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17th International Conference on

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October 08-09, 2018 | Edinburgh, Scotland

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Itika Kumar et al., RRJMHS 2018
Volume: 7

AN AUDIT OF PLACENTAL SPECIMENS, THEIR CLINICAL INDICATIONS AND SUITABILITY FOR ASSESSMENT

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Background: The Royal College of Pathologists has issued guidance on specimens of little clinical value; this includes placentas. It has been agreed nationally that there are specific indications for processing these specimens; most of the important features can be recorded by midwives at the time of delivery and microscopic examination reveals little else except for certain clinical circumstances. We wished to determine if we were being referred appropriate cases.

Methods: A pathology database search was utilized and identified 140 specimens for the 2016 period. 32 were selected randomly. All were audited against the standard.

Results: In every report that was analysed the mother's details such as date of birth was reported. On the contrary, none of the infant's details which include foetal birth weight or condition was reported. This was the most neglected field and is extremely important to provide context for the microscopic examination being requested.

Conclusion: The results of this audit showed that 100% of the mother's details and responsible consultant was stated in every report. Unfortunately, infant details were not provided on any of the requests; there is an opportunity to improve.

Biography

Itika Kumar is Currently working in The James Cook University Hospital, UK

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Alaa Salah Jummah et al., RRJMHS 2018
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FOLD CHANGE IN *PTEN* GENE EXPRESSION IN ENDOMETRIAL CARCINOMA PATIENTS WHO LIVED IN DEPLETED URANIUM POLLUTED AREA

Alaa Salah Jummah, Hawraa Sahib Al-Haddad, Emad Hatem and **Akeel A Yaseen Al-Kufi**

University of Kufa, Iraq

To investigate whether there is any change in *PTEN* gene expression profile and tumor aggressiveness in endometrial carcinoma patients who lived in (DU) polluted area with those patients who lived in unpolluted area. An elevation in the *PTEN* gene expression profile was recorded in patients who lived in (DU) polluted area in comparison with the patients who have had the tumor though they lived in unpolluted area. The increase in gene expression was highly significant (P=0.001). No difference was noticed in the *PTEN* gene expression with regard to different grades of endometriosis carcinoma (P=0.286). Likewise, no significant *PTEN* gene expression changes were observed between the two groups when the age of the patients was introduced for comparison (P=0.45). Similarly, no significant differences in *PTEN* gene expression between the potentially exposed and unexposed subjects with regard to different stages of the tumor (P=0.98), to cervix involvement (P=0.532), or to ovarian involvement (P=0.518). *PTEN* genetic alteration plays an important role in pathogenesis of endometrial carcinoma. An obvious and significant increase in *PTEN* gene expression profile was spotted between the alleged exposed and unexposed patients. This observation urges the need for further molecular study to unfold the extent of DNA damages caused most probably by the use of DU on the Iraqi population and the types of damages that DU may cause. The results may conclude the most disputed arguments about the reasons behind the high incidence of all types of cancer in the middle and southern part of Iraq.

Biography

Akeel A, Yasseen, M.Sc(UK0, PhD(UK) M.Sc. and Ph.D. from Queens University of Belfast and University of Ulster (United Kingdom) in cytogenetics, molecular genetics and cancer research. Research fellow at the International Centre for Genetic Engineering and Biotechnology (United Nation, UNEDO), Trieste, Italy (1989). Research fellow at the Italian National Research Centre (CNR) and at the Instituto Superiora Di Sanita in Rome (1990). Visiting Professor at the University of Ulster School of Biomedical Sciences. (2005). Honorary Appointing Visiting Professor at the school of Biomedical Science, University of Ulster (2006 – 2010). Deputy president of the University of Kufa (1991-2001) and President of the University of Kufa (2011-2017). Patent holder on the Lymphocytes stimulation of peripheral blood culture by He-Ne Laser. Currently, Emeritus professor of Medical and Molecular Genetics at the Department of Pathology and Forensic Medicine, Faculty of Medicine, University of Kufa, Iraq. Substantial publication record in peer reviewing journals and skilled in delivering oral presentations: 50 peer reviewed papers; 53 National and International Presentations; 2 books Widely ranging research expertise in: molecular genetics, medical genetics and genetic counseling, clinical cytogenetics, cell and tissue culture, DNA repair.

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Pathology & Cancer Epidemiology

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Gozzi Michela et al., RRJMHS 2018
Volume: 7

USE OF THE CYTOLOGICAL METHOD OF LIQUID PHASE IN NASAL CYTOLOGY

Gozzi Michela, Sergio Fiaccavento and **Cordoni Rosangela**
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In case of rhinitis the diagnosis requires a precise diagnostic procedure and is essentially based on the exclusion of allergies, infections or defects of the nose. The clinical di usion of nasal cytology has allowed recognizing the non-allergic rhinitis. Nasal Cytology allows identifying non-allergic cell-mediated rhinitis from neutrophilis (NARNE), eosinophils (NARES) and mast cells (NARMA). The enrichment technique in the liquid phase also allows improving the quality of the sample making it easier to read by the pathologist. The poster describes the technique used to set up the samples and the results obtained.

Biography

Gozzi Michela, born in 1973, obtained a degree in 1997 from the Faculty of Medicine and Surgery of Brescia in a Biomedical laboratory techniques with a score of 110/110 with honors. From 1997 to 2005 she worked at the Service of Pathological Anatomy of the Poliambulanza Foundation, then she worked as co-ordinator of the Cytology service of the OxigenLab medical analysis laboratory. From 2014 she started working as a freelance cytologist in the cytopathology service of the Clinical Institute of the City of Brescia.

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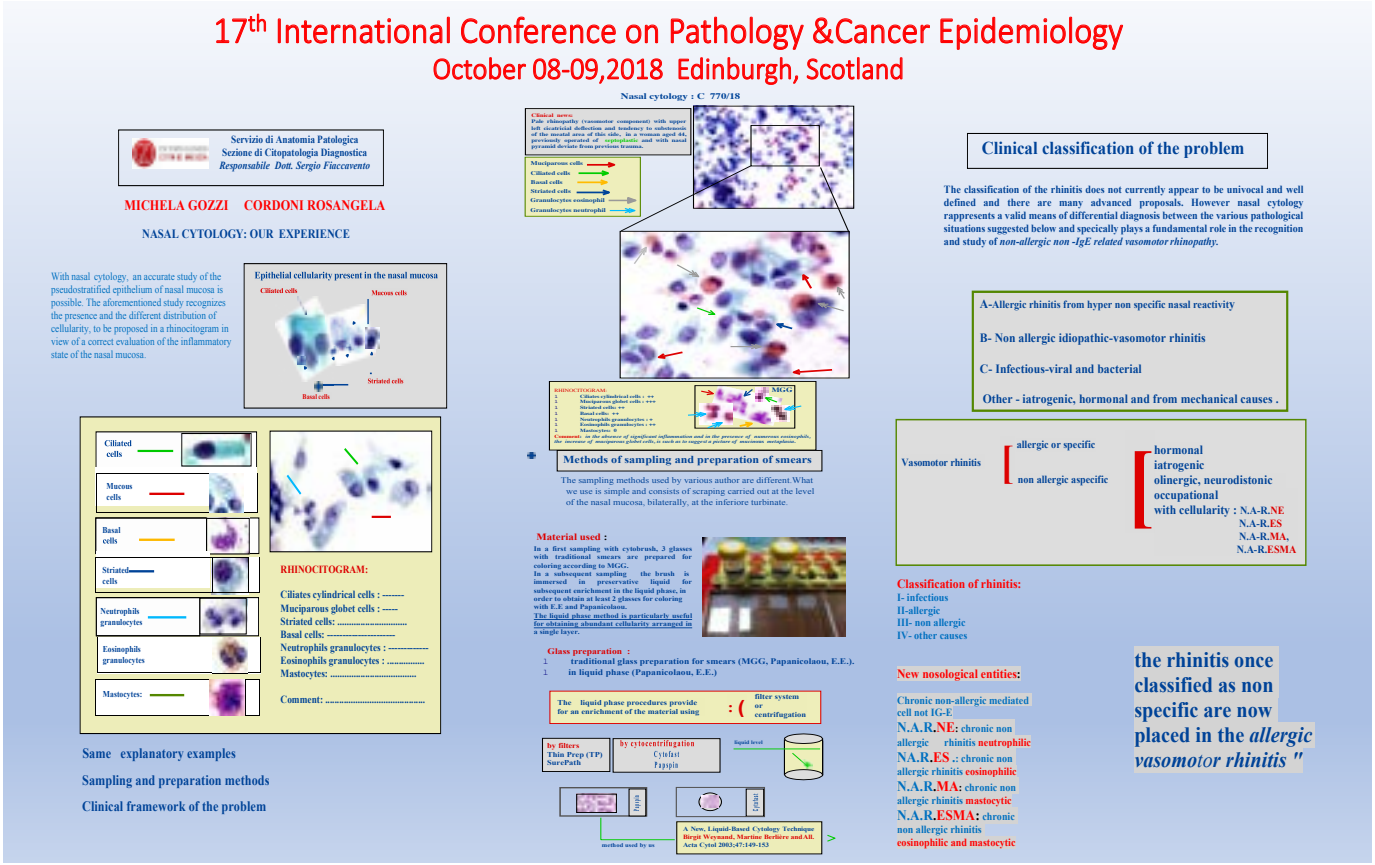

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Vivian G D Rouston et al., RRJMHS 2018
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SURVIVIN AND CASPASE-3 AS A DIAGNOSTIC AND PREDICTIVE BIOMARKERS OF RECURRENCE FOR URINARY BLADDER CARCINOMA AFTER TURBT

Vivian G D Rouston, Amal A A Shaaban, Dina M Abd Allah and **Ahmed F Kotb**
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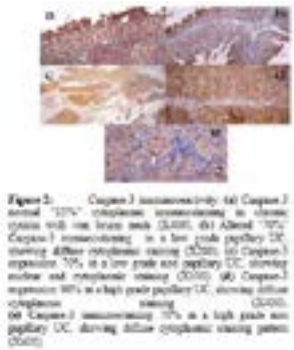
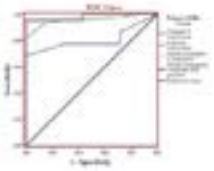
Background: Bladder cancer even in early stage develop recurrence. Poor sensitivity of cytology and invasiveness of urethrocystoscopy have generated interest in non-invasive tools to monitor for recurrence. Caspase-3 and survivin have central role in regulation of apoptosis. Survivin can aid early diagnosis, determine prognosis in multiple cancer types and predict response to anti-cancer therapies. Its combination with other biomarkers as caspase-3 enhance prognostication and prediction of treatment response in UBC.

Methods: Immunohistochemical expression of survivin and caspase-3 were assessed in 44 Egyptian consecutive patients with UBC and 7 cystoscopic biopsies of cystitis as control reactive benign urothelium. Relationships between their expression, clinicopathological characteristics, diagnostic and prognostic performance were statistically analyzed.

Findings: No survivin immunoreactivity was identified in non-neoplastic bladder tissue. Expression of survivin and caspase-3 was altered in 42(95.5%) and 10(22.7%) cases, respectively. There was statistically significant moderate positive correlation between survivin and caspase-3 expression among whole studied cases (p=0.006). Expression of either survivin or caspase-3 protein individually significantly differ (p=0.000) in cancer status from control cases. Survivin was an independent predictor of UBC in multivariable analyses. Diagnostic accuracy of survivin alone was significantly better than caspase-3 alone (sensitivity 81.82% vs. 68.18%, p=0.027). Addition of survivin immunoreactivity to model including caspase-3 expression improved diagnostic accuracy with a sensitivity of 93.18%. Addition of gender to the previous model improved more diagnostic accuracy with sensitivity of 100%.

Interpretation: Survivin alone is very promising marker and reliable indicator in UBC. Survivin and caspase-3 antigens have a cooperative effect on bladder cancer, their simultaneous evaluation augments diagnostic sensitivity.





Biography

Vivian G D Rouston obtained her MBBCh in 2004 and Masters in Pathology in 2015 from Faculty of Medicine Alexandria University. She was trained for Histopathology and Cytopathology at Histopathology Division of the Department of Pathology, St James's University Hospital, the Leeds Teaching Hospitals, NHS Trust, United Kingdom. She is working as a Histopathology Specialist in a general hospital in Egypt.

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Pathology & Cancer Epidemiology

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Weidong Xie et al., RRJMHS 2018
Volume: 7

CLASSIFICATION OF BREAST CANCER HISTOLOGY IMAGES USING DEEP LEARNING

Weidong Xie[1], Anjia Han[2], Xunzhang Wang[3], Tiantian Zhen[2], Yan Yang[1], Huijuan Shi[2], Elyas Mamatkadir[1] and **Jinwen Wang[3]**

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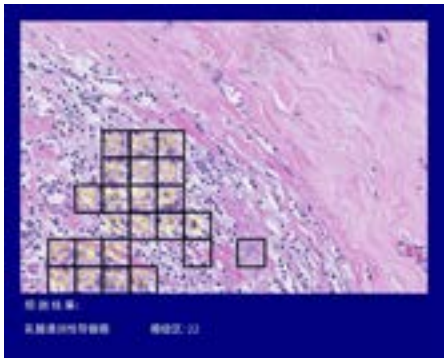
Cancer is the second important morbidity and mortality factor among women and the most incident type is breast cancer. The diagnosis of biopsy tissue with hematoxylin and eosin (H&E) stained images is non-trivial and specialists often disagree on the final diagnosis. Actually, computer-aided diagnosis systems contribute to reduce the cost and increase the efficiency of this process. Therefore, we have established a diagnostic tool based on a deep-learning framework for the screening of patients with invasive ductal carcinoma. The dataset of tissue slides used in this project consists of 30,000 samples from eligible patients in our hospital. Available tissue samples above were split into a training set, for learning the CNN parameters, and test set, for evaluating its performance. An accuracy of 94% was obtained for non-cancer (i.e. normal or benign) vs. malignant (i.e. invasive carcinoma). This will be helping specialists identify cancerization which is not visible under a single microscope, and this is just the start of what we have planned.



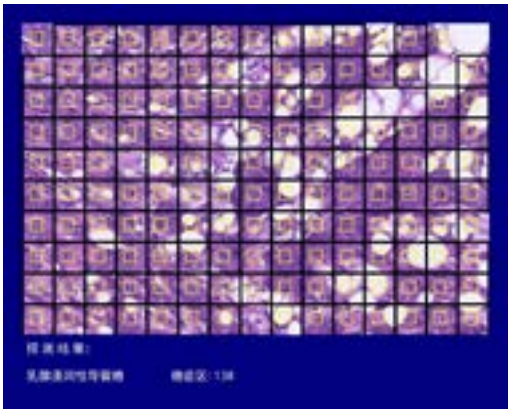


Figure: The prediction results of 2 samples in the validation set AI(the black box)vs. pathologists (the yellow box).

Biography

Weidong Xie is a inventor, founder and CEO of DM Intelligence. Following graduation from Imperial College London with honor in Biological Medicine he took office as Associate Professor in Sun Yat-sen University and Director/PI in St. Jude Children's Research Hospital, USA. His research results in regards to T-cell viral immunity which is listed as the remarkable scientific breakthroughs by famous journals. After a decade of experience in small molecule drug discovery, he leads technology startups successfully and AI in medical imaging & pathology diagnosis is the key point he focuses on.

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ADVANTAGE OF Z-STACKING FOR TELE CONSULTATION BETWEEN THE USA AND COLOMBIA

Andres Mosquera Zamudio[1], Matthew G Hanna[2], Rafael Parra Medina[3], Ana Carolina Piedrahita[1], Paula A Rodriguez Urrego[4] and **Liron Pantanowitz[2]**

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Introduction & Aim: There is an emerging need for tele cytology in Colombia as the demand for cytopathology has increased. However, due to economic and technological constraints tele cytology services are limited. Our aim was to evaluate the diagnostic feasibility of using whole slide imaging with and without Z-stacking for tele cytology in Colombia, South America.

Methods: Archival glass slides from 17 fine needle aspiration smears were digitized employing whole slide imaging (WSI) (Nanozoomer 2.0 HT, Hamamatsu) in one Z-plane at 40x and panoramic digital imaging (Panoptiq system, Views IQ) combining low-magnification digital maps with embedded 40x Z stacks of representative regions of interest. Fourteen Colombian pathologists reviewed both sets of digital images. Diagnostic concordance, time to diagnosis, image quality (scale 1-10), and usefulness of Z stacking, and technical difficulties were recorded.

Results: Image quality scored by pathologists was on average 8.3 for WSI and 8.7 for panoramic images with Z stacks (p=0.03). However, diagnostic concordance was not impacted by image quality ranking. In the majority of cases (72.4%) pathologists deemed Z-stacking to be diagnostically helpful. Technical issues related to Z-stack video performance constituted only a minor proportion of technical problems reported. Slow downloads and crashing of files while viewing was mostly experienced with larger WSI files.

Conclusion: This study demonstrated that international tele cytology for diagnostic purposes is feasible. Panoramic images had to be acquired manually but were of suitable diagnostic quality and generated smaller image files associated with fewer technical errors. Z-stacking proved to be useful in the majority of cases and is thus recommended for tele cytology.

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RRJMHS 2018
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ENDOCYTOSIS OF CEMENT DUST EXPOSURE AS A CAUSE OF ALTERED MITOCHONDRIAL MEMBRANE POTENTIAL, APOPTOSIS, NADP/NADPH AND OXIDATIVE STRESS IN HUMAN TYPE II EPITHELIAL CELLS

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Mechanisms of cement dust induced toxicity in lung cells have been scarcely studied. In the present study, we investigated endocytosis of cement dust and clinker particles, apoptosis, mitochondrial membrane potential ($\Delta\Psi_m$) alteration, NADP+, NADPH and NADP/NADPH ratio, *in situ* DNA fragmentation and oxidative stress in human alveolar type II epithelial cells (A549) exposed to cement dust particles. The endocytosis of particles was evaluated using transmission electron microscope (TEM), 3-(4, 5-dimethylthiazol-2-yl)-2, 5 diphenyl tetrazolium bromide (MTT) assay, LDH leakage, NADP/NADPH by enzyme linked immunosorbent assay (ELISA) and $\Delta\Psi_m$ using JC-1 dye. Additionally, apoptosis, intracellular reactive oxygen species (ROS) production and reduction of intracellular reduced glutathione (GSH) were quantified using flow cytometry method, while in situ DNA strand break was examined using TUNEL assay. Alveolar epithelial cells evaluation shows endocytosis of cement dust or clinker particles into the cytoplasmic vacuoles. Though, cells exposed to clinker were found to internalized clinker predominantly at the membrane bound vacuoles. Also, both cement dust samples and clinker induced reduction of $\Delta\Psi_m$ and NADP/NADPH ratio with subsequent increased induction of apoptosis and ROS generation. All dust samples induced profound reduction NADP/NADPH ratio which suggests reduction in intracellular reducing power. Collectively, data from this study show that endocytosis of cement dust and subsequent reduction of $\Delta\Psi_m$ and NADP/NADPH ratio, increased apoptosis, intracellular ROS production and reduction of GSH in type II epithelial cells may be key mechanisms of cement dust induced lung cells damage and may contribute significantly to cement dust induced lung fibrosis.

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RRJMHS 2018
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FIRST DO NO HARM – CHALLENGES TO BE OVERCOME IN THE MODERN PRACTICE OF PATHOLOGY

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The modern practice of pathology faces two immediate and major challenges – the need to satisfy a high level of clinical demand for reliable testing to make treatment as well as diagnostic decisions and the requirement that this to be done in an environment where healthcare spending is increasingly constrained. These international trends have driven widespread and often rapid changes in the way in which pathology services are delivered. New models of operation have utilized amalgamation, centralization, automation and digitization to deliver services with varying success. As safe and reliable pathology testing underpins modern healthcare, any failures impact directly on the care of individuals or a very large numbers of patients and disrupt the delivery of acute as well as community-based care. There is an urgent need to reassess these models to ensure that any risks to patient safety which have arisen during this period of change are identified and managed. Data from a review of errors known to be associated patient harm, including a review of claims from a large medical indemnity insurer, will be presented and a path forward for the effective management of risks to patients as a consequence of pathology testing is proposed.

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RRJMHS 2018
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DISTINCTIVE CLINICO-PATHOLOGICAL FEATURES AND DISEASE-SPECIFIC SURVIVAL OF ADENOID CYSTIC CARCINOMAS IN THE LOWER FEMALE GENITAL TRACT

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We have previously demonstrated that uterine cervical mixed carcinomas with adenoid cystic differentiation are high-risk human papillomavirus (HPV) related but pure adenoid cystic carcinomas (ACCs) of vulvar and uterine cervical origin appear to be unrelated to high risk HPV and contain NFIB related chromosome translocation. However, data on clinicopathologic features and survival outcomes of ACCs in lower female genital tract are limited to case reports and small case series studies. Here we systemically analyzed 84 cervical ACCs and 71 vulvar ACCs to identify clinicopathologic features and survival factors in a population based surveillance, epidemiology and end results study. While cervical ACCs tended to occur in the elderly (median, 72 years), vulvar ACCs commonly occurred in the patients a decade younger (median, 59 years, p<0.001). The median size of cervical and vulvar ACCs were 3.3 cm and 3.4 cm respectively. The patients with cervical and vulvar ACCs tended to have higher stage disease and a significant proportion of these patients received radiotherapy with or without surgery. The patients with cervical ACC had poor prognosis compared to that of vulvar ACC. The 10-year cause specific survival (CSS) rates for patients with cervical ACC were 57.9% and vulvar ACC are 80.7% (p<0.001). Increased age and high stage were significantly associated with a worse prognosis in the patients with cervical and vulvar ACCs by univariate and multivariate analysis. Our data demonstrated the distinctive clinicopathologic features and survival outcomes differing significantly among ACCs in lower female genital tract, thus providing a rationale for location/pathologic type-based treatment modalities.

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SPONTANEOUS *IN VITRO* CONVERSION OF VARIOUS PHENOTYPE FORMS OF FACTOR B

Dragana Begovic and **Dragisa Misovic**
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Objective: Several phenotype variants of factor B (FB) can be identified in human serum. We have previously shown that there are differences in concentration and activity of various phenotypes FB. It was also observed that during serum storage a slow conversion rate between FB phenotypes is accelerated at 37 . The purpose of this work is to determine the difference of conversion rate between different FB phenotype variants.

Methodology: 107 serum samples of healthy individuals were investigated. Electrophoresis with immuno fixation was used for phenotyping. Activity of FB was determined using the kinetic, nephelometric test with FB deficient serum. RID and electro immuno assay were used for determination of FB concentration. C3 component conversion was investigated by cross- electrophoresis.

Results: In analyzed samples 60 SS, 43 FS, 3 FF and one F1S phenotype was found. Three serum samples of each phenotype were stored at 37ºC. After 24 h, 3 and 7 days in each sample FB concentration and activity and complement alternative pathway activity were determined. During conversion it was noticed that complement activity was lost on the 7th day, while FB activity remained unchanged. Using cross-electrophoresis we found that on 7th day, C3 component was completely converted leading to the loss of complement hemolytic activity.

Conclusion: Phenotype FF had the fastest conversion rate, FS phenotype slower and the slowest conversion rate had SS phenotype. The differences were most obvious on the third day of conversion. Various FB phenotypes had no influence on C3 component conversion.

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RRJMHS 2018
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CYTOPATHOLOGY – THE LEADING EDGE TO THERANOSTICS AND PERSONALIZED MEDICINE

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The objective of the study is to describe the companion diagnostics that are necessary to differentiate specific cancers; describe the therapeutic modalities or personalized drugs that are coupled with the companion diagnostic; Understand the relationship between cytopathologic diagnosis of cancer from multiple organ sites and its relationship to theranostics; describe the FDA approved drugs that are used to treat leukemias and lymphomas, carcinomas and sarcomas and also to describe the tumor suppressor genes and their subsequent mutations that are associated with triaging patients with specific personalized therapies. The field of cytopathology has evolved from basic Pap staining of tumors followed by H&E tissue diagnosis of disease to the use of immunocytochemistry and complementary ancillary molecular diagnostics to aid in specifying the disease. However, due to the sequencing of the human genome and the subsequent genomic revolution, the field of theranostics has evolved. Theranostics is the coupling of companion diagnostic tools (in particular, molecular profiling) with specific therapeutic drugs. This personalized approach to diagnosis allows the clinician to provide therapy based on specific genetic mutations of the tumors from their patients. The FDA has dramatically increased the number of cleared/approved *in vitro* assays for patients with genetic mutations that respond to drugs that prevent the expression of the mutations, such as tyrosine kinase inhibitors. These alternative forms of therapy have dramatically increased the survival rate in patients with stage four and metastatic cancer. It is imperative that pathologists and laboratory professionals determine which companion diagnostic assay should be chosen and recommend the clinically actionable drugs tailored to their genetic mutation to the clinician. This change in the scope of practice creates unprecedented opportunities to more accurately diagnose patients and guide the selection of personalized therapies.

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A STUDY OF THE EFFECT OF IRON DEFICIENCY ANEMIA ON HBA1C IN DIABETES

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Adesh Institute of Medical Sciences & Research, India

Introduction: Diabetes mellitus is characterized by hyperglycemia resulting from defects of insulin and is associated with long-term damage of various organs. Glycated hemoglobin is widely used as a gold standard for monitoring glycemic control over the previous three months but it may be affected by genetic, physiological, hematological and illness-related factors. Two known factors which can modulate the glycation of proteins are the prevailing concentration of glucose and the half life of the proteins. Eventhough, HbA1c is a precise diagnostic tool for diabetic patients there are different factors like iron deficiency anemia (IDA) which can give false result of HbA1c.

Aim: The aim is to study the effect of iron deficiency anemia on levels of HbA1c in diabetic patients.

Methodology: Fifty diabetic, iron deficient anaemic patients (cases) and 50 age-matched diabetic patients (controls) were enrolled. The patients with haemoglobinopathies, haemolytic anaemia, chronic alcohol ingestion and chronic renal failure were excluded. Haemato¬logic investigations, fasting glucose and HbA1c levels were measured.

Results: The mean HbA1c in cases was 7.91±1.20 and in controls was 7.11±0.89, which was significant statistically as the p value was 0.0003 (<0.05). There was a significant difference between the values of hemoglobin between the cases and controls and no difference between the fasting glucose levels.

Conclusion: Iron deficiency anemia is the most prevalent nutritional anemia in India. Our study showed that IDA spuriously elevates HbA1C levels in the diabetic patients independent of plasma glucose concentration. Hence, it is important to exclude iron deficiency anemia and correct it before making any diagnostic/ therapeutic decision in a patient of diabetes mellitus.

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RRJMHS 2018
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PROBE BASED MELTING CURVE ANALYSIS IN ANTI-HBV DRUG RESISTANCE GENE MUTATION DETECTION

Muhammad Ammar Athar[1,2], Yi Mou[1,2], Yuzhen Wu[1,2], Ye Xu[1,2], Jianhua Wu[3], Zhenxing Xu[3], Zulfiqar Hayder[4], Saeed Khan[5], Muhammad Idrees Khan[6], Muhammad Israr Nasir[7], Yiqun Liao[1] and **Qingge Li[1,2]**

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[7]Liaquat National Hospital, Pakistan

Chronic hepatitis B (CHB) caused by Hepatitis B virus infection is a global public health issue. Individualized treatment of CHB becomes increasingly important and a best individualized treatment plan cannot be established without the information of HBV genetic diagnosis. Nowadays, HBV DNA quantification by real-time PCR is widely used in clinical diagnosis. However, there is an urgent need to establish some simple and efficient clinical detection methods for HBV drug resistance gene mutations detection. To address these issues, we proposed a study on the establishment of convenient and efficient methods for HBV drug resistance gene mutations detection. We described a real-time PCR-based assay using melting curve analysis that could accurately detect 24 HBV nucleotide mutations at 10 amino acid positions in the reverse transcriptase region of the HBV polymerase gene. The two-reaction assay had a limit of detection of five copies per reaction and could detect 5% rtM204V in the presence of the wild-type when the overall concentration was 104 copies/μL. The assay could be finished within three h and the material cost for each sample was less than 10 USD. Clinical study using three groups of samples involving both nucleotide analogs-treated and untreated patients showed that 99.3% (840/846) samples and 99.9% (8454/8460) amino acids were concordant with PCR sequencing. The six minor mutation containing samples undetected by PCR sequencing were confirmed by co-amplification at lower denaturation temperature-PCR sequencing. In the treated patients, 48.6% (103/212) were mutant comprising lamivudine-monoresistance, adefovir-monoresistance, entecavir resistance and lamivudine+adefovir resistance, respectively. Among the untreated patients, Chinese group had more mutation containing samples than did the Pakistani group (3.3% vs 0.56%). Because of its accuracy, rapidness, wide coverage and cost-effectiveness, the real-time PCR assay could be a robust tool for anti HBV drug resistance mutations detection in resources-limiting countries.

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HISTOPATHOLOGICAL STUDY OF MINOR SALIVARY GLAND TUMORS: AN OBSERVATIONAL STUDY IN THE MALWA BELT OF SOUTH WEST PART OF PUNJAB

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Adesh Institute of Medical Sciences & Research, India

Introduction: Minor salivary gland neoplasms represent less than 25% of the intraoral salivary neoplasms and only 0.3-1.5% of all the biopsies received in oral pathology laboratories.

Aim & Objective: Histopathological study of minor salivary gland tumors: An observational study in the Malwa belt of south west part of Punjab.

Material & Method: A prospective clinico-pathological study of 15 cases of benign and malignant neoplastic tumors of intraoral minor salivary glands was conducted in Department of Pathology at Adesh Institute of Medical Sciences and Research, Bathinda over the period of 6 months. The lesions from representative sections were studied and classified according to World Health Organization (WHO) classification.

Result: Palate was the most common site constituting 46.6% followed by retromolar region contributing 26%. Histopathologically amongst the 15 cases studied during study period, 8 were benign and remaining 7 were malignant. The most common benign tumor found was Pleomorphic adenoma (87.5%) followed by a single case of oncocytoma (12.5%). Among the 7 malignant tumours most commonly seen lesion was serous polymorphous low grade adenocarcinoma (PLGA) contributing 42.8% of all the malignant minor salivary gland lesions followed by adenoid cystic carcinoma (28.5%), mucoepidermoid carcinoma (14.2%).

Conclusion: Most of the benign tumors were observed in the age group of 20-40 years, while most of the malignant tumor cases were common in elderly (>40 years) age group. The most commonly seen benign neoplastic lesion was pleomorphic adenoma whereas polymorphous low grade adenocarcinoma (PLGA) was the most common malignant salivary gland neoplasm. Histopathology remains the gold standard for the diagnosis along with all other advanced ancillary techniques such as immunohistochemistry.

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MICROSATELLITE INSTABILITY IN COLORECTAL CARCINOMA: DOES SEX MATTER?

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The aim of this study was to evaluate sex diffrerences in microsatellite instability frequency and clinicopathological features of colorectal carcinoma (CRC). 177 patients (88 females and 89 males) with CRC who underwent microsatellite instability (MSI) testing were enrolled in this study. The overall incidence of MSI-H status among observed patients with CRC was 14.7%. The frequency of MSI was significantly higher in men (25.35%), comparing with women (10%) (P=0.0369). The MSI-H status was associated with the younger age (P=0.0020) in men. In addition, vast majority of MSI-H tumors were found in proximal part of large intestine (P<0.0001). In most of cases, MSI was due to lack of MLH1 and PMS2 expression (64%). MLH1 deficiency was higher in men rather than women (70.6% vs. 50%). In contrast, women demonstrated more often lack of MSH2+MSH6 (37.5% vs. 11.8%). Lack of MSH2 and MSH6 extression, as well as isolated block of PMS2 expression, were associated with the highest tumor grade (P<0.0001). In addition to grade, we found association of MSI-H status with some histological types of colorectal carcinoma. In particular, medullary and mucinous carcinoma were tightly associated with MSI (P=0.000767). Interestingly that most of these histological types were found in men in age up to 50 (P=0.0269). Finally, assessment of MSI-H status relation to tumor staging allowed us to find the lower frequency of metastasis in patietns with MSI-H status, comparing with patients with microsatellite stable tumors regardless of sex.

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EuroSciCon

17th International Conference on

Pathology & Cancer Epidemiology

October 08-09, 2018
Edinburgh, Scotland

RRJMHS 2018
Volume: 7

THROMBOTIC THROMBOCYTOPENIC PURPURA AND THE ROLE OF ADAMTS13 AS A KEY ENZYME IN THE PATHOGENESIS OF TTP

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Thrombotic thrombocytopenic purpura (TTP) is one of the most serious and life-threatening form of thrombotic microangiopathy characterized by microangiopathic hemolytic anemia, severe thrombocytopenia, and multiple organs damage due to VWF–platelet aggregations in the arterioles and capillaries of end organs. The thrombi are found most extensively in the heart, brain, kidney, pancreas, spleen, mesentery and adrenal glands. Thrombocytopenia results from consumption of platelets in the thrombotic process, while erythrocyte fragmentation and hemolysis result from mechanical injury induced by abnormally high shear stress in the microvasculature. Pathophysiology involves the absence of von Willebrand factor cleaving enzyme (ADAMTS-13), resulting in unusually large von Willebrand multimers. These multimers lead to platelet aggregations, microthrombi and subsequent thrombocytopenia. About 35% of adult patients have idiopathic (acquired) TTP due to formation of antibodies/inhibitors against ADAMTS13 (a disintegrin and metalloprotease with thrombospondin type 1 repeats, member 13). These patients develop severe ADAMTS13 deficiency and acute TTP. The inhibitors are primarily IgG but less often IgM. The plasma ADAMTS13 activity level is less than 10% or 5% in acute TTP. Inherited form of TTP is also described in children due to mutations of ADAMTS13 gene located on the long arm of chromosome 9 An ADAMTS13 level >10% excludes the diagnosis of TTP. Early diagnosis of TTP is essential to initiate appropriate treatment. The first-line therapy for acute TTP is based on daily therapeutic plasma exchange supplying deficient ADAMTS13. Immune modulators are humanized anti-CD20 monoclonal antibody rituximab.

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EuroSciCon

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Pathology & Cancer Epidemiology

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RRJMHS 2018
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MOLECULAR SIGNATURE AND SUB CLASSIFICATION OF LUNG CANCERS USING SMALL BIOPSY SAMPLES – MOVING FROM TARGETED THERAPY TO IMMUNOTHERAPY

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The majority of lung cancer patients present with locally advanced disease or with distant metastasis at the time of diagnosis. Fine needle biopsy (FNA) is an important approach for diagnosis and staging of lung cancer as well as for molecular characterization of the tumor. The new 2015 edition of the WHO classification and recommendations of IASLC (International Association of Study of Lung Cancer) emphasize the importance of accurate subclassification of lung cancers for targeted therapy. Lung cancer is a heterogeneous group of neoplasms and accurate diagnosis on small biopsies can be challenging. Recent systematic reviews and meta-analyses have shown that interobserver disagreement rates on the subclassification of non–small cell lung cancer (NSCLC) are approximately 10-20% in resected tumor specimens and 20-30% in small biopsy specimen without immunohistochemical (IHC) stains. The morphological heterogeneity of the lung cancer is also correlated with certain molecular alterations. Therefore, it is necessary to introduce newly updated guidelines of WHO and IASLC into our daily practice to improve the accuracy of subclassification of NSCLC for molecular profile and targeted therapy.

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Pathology & Cancer Epidemiology

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RRJMHS 2018
Volume: 7

OVARIAN NEOPLASMS IN PEDIATRIC AGE

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Ovarian neoplasms, although rare, are the most common gynecological tumors in the pediatric population. Few studies exist in the literature, demonstrating that the distribution of ovarian tumors histology in pediatric patients is quite different compared to adult age, with germ cell tumors and serous/mucinous surface epithelial neoplasms accounting for the majority of pathologic types. Although benign neoplasms greatly outnumber malignant ones it is critical to determine the possibility of malignancy at an early stage by multimodal diagnostic methods. Germ cell neoplasms are the most common, constituting nearly 80% of all ovarian tumors in the pediatric population. About teratomas the main criticities concern the grading of immaturity and the identification of microfoci of malignant tumors. Tumors as dysgerminoma and malignant mixed germ cell tumors are typical of prepubertal age and generally don't present diagnostic difficulty: immunohistochemistry may be useful for differential diagnosis. Epithelial neoplasms are uncommon in pediatric age accounting for about 15%, the most common type encountered being benign cystodenoma, followed by borderline tumors. The sex-cord stromal, for their rarity, can create diagnostic difficulties and may require immunohistochemical stains for differential diagnosis. Since today few attempts have been made to analyze the whole spectrum of ovarian neoplastic pathology in children and treatment guidelines dedicated to children are still not established. So it is very important to expand the knowledge of these rare tumors in order to allow the most appropriate therapeutic decisions.

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EuroSciCon

17th International Conference on

Pathology & Cancer Epidemiology

October 08-09, 2018
Edinburgh, Scotland

RRJMHS 2018
Volume: 7

DIRECT EVIDENCE OF VIRAL INFECTION AND MITOCHONDRIAL ALTERATIONS IN THE BRAIN OF FETUSES AT HIGH RISK FOR SCHIZOPHRENIA

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Background: There is increasing evidences that favor the prenatal beginning of schizophrenia. These evidences point toward intra-uterine environmental factors that act specifically during the second pregnancy trimester producing a direct damage of the brain of the fetus. The current available technology doesn't allow observing what is happening at cellular level since the human brain is not exposed to a direct analysis in that stage of the life in subjects at high risk of developing schizophrenia.

Methods: In 1977 we began a direct electron microscopic research of the brain of fetuses at high risk from schizophrenic mothers in order to finding differences at cellular level in relation to controls.

Results: In these studies we have observed within the nuclei of neurons the presence of complete and incomplete viral particles that reacted in positive form with antibodies to herpes simplex hominis type I [HSV1] virus, and mitochondria alterations.

Conclusion: The importance of these findings can have practical applications in the prevention of the illness keeping in mind its direct relation to the aetiology and physiopathology of schizophrenia. A study of the gametes or the amniotic fluid cells in women at risk of having a schizophrenic offspring is considered. Of being observed the same alterations that those observed previously in the cells of the brain of the studied foetuses, it would intend to these women in risk of having a schizophrenic descendant, previous information of the results, the voluntary medical interruption of the pregnancy or an early anti HSV1 viral treatment as preventive measure of the later development of the illness.

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Pathology & Cancer Epidemiology

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RRJMHS 2018
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ROLE OF EPIGENETIC MECHANISM IN THE PATHOLOGY OF ABDOMINAL AORTIC ANEURYSM

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Abdominal aortic aneurysm (AAA) is an abnormal dilatation in a weakened region of the main abdominal blood vessel. Approximately 5% of men over 65 years of age have an AAA. Prevalence of AAA is increasing rapidly in an aging population and becoming increasingly common in women. Patients with AAA present an increased risk of major cardiovascular events such as stroke and myocardial infarction, and AAA is amongst the leading 15 causes of death for people aged >60 years. Surgical intervention is currently the method for AAA correction but is associated with significant peri-operative mortality and currently there is no medical cure for AAA. Detailed information regarding the aneurysms is a prerequisite for targeted drug development for AAAs and currently it is still limited even after numerous genetic studies conducted in the past. Analysis of disease-state epigenome when compared to the normal epigenome provides a valuable foundation to study the regulation of gene expression crucial to the development of complex diseases. DNA methylation and histone modifications are two important epigenetic mediators of transcriptional repression. Several lines of evidences suggest an important role of altered epigenetic status in inflammation, proliferation and remodelling processes, which are also associated with the development of AAA indicating that epigenetic changes are crucial in the development and progression of AAA. In this study, an over view of evidences of the role of epigentic mechanisms in AAA pathology is presented.

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RRJMHS 2018
Volume: 7

HORMONE RECEPTOR – POSITIVE BREAST CANCER HAS A WORSE PROGNOSIS IN MALE THAN IN FEMALE PATIENTS

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Purpose: Male breast carcinoma (MBC) is treated similarly to female breast carcinoma (FBC), and similar survival rates for both have been assumed. We analyzed prognostic and clinico-pathologic features of MBC to determine whether MBC subtypes differ from FBC subtypes.

Methods: We reviewed data for 172,847 FBC and 1,442 MBC patients from 2010 to 2012 from the National Cancer Institute Surveillance, epidemiology, and end results database. Carcinomas were subtyped by hormone receptor (HR) and human epidermal growth factor 2 (HER2) status as HR+/HER2–, HR+/HER2+, HR–/HER2+, and HR–/HER2–.

Results: The overall incidence of MBC in all breast carcinoma cases was 0.8%. MBC was more frequently HR+/HER2– than FBC was (78.3% vs. 67.4%) and less frequently HR–/HER2– (2.1% vs 10.9%). More MBC was staged as III or IV (24.9% vs. 17.2%). MBC had significantly worse overall survival (OS) than FBC (P<0.0001). After adjustment for age, ethnicity, and tumor grade, stage I and II MBC had significantly worse OS time than stage-matched FBC had (P=0.0011 for stage I, P=0.0229 for stage II). When stage- and subtype-matched patients were compared, MBC had significantly worse OS than FBC for stage I overall, for sub-stages IA and IIB HR+/HER2– carcinoma, and for stage III HR+/HER2+ carcinoma. Furthermore, MBC patients with HR+/HER2– T1aN0 carcinomas had worse OS than FBC patients had.

Conclusions: Patients with MBC have worse survival than patients with FBC, especially for early-stage HR+ breast cancers. More studies are needed to optimize treatment for MBC.

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DIRECTLY SAMPLED ENDOMETRIAL CYTOLOGY FOR SCREENING OF ENDOMETRIAL CANCERS

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Objective: Currently, directly sampled endometrial cytology is the most common method of screening for endometrial cancer in Japan. The purpose of this study are as follows: comparison of the detection rate between endometrial cytology and biopsy for diagnosis of endometrial cancers, and comparison of the diagnostic value of conventional and liquid-based preparation for endometrial cytology.

Materials & Methods: From 2000 to 2016, a total number of 2,326 patients with endometrial cancer underwent surgery at Cancer Institute Hospital, Tokyo Japan. Among them, we reviewed preoperative cytology and biopsy specimens of 1860 cases. The direct endometrial sampling method was applied for endometrial cytology.

Results: The detection rate of endometrial cancers between cytology and biopsy in all stages was 83.9% and 95.7% respectively, and in early stage was 79.4% and 90.0% respectively. There were significant differences between them. Comparison of the two preparation methods (conventional and liquid-based preparation). Even though there were some differences between conventional and liquid-based preparation, our results indicated that both methods are useful for detecting endometrial cancers.

Conclusions: Although, there were significant differences between cytology and biopsy in the detection rates of endometrial cancers, compared to the endometrial biopsy, endometrial cytology is easier to insert into the uterine cavity and is less painful. Therefore endometrial cytology has been used as a screening for endometrial cancer in Japan. Even though there were some differences between conventional and liquid-based cytology, our results indicated that both methods are useful for detecting endometrial cancers.

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RRJMHS 2018
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MILAN SALIVARY GLAND REPORTING SYSTEM: HIGHLIGHTS AND CLASSIFICATION SCHEMES

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Salivary gland lesions are relatively uncommon and fine needle aspiration (FNA) is routinely performed to evaluate these lesions. Although it is possible to reach a definitive diagnosis in some cases, there are a considerable number of remaining problematic cases. The issues precluding a definitive diagnosis on aspirated material of salivary gland lesions are as follows: scant cellularity, poorly preserved cells, cellular heterogeneity, squamous metaplasia, variable ratio of the cells and the matrix, uncommon presentation of common entities and finally, rare neoplasms. Therefore, rendering a definitive diagnosis on aspirated material can be a diagnostic challenge. Moreover, the clinicians and surgeons rely heavily on diagnosis of salivary gland FNAs for their patient care and management. The Milan salivary gland reporting system is introduced to provide a classification scheme for salivary gland FNA to improve the rendering of diagnoses of these cases. This workshop will review the Milan system and its application on routine daily practices for pathologists.

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EuroSciCon

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Pathology & Cancer Epidemiology

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RRJMHS 2018
Volume: 7

HISTOPATHOLOGIC EVALUATION AND PREVALENCE OF GASTRIC CANCER IN HERAT PROVNICE OF AFGHANISTAN FOR THE FIRST TIME

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Background: Gastric cancer is one of the leading causes of cancer related death worldwide. Many patients have in operable diseases at diagnosis or have recurrent diseases after resection with curative intent. Gastric cancer is seperated anatomically into true gastric adenocarcinoms and gastro oesophageal junction adenocarcinomas and histologically into diffuse and intestinal types. Gastric cancer should be treated by team of experts from different discipline. Surgery is the only curative treatment for locally advanced diseases. Chemotherapy is usually implemented in combination with surgery. In metastatic diseases, outcomes are poor with median survival being around one year. For the first time in Herat province of Afghanistan I decided to have a research on gastric cancers. Since there was no pathology laboratory in the past, no data is available about prevalence and incidence of this diseases. I collected the data and related possible causes of gastric cancer in my cancer diagnostic center, in order to inform the community about this dangerous diseases. Unfortunately in our country most of patients diagnose in late stages of cancer because of lack of facilities and awaraness of diagnostic methods.

Objective: To evaluate the histopathologic types of gastric cancer and related risk factors in Herat city.

Methods: This research is a descriptive study (based on existing data) or cross sectional study. The study population consists of 152 gastric biopsies from the patients who were suffering form gastric disorders. Endoscopically mucosal resection (biopsy) is taken by endoscopists and referred to Firooz pathology laboratory for diagnosis. The research data is from 01/01/2015 to 01/01/2017.

Materials: All tissues were excised by endoscopy as mucosal resections (biopsies). The diagnosis of the tissue samples were according to histologic prepared and stained slides (H&E) after standard histotechnology.

Results: In this study, 152 biopsies were assessed. 137 patients diagnosed gastric cancer, among them 95 (69.2%) were males and 42 (30.7%) females, 45.26% of cancer patients aged over 60 years old. In (71.05%) of biopsies revealed intestinal type adenocarcinoma. (11.8%) of patients the biopsies showed diffuse type carcinoma. Dysplasia were noted in (6.57%) of biopsies. Finally (2.70%) of biopsies revealed atrophic gastritis and (0.65%) of cases revealed lymphoma NHL. In 49.6% of cases the tumors had proximal location and in 50.44% of cases the tumor had distal location. Low grade adenocarcinoma were seen in 22.6% of cases, moderately differentiated were seen in 19.7% of cases and poorly differentiated were seen in 57.7% of cases. In this study 41.6% of cases revealed *Helicobacter pylori* in gastric mucosa. Patients who diagnosed gastric cancer did not use alcohol and Tobacco, most used meat in their daily diet.

Conclusion: By considering this fact that gastric cancer is a dangerous disease specially in undeveloped countries like Afghanistan and kills many people, it is mandatory for physician to diagnose gastric cancer in onset and early stages, in order to survive patients. Acording to our study most of referring patients (57.7%) suffered from Grade III adenocarcinoma and diagnosed poorly differentiated adenocarcinoma during there first endoscopy and histopathologic examination and the mean age for gastric cancer was 57.8 therfore, it is recommended for doctors to consider abdominal discomfort and gastric disorders as a serious problem and do necessary investigative methods especially in ages above 45 years with special emphasis on early diagnosis of disease inorder to reduce and decrease the death rates.

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EuroSciCon

17th International Conference on

Pathology & Cancer Epidemiology

October 08-09, 2018
Edinburgh, Scotland

RRJMHS 2018
Volume: 7

CASE STUDY

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37 years old female, married, G5P4, suffered from left breast mass in the supraareolar region (at 12 o'clock), no consult was done, she noted gradual enlargement of the mass over nine months, she came in for consult, with the persistence of the above symptoms with now accompanying tenderness, skin tethering and nipple retraction. She was nonsmoker, with regular menstruation and negative family history for breast cancer. Ultrasonography revealed ill-defined speculated hyperechoic mass with central calcification, measured 31x28 mm, and classified as score 5 by elastography. Fine needle aspiration and excisional biopsy revealed invasive ductal carcinoma, and it was triple positive by immunohistochemistry.

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