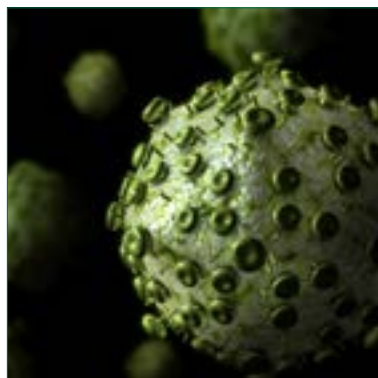

Accepted Abstracts

Emerging Diseases and Case Studies & Influenza 2018



International Conference on

Emerging Diseases, Outbreaks & Case Studies &

16th Annual Meeting on **Influenza** March 28-29, 2018 | Orlando, USA

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Emergence of Zika virus and global implications

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After initial isolation from macaque monkeys living in the Zika forest of Uganda in 1947, Zika virus remained dormant for years, aside from sporadic outbreaks in Asia, tropical Africa and the South Pacific. In 2015, the virus made international headlines after the World Cup in Brazil, when numerous cases of birth defects including microcephaly were linked to the virus. By December 2015, over 1.3 million Zika cases were reported in Brazil. Shortly after Puerto Rico fell victim to Zika, with over 36,000 cases in 2016, and continued spread due to vulnerability from recent hurricanes. Zika virus, a member of the family *Flaviviridae*, spreads rapidly via its primary vector, the daytime-active *Aedes aegypti* mosquito. Additional modes of transmission include sexual, blood-borne and maternal-fetal transmission. Areas with active Zika outbreaks include warm/temperate regions in Mexico, Central and South America, the Caribbean, mid-Africa, and southern Asia. Viral incubation averages 7-10 days. Symptoms of active infection are similar to those of dengue or chikungunya, and include headache, fever, rash, conjunctivitis, arthralgias, and gastrointestinal symptoms, although many may be asymptomatic. Illness is generally

mild, although neurologic complications such as Guillain Barré may occur. Maternal-fetal transmission with resultant microcephaly is well documented, and pregnant women are at greatest risk during the first trimester. Pregnant women presenting with symptoms should be referred for testing. As treatment remains supportive, measures to prevent disease are paramount. Healthcare providers must play a strong role in the education of individuals planning travel to endemic areas, including protective measures such as mosquito repellent and window screens. Routine mosquito spraying of susceptible areas is particularly important, and has been effective in preventing Zika infection in San Pedro and the Cayman islands. Prenatal counseling plays a vital role, as viral RNA can remain in semen for up to three months post infection. Although there are no effective vaccines to prevent infection, a great deal of research is underway. Zika has become a significant global public health issue, raising concerns regarding international travel, sexual transmission, and blood product safety. Only through global partnerships can we hope to halt the spread of the virus.

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Apparent poor prognosis for patients infected with MERS-CoV through human-human mode than animal-human

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Background: Many cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) have been identified in the Kingdom of Saudi Arabia (KSA) since 2012. As of early December 2015, 549 of 1,277 patients (43%) with laboratory-confirmed MERS-CoV whom treated in Ministry of Health hospitals in KSA, confirmed to have died. Two main pathways by which MERS-CoV were reported to be transmitted: animal-to-human (AH) (primary infection); and human-to-human (HH) (secondary infection), most human cases reported to date have resulted from human-to-human transmission in health care settings. Although our knowledge of the clinical features of MERS-CoV infection has grown over the past three years, however, the pathogenesis of disease and treatment outcomes are still not well known. We aim in this study to investigate the differences between MERS-CoV animal-to-human and human-to-human transmitted cases, in relation to virulence and response to treatment.

Methods: All cases of laboratory-confirmed MERS-CoV occurring at King Fahad Hofuf Hospital in Al-Ahsa, Saudi Arabia, from April 1, 2012 to November 30, 2016 were reviewed retrospectively. Virulence (symptoms/severity of disease) was identified by using Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scoring systems, mode of MERS-CoV transmission, patients' demography, baseline characteristics, X-ray and laboratory findings, co-morbidities, prognosis and treatments' outcomes were identified.

Results: From April 1, 2012 to November 30, 2016, there were 107 laboratory-confirmed MERS-CoV cases, of which 23 (21.4%) cases were transmitted from AH and 84 (78.6%) were

transmitted from HH mode. Ten (43%) AH and 43 HH MERS-CoV Patients' groups were admitted to ICU, time from onset of symptoms to ICU admission was (8 days (3-14) median AH group and 4 days (3-11) median for HH group. APACHE II score was higher in (AH, 11.2) group than (HH, 23) group P value 0.043. In AH group, n=2 patients were recovered, (n=2 transferred) to another care center, (n=9 died) and (n=4 discharged), whereas in HH group (n=5 recovered), (n=22 transferred), (n=45 died) and (n=12 discharged). Time from onset of MERS-CoV symptoms to death was (11 days, (8-17) median) for AH group and (5 days (6-9) median) HH group, P value 0.043. Piperacillin, tazobactam and levofloxacin was the most common combination prescribed to treat pneumonia in AH MERS CoV group (n=9, 39%), and (n=15, 18%) for HH group, whereas ribavirin was the most common used antiviral drug in AH (n=8m 35% for 11 days) and HH (n=53, 63% for 18 days) MERS-CoV groups.

Conclusion: Despite the small sample size of our study, higher APACHE II score was observed in human-human MERS CoV transmitted group in compare to animal to human group, accompanied with poor prognosis witnessed by short time from appearance of symptoms and transferring to ICU and death.

Speaker Biography

Mansour Tobaigy is an Assistant Professor of Clinical Pharmacology in the Faculty of Medicine, University of Jeddah, KSA. He is also the General Supervisor of the Human Resources Development Centre in the same university and he has completed his PhD in Medicine and Therapeutics from the School of Medicine, University of Aberdeen, UK. He is also a Visiting Professor at RGU, UK. He has done several researches on the safety medicines in children and pharmacovigilance in general

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 Notes:

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Blocking the transmission of vector borne diseases with fungal metabolites

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Mosquitoes transmitted many diseases including Zika and Malaria. Malaria alone is responsible for about two hundred million clinical cases worldwide and kills nearly one million a year. Malaria is caused by *Plasmodium* parasites and transmitted by *Anopheles* mosquitoes. Zika can trigger paralysis and birth defects. Inhibiting pathogen development in mosquitoes will block disease transmission. My research aims to find target genes that are essential for pathogen transmission in mosquitoes, and further to develop drugs targeting these critical genes to stop disease transmission. By genomic approaches, several critical genes have been discovered for *Plasmodium* parasite transmission to *Anopheles* mosquitoes. Furthermore, we tested the hypothesis that small molecule compounds disrupting

the interaction would prevent parasites from infecting mosquitoes. We screened a large fungal extract library from more than 12,000 different fungal species, and found several bioactive compounds including *P*-orlandin that specifically inhibits the interaction between FREP1 and *P. falciparum*. Notably, feeding mosquitoes with candidate fungal metabolites significantly inhibited *P. falciparum* transmission to mosquitoes. Surprisingly, spraying one non-toxic candidate compound could prevent mosquitoes from transmitting malaria. Therefore, targeting molecules that are responsible for pathogen invasion with bioactive compounds is an effective novel approach to block the spread of vector-borne diseases.

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16th Annual Meeting on **Influenza** March 28-29, 2018 | Orlando, USA

Automated chest X-ray screening: Can lung region symmetry help detect pulmonary abnormalities?

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Our primary motivator is the need for screening HIV+ populations in resource-constrained regions for exposure to Tuberculosis (TB), using poster anterior chest radiographs (CXRs). The proposed method is motivated by the observation that radiological examinations routinely conduct bilateral comparisons of the lung field. Also, abnormal CXRs tend to exhibit changes in the lung shape, size and content (textures), and in overall, reflection symmetry between them. We analyze lung region symmetry using multi-scale shape features, and edge plus texture features. Shape features exploit local and global representation of the lung regions, while edge and texture features take internal content, including spatial arrangements of the structures. For classification, we have performed voting-based combination

of three different classifiers: Bayesian network (BN), multilayer perception (MLP) neural networks and random forest (RF). We have used three CXR benchmark collections made available by the US National Library of Medicine, and National Institute of Tuberculosis and Respiratory Diseases, India, and have achieved maximum abnormality detection accuracy (ACC) of 91.00% and area under the ROC curve (AUC) of 0.96. The proposed method outperforms the previously reported methods by more than 5% in ACC and 3% in AUC.

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Foreign circular element detection in chest X-rays for effective automated pulmonary abnormality screening

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In automated chest X-ray screening (to detect pulmonary abnormality: Tuberculosis (TB), for instance), the presence of foreign element such as buttons and medical devices hinders its performance. In this paper, using digital chest radiographs, the authors present a new technique to detect circular foreign element, within the lung regions. They first compute edge map by using several different edge detection algorithms, which is followed by morphological operations

for potential candidate selection. These candidates are then confirmed by using circular Hough transform (CHT). In their test, the authors have achieved precision, recall, and F1 score of 96%, 90%, and 92%, respectively with lung segmentation. Compared to state-of-the-art work, their technique excels performance in terms of both detection accuracy and computational time.

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Combination of texture and shape features to detect pulmonary abnormalities in digital chest X-rays

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The objective of the study is to improve detection of pulmonary and pleural abnormalities caused by pneumonia or tuberculosis (TB) in digital chest X-rays (CXRs). A method was developed and tested by combining shape and texture features based on which CXRs are classified into two categories: TB and non-TB cases. Based on observation, we found that radiologist interpretation is typically comparative between left and right lung fields, the algorithm uses shape

features to describe the overall geometrical characteristics of the lung fields and texture features to represent image characteristics inside them. Our algorithm was evaluated on two different datasets containing tuberculosis and pneumonia cases. Using our proposed algorithm, we were able to increase the overall performance, measured as area under the (ROC) curve (AUC) by 2.4% over our previous work.

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Human diseases related with leucine rich repeats

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Leucine rich repeats (LRRs) are unusually rich in the hydrophobic, amino acid leucine. LRRs have been reported in over 100,000 proteins from viruses to eukaryotes. The LRRs are composed of 20-30 residues stretches and repeat in tandem. The repeat numbers range from two to ninety-seven. LRR units are divided into a highly conserved segment (HCS) and a variable segment (VS). Twenty-three types of LRRs including eight classes well recognized have been proposed. The HCS part consists of an eleven or twelve residue stretch, LxxLxLxx(N/C)(x/-)L, in which "L" is Leu, Ile, Val, or Phe, "N" is Asn, Thr, Ser, or Cys, "C" is Cys, Ser or Asn, "x" is any amino acid, and "-" is a deletion. Three residues at positions 3 to 5 in the HCS part form a short β -strand. These β -strands stack parallel; they have the pattern of H-bonding (N-H \rightarrow O=C), and then tandem repeats of LRRs assume their super helical arrangements called a solenoid structure. Structural data of LRR proteins have increased. Meanwhile, a number of human diseases have been shown

to be associated with mutation in the genes encoding LRR proteins which count over forty. The LRR proteins include opticon, lumican, fibromodulin, FLRT3, F-box/LRR-repeat protein 4, LGI1, Trk-A, nyctalopin, FSHR, LH/CGR, TSHR, keratocan, GPIIb/IIIa, GPIIb/IIIa, GPIX, LRRK2, CIAS1, CIITA, and Nod2. The mutations of these proteins are associated with high myopia, congenital hypogonadotropic hypogonadism, mitochondrial encephalomyopathy, ADLTE/ADPEAF, CIPA, CSNB1/XLCSNB, ODG1, LCH, Graves disease, thyrotropin resistance, FGH, papillary cancer, hyperthyroidism, CNA2, BSS, PT-vWD, Parkinson's disease, CINCA/NOMID, BLS II, and Crohn's disease. The mutations occur frequently within the LRR domains as well as in their neighboring domains at the N- and C-termini. Here, we review the adverse effects of different sequence variants based on the sequence analysis of the LRR domains and the known structures of LRR proteins.

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Application of endometrial stem cells for Parkinson's treatment

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Stem cell therapy has been suggested as a novel treatment for the management of Parkinson's diseases. The previous studies demonstrated that the pluripotent embryonic stem cells and adult stem cells are capable of differentiating into dopaminergic neurons types'. Recently, stem cells were isolated from human endometrium, using dopaminergic neurons differentiation medium. Herein, we postulate that because of the outcome and complication of the other sources of stem cells, stem cell therapy through application of endometrial stem cells can open a new horizon for the treatment of neurodegenerative disorders such as Parkinson with lesser degree of complications and better efficacy and outcome. Endometrial stem cells evaluated by using flow-cytometry for detection of stem cell markers such as CD146, CD90 in the isolated endometrial stem cells. Also, isolated stromal cells will be examined to be free from hematopoietic cells using CD34 staining. The next step was to investigate the ability of human endometrial adult stem cells to differentiate into the dopaminergic neurons showing characteristics of dopaminergic neurons. For this purpose, the endometrial stem cells induced by dopaminergic neurons differentiation

medium. Subsequently, immunocytochemistry used for the confirmation of dopaminergic neurons markers expression such as FOXA2 and GIRK2. Multipotent adult stem/progenitor cells in the endometrium were characterized by a remarkable regenerative capacity of undergoing repetitive cycles of growth and differentiation. Endometrial regenerative cells possess the potential to differentiate into adipocytes, endothelial cells, pancreatic cells and neurons. In the past few years, for neurodegenerative diseases therapy, research has focused on the stem cells therapy. Due to promising results in stem cell therapy, there are different sources of stem cells for transplantation in human. Recently, a highly promising source of accessible, abundant and multipotent adult stem cells is human endometrial stem cells. Consequently, we could that endometrial adult stem cells differentiated into dopaminergic neurons when they are exposed to specific differentiated conditions. The stem cells have potential advantages over other stem cells and are attractive candidate for treatment of Parkinson.

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Mycobacterial lineages causing pulmonary and extra pulmonary tuberculosis, Ethiopia

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Molecular typing of 964 specimens from patients in Ethiopia with lymph node or pulmonary tuberculosis showed a similar distribution of *Mycobacterium tuberculosis* strains between the two disease manifestations and a minimal role for *M. bovis*. We report a novel phylogenetic lineage of *M. tuberculosis* strongly associated with the Horn of Africa. Ethiopia is among the countries with the highest incidence of tuberculosis (TB) and has a yearly incidence of 261 cases/100,000 population. TB lymphadenitis in cervical lymph nodes (TBLN) accounts for ≈33% of all new cases in this country, which is greater than the global average of ≈15%.

Ethiopia has the largest livestock population in Africa (≈51 million cattle), and recent studies have shown that bovine TB is endemic in this country (estimated prevalence 1%–10%). To explore the public health risk for bovine TB in Ethiopia, we have used molecular typing to characterize mycobacterial isolates from persons with TBLN and pulmonary TB who were visiting hospitals throughout the country. Our aim was to define the role of *Mycobacterium bovis* in human TB and to define the overall structure of the *M. tuberculosis* complex in Ethiopia.

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A matched case-control study of risk factors for equine influenza epidemic 2015-2016 in equine in Khyber Pakhtunkhwa, Pakistan

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Equine influenza in non-vaccinated equine population causes disruption and economic losses. To identify the risk factors associated with the equine influenza epidemics in equids in Pakistan, a 1:1 matched case control study was conducted during 2015-2016, including laboratory confirmed 197 positive cases and negative controls, matched on the basis of geography, time of sampling, specie and age. A piloted questionnaire was used to obtain the information about the risk factors associated with the occurrence of equine influenza in face to face interviews. Conditional logistic regression was performed to analyze the data. A total of 16 out of 23 variables were found associated as risk factors on univariate conditional logistic regression. Multivariate conditional logistic-regression model was also performed. The key potential risk factors identified in this model were

local equine density and manure removal frequency. Due to lack of vaccination against equine influenza; the spread of disease is favored by high local equine density. Investigating the index-case it was recorded that infected cases were imported from Afghanistan. Most of these risk factors related to biosecurity and management were due to the low awareness level regarding equine influenza amongst the respondents. These findings are in line with the results of many other studies identifying similar risk factors for equine influenza infection in various countries. Improving protective and controlling the risk factors identified in the present study could reduce the spread and future outbreaks of equine influenza in Pakistan.

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16th Annual Meeting on **Influenza** March 28-29, 2018 | Orlando, USA

The effective role of complementary and alternative medicine in treating diabetes mellitus

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Over the last few decades, the incidence of diabetes mellitus (DM) has increased drastically. This has resulted in the rise of morbidity and mortality. Treatment of complications arising due to DM is a big challenge. In this regard, the role of complementary and alternative medicine is pertinent to mention. This is because of less complication, lesser cost, easy availability and better patient compliance while using these herbal products. Our quest for treating the DM complications with complementary and alternative medicine showed promising results. Over the last decade, we created experimental animal model of DM and treated it with herbal extracts such as *Piper sarmentosum*,

Piper betle and *Momordica charantia*. The oxidative damage to the tissues was seen to be less once the experimental animals were treated with such herbal products. Epithelial wounds even healed faster, and integrity of the epithelium was restored to normal. The biochemical tests such as wound contraction rate and total protein content also proved that these herbal extracts acted as excellent antioxidants. Based on our research findings, it could be concluded that herbal extracts have a greater role to play in the treatment of DM and its complications.

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Invasive origin and parasite subsistence of human cancer

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The ability of human cancer to invade tissues and cells is out of the mainstream of discoveries of cancer pathogenesis and subsistence. Our goal is to present maximally exhaustive epidemiological, clinical, genetic and immunological evidence of invasive origin of cancerous disease. The investigation is grounded on a multidisciplinary integrative reassessment and reinterpretation of relevant cancer data from the viewpoint of recent achievements in epidemiology, immunology, molecular interspecies ecology and the theory of biological evolution. There exist a lot of cancer features that united cancer with undoubtedly invasive parasitic diseases. Main features includes: Interethnic differences in susceptibility to cancer; Individual differences in susceptibility to cancer; Individual differences in intrabody locations of cancer affections; and Individual differences in intraorgan locations of cancer affection the gressivness (gobbleness) the subsistence at the expense of materials, energy and functions of victim. The multiplicity

of functions that belong to human cancer are performed by a causative agent of the disease, unprecedently specialized monocellular biological entity that evolved to invade human body and to subsist in it at the expense of the materials, energy and functions of the invaded organism. The human cancer has been provided in it evolution by a set of genetic adaptations. Cancerous cells are absolutely resistant to defense performed by immune system of invaded organism but ignore physiological regulation of cells dividing and tissues growth. These features are in contradiction to existed paradigm of mutations origin of initial cancer cell and its subsequent dispersion (metastasis) around invaded human body. What is more, in contrast to other micro-parasites population of cancerous cells exists as a present whole entity? Populations of West Africa, Abyssinia and India are most resistant to cancer.

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16th Annual Meeting on **Influenza** March 28-29, 2018 | Orlando, USA

Molecular epidemiology of a novel re-assorted epidemic strain of equine influenza virus in Pakistan in 2015-16

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A widespread epidemic of equine influenza (EI) occurred in nonvaccinated equine population across multiple districts in Khyber Pakhtunkhwa Province of Pakistan during 2015-2016. An epidemiological surveillance study was conducted from Oct 2015 to April 2016 to investigate the outbreak. EI virus strains were isolated in embryonated eggs from suspected equines swab samples and were subjected to genome sequencing using M13 tagged segment specific primers. Phylogenetic analyses of the nucleotide sequences were concluded using Geneious. Haemagglutinin (HA), Neuraminidase (NA), Matrix (M) and nucleoprotein (NP) genes nucleotide and amino acid sequences of the isolated viruses were aligned with those of OIE recommended, FC-1, FC-2, and contemporary isolates of influenza A viruses from other species. HA and NA genes amino acid sequences were very similar to Tennessee/14 and Malaysia/15 of FC-1 and clustered with the contemporary isolates recently reported in the USA. Phylogenetic analysis showed that these viruses were mostly identical (with 99.6% and 97.4% nucleotide homology) to, and were reassortants containing chicken/

Pakistan/14 (H7N3) and Canine/Beijing/10 (H3N2) like M and NP genes. Genetic analysis indicated that A/equine/Pakistan/16 viruses were most probably the result of several re-assortments between the co-circulating avian and equine viruses, and were genetically unlike the other equine viruses due to the presence of H7N3 or H3N2 like M and NP genes. Epidemiological data analysis indicated the potential chance of mixed, and management such as mixed farming system by keeping equine, canine and backyard poultry together in confined premises as the greater risk factors responsible for the re-assortments. Other factors might have contributed to the spread of the epidemic, including low awareness level, poor control of equine movements, and absence of border control disease strategies.

Speaker Biography

Amjad Khan has completed his PhD from the University of Veterinary and Animal Sciences, Lahore. He currently a Research Associate working in a project on surveillance of influenza viruses in Pakistan. He has published more than 20 research articles in peer reviewed journals.

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