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A predictive multiscale computational tool for simulation of lung absorption and pharmacokinetics and optimization of pulmonary drug delivery

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Pulmonary drug delivery via oral inhalation is increasingly used for both treatment of lung diseases and for delivering drugs to the systemic circulation. Efficacy and safety of orally inhaled drugs is dependent on deposition and absorption of drugs in targeted region. However, due to the complex pharmaceutical and physiological factors involved in drug transfer from the administration site to the target region, it is difficult to experimentally capture the detailed mechanistic insights of involved pulmonary drug delivery processes.

In the present study, we have developed a novel predictive multi scale computational tool to simulate delivery, deposition, dissolution, absorption, distribution, metabolism, excretion, and actions of inhaled drug products within an integral framework of computational fluid dynamics (CFD) and PBPK-PD models. The tools and models will be used in predicting the effects of inhalation devices, drug formulation, compound physiochemical characteristics, physiological settings, and various pathological factors on drug deposition and distribution. Ultimately, we aim to provide not only the detailed mechanistic insights into key aspects affecting efficacy and safety of inhaled drug products, but also to guide optimal designs of pulmonary drug delivery systems, inhaled formulations, to prescribe these therapies optimally. Research reported in this study is supported by the U.S. Food and Drug Administration (FDA) under award number 1U01FD005214-01.

Biography

Ravishakar Kannan is a Principal Scientist at CFDR. He obtained his Ph.D. degree in 2008 from the Department of Aerospace Engineering, Iowa State University. His research interests include particle transport methods, computational drug delivery, moving boundary problems, parallel programming, algorithm development for high order methods, fluid structure interactions and High Performance Computing (HPC). He has published a series of research papers on the above in well-known international journals. Some of his latest contributions include the development of the Wind-Kessel algorithm for truncated lung models, the Q3D model for lung airways, novel high order viscous flux schemes, optimized partitioning and communication routine for HPC and development of an algorithm to detect and quantify blast injuries. Currently Dr. Kannan works on the multiscale modelling of the pulmonary drug particle deposition, dissolution, clearance and systemic circulation, collaborating with the FDA, NIH and Merck teams. Dr. Kannan has been invited to present his research at several universities worldwide in the above mentioned areas. Dr. Kannan is in the editorial board of "Journal of Aerospace Engineering and Technology" and "International Journal of Biomedical Engineering".

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Clinical and epidemiological profile of patients with chronic obstructive pulmonary disease in a medical institution from the city of Medellin, Colombia

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Introduction: Chronic obstructive pulmonary disease is a common condition, characterized by a persistent blockage of airflow, partially reversible and progressive, that represents 5% of the total deaths around the world, and is expected to become the third leading cause of death by 2030.

Objective: To establish the clinical and epidemiological profile of patients with chronic obstructive pulmonary disease in a medical institution from the city of Medellin, Colombia.

Methods: A cross-sectional study was performed, with a sample of 50 patients with a diagnosis of chronic obstructive pulmonary disease in a private institution in Medellin, during 2015. For the statistical analysis, the software SPSS ver.20 was used. For the quantitative variables mean, standard deviations, and minimum and maximum values were calculated; while for ordinal and nominal qualitative variables, proportions were estimated.

Results: The average age was 73.5 ± 9.3 years, 52% of the patients were women, 50% of them had retired, 46% were married and 80% lived in the city of Medellin. The mean time of diagnosis was 7.8 ± 1.3 years and 100% of the patients were treated at the internal medicine service. The most common clinical features were: 36% classified as class D for the disease, 34% had a FEV1 <30%, 88% had a history of smoking and 52% had oxygen therapy at home.

Conclusion: It was found that class D was the most common, and the majority of the patients had a history of smoking, indicating the need to strengthen promotion and prevention strategies in this regard.

Biography

Camilo Ruiz Mejia has completed his high school studies at from Colegio Calasanz de Medellin and is currently a third year Medical student at Universidad Pontificia Bolivariana. He is an active Member of the Systems Biology Research Group at Universidad Pontificia Bolivariana, Colombia.

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Design, synthesis and anti-tubercular potential of some new substituted 1,2,4-triazoles derived from isonicotinic acid hydrazides

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Objective of the study was to design and synthesize some new substitutes of 1,2,4-triazoles derived from isonicotinic acid hydrazides and screen for anti-tubercular activity. A series of new substituted 1,2,4-triazoles; isonicotinic acid hydrazide derivative (1–28) were synthesized. Potassium dithiocarbazinate (1) was obtained from the reaction of isonicotinic acid hydrazide with carbon disulfide in basic medium (KOH) and converted into 4-amino-5-(pyridin-4-yl)-4H-1,2,4-triazole-3-thiol (2) by the treatment with hydrazine hydrate. The synthesis of the other compound was performed from the reaction of (2) with seven different benzaldehyde resulted in the formation of 4-[(substituted phenyl)-methylene]-amino-5-(pyridine-4-yl)-4H-1,2,4-triazol-3-thiol (3). The final compound synthesized from the reaction of 3 with four different acetanilide resulted in the formation of 4-[(substituted phenyl)-methylene]-amino-3-(N-substitutedcarboxamidomethylthio)-5-(pyridine-4-yl)-4H-1,2,4-triazoles (4). The structures of the synthesized compounds (1-28) were characterized by IR, ¹H NMR, ¹³C NMR, mass spectroscopy and elemental method of analysis. IR data, ¹H NMR spectra, ¹³C NMR spectra, mass spectra and elemental analysis indicates that 28 compounds were synthesized as proposed. In conclusion, their biological activities and study for toxicity are required.

Biography

Varsha Kashaw has completed her PhD in 2007 from Dr Harisingh Gour University, (A Central University; 'A' Grade by UGC-NAAC), India. Currently, she is working at the Department of Pharmaceutical Sciences, SVN University, India as an Associate Professor. To her credit, she is handling two research projects which are sponsored by State and Indian Government. She has published many research papers in the journals of great repute. At present she is pursuing her MBA from Global University.

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The dangers of judicious amiodarone use: An unusual case of amiodarone toxicity

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Amiodarone is highly efficacious as a medical therapy for cardiac arrhythmias. Amiodarone pulmonary toxicity, which can be presented as eosinophilic pneumonia, organizing pneumonia, acute respiratory distress syndrome (ARDS), diffuse alveolar hemorrhage, or pulmonary nodules and masses, is one of many severe potential side effects of this medication. The mechanisms involved in amiodarone-induced lung injury remain unclear, but may include direct toxic effect or an indirect immunologic reaction. This case involves a patient who developed amiodarone toxicity requiring intubation secondary to ARDS after a short course on a low dose of the medication. In this study a 79-year-old female who was presented to the emergency department with a two-day history of productive cough, pleurisy, worsening fatigue, and shortness of breath was considered. She had been on amiodarone for the previous six weeks for treatment of atrial flutter/fibrillation. Chest computed tomography showed diffused patchy foci of ground glass opacification in both lungs, likely secondary to a drug reaction from amiodarone toxicity. Patient had increased oxygen requirements throughout her hospitalization despite treatment with high dose steroids, diuresis and empiric antibiotic coverage. She required non-invasive ventilation with increasing frequency, later requiring intubation, and eventual withdrawal from life-sustaining measures. Amiodarone toxicity is a diagnosis of exclusion and remains perplexing from both a management and prognostic perspective. There are documented effects on the thyroid, heart, liver, skin, bone marrow, eyes, and lungs. While toxicity is rare, the potential complications can be lethal. Therefore, this medication should be used with caution due to its potential unpredictable side effect profile.

Biography

Kathryn Tapper has completed her Medical degree from the George Washington University School of Medicine and Health Sciences in Washington. She is currently pursuing her final year of Residency in Family Medicine at the Mayo Clinic in Jacksonville, Florida. She is currently serving as one of the Chief Residents of the Family Medicine Residency Program at Mayo Clinic.

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Development of in-silico QSAR models of 1,2,4 oxadiazole derivatives as potential apoptosis inducer and anticancer agents

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The quest for the novel structural scaffolds to treat cancer is always at the heart of pharmaceutical industry. Novel caspase-3 activator 1,2,4-oxadiazole derivatives have for a long time enthused the curiosity of research workers. In order to explore the potential caspase-3-activators class of compounds for anti-cancer activity, we have carried out computational studies on cell-lines DLD1 and T47. The studies involved 2D, 3D and group QSAR analysis which have been carried out to establish the relationship between physicochemical descriptors and the biological activity. In addition, group QSAR also helped to investigate structure activity relationships based on molecular fragments of set of molecules. The regression analysis was done by partial least square analysis (PLS) and kNN (k-nearest neighbor) method. The descriptors which were found to influence the activity involve T_C_C_5, T_S_Cl_3, T_C_S_3 and Sdss count on cell line DLD1 and descriptors such as T_N_N_6, T_N_Cl_4, T_C_S_3 and T_N_Br_7 influenced the activity on cell line T47. The studies were further extended to the pharmacophore analysis which involves the identification of the basic pharmacophore and the key features essential for the activity. Based on the survival scores, the best four featured pharmacophore hypothesis AAHR.9 was generated by PLS method which showed that the presence of two acceptor group, one hydrophobic group and one aromatic ring is essential for anticancer activity. The information provided by the present studies may be used to design novel potential compounds against cancer.

Biography

Sushil K Kashaw has completed his PhD in 2009 from Dr. Harisingh Gour University, (A Central University; 'A' Grade by UGC-NAAC), India. Currently, he has joined the Department of Pharmaceutical Sciences, Wayne State University, Detroit under the mentorship of Dr. Arun K Iyer as Post-doctoral Fellow under the visitor exchange program. To his credit, he has completed three research projects and two research projects are ongoing which are sponsored by State and Indian Government. Currently, he is guiding four PhD scholars and 34 MPharm students. He has published 58 research papers in the journals of great repute along with one book entitled "Text book of organic name reactions".

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Depression and its frequency in patients with chronic obstructive pulmonary disease (COPD)

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Introduction: COPD is one of the most prevailing chronic respiratory illnesses which are progressive and irreversible. Many people die prematurely from its complications. Depression is a common co-morbidity in patients with COPD who are facing embarrassing symptoms like dyspnea and productive cough. Early diagnosis and treatment of depression in COPD patients is now taken to be an important aspect for COPD management. Depression has a significant impact on COPD patients and their families. Prolonged illness may cause hopelessness and depressive symptoms like self-neglect, low energy and sleep disturbance. No such data exist for patients in our population.

Objective: To find out the frequency of depression in patients with chronic obstructive pulmonary disease.

Materials & Methods: 100 consecutive patients with diagnosed COPD (on history, physical examination, chest X-ray and spirometry), with FEV1/FVC<70% and <12% reversibility after inhaled bronchodilator and fulfilling the inclusion and exclusion criteria were included in the study.

Results: N=100 patients with COPD, 85% males and 15% females. Mean age was 54.79+10.55 years. Mean duration of disease was 5.35+3.24. Mean for duration of treatment was 5.34+3.24 years. Mean number of smoking pack years was 23.24+8.9. Overall 47 patients (47%) were found to have depression. There were only 15 (31.9%) patients with mild to moderate depression, 14 (29.7%) with moderate to severe depression and 18 (38.2%) with severe depression. Depression was seen in 45.7% patients with age >50 years and in 48.7% patients with age <50 years. Those with smoking <20 pack years, 41.3% were having depression whereas those with smoking >20 pack years 51.8% were found to have depression. Depression was seen in 6.67% patient with mild COPD, 44.6% patients with moderate COPD, 58.6% with severe COPD and 80% patients with very severe COPD.

Conclusion: There was a high frequency of depression in patients with COPD. Depression was found to be associated with longer duration of disease, higher number of smoking pack years and with increasing severity of COPD. Keeping in view this higher percentage of depression in COPD patients in our population, it's necessary to focus on this important co-morbidity in order to improve the quality of life and to reduce the health care burden.

Biography

Gillani Seemab is a clinical psychologist His international experience includes various programs, contributions and participation in different countries for diverse fields of study. His research interests reflect in his wide range of publications in various national and international journals.

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Hemoptysis and a purpuric rash: A rare presentation of amyloidosis

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A middle aged man was admitted with a 2-3 year history of recurrent hemoptysis on exertion, culminating in a requirement for home oxygen therapy. On examination, he had a diffuse purpuric rash, subconjunctival hemorrhages, oral ulcers, macroglossia and dystrophic nails. He was initially investigated for connective tissue disease (CTD) as a cause of HRCT-demonstrated lung fibrosis. However, further investigations found a lambda light-chain band on electrophoresis and a plasma cell dyscrasia on flow cytometry. Serum amyloid protein (SAP) scan, dermatological biopsy and bone marrow biopsy confirmed primary systemic amyloidosis secondary to multiple myeloma. It is believed that the cause of his hemoptysis is amyloid deposition in the lungs, though the SAP scan and CT report did not confirm this. His cause of hemoptysis remained controversial, though the clinical picture was one of amyloidosis. He underwent chemotherapy and clinically improved with no further reports of hemoptysis, resolution of his dermatological features and now he no longer requires home oxygen. Our aim is to promote the consideration of other potential causes of hemoptysis when in conjunction with other systemic features of disease. We also aim to elaborate on our case's recovery of his respiratory symptoms when the hematological diagnosis had been targeted with relevant chemotherapy.

Biography

Anne-marie Ionescu has done BSc and MBBS from the University College London (UCL) Medical School in the year 2015.

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A rare case of pleural empyema caused by *Clostridium baratii*

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Introduction: *Clostridium baratii* is an anaerobic, motile, Gram-positive bacterium. It is a rare cause of infant botulinum. We present a rare case of pleural empyema caused by *C. baratii*.

Case Presentation: A 74-year-old female presented to ER with chief complaint of right-sided chest pain and shortness of breath. She was discharged from the hospital 10 days ago due to small bowel obstruction caused by internal hernia resulting in laparotomy. On examination, she was afebrile and hypoxic with O₂ saturation of 89%. She had diminished breath sounds in the right lung field. CT chest showed moderate right pleural effusion with compressive atelectasis and right lower lobe infiltrate. She was given vancomycin, levofloxacin and cefepime for possible healthcare associated pneumonia. Ultrasound guided right sided thoracentesis revealed exudative effusion. A 14F pigtail catheter was placed under CT guidance and tissue plasminogen activator (tPA) was infused via catheter to help drain the fluid. Total of 3.5L pleural fluid was drained over 5 days with the tPA infusion. Repeat cultures of pleural fluid came back positive for *Clostridium baratii* which was sensitive to Penicillin. The catheter was removed and she received a PICC line. She was discharged home with home healthcare on Ampicillin-Sulbactam to complete total of 3 weeks' treatment. During the course of treatment her symptoms resolved.

Discussion: Clostridial pleuropulmonary infections are rare; most of these infections are attributed to *Clostridium perfringens*. *Clostridium baratii*, usually associated with infant botulisms has not been reported to cause pulmonary infections. Trauma, chest surgery or other invasive procedures and underlying lung disease are often found to precede clostridial empyema. In our patient, spread of *C. baratii* most likely occurred after a recent abdominal surgery which may have resulted from transdiaphragmatic lymphatic translocation. Intra-pleural infusion of tPA is a controversial treatment for empyema. If combined with DNase may result in better drainage. This treatment was effective in our patient and resulted in resolution of the empyema.

Conclusions: Although mostly associated with infant botulisms, *Clostridium baratii* may be associated with other infections in immunocompetent patients particularly pulmonary infections. Infusion of tPA via catheter is an effective option before considering surgery in cases with pleural empyema.

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Curcumin has a dual effect on targeting the lung cancer cell lines

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Exposure to arsenic is one of the major causes of lung cancer due to production of Reactive Oxygen Species (ROS). Herbal medicine is a new approach used for prevention or treatment of cancers. Among various herbal compounds, a lot of attention has been paid to curcumin, as antioxidant, anti-proliferative, anti-carcinogenic and anti-tumour and pro-apoptotic properties of curcumin have been well studied. In the present study, we investigated the effects of curcumin on lung cancer cell lines and arsenic-treated lung cancer cell lines, originated from different stages of lung cancer development. Here, we measured ROS generation and caspase 3/7 activity for both curcumin-treated cell lines and those co-treated with arsenic and curcumin. Then, we studied lipid peroxidation, intracellular ATP content, and cytochrome c release to further investigate how ROS generation and curcumin exert synergistic effects and direct cells toward apoptosis. According to our data, curcumin has a dual effect on ROS generation which is dependent on specific concentration as a threshold and seems to induce apoptosis by two different mechanisms. Moreover, for the first time we report that curcumin delays the drop in ATP levels in these cell lines and hence provides required energy for apoptosis process. Furthermore, western blot analysis reveals that release of cytochrome c is highest when ATP begins to drop in the presence of curcumin. To sum it up, it seems that curcumin is strong candidate for prevention or treatment of lung cancer, especially at stage 2.

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Diagnosing techniques in lung disease

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Background: Fiberoptic bronchoscopy is the most commonly used method for diagnosing lung cancer. Several techniques such as biopsy, bronchial brushing and bronchial washing are traditionally used together because of their combined high diagnostic value.

Objective: To evaluate the efficacy of bronchial brush (BB) cytology in comparison to bronchial wash cytology (BW) in the diagnosis of bronchopulmonary lesions.

Methods: Totally 1691 patients (77% males and 23% females) were investigated for suspected lung cancer between January 2000 and December 2010 in Rizgary Teaching Hospital in Erbil, Kurdistan. The age of patients varied between 11 to 100 years. Flexible bronchoscopic samples of bronchoalveolar lavage (wash) and bronchial brush cytology were taken and processed as per standard procedures of cytology.

Results: Mean age was 62.2 ± 0.35 for the male patients and 57.5 ± 0.77 for female patients. We found that 92.5% of the male patients and 54.1% of the female patients were smokers. Clinical findings and bronchoscopy examination showed that 693 patients had lung cancer, 83.7% of them were males and only 16.3% were female patients, with male to female ratio approximately 5:1. Pulmonary cytology from BB and BW is valuable tool in the diagnosis of lung malignancies and has been used in the present study. Complete cytological results were available from 1074 patients. Cytology revealed 19% cases of malignancy and 10% were diagnosed as atypical/suspicious. Benign and inadequate (hypocellular specimens) were 74% and 7.2%, respectively. Interestingly, it has been found that 57% of the malignant samples were from BB cytology compared to 43% from BW cytology. Further, it was found that atypical/suspicious and hypocellular samples from BB cytology were 20% and 9%, respectively, compared to 80% and 91% respectively, from BW cytology ($p < 0.001$). BB cytology showed 65% sensitivity, 90% specificity and 71% accuracy, while BW cytology showed 48.5% sensitivity, 81% specificity and 68% accuracy. Positive predictive value and negative predictive value from BB cytology were 95% and 44.3% respectively, while the values for BW cytology were 62% and 71%, respectively. The most common type of tumors found in this study was squamous cell carcinoma.

Conclusion: Bronchial brush cytology was superior to bronchial wash cytology in the diagnosis and morphological typing of lung cancers.

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Pulmonary functions test in pre and post-menopausal women

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Abstract: Pulmonary function test is one of the most important parametric tests for diagnosing obstructive and restrictive pulmonary disease; these tests in physiology are also considered as an effective test in organizing research in different physiological status, one of this in pre and post-menopausal status of women. Therefore, a study was carried out to find any difference in this parametric test between pre and post-menopausal women, and the rationale behind the difference. The result showed the significant difference in some of the effective parameter of the pulmonary function test.

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Active case findings (ACF) at Tengecha Boys High School, Bureti sub-county, Kericho County

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Background: TB still remains a major cause of morbidity and mortality in Kenya. Early and routine screening plus lab work is critical to promptly identify and treat TB. Tuberculosis control depends on successful case finding and treatment of individuals infected with *Mycobacterium tuberculosis*. Passive case finding is widely practiced which barely little results.

Aim: The present study aims to ascertain the consensus and possible improvements in active case finding across the country especially boarding schools.

Objective: To evaluate active TB case finding among students and teachers of Tengecha Boys High School in Bureti sub-county.

Methodology: Prospective study was conducted in Tengecha Boy's High School for active case finding by the hospital team. This was triggered by smear positive students screened and treated for TB in the hospital. The study was conducted in the school from July, 2014 to November 2014. Screening was conducted for all students and teachers, those found with signs and symptoms; sputum smears was done. Those found to be smear positive were initiated on anti-TB drugs and were followed up in the hospital. Health education was conducted weekly by the hospital staff in the school during the study period.

Summary: From the findings, 920 student were screened and 80 teachers, for students 10.8% (n=100) had signs and symptoms, 22% (n=22) were smear positive. For teachers 6.25% (n=5) had signs and symptoms and 20% (n=1) was smear positive. All smear positive were initiated anti-TB medication.

Conclusion: Active contact tracing of SS+ve index cases have high yields in reduction in TB transmission. The intervention has resulted in improved compliance and reduction in complication this has significantly reduced previously high mortality rates. There are still missed opportunities which need to be addressed by ensuring all boarding schools children need to be routinely screened for TB and Health education need to be scheduled in all boarding schools.

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The *Mycobacterium tuberculosis* tm-RNA *ssr* is required for intracellular survival and resistance to nitric oxide

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A genome of almost 4,200 predicted genes encoding an abundance of readily recognized transcriptional regulatory factors functions to allow the tubercle bacillus to survive in different environments during infection and survive aerosol transmission to new host. Screening for bacterial RNAs produced in response to host interaction produced candidate lists where we noted *ssr*, annotated as small stable RNA. *M. tuberculosis ssr* encodes small stable tmRNA with both transfer and messenger function that is highly important to keep bacterial cell in fully operational state. We investigated the contribution of *ssr* to *M. tuberculosis* pathogenesis. Genetic DNA manipulations revealed that *ssr-Rv3099c-smpB* genes are indeed not essential for growth. An H37Rv *ssr-Rv3099c-smpB* mutant was greatly impaired intracellular survival and growth relative to H37Rv and Rvs2O strains. In addition, mutant strain was more sensitive to various in vitro stress conditions including heat, SDS treatment, sub-lethal concentration of translation specific antibiotic, and more interestingly to nitric oxide, which is along with reactive nitrogen intermediates represent an important mean through which macrophages partially control *M. tuberculosis* infection. Our findings indicate an important role of *ssr-Rv3099c-smpB* genes in *M. tuberculosis* pathogenesis and tolerance to various stress conditions.

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Advanced non small cell lung cancer at the National Cancer Institute in Egypt: A descriptive analysis

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Background: Worldwide, lung cancer is the most commonly diagnosed cancer and causes more deaths than any other cancer. In Egypt, it accounts for 7% of male cancer and 3% in females. It is considered to be 3rd most common cancer in Egyptian males and 6th most common of both sexes.

Materials & Methods: A total of 99 advanced non-small cell lung cancer patients who underwent first line platinum containing chemotherapy in our institute were included in this study. All clinical and pathological data were collected from patient's files retrospectively between 2012-2014.

Results: All 99 cases were diagnosed at late stage IIIB-IV (59 cases were IIIB). The median age was 54 years (range; 30-70) with 53% of cases are ≥ 54 years. 71% were males with male: female ratio of 2.4:1. All male patients were chronic smokers. The most frequent symptom was coughing (68%). Most of the patients had primary lung cancer in the right lung (77%). The most common histological subtype was squamous cell carcinoma (35.4%) with 54 cases present with PS-I, the remain was PS-II. All cases received platinum containing chemotherapy. The majority of cases experienced a progressive disease 60.6%. The median progression free survival (PFS) was 6 months and median overall survival (OS) was 18 months. We found that PS, disease stage, pathological subtypes and response to treatment statistically affects both median OS and PFS. Age affects only OS.

Conclusions: Our analysis suggests that some of the clinico-pathological factors and response to first line platinum containing regimens affect both OS and PFS of advanced NSCLC. This may be beneficial as prognostic markers and further studies were needed to aid in identification and treatment of these patients.

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Oral tuberculosis: The often forgotten entity

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Tuberculosis (TB) is a major global health problem. According to latest WHO Global Health Tuberculosis Report 2015, TB causes ill health among millions of people each year and ranks alongside HIV as a leading cause of death worldwide. In 2014, there were an estimated 9.6 million new TB cases: 5.4 million among men, 3.2 million among women and 1.0 million among children. Of the 9.6 million new TB cases in 2014, 58% were in the South-East Asia and Western Pacific regions. The African Region had 28% of the world's cases in 2014, India, Indonesia and China had the largest number of cases: 23%, 10% and 10% of the global total, respectively. Oral tuberculosis (Oral TB) has been considered to account for 0.1-5% of all TB infections. Primary tuberculosis is extremely rare, secondary tuberculosis is more frequent and often involves the tongue, followed by palate, lips, buccal mucosa, gingiva and frenum. The lesion usually appears in form of ulcers, patches, indurated soft tissue or occasionally within jaw as tuberculosis osteomyelitis. Oral TB can be a diagnostic challenge to the clinician, because of its varied clinical presentation. Hence, a complete physical, radiographic and sputum examination along with anti-tuberculin tests should be done. Biopsy and molecular techniques can also play a crucial role in successful diagnosis of oral TB. This paper highlights few case presentations discussing clinical features, diagnosis, differential diagnosis and treatment modalities for the often forgotten and rare entity the oral TB.

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Consequence of obstructive sleep apnea on functioning of nervous system

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Obstructive sleep apnea (OSA) is highly prevalent within the primary care community and yet it is frequently undiagnosed. OSA per se is not looked as disease by the masses and is thought as deviations from the usual sleep pattern. In fact, OSA is a major risk factor for cardiopulmonary insufficiency and other complications if not intervened appropriately. Until now no study has characterized the severity of OSA and its impact on functioning of nervous system in Indian subjects. The objective of this study was to evaluate the prevalence of OSA in a South Indian population, to assess the neurocognitive functioning in patients and also to correlate the changes in higher mental functions, nerve conduction velocities and brain natriuretic peptide (BNP) with the duration and severity of OSA. A retrospective analysis of data accrued in patients undergoing polysomnography (PSG) was undertaken. Cognitive functioning was assessed by mini-mental state examination (MMSE) and depression was evaluated using Zung self-report depression scale. Two hundred fifty-four patients of either sex in the age of 54±11 years who tested positive for OSA were compared with control group. An apnea hypopnea index (AHI) of >5 in the presence of snoring and daytime somnolence was taken to define sleep apnea. The OSA patients were divided into three subgroups: mild, moderate and severe depending upon AHI. The mean AHI among the study group with OSA was 31.3±18.6 as compared with 1.2±0.5 in the control group. Among OSA patients (31%) were having mild OSA, moderate (33%) and severe (59%), respectively. The BMI among patients with OSA was 32±6 as compared with 24±4 in comparison group (p<0.001). A significant decrease in cognitive impairment (by MMSE score) in OSA patients was observed when compared to control. Orientation, memory, registration, attention, calculation skills, language and constructive praxis were significantly low in OSA patients in contrast with controls. A higher decline in depression score was observed in severe OSA patients when compared to patients having moderate OSA. Autonomic dysfunctioning was observed with severe OSA, which may play a key factor in the causal link between OSA and cardiovascular disease. The risk of metabolic syndrome in OSA syndrome patients was almost three times more than that of the comparing group. Our study found a noticeable relation between the severity of the Mallampati score and a restrictive type of defect on spirometry in OSA patients. Our data also provided compelling evidence that OSA is associated with cognitive decline and depression. Although hypoxemic stress and sleep disruption are likely the key players in the pathogenetic mechanisms behind such derangements, the role of an underlying common denominator needs to be scrutinized. We are doing further studies to define the driving mechanisms through which sleep-disordered breathing promotes many of these consequences. Nevertheless, the present study was a novel approach to nervous system effects of OSA, which may help the clinicians to diagnosis and prognosis and the researchers to look into new era in OSA research.

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Treatment of community acquired pneumonia: Assessment of antibiotic prescription

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Background: Community acquired pneumonia (CAP) affects 0.5-1% of UK adults annually, more than half of them are aged over 84. Hospitalized patients have 5-14% mortality, with annual costs exceeding £400 million. The British Thoracic Society (BTS) have devised guidelines for CAP management. This involves documentation of severity using CURB65 score, and antibiotic prescription according to this score.

Aim: To assess compliance with BTS guidelines (2009) in the Elderly Care ward of the Queen Elizabeth Hospital.

Methods: Notes of geriatric patients treated for CAP during July, August and September were retrospectively studied for CURB65 score, antibiotic treatment, treatment duration and time before IV medication changed to oral (if applicable). The PICS online system was used as confirmation, and to identify if a prescribing note (for indication) had been issued. Data was analyzed on Microsoft Excel.

Results: CURB65 recorded in 50% (24/48). Treatment was appropriate to the score in 54% of cases (no significant differences between scores, $p=0.2393$). Prescription note compliance was 69% and the average treatment duration was 6.21 (± 0.86) days.

Conclusions: CURB65 was poorly documented in CAP. When documented, compliance with guidelines was poor. Prescriptions notes were absent in medical notes, and require improvement on PICS. Increased staff training for prescription notes and audit has been planned.

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Characterization of mutations causing rifampicin and isoniazid resistance of *Mycobacterium tuberculosis*

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Objective: To characterize mutations causing rifampicin and isoniazid resistance of *M. tuberculosis* in Syria.

Methods: 69 rifampicin resistant (RIFr) and 72 isoniazid resistant (INHr) isolates were screened for point mutations in hot spots of the *rpoB*, *katG* and *inhA* genes by DNA sequencing and real time PCR.

Results: Of the 69 RIFr isolates, 62 (90%) had mutations in the rifampin resistance determining region (RRDR) of the *rpoB* gene, with codons 531 (61%), 526 (13%) and 516 (8.7%) being the most commonly mutated. We found two new mutations (Asp516Thr and Ser531Gly) described for the first time in the *rpoB*-RRDR in association with rifampicin resistance. Only one mutation (Ile572Phe) was found outside the *rpoB*-RRDR. Of 72 INHr strains, 30 (41.6%) had a mutation in *katG* codon 315 (with Ser315Thr being the predominant alteration), and 23 (32%) harbored the *inhA*-15C<T mutation. While the general pattern of *rpoB*-RRDR and *katG* mutations reflected those found worldwide, the prevalence of the *inhA*-15C<T mutation was above the value found in most other countries.

Conclusion: Emphasizing the great importance of testing the *inhA*-15C<T mutation for prediction of isoniazid resistance in Syria. Sensitivity of a rapid test using real time PCR and 3'-minor groove binder (MGB) probes in detecting RIFr and INHr isolates was 90% and 69.4%, respectively. This demonstrates that a small set of MGB-probes can be used in real time PCR in order to detect most mutations causing resistance to Rifampicin and Isoniazid.

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