessons learnt.

Material/Methods: Prospective analysis of pancreaticoduodenectomiescarried out at Shaukat Khanum Memorial Cancer Hospital and Research center from October 2014 to May 2016. We report patient's characteristics including age, gender, presenting symptoms, American Society of Anesthesiology (ASA) score, surgical technique and 30 days morbidity and mortality. International Study Group of Pancreatic Fistula (ISGPF) classification was used to define post-operative pancreatic fistula and Clavien-Dindo classification to grade complications. SPSS 20.0 was used for statistical analysis.

Results: A total number of 65 patients underwent trial of dissection, 50 had pancreaticoduodenectomy and 15 patients underwent palliative bypass due to locally advanced disease and were excluded from analysis. The most common tumour was periampullary (N=29, 58%) followed by pancreatic head (N=14, 28%) and duodenal (N=7, 14%). Median age was 50.9 years (range 19-76). Median operating time was 423.3 mins (300-550) and blood loss 3985 mls (200-2000). Pancreaticogastrostomy was the preferred reconstruction technique (N=37, 75%) verses pancreaticojejunostomy (N=13, 25%). Four patients needed portal vein and two replaced right hepatic artery resection and reconstruction due to tumor involvement. We noted seven Grade A and 1 each Grade B and C pancreatic fistulae. Pancreatic fistula was more common after PJ (N=5, 38.5%) as compared to PG anastomosis (N=4, 10.8% p= 0.026). Three patients needed endoscopic therapy for gastrointestinal hemorrhage from pancreatic stump. There was one death in postoperative period.

Conclusion: Pancreaticoduodenectomy has evolved as a safe procedure with excellent post-operative outcome if carried out in a specialized hepato-pancreato-biliary unit. As most of our patients' hadperiampullarytumours with soft pancreas and non-dilated pancreatic duct, a PG reconstruction can be a safer alternative to PJ. Suitable patients with short segment portal vein involvement may benefit from surgery and should be given chance for curative resection.

PANCREATICOGASTROSTOMY - AN ALTERNATE FOR DEALING WITH PANCREATIC REMNANT AFTER PANCREATICODUODENECTOMY - EXPERIENCE FROM A TERTIARY CARE CENTER OF PAKISTAN

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Purpose/Objective: Whipple's pancreaticoduodenectomy (PD) has been refined over the years to be a safe operation with a reported mortality rate of less than 3% in most of the recent series though the morbidity rate still remains high (30-50%). Pancreatic fistula is the single most important cause of mortality following pancreaticoduodenectomy. To manage the pancreatic remnant and prevent these complications, surgeons have used two main anastomotic techniques: pancreaticojejunostomy (PJ) and pancreaticogastrostomy (PG).

Results of recent studies have shown significant differences in the incidence of pancreatic fistulas between these two methods, it has been found that PG is associated with fewer overall complications than PJ. Presented here is, technique and our experience of PG in Whipple's procedure performed at Aga Khan University Hospital, Karachi.

Material/Methods: Retrospective review of charts was done for the patients who underwent Whipple's pancreaticoduodenectomy at AGA Khan University Hospital and had pancreaticogastrostomy as a preferred anastomosis for pancreatic stump.

Results:2 patients met the inclusion criteria. 27 patients were male. None of our patients had the complication of post-operative pancreatic fistula. 13 (31 %) of our patients had morbidities including delayed gastric emptying (4 patients), wound infection (3 patients), haemorrhage from pancreatic stump (5 patients) and Choledochojejunostomy leak (1 patient). Mortality is reported to be 11.9 % (5 patients) in this case series.

Conclusion: Pancreaticogastrostomy seems to be a safe alternative and easier anastomosis to perform with less post-operative morbidity and mortality. Further data should become available with greater numbers in the future.

STEM CELL SPHERES IN PRIMARY CULTURES OF HUMAN COLON CANCER, NON-CANCER COLON POLYPS AND NORMAL COLON

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Purpose/Objective: A phenotypic sub-population of cells called cancer stem cells (CSCs) have been demonstrated to exist in several malignancies including colon carcinoma. These cells are able to initiate and sustain tumor growth and cause its recurrence. The aim of our pilot study was to isolate CD44+CD26+CD133+ CSCs from patient colon tumors (site-specific fresh surgical specimen), grow spheres and observe their physical characteristics and proliferation in primary cultures. Parallel cultures of colon normal lining (non-cancer) and benign polyp (non-cancer) were set up as controls.

Material/Methods: Magnetic activated cell sorting (MACS) was used to isolate CD44+CD26+CD133+ cell populations

followed by primary cell culturing under stem cell culture conditions.

Results: Both colon tumor and colon benign polyp biopsies produced floating spheres in suspension; however those grown in benign polyp cultures did not exhibit self-renewal properties for more than 1 passage. Normal colon single-cell suspension did not create spheres under stem cell culture conditions. Metastatic colon tumors produce cancer cell spheres in larger numbers and rapidly (less than 24 hours) compared to nonmetastatic colon tumors (1-3 weeks). In addition, metastatic colon tumor spheres have the capacity for proliferation for up to five generations in primary culture as compared to three generations for nonmetastatic tumors.

Conclusion: This in vitro CSC model will help study colon cancer biology and assist in redesigning and upgrading current treatment modalities targeting CSC and the specific biochemical pathways responsible for resistant behavior towards chemotherapy and radiation.

MODULAR APPAROCH FOR TRAINING IN LAPAROSCOPIC COLORECTAL SURGERY: EXPERIENCE FROM 1000 CONSECTIVE CASES

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Purpose/Objective: Laparoscopic approach has become a gold standard for colorectal cancer surgery. To learn laparoscopic skills appropriate mentoring and training are essential. Consistent and standardized techniques are fundamental to master in laparoscopic skills. Development of reproducible surgical techniques and recognisable patterns for training purposes are helpful in shortening the learning curve and becoming proficient in laparoscopic skills.

The aim of this study is to analyse the short and long term surgical outcomes of all patients undergoing colorectal resections with a modular approach over a period of nine years.

Material/Methods: Data of 1021 consecutive patients undergoing colorectal resection from February 2006 to March 2015 was included in the study. Both short-term clinical outcomes and long term oncological survival were analysed.

Results: Consecutive 1021 patients (551 males) underwent laparoscopic colorectal resections performed or closely supervised by a senior surgeon at a single center. Over 90% of procedures were closely supervised using a modular approach to train. 759 (74 %) had colorectal cancer while 262 (26%) were operated for benign disease. Median operating time was 145 mins (40 to 410 mins) while conversion to open surgery was required in 1 % of cases. An overall anastomotic leak rate of 1.7% and median length of stay of 5 days was noted, whereas an overall 30-day readmission rate of 11.5%, re-operation rate of 3.6% and mortality rate of 0.29% was noted. R0 resection was seen in 98.7% with median lymph node number of 18 (14 to 58). Overall cancer local recurrence rate of 1.58% and disease free survival of 87.5% was seen after curative resections.

Conclusion: Modular approach for laparoscopic colorectal surgery leads to favourable clinical outcomes. This effect was seen both in service delivery as well as teaching and training.

LAPAROSCOPIC VS OPEN RESECTION FOR RECTAL CANCER: A LOWER MIDDLE INCOME COUNTRY EXPERIENCE

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Purpose/Objective: To measure the short and long term surgical outcomes of laparoscopic rectal cancer surgery at a cancer hospital in a lower middle income country.

Material/Methods: All patients with a diagnosis of rectal cancer from Jun 2006 to Jun 2015 were studied. Patient demographics were recorded. Short term surgical outcomes were recorded. Oncological factors indicating an adequate surgical resection were identified. Successful resection was defined as having negative linear and radial margins and a complete TME. LN yield was also recorded. Post op complications were also compared.

Results: A total of 440 surgeries were performed. 154 abdominoperineal resections, 35 extra levator abdominoperineal resections, 151 anterior resections, 40 ultralow resections, 40 hartman's procedures and 20 total colectomies were performed. 262 were laparoscopic and 178 were open. There were 27 conversions (10%). Tumours in the open group were more aggressive and more advanced. There were more T4 lesions (5.2% vs 0.6%), more mucinous (38.7 vs 26.7%) and more nodal involvement (45% vs 34%). Distal resection margins were negative in all open and laparoscopic resections. CRM was clear in 83.9% in open resections vs 88.8 % in laparoscopic resections. TME was complete in in 86% in open surgery and 91% in laparoscopic surgery. Median number of LNs excised were similar in both groups (median of 13). Complications were seen in 8.4% patients in open group versus 5.7% patients in laparoscopic group.

Conclusion: Laparoscopic surgery is similar to open surgery in terms of early surgical and oncological outcomes. A long term comparison of oncological outcomes in terms of recurrence and survival is required.

SINGLE DOCKING ROBOTIC RECTAL SURGERY STANDARDISED TECHNIQUE WITH THE DA VINCI XI SYSTEM AND INTEGRATED TABLE MOTION: FIRST 26 CASES

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Purpose/Objective: Robotic surgery is increasingly becoming an attractive option for rectal surgery. Currently several approaches are in practice, such as the hybrid, reverse hybrid, single or multiple docking techniques. The da Vinci Xi is the new robotic system from Intuitive Surgical and coupled with the integrated table motion enables the surgeon to perform single docking robotic surgery without having to change the port configuration during the operation and reduces the time the patient spends in the steep Trendelenburg position. The aim of this study is to present a standardised technique for single docking robotic rectal resection surgery with the da Vinci Xi system and to analyse the short term clinical outcomes of the first 26 cases we performed in our unit.

Material/Methods: Prospectively collected data for consecutive patients who underwent robotic rectal cancer surgery with the da Vinci Xi between November 2015 and July 2016 was analysed. The time the patients spent on the reverse Trendelenburg position during splenic flexure mobilisation was recorded.

Results: Twenty six patients (20 male, 6 female) were identified. Seven (27%) of them received neoadjuvant chemoradiotherapy. 23 (88%) patients had anterior resections, 2 abdominoperineal excisions and one a sigmoid colectomy. There were no conversions to open, no anastomotic leaks and no mortality. Median operation time was 331 minutes, blood loss 20 mls and length of stay 7 days. 30-day readmission rate and re-operation rates were 3.8% (n=1) and 7.7% (n=2) respectively. Median reverse Trendelenburg time was 30 minutes.

Conclusion: By standardising the technique and applying a modular approach the single docking procedure with the da Vinci Xi is feasible, reproducible and offers good short term outcomes. The technological advances of this new model coupled with the integrated table motion increase the feasibility of the totally robotic single docking approach and reduce the time spend in the steep Trendelenburg position.

ROBOTIC VERSUS LAPAROSCOPIC RECTAL SURGERY IN HIGH-RISK PATIENTS

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Purpose/Objective: Laparoscopic rectal surgery is associated with a steep learning curve and high conversion rate despite progress in equipment design and consistent practice. Certain patient groups present additional technical challenges during laparoscopic approach. In providing stable and better views, improved dexterity and ergonomics, robotic systems have the potential to overcome these limitations. In this study we compared the perioperative outcomes of laparoscopic and robotic rectal cancer surgery in high-risk patients.

Material/Methods: Material/Methods: Prospective data for high-risk patients was undertaken for consecutive cases between May 2013 and November 2015. Inclusion criteria were defined as patients with any one of the following characteristics: BMI of \geq 30, male gender, preoperative chemo-radiotherapy, tumour < 8cm from the anal verge and previous abdominal surgery. Categorical and continuous data analysis was performed using Chi Square and Mann Whitney's U-tests.

Results: A total of 184 high-risk patients were identified. The robotic (n=99) and laparoscopic (n=85) group had similar baseline characteristics. Robotic surgery was associated with a significantly higher sphincter preservation rate (86% vs 74%, P=0.045), shorter operative time (240 vs. 270 minutes, p=0.013) and hospital stay (7 vs. 9 days, p=0.001), less blood loss (10 vs. 100mls, p<0.001) and conversion rate to open surgery (0% vs. 5%, p=0.043) when compared with laparoscopic technique. Re-operation, anastomotic leak rate, 30 days mortality and oncological outcomes were comparable.

Conclusion: Robotic rectal surgery in high-risk patients may be associated with higher sphincter preservation, reduced blood loss, better conversion rates, shorter operating time, and shorter length of stay.

UROGENITAL FUNCTIONAL OUTCOMES IN ROBOTIC VS LAPAROSCOPIC RECTAL CANCER SURGERY: A COMPARATIVE STUDY

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Purpose/Objective: Urological and sexual dysfunction are recognised risks of rectal cancer surgery, however, there is limited evidence regarding urogenital function comparing robotic to laparoscopic approach. The aim of this study was to assess the urological and sexual outcomes of patients undergoing laparoscopic and robotic rectal cancer surgery.

Material/Methods: Urological and sexual functions were assessed using gender specific validated standardised questionnaires. Questionnaires were sent a minimum of 6 months after surgery and patients were asked to report their urogenital function pre and post-operatively, allowing changes in urogenital function to be identified. Questionnaires were sent to 158 patients (89 laparoscopy, 69 robotic) of whom 126 (80%) responded. 78 (49 male, 29 female) of the responders underwent laparoscopic and 48 (35 male, 13 female) robotic surgery. Of those 45 (36 male, 9 female) were sexually active in the laparoscopic group and 17 (13 male, 4 female) in the robotic group.

Results: Male patients in the robotic group deteriorated less across all components of sexual function (libido, p=0.001; erection, p<0.001; stiffness for penetration, p<0.001; orgasm/ejaculation, p<0.001) and in five components of urological function (frequency, p=0.002; nocturia, p=0.002; incontinence, p<0.001; poof flow, p=0.002; incomplete bladder emptying, p=0.017). Composite male urological and sexual function scores change from baseline were better in the robotic cohort (p<0.001). In females, there was no difference between the two groups in any of the components of urological or sexual function. However, composite female urological function score change from baseline was better in the robotic group (p=0.003).

Conclusion: Robotic rectal cancer surgery might offer better postoperative urological and sexual outcomes compared to laparoscopic surgery in male patients and better urological outcomes in females. Larger scale, prospective randomised control studies including urodynamic assessment of urogenital function are required to validate these results.

PARTICPANT ENROLMENT IN GENETIC RESEARCH STUDIES - SINGLE CENTRE EXPERIENCE AT SHAUKAT KHANUM MEMORIAL CANCER HOSPITAL AND RESEARCH CENTRE

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Purpose/Objective: three basic elements of an informed consent namely capacity, disclosure and voluntariness present unique challenges especially when conducting genetic research in a developing country like Pakistan .The abstract below summarizes our single centre experience for patient enrolment in genetic studies.

Material/Methods: The Clinical Research Office (CRO) is the standing office of the research wing at SKMCH&RC. Since 2001 CRO has been involved in patient enrolment for six genetic studies involving patients with hereditary cancers including familial breast, ovarian and colorectal cancers. All patients eligible for participation in genetic research are contacted either directly by research officers or referred via primary oncologists for informed consent discussion. All studies use an IRB approved written informed consent. The required elements of a written informed consent used in genetic studies are summarized in Table 1.

Results: A total of 1190 patients and 433 family members have been enrolled across all six studies. Although figures for all aspects related to participant enrolment in genetic studies are not available, enrolment data collected over two years (August 2013-August 2015) showed that nearly 180 patients were eligible for participation over a two year period. Of these we were able to contact 150 (83.33% of total eligible) patients and 99 (66%) of contacted patients were enrolled after consent. Commonly expressed motivators for participation were: to know cause of cancer, to know cancer risk for family, to help out researchers and to contribute to care of future patients. Major challenges experienced by research officers during these discussions included explaining complicated concepts such as genes, mutations and cancer risk probabilities, negotiating the relational autonomy and family dynamics while respecting patient privacy and ensuring adequate disclosure and voluntariness. Reasons for non participation included consent refusals, being lost to follow up and patient death. Commonly seen reasons for consent refusal included, fear of stigmatization, lack of interest and/or anxiety related to knowing genetic risk.

Conclusion: Genetic research poses unique challenges for participant enrolment in genetic studies. There is need for development of framework that simplifies complex genetic information for research participants and trained genetic counsellors.

OVERVIEW OF GIANT CELL TUMOUR, 10 YEARS REPORTED CASES AT GHURKI TRUST TEACHING HOSPITAL, LAHORE

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Purpose/Objective: Giant cell tumor (GCT) of bone was described by Cooper and Travers in 1818. They are rare and occur in roughly one out of every million people per year. Giant cell tumor of bone is an aggressive bone tumor that arises adjacent to the subchondral bone of major joints. It is thought to originate at the metaphyseoepiphyseal junction and may extend into the metaphysis. The areas of bone most often involved are the distal femur, proximal tibia, proximal humerus, and distal radius. Although histologically benign, giant cell tumor shows locally destructive behavior and frequent local recurrence postoperatively. Treatments ranging from surgical curettage to wide resection To determine the frequency of the different bones involved and surgical procedures as well as outcome in patients suffering from Giant cell tumour.

Material/Methods: The data of 108 patients having biopsy proved Giant cell tumour and were followed for atleast 1 year were analyzed retrospectively in the Department of Orthopaedics and spine surgery of Ghurki trust teaching hospital, Lahore. All patients The patients whose record were incomplete and having follow up less than 1 year between 2004- 2016 were excluded from the study. A total of 108 patients presented with a mean age of 28.66 ± 11.23 . There were 58 males and 50 females. The male to female ratio were 1.16:1. The lesion of all patients were staged according to the system of Campanacci et al. 70 patients had a Grade II lesion and 38 had a Grade III lesion. The data was analyzed using SPSS 17.0 version.

Results: The patients with age less than 20 years were 30 (27.8%),those between 21- 40 years were 68(63.0%) and above 40 were 10 (9.3%). The average duration first time onset of symptom and presentation were 12.44 ± 9.181 . The 66(61.1%) patients presented for the first time while the remaining 42(38.9%) were operated elsewhere and were referred. The patients with presenting symptom of only pain were 38(35.2%), with swelling only were 18 (16.7%), with both pain and swelling were 46(42.6%) and those with pain and fracture were 6(5.6%). The commonest site were proximal tibia 32(29.63%) followed by distal femur 20(18.52%) and then proximal humerus 16(14.82%). The commonest surgical procedure performed were curettage and bone cementation i-e 36(33.33%), followed by wide excision of bone \pm cementation and usage of implant i-e 34(31.5%). Curettage and bone grafting were done in 14(13%) patients, 10(9.3%) patients with recurrent tumor underwent above knee amputation, 6(5.55%) patients underwent custom made arthroplasties, 8(7.40%) patients underwent disarticulation. 18 patients were lost in 1 year follow up, 7(6.48%) presented with recurrent tumour whose were managed accordingly.

Conclusion: Giant cell tumour can occur at any age,most commonly in 3rd & 4th decade and any bone can be involved but mostly proximal tibia and distal femur. The choice of surgical treatment varies among individuals which depends on the extent of bone destruction, risk of tumor recurrence and type of bone involved. The delayed presentation of the patients is most common cause for wide excision.

PATHOLOGICAL EVALUATION OF NEOADJUVANT CHEMOTHERAPY TREATED AMPUTATIONS IN OSTEOSARCOMA PATIENTS

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Purpose/Objective: Osteosarcoma is a primary malignant bone tumor with the major peak incidence in early adolescence. Current management of osteosarcoma includes a combination of systemic chemotherapy and surgical resection. Assessment of post-neoadjuvant chemotherapy is used to predict prognosis after surgery. This study was done to assess the pathologic response of neoadjuvant chemotherapy in patients of osteosarcoma.

Material/Methods: this was a cross-sectional study, conducted at shaukat khanum memorial cancer hospital, lahore, from 06/01/16 to 05/07/16. A total of 60 cases of osteosarcoma were included. Demographic details such as sex and age were collected. A representative tumor grid was sampled from each case using standard grossing protocol. Sections were stained with hematoxylin and eosin. The percentage of necrosis was assessed by two histopathologists, independently.

Results: Sixty percent patients(n=36) were between 07-18 years of age while 40% (n=24) were between 19-45 years of age, mean age was calculated as 17.65 years, 58.33% (n=35) were male and 41.67% (n=25) were females, pathologic response of osteosarcoma in amputation specimens after neoadjuvant chemotherapy in terms of good response($\geq 90\%$ tumor necrosis) and poor response(< 90% tumor necrosis) was recorded as 30% (n=18) with good response and 70% (n=42) with poor response.

Conclusion: Early detection and more aggressive therapy regimes might help in improving dismal figures in terms of response to chemotherapy.

DIAGNOSTIC ACCURACY OF A LIMITED IMMNUO-PANEL OF CALRETININ AND BER-EP4 FOR DIAGNOSIS OF MALIGNANT EFFUSIONS

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Purpose/Objective: The objective of the study is to evaluate the diagnostic accuracy of limited immuno-panel of two antibodies for differentiation of reactive mesothelial cells and malignant epithelial cells in effusions; Calretinin and Ber-EP4 respectively.

Material/Methods: The study was conducted at the Histopathology, Oncology and Surgical departments of Allama Iqbal Medical College, Jinnah Hospital Lahore, Pakistan over a period of one year (October 2014 to October 2015). A total of 97 suspected malignant pleural and peritoneal effusions were collected. Cytological smears and cell blocks were prepared from centrifuged deposit of aspirates. Giemsa and Papanicolaou stained smears were screened for malignant cells. Immunohistochemical markers (Calretinin and Ber-ER4) were applied to the cell block. The cytological diagnosis of malignant cells and reactive mesothelial cells was verified with the cell block, histopathological diagnosis and immunohistochemistry results.

Results: Out of total 97 cases, cytological examination diagnosed 55 cases as definitive malignant, 21 cases as confirmed benign, 18 were suspicious for malignant cells and 3 were inconclusive due to low cellularity.

Antibodies (Ber-EP4 and Calretinin) were applied on cell blocks. Ber-EP4 showed positive results in 72 cases, out of 73 histologically proved malignant effusion cases while Calretinin revealed positive results in 19 out of 24 confirmed benign/ reactive cases.

Cross tabulation was done between results of Immunocytochemistry on cell blocks and histopathological diagnosis which is taken as gold standard. This showed that Sensitivity of Ber-EP4 is 98.6%, specificity is 100%, PPV is 100% and NPV is 96%. Sensitivity of Calretinin is 79.2%, specificity is 100%, PPV is 100% and NPV is 93.6%.

Conclusion: Limited immuno-panel of Calretinin and Ber-EP4 has a high positive and negative predictive value and is cost effective in resource limited set up for differentiation of Adenocarcinoma cells and Reactive Mesothelial cells in serous effusions.

PREDICTIVE IMPACT OF EGFR MUTATION IN METASTATIC NSCLC PATIENTS WITH TYROSINE KINASE THERAPY.

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Purpose/Objective: To identify EGFR mutations, linked to favorable outcome for tyrosine kinase therapy, in metastatic NSCLC patients.

IntroductionTumor cells of Non-small cell lung cancer patients harboring activating mutations in EGFR gene tend to do significantly better when treated with oral tyrosine kinase inhibitors, as compared to those with wild type EGFR.

Material/Methods: EGFR mutations in tumor samples were screened by multiplex real time PCR (Roche Diagnostics, USA) according to the manufacturer's instructions. DNA from FFPE tissue, was amplified with primers and probes specific to 43 different EGFR mutations.

Results: Out of 114 patients, 75 were male and 39 females; male to female ratio was 1.9. Mean age of the patients was 60 years, which ranged between 5.5 and 85 years. EGFR mutation Del 19 was detected in 18 patients, whereas L858R mutation was found in 9 patients. In 2 patients compound mutation [S768I and G719X] was observed.. EGFR mutations were more common in male patients compared to females, In addition, none of the 43 mutations was detected in 84 tumors samples, indicating an overall 27% mutation positivity in Pakistani NSCLC patients.

Conclusion: According to our study, frequency of mutation positive samples (27%) was smaller compared to other South Asian countries. However, positivity in female patients was higher compared to male patients. A study with larger sample size may better portray general mutation distribution.

CHARACTERISTIC AND OUTCOME OF MULTIPLE MYELOMA: A SINGLE CENTER EXPERIENCE

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Purpose/Objective: Multiple myeloma is plasma cells disorder characterized by presence of monoclonal protein in serum or urine or both, increased bone marrow plasma cells, osteolytic lesion, hypercalcemia and anemia. Several combination regimens are commonly recommended for treatment of multiple myeloma. Aim of this study is to determine characteristics and outcome of multiple myeloma treated at SKMH.

Material/Methods: All patients from January 2012 to July 2015 with a proven diagnosis of Multiple were enrolled in study. Data abstracted from hospital information system .All patients Characteristics and outcomes were calculated. Progression free survival and overall survival of patients estimated with different chemo regimens.

Results: Total of 82 patients were available for final analysis. The median age was 51 years (Range23–64 years). There were 46 (56.1%) males and 36 (43.9%) females. Number of patients with IgG and IgA type was 48 (58.5%) and 15(18.3%) respectively. There were 7(8.5%) patients with non secretory type, and 74 (90.2%) with secretory type disease. Majority of the patients 59(71.9%) were treated with CTD regimen and only 13(15.8%) patients received Bortezomib based treatment. The median progression-free survival time was 30 months and median overall survival time was 48 months.

Conclusion: Based on our results, onset of multiple myeloma is in a relatively younger age group. Small number of patients received Bortezomib due to cost issues. PFS and OS in our study are comparable with published literature.

INTERNATIONAL SCORING SYSTEM IN SYMPTOMATIC MULTIPLE MYELOMA: EXPERIENCE FROM A TERTIARY CARE CENTER

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Purpose/Objective: Symptomatic multiple myeloma (MM) is a plasma cell dyscrasia that is characterized by clonal plasma cells infiltration, presence of M-paraprotein, and an associated end organ failure. Limited data is available from Pakistan, which prompted us to conduct this study. Our aim is to study demographics, clinicopathological features and to determine the stage stratification according to an international scoring system (ISS) in adult Pakistani MM patients at disease presentation.

Material/Methods: This single centre cross-sectional study extended from January 2010 to December 2014. Data were retrieved from the departmental patients' maintained archive.

Results: Overall, 61 patients were diagnosed at our institution with MM during the study period. There were 43 males and 18 females. Age ranged between 34 and 81 years with a mean of 56.1±12.8 and a median of 57 years. The male to female ratio was ~2:1. Common presenting complaints included fatigue (81.9%); backache (80.3%) and bony pain (67.2%). Physical findings revealed pallor (44.2%) as a presenting clinical feature. The mean hemoglobin value was 8.9±1.7g/dl. Severe anemia with hemoglobin <8.5 gm/dl was seen in 40.9%.

Out of 61 study subjects, 39 patients data were available for disease types and stage stratifications. Overall, 9 patients were in ISS stage I (23%), 12 were in stage II (30.7%) and 18 were in stage III (46.1%). IgG myeloma was commonest, seen in 26 (66.6%) followed by IgA in 11 (28.2%) patients with non secretory myeloma in one (2.5%) and light chain disease also in one patient (2.5%). Kappa immunoglobulin was detected in 29 (74.3%) and the remaining 10 (25.6%) patients had lambda type myelomas.

Conclusion: MM in Pakistani patients is seen in a relatively young population with male preponderance. The majority of patients present with symptomatic anemia and backache to seek medical attention. IgG Kappa was diagnosed as commonest type. Primarily patients were symptomatic and risk stratification revealed a predominance of advanced stage III disease at presentation.

SINGLE CENTER EXPERIENCE OF DIFFUSE LARGE B-CELL LYMPHOMA PATIENTS WITH CENTRAL NERVOUS SYSTEM RELAPSE

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Purpose/Objective: Central nervous system (CNS) relapse of diffuse large B cell lymphoma (DLBCL) is relatively uncommon and nearly fatal. We analyzed characteristics of patients of DLBCL presenting with CNS relapse.

Material/Methods: All patients of DLBCL with CNS relapse from 2006 to 2014 were included. Data were collected from hospital information system and analyzed for characteristics and median survival.

Results: Out of twenty one patients included in the study, 14(66.3%) males and 7(33.7%) were females. On initial diagnosis of DLBCL, median age was 37.4 years. Stage IV was in 12(57.1%) patients; 4(19.0%), 2(9.5%) and 3 (14.3%) patients had stage III, II, I disease respectively. Extra-nodal involvement was in 16(76.2%), high LDH in 18(85.7%), bone marrow involvement in 8(38.1%) and bulky disease in 5(23.8%) patients. International Prognostic Index (IPI) was 1 in 4(19%), 2 in 9(42.9%), 3 in 8(38.1%) patients. Extra-nodal sites were gut in 2(9.1%) while 1(4.5%) patient of each of following organs; cervix, gluteal muscle, iliac bone, liver, ovaries, pancreas, parotid gland and testes. Chemotherapy CHOP was given to 16(76.2%), RCHOP 5(23.8%) patients. Intra-thecal methotrexate was given to 10(47.6%) patients. Complete response was in 10 (47.6%), partial response was in 3 (14.3%) and disease progression was in 8 (38.1%) patients. CNS relapse occurred in 10 (81%) patients within six months after completion therapy. Isolated CNS relapse was in 7(33.3%) patients. Overall median survival of CNS relapsed patients was 54 days.

Conclusion: Patients with DLBCL who had advanced stage, high LDH and extra-anodal involvement at initial presentation are high risk for CNS relapse. Once relapsed in CNS, these patients have very poor prognosis.

UTILITY F18 FDG PET-CT IN NK CELL LYMPHOMA: AN INSTITUTIONAL REVIEW

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Purpose/Objective: Institutional review of the utility of F18 FDG PET-CT in NK cell lymphoma. Natural killer (NK)/T-cell lymphoma is a newly recognized distinctive entity in the World Health Organization (WHO) classification of lymphomas. It accounts for less than 3% to 9% of all lymphomas in Asia. NKTL is an aggressive lymphoma with cumulative probability of 5-year survival ranging from 37.9% to 49.5%.

Material/Methods: Retrospective review of 12 patients who underwent22 FDG PET-CT scans between January 2011 and June 2016 in histopathologically proven NK T cell lymphomas at a tertiary care cancer centre. One patient was excluded due to inadequate information on follow-up. FDG PET CT scan was performed in 8 patients for baseline staging workup and in 4 patients for response evaluation/restaging. Median follow up: 14 months (range 3-36 months). Kaplan-Meier disease free survival and overall survival curves were generated for multiple variables including gender, stage, SUVmax, disease sites and Ki 67%.

Results: 11 patients had nasal presentation while 1 had pharyngeal disease. Out of 8 patients for baseline workup, six were males and two females [age = 45 years ± 13SD]. SUVmax range 4-20. PET-CT identified stage I[n=3], II[n=2], III [1] and IV[n=2]. At staging, 3[37.5%] had visceral involvement. No statistically significant correlation was found between Ki67 index and SUV values (p value=0.43) Kaplan-Meier 36 months disease free survival based on gender: males (40%), females (50%); stage: I (67%), II (100%), III (0%) and IV (0%); disease site: Nodal (60%), visceral (0%); and Ki67 index: <70% (70%), >70% (0%). None of these factors showed statistically significant results due to small number of data sets. Overall, 4 [50%] patients expired during follow-up and once again no significant correlation was found between overall survival and the aforementioned variables due to small data set of patients.

Conclusion: NK Cell lymphomas are FDG avid and given its rarity, role of PET-CT in its management is evolving.

CYTOGENETIC INVESTIGATION IN CHRONIC MYELOID LEUKEMIA - A STUDY FROM SHAUKAT KHANUM MEMORIAL CANCER HOSPITAL (SKMCH)

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Purpose/Objective:

Chronic myeloid leukemia (CML) is a myeloproliferative disorder characterized by t(9;22)(q34;q11.2) reciprocal transloclation, resulting in fusion of BCR gene at 9q34 to ABL gene at 22q11.2. The resulting BCR/ABL fusion gene (Philadelphia chromosome) encodes constitutively active tyrosine kinase, that is present in >90% of the patients, is believed to play a role in leukomogenesis of CML and is targeted by imatinib mesylate (Gleevec). Objective Cytogenetic analysis plays a pivatol role in diagnosing CML patients. Data on cytogenetic abnormalites (both common as well as rare variants) in CML remains scarce. In view of this, we conducted a retrospective study on samples from SKMCH to identify simple and complex chromosomal aberrations in CML using conventional cytogenetic analyses. The prevalence as well as frequency of common t(9;22)(q34;q11.2) and complex variant translocations was assessed.

Material/Methods: This study was conducted retrospectively on 400 samples submitted to the cytogenetic laboratory at SKMCH. Cytogenetic analyses were performed on heparinized bone marrow (BM) or blood (more than 10% blast) samples. Cells were harvested to obtain chromosomes using standard techniques after overnight or 48 hour incubation. The fixed cells were dropped onto the slides, stained and G-banded. At least 20 metaphase chromosomes were analyzed from each sample and aneuploidy, translocations, deletions and other abnormalities were scored. Cells were karyotyped using Cytovision software 7.3.

Results: Conventional cytogenetic analysis was performed on hematological confirmed CML cases. The data from SKMCH showed that out of 400 reported cases, 96 (24%) showed normal karyotypes; of 304 (76%) abnormal cases 211 (69.4%) scored positive for t(9;22)(q34;q11.2) translocation. Within Philadelphia chromosome positive (Ph'+ve) samples, 59 (28%) cases showed additional chromosomal aberrations (ACAs) including +8, i(17)q, del 11q, +mar and translocations t(1;19), t(8;20), t(8;14), t(1;4). Patients harboring variant translocations were detected in 16 (7.6%) cases involving three way translocation of t(9;22) with chromosomes 1, 2, 10, 11 & 14. Ph'-ve CML showed additional chromosomal aberrations (+8, del 12p & polyploidy) detected in 18 (5.9%) cases. The proportion of Ph + CML cases in males and females was 63.5% and 36.5%, respectively. Abnormal karyotypes were significantly higher in males (i.e., 67%) as compared to females (i.e., 33%) and were highest (i.e., 69.3%) in 21-60 age groups.

Conclusion: Cytogenetic evaluation has prognostic and predictive significance in hematological malignancies. Conventional cytogenetic analysis plays an important role in initial diagnosis and disease monitoring of leukemia. CML which is characterized by t(9;22)(q34;q11.2) translocation is present in about 90% cases. In 5-6 % of cases, Philadelphia chromosome is produced by complex translocations. This study shows that Ph +ve CML predominates in males than females and especially in higher age groups. Secondary chromosomal aberrations are also more frequent in males. Although other molecular and FISH (fluorescence in situ hybridyzation) tests may be employed to detect t(9;22)(q34;q11.2) translocations, carrying out conventional cytogenetic analyses remains absolutely necessary for any cancer research/diagnostic laboratory.

YIELD OF BLOOD CULTURES IN CANCER AND NON-CANCER PATIENTS

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Purpose/Objective: Limited data is available on the yield from blood cultures in cancer patients. We therefore undertook a review of the yield of blood cultures taken from cancer patients as well as from non-cancer patients to serve as a comparator group.

Material/Methods: This retrospective review was conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan. Data pertaining to all the blood cultures from January 2011 to December 2015 was retrieved from electronic hospital record system.

Inclusion criteria included all cancer patients from our hospital and culture received from our network of laboratory phlebotomy centers, located all over Pakistan. Hospital employees' data was excluded. Blood cultures were classified into three categories, true positive, false positive (contamination) and negative blood cultures. True positive and false positive blood cultures were determined by the infectious disease specialist and microbiologist, together.

During the study period all blood cultures had processed by the BACTEC 9240 system (Becton Dickinson), with an incubation period of 7 days. Isolates were identified by standard techniques and anti-microbial susceptibility testing was performed and interpreted according to Clinical Laboratory Standards Institute (CLSI) criteria using the disk diffusion methodology.

Results: A total of 39,752 blood cultures were received at our microbiology lab during the study period from all over the country. Out of these 30,116 were reported as negative and 5,247 blood cultures were found to be true positives. Culture positive rate among cancer patients was 29.2% whereas it was 18.1% in samples received from phlebotomy centers across the country, the large majority of whom is likely to be non-malignant diagnoses. Overall, true positive rate in cancer patients was 16.2%, where it was 9.5% in those without any cancer.

Coagulase negative Staphylococci and Staphylococcus epidermidis were the most common contaminants at 74.3%, followed by Diptheroid (10.1%), Micrococcus (7.8%), Bacillus (7.3%) and Corynebacterium species (0.5%). Among true positive cultures, Escherichia.coli was the most commonly isolated pathogen (20.6%) followed by Salmonella species and klebsiella pneumonia.

Conclusion: The yield of blood cultures in hospital patients was higher than those of other patients. Sampling technique is critical in avoiding contamination, which can lead to unnecessary antibiotics administration and increase cost.

SYNTHESIS AND CHARACTERIZATION OF NANOBIOMATERIAL FOR CANCER DIAGNOSTICS

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Purpose/Objective:

Cancer diagnostic is one of burgeoning area of research. Research in cancer diagnostic lies at interface of molecular biology and interdisciplinary science. Traditional cancer diagnostics utilizes conventional techniques such as PCR, ELISA and MRI. However immediate need for real time and time efficient sensors is imminent for cancer diagnostics. Nanobiomaterials have emerged as saviour in this paradigm shift. Nanoparticles and graphene oxide are one of most popular nanomaterials in area. Combining graphene oxide and nanoparticles together give us desired tailor ability to nanosystem. In this research work, an effort was put forth for the synthesis and fabrication of a nanocomposite that can mimic peroxidase enzyme activity and therefore can be used for colorimetric detection of peroxides in the abnormal or cancer cells with improved limit of detection (LOD).

Material/Methods: Graphite flakes, Iron nitrate and cobalt nitrate, Dimethyl Sulfoxide (DMSO), Oleylamine (OAM) (70%) and 3,3',5,5'-Tetramethylbenzidine (TMB) were used as raw material without any further processing. Techniques such as scanning electron microscope (SEM), Fourier Transform Infrared Spectrophotometer (FTIR), X-ray diffraction (XRD) and UV visible spectroscopy were used for the characterization of synthesized nanomaterial. Peroxidase like activity was tested using UV Vis spectroscopy at wavelength (400-800nm)

Results: XRD analysis, SEM micrographs show successful synthesis of graphene oxide sheets, spherical nanoparticles and graphene oxide containing embedded nanoparticles on its surface. This water dispersible nanocomposite exhibited colloidal stability for a month.

Peroxidase like activity was found in this physical composite with LoD 0.3µM. Physical GO-CoFe nanocomposite had uniform dispersion of CoFe particles on GO sheets.

Conclusion: Synthesized nanocomposite exhibited stable and effective peroxidase like activity for H2O2 detection. In comparison to natural enzymes, this nanocomposite show advantages such as low cost and ease of modifications. We expect broader utilization of this engineered nanomaterial as a signal transducer to develop a colorimetric assay towards cancer diagnostics through its conjugation with various recognition elements such as aptamers and peptides.

A RE-AUDIT ON USE OF PERCUTANEOUS NEPHROSTOMY IN ADULT PATIENTS WITH MALIGNANT URETERIC OBSTRUCTION

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Purpose/Objective: Pelvic and retroperitoneal malignancies can cause obstructive uropathy leading to uraemia and severe acute kidney injury (AKI). Palliative decompression of the obstructed urinary system, either by percutaneous nephrostomy (PCN), ureteric stent or a combination of both can be used but offer uncertain benefits in improving renal and patient outcomes in people with advanced cancer.

Aims and Objectives:

We aim to compare rates of complications post PCN insertion at our centre to society of interventional radiology standards and incidence of such complications to previous audit performed in 2008. We also looked at patient and renal outcomes post PCN insertion.

Material/Methods: 300 patients, who received either unilateral or bilateral PCN between January 2015 and June 2016, were identified via hospital Medical Information System (MIS). We looked at every 3rd consecutive patient's medical notes retrospectively for demographics, details of malignancy, change in renal function, emergency presentation and need for admission post- PCN insertion and patient outcomes (n= 100). All these patients were receiving active treatment for underlying malignancy at SKMCH&RC.

Results: 72% were male and locally advanced bladder cancer was the most common malignancy in this group. None of the patients had any major complications post PCN insertion. Almost half of the patients (47%) returned to Emergency room within 30 days of PCN insertion, due to symptoms related to minor complications post PCN insertion with catheter displacement being commonest (27%). 1/3rd of patients required repeat PCN insertion within 60 days. Renal function never recovered in 24%. 56% either died or were lost to follow up. Rates of minor complications (including catheter displacement and infection) were lower compared to previous audit.

Conclusion: PCN insertion is a safe procedure however does not offer improved renal and patient outcomes in people with advanced malignancy. Benefits vs. risks of PCN insertion as part of therapeutic or palliative procedure should be discussed on an individual basis.