Case Series with Review of Literature

Our Experiences of Swine Flu Cases in Office Practice in Jan-Feb: 2015

*Rathinasamy M, *Srinivasan K, *Umadevi L ,**Manikumar, *Sujatha Sridharan, *Kathir Subramaniam, **Subhadevi S, *Jaishree Vasudevan, ***Jenifer Jabakani E

*Professor, **Assistant Professor, ***Junior Resident, Department of Paediatrics and Neonatology, Chettinad Hospital & Research Institute , Chennai,India.

Dr.Rathinasamy completed MD Paediatrics from Madras Medical College in 1990 and worked there till 2006.Then he served in Coimbatore& Salem Medical Colleges. He is an examiner for MBBS, DCH, MD and Paramedical courses. He also served as MCI inspector in 2011 and 2012. He has presented many papers in conferences and published articles in Journals. He has given many guest lectures in various fora. He is currently working as a Professor of Paediatrics/Professor of Neonatology at Chettinad Medical College since 2012, and he also teaches MBBS, MD (Paed), DM (Neo) for post graduates. He is a Governing Council member for DM courses at Chettinad Hospital & Research Institute.

Corresponding author - Rathinasamy (dr.rathinasamy@gmail.com)

Chettinad Health City Medical Journal 2015; 4(2): 86 - 91

Abstract

Human Influenza Virus when it got mixed with swine/bird influenza virus it manifested as Swine flu in 2009.Subsequently it caused epidemics and pandemics and has remained as endemic disease. Clinically swine flu and seasonal flu present with similar presentation. Hence there is a need for categorization of disease, sub typing and laboratory confirmation. In our OPD out of 27 cases tested for swine flu, 13 were positive including 2 cases of pneumonia, all of which recovered. In this article early diagnosis and appropriate management is highlighted. Also a review of literature from India between 2009 to 2014 has been discussed.

Key Words: Influenza virus, Swine flu, Management

Introduction

Common cold(seasonal flu) caused by viruses like influenza virus, adenovirus, respiratory syncytial virus, etc, presents as running nose, sore throat, mild cough and fever[1]. Influenza in swine having genomes of avian, human and swine were notified in 1998. Those assorted viral genomes were demonstrated in humans in 2005[2]. In 2009 unique combination of viral structure which was not known earlier neither in swine nor in human were shown in United States in April 2009 and later in Mexico. It was termed novel H1N1 flu which exhibited two main surface antigens, H1 (hemagglutinin type 1) and N1 (neuraminidase type1)[2]. It manifests in humans as influenza like illness (ILI) and it is called swine flu. After the epidemics and pandemics, humans are the reservoirs of the virus and spreads from one person to another (Fig 1).

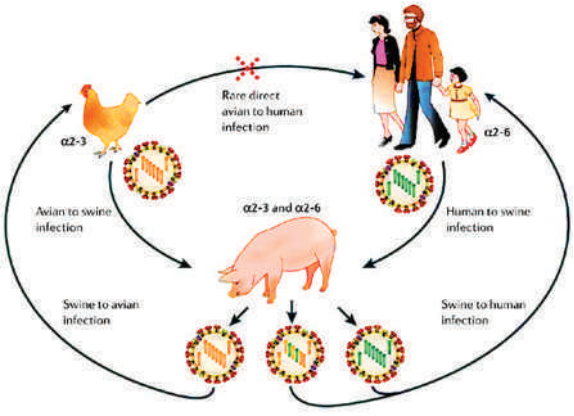


Fig 1 - Reservoir and spread of Swine Flu Virus

Causative Organism

Influenza viruses are members of the family orthomyxoviridae. Electron microscope image of the re-assorted H1N1 influenza virus photographed at the CDC Influenza Laboratory was similar to 2009 isolates in India; A/California/7/2009(H1N1)pdm09-like virus (Table 1)[3]. This influenza virion is 80–120 nanometers in diameter, roughly spherical. The viral genome is enveloped by a lipid membrane layer which is taken from the host cell in which the virus multiplies. Inserted into the lipid membrane are 'spikes', which are glycoproteins, consisting of proteins linked to sugars – known as HA (hemagglutinin) and NA (neuraminidase) (Fig 2). These are the proteins that determine the subtype of influenza virus (for example A/H1N1)[2, 3]. The HA and NA are important in the immune response against the virus; antibodies against these spikes may protect against infection.

The eight RNA strands from novel H1N1 flu have one strand derived from human flu strains (polymerase pb1 gene), two from avian (bird) strains (polymerase pb2 and polymerase pa genes), and five from swine strains (hemagglutinin-HA, nucleoprotein-NP, neuraminidase - NA, non structural proteins - NS genes and M-protein)[2].

A	Virus strain designation
California	Geographic origin
10	Laboratory strain number
1978	Year of isolation
H1N1	Subtype

Table 1 - WHO nomenclature-A/California/10/78 [H1N1]

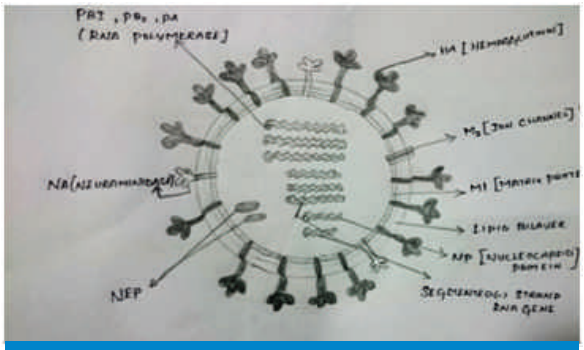


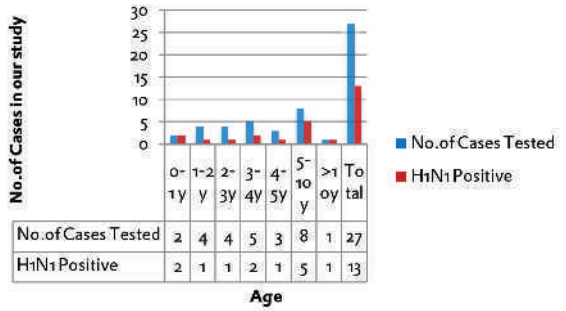
Fig 2 - Diagrammatic Representation of Virus

There are 3 types of influenza viruses :

- Type A causes moderate to severe illness in all age groups in humans and animals. They can produce epidemics and pandemics. There are many sub types (16 H and 9 N).
- Type B usually causes mild illness in humans only and primarily in children. They are genetically more stable.
- Type C is rarely reported in human and does not cause epidemics.

Case Series in our Study

During the flu season between January to February 2015, 27 patients including children of 0-18 years and 1 mother presented with fever, nasal discharge, cough, sore throat, headache, body ache, fatigue, vomiting, diarrhea. Out of the 27patients 13 tested positive(Fig 3). They had history of contact with a proven case or travelled to an endemic area. None had previous flu immunizations. Nasopharyngeal swabs were taken, put in viral transport medium and sent in reverse cold chain for testing for influenza A (H1N1) by reverse-transcriptase polymerase-chain-reaction (rt-PCR) assay in a regional laboratory accredited by WHO.



	0-1y	1-2 y	2-3y	3-4y	4-5y	5-10 y	>10y	Total
No.of Cases Tested	2	4	4	5	3	8	1	27
H1N1 Positive	2	1	1	2	1	5	1	13

Fig 3 - No. of H1N1 positive cases

Results: Out of 27 patients 13 tested positive (males-7, females-6). The lowest age group was 2 months old. 3 children needed admission with following clinical presentation .

Case 1: 8 ½ month infant presented with crying during micturition for 2days, high grade fever, rhinitis, severe pharyngitis, measles like rashes all over the body, sick looking . Urine Culture grew E.coli. Dengue and measles were ruled out by antibody titer.

Case 2: 5months baby presented with complaints of high grade fever, rhinitis, pharyngitis and fast breathing. The baby had bronchopneumonia clinically and radiologically. Mother had similar illness and was H1N1 positive.

Case 3 : 1year 8month boy presented with high grade fever, rhinitis, fast breathing and pharyngitis. Child had tachycardia, bilateral crepitations and rhonchus with tachypnoea. X ray showed pneumonia in right middle lobe.

The above mentioned cases were given supportive treatment and Tamiflu. All other cases were followed by treatment with oseltamivir (Tamiflu) as out-patients. All the patients recovered.

Discussion

In our study, the most common presentation among our patients was - onset of symptoms within 12 hours, fever (92.6%), cough(88.9%), nasal discharge(81.4%), sore throat(70.4%), family history of ARI within the last 2 weeks(48.1%), chills and rigors(40.7%), breathlessness(14.8%), headache(7.4%), body ache(7.4%), and vomiting(7.4%).The lowest age was 2 months. The contact in this infant probably was the waiting area in a clinic where he was vaccinated one week prior to the onset of illness. He had sudden onset of high grade fever and pharyngitis.

In a similar study published in Indian Journal of Paediatrics, a total of 100 children were hospitalized with suspected 2009 H1N1 influenza with Category "C"[4]. Twenty five patients were positive for H1N1 and 9 for seasonal influenza A. The most common presentation (H1N1 positive) was with fever (100%), cough (100%), coryza (52%), respiratory distress (88%), vomiting (28%) and diarrhea (16%). One child presented with hypernatremic dehydration and seizures (Serum sodium 174 meq/l)[4]. In another study conducted in a similar tertiary care setup in Chandigarh stated that the prevalence of influenza A H1N1 is high in the younger population, and fever, cough and sore throat are the most common symptoms with which the patients usually present[5]. Our study is in accordance with the results of the above studies.

Review of literature

The trachea of pigs produce both alpha (2,3) and alpha (2,6) linked sialic acids. This is believed to be the reason why pigs can be infected with both avian and human influenza virus strains and serve as a 'mixing vessel' for the emergence of new viruses[6].

Symptoms and signs

Swine Flu most of the time presents as seasonal(mild) flu, resembling common cold (ILI), presenting with fever, sore throat, running nose, cough, head & body ache, fatigue, vomiting, diarrhea[1]. Severe disease presents with high fever, chills and rigors, severe sore throat somnolence, lethargy, convulsions. Most of the cases are not diagnosed as swine flu because they manifest as ordinary common cold. Most of them recover without any treatment. Severity of disease increases when associated with risk factors. If antiviral are started early, in cases with risk factors, they recover fully. The following are the risk factors -

- All children 6 months to 4 years (59 months) of age
- All people 50 years of age and older
- Adults and children who have chronic pulmonary (including asthma) or cardiovascular (except isolated hypertension), renal, hepatic, neurologi cal, hemato logic, or metabolic disorders (including diabetes mellitus)
- People who are immunosuppressed (including immunosuppression caused by medications or by HIV)
- Women who are or will be pregnant during the influenza season
- Children and adolescents (6 months to 18 years of ge) who are receiving long-term aspirin therapy and who might be at risk for experiencing Reye's syndrome after influenza virus infection
- Residents of nursing homes and other long-term-care facilities
- American Indians/Alaska natives

  People who are morbidly obese (BMI ≥40)
- Health-care professionals (doctors, nurses, health-care personnel treating patients)
- Household contacts and caregivers of children under 5 years of age and adults 50 years of age and older, with particular emphasis on vaccinating contacts of children less than 6 months age
- Household contacts and caregivers of people with medical conditions that put them at higher risk for severe complications from influenza

Diagnosis

Acute febrile respiratory illness in a person who develops symptoms within seven days of close contact with a person who is a confirmed case of H1N1 influenza A virus infection, or develops symptoms within seven days of travel or resides in a community where there are one or more confirmed A H1N1 influenza cases. Acute febrile respiratory illness with laboratory-confirmed by identifying antigens H1N1 influenza A virus through detection by real-time reverse transcriptase PCR (RT-PCR) or culture. Blood counts seem to be useful. Relative lymphopenia has been noted in many. Neutrophil to Lymphocyte ratio (N/L) less than or equal to 2 appears to be a marker to identify those likely to have H1N1 infection. N/L ratio < 2 as a screening tool was found to be sensitive and specific for swine influenza virus infection in adults[5]. As a screening test, Gene Xpert – is quick,useful and may be done in epidemic situations.

Treatment

If a person becomes sick with swine flu, antiviral drugs can make the illness milder and make the patient feel better faster. They may also prevent serious flu complications[5]. For treatment, antiviral drugs work best if started within two days of symptoms. Besides antiviral therapy, supportive care at home or in a hospital focusing on controlling fevers, relieving pain and maintaining fluid balance, as well as identifying and treating any secondary infections or other medical problems.

recommends the use of oseltamivir (Tamiflu) or zanamivir (Relenza) for the treatment and/or prevention of infection with swine influenza viruses(Fig 4). These drugs should not be used indiscriminately, because viral resistance can occur. The viruses isolated in the 2009 outbreak have been found resistant to amantadine and rimantadine.

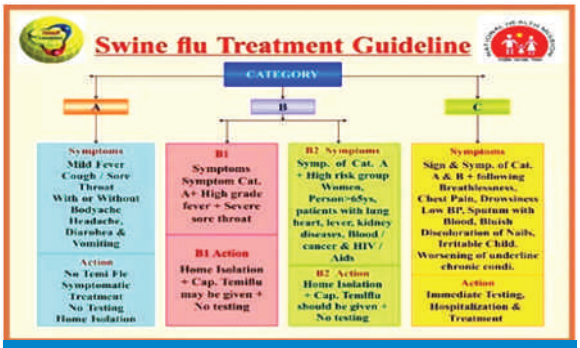


Fig 4 - National health mission guidelines for management of swine flu cases

Drug dosage guidelines

1. Oseltamivir (Tamiflu®)[7] : Mechanism of action- Oseltamivir carboxylate acts by selective inhibition of influenza A and B viral neuraminidase. A lipophilic side chain of the active drug binds to the virus enzyme, by blocking its ability to cleave sialic acid residues on the surface of the infected cell and resulting in an inability to release progeny virions. The dosage guidelines are given in table 2 and 3.

Weight	Dosage	Treatment	Prophylaxis
<15kg	30mg	BID for 5 days	OD for 10 days
15-23kg	45mg	BID for 5 days	OD for 10 days
24-40kg	60mg	BID for 5 days	OD for 10 days
>41kg	75mg	BID for 5 days	OD for 10 days

Table 2 - Oseltamivir WHO dosage guidelines (capsules 75mg)

Age	Dosage	Treatment	Chemoprophylaxis
<38WEEKS 38-40 WEEKS >40 WEEKS	1mg/kg/dose 1.5mg/kg/dose 3mg/kg/dose	Twice daily orally for 5days	Not Recommended
<3MONTHS	3mg/kg/dose	Twice daily orally for 5days	Recommended if needed (in critical case)
3-11MONTHS	3mg/kg/dose	Twice daily orally for 5days	3mg/kg/dose once daily for 7days

Table 3 - Oseltamivir CDC guidelines for newborns and infants (syrup 12mg/ml)(maya-ped.nursing)

2. Zanamavir (Relenza®)[7] :

Available in blisters of powder for inhalation (5mg)

Dosage : allowed over 2 yrs of age.
<7yr : They may not cooperate.
>7yr : 10mg 12th hourly

3. Amantadine (Symmetrel®)[7] :

The viruses isolated in the 2009 outbreak have been found resistant to amantadine and rimantadine.

Amantadine group of drugs has developed resist ance & so better avoided.

Available in Cap.100mg and Syrup 50mg/5ml

Dosage: 1-9yr or <40kg: 5mg/kg/24hr divided 12th hourly

>9yr or >40kg and Adults: 200mg/24hr divided 12th hourly

4. Rimantadine (Flumadine®)[7]

Available in Tab.100mg and Syrup 50mg/5ml

Dosage: 1-9yr or <40kg: 5mg/kg/24hr divided 12th hourly

>9yr or >40kg and Adults: 200mg/24hr divided 12th hourly

5. Peramivir (Rapivab®)[7]

Used as an intravenous antiviral against Swine Flu, in severely ill, in addition to Oseltamivir.

It is FDA approved and recommended for use in Adults 18 years or older. Use in children is controversial and contraindicated.

Dosage: Single dose 600mg as intravenous infusion for 15-30 mins.

The most common cause of death is respiratory failure. Other causes of death are pneumonia (leading to sepsis), high fever (leading to neurological problems), dehydration (from excessive vomiting and diarrhea), electrolyte imbalance (increased Sodium) and kidney failure. Fatalities are more likely in young children, the elderly and those presenting at the late stage of the disease. More deaths at a particular year probably due to the antigenic shift and antigenic drift and increased resistance to known antiviral drugs.

Fortunately, although H1N1 developed into a pandemic (worldwide) flu strain, the mortality rate in the U.S. and many other countries only approximated the usual numbers of flu deaths worldwide. Speculation about why the mortality rate remained much lower than

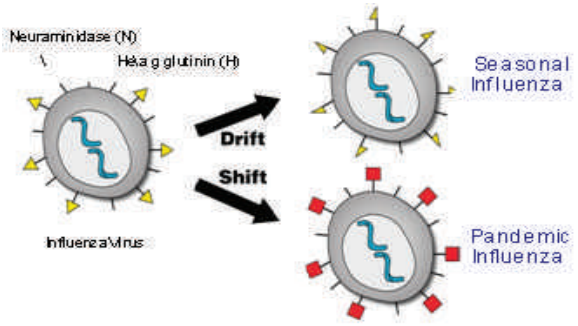


Fig 5 - Influenza - Antigenic Drift and Shift

H1N1 virus followed by Delhi. However, Tamil Nadu witnessed 93 cases with 7 (8%) lives claimed by the disease[8].

Prevention

Facility management includes using disinfectants and ambient temperature to control viruses in the environment. They are unlikely to survive outside living cells for more than two weeks, except in cold (but above freezing) conditions, and are readily inactivated by disinfectants.

Prevention of human-to-human transmission

Avoid visiting Swine Flu infected areas. Influenza spreads between humans when infected people cough or sneeze, small droplets containing the virus can linger on tabletops, telephones and other surfaces and be transferred via the fingers to the eyes, nose or mouth. In humans it is most contagious during the first 5 days of the illness although some people, most commonly

	MAY 2009	JAN 2010	JAN 2011	JAN 2012	JAN 2013	JAN 2014	JAN 2015
PERIOD	DEC 2009	DEC 2010	DEC 2011	DEC 2012	DEC 2013	DEC 2014	FEB 2015*
CLASES	27236	20604	603	5044	5253	937	5157
MORTALITY	3.60%	8.55%	12.44%	8.03%	13.31%	25.40%	7.89%
MORTALITY RATIO	3.60%	8.55%	12.44%	8.03%	13.31%	25.40%	7.89%

Table 4 - Cases And Death Caused By Influenza H1n1 (Swine Flu) Year-Wise2009-2015 India[8]

Year	Samples	Positives	Positivity Rate	Deaths	CFR
2010	9630	1405	14.6	24	1.71
2011	786	34	4.3	4	11.76
2012	5058	750	14.8	40	5.33
2013	2528	37	1.5	6	16.22
2014	1363	58	4.3	8	13.79
2015*	196	36	18.4	4	11.11

Table 5 - Swine flu-cases and deaths: Tamil Nadu statistics[9].

predicted includes increased public awareness and action that produced an increase in hygiene (especially hand washing), a fairly rapid development of a new vaccine and patient self-isolation if symptoms developed. Research is ongoing to develop data-based answers to such questions. Jan 2015 epidemic, the total number of cases of swine flu coming to light across India in January stood at 2,038 which claimed 191 (9%) deaths all over India with Telangana reporting the highest number of cases of people afflicted with the

children, can remain contagious for up to 10 days. It spreads when people may breathe in the virus or touch something with the virus on it and then touch their own face. So avoid touching eyes, nose or mouth. Alcohol-based gel or foam hand sanitizers work well to destroy viruses and bacteria. Surfaces, which can be done effectively with diluted chlorine, bleach solution[10].

Recently, the use of N95 Masks or Respirators has become popular. An N95 respirator is a respiratory protective device designed to achieve a very close facial fit and very efficient filtration of airborne particles. In addition to blocking splashes, sprays and large droplets, the respirator is also designed to prevent the wearer from breathing in very small particles that may be in the air. The 'N95' designation means that when subjected to careful testing, the respirator blocks at least 95% of very small test particles.

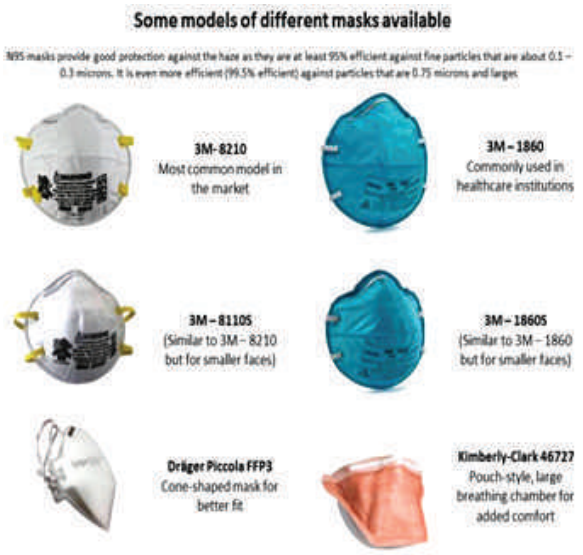


Fig 6 - N95 masks

Till April 2015 the vaccines with the following contents were used, Trivalent injectable vaccine

A/California/7/2009(H1N1) pdm09,

B/Massachusetts/2/2012, A/TEXAS/50/2012-H3N2 is used from 6 months onwards.

From May 2015 onwards, the contents of the vaccine was changed according to the WHO recommendation[11,12]

A/California/7/2009 (H1N1) pdm09-derived strain used (NYMC X-179A)

A/Switzerland/9715293/2013 (H3N2) - like strain used (IVR-175) derived from A/south

Australia/55/2014

B/Phuket/3073/2013. All 7.5 micrograms HA** per 0.25ml dose.

Live nasal vaccines are used from two years and above.

Post vaccination antibody titers peak 2-4 weeks in primed individuals and 4 weeks or later in unprimed individuals. Protection lasts for at least 6-8 months. Hence, yearly vaccination is recommended in high risk individuals[11,12].

Age	6-35 months	3-8 years	From 9 years of age
Dose	0.25 ml	0.5 ml	0.5 ml
No. of Doses	1 or 2*	1 or 2*	1

Fig 6 Dosage and schedule of TIVs

Brand Names	Manufacturer	Type of Vaccine	Composition
Vaxigrip	Sanofi Pasteur India Private Limited	Split-Virion, inactivated	TIV (Both SH and NH)
Agrippal	Chiron Panacea (Panacea Biotech Ltd)	Surface Antigen, inactivated	TIV (NH)
Influgen	Lupin Laboratories Ltd	Split-Virions, inactivated	TIV (NH)
Influvac	Solvay Pharma India Ltd	Split-Virion, inactivated	TIV (NH)
Fluarix	GalaxoSmithkline Pharmaceuticals Ltd.	Split-Virion, inactivated	TIV (NH)
Vaxiflu	Zydus Cadila	Purified H1N1 Monovalent inactivated	TIV (NH)
Nasovac	Serum Institute of India Ltd	Live attenuated monovalent	LAIV (A/H1N1pdm)

Fig 7 Influenza vaccines licensed in India

*SH: Southern Hemisphere; NH: Northern Hemisphere; TIV: Trivalent inactivated vaccine; LAIV: Live attenuated influenza vaccine

If properly fitted, the filtration capabilities of N95 respirators exceed those of face masks. The price of an N95 mask ranges from Rs.150 to Rs.300 in India. Anyone with flu-like symptoms, such as a sudden fever, cough or muscle aches, should stay away from work or public transportation, drink lot of fluids, take paracetamol, do not spit in public places and should contact a doctor for advice. Chance of transmission is also reduced by disinfecting household.

Vaccine

Vaccination to prevent influenza is particularly important for people who are at increased risk for severe complications from influenza[4]. When vaccine supply is limited, vaccination efforts should focus on delivering vaccination to the following people since these populations have a higher risk for H1N1 and some other viral infections according to the CDC:

References

1) Davis C. Swine Flu: Read About Symptoms, Treatment and H1N1 Vaccine. (Available from: http://www.medicinenet.com/swine_flu/article.htm) accessed July 22, 2015.

2) Dawood FS, Jain S, Fineli L, Shaw MW, Lindstrom S, et al. Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine_origin Influenza A (H1N1) virus in humans. N Engl J Med 2009; 360:2605-15.

3) Virology.ws. Structure of influenza virus . (Available from: http://www.virology.ws/2009/04/30/structure-of-influenza-virus/) accessed July 22, 2015.

4) Ankit Parakh A, Kumar A, Kumar V, Kumar Dutta A, Khare S. Pediatric Hospitalizations Associated with 2009 Pandemic Influenza A (H1N1): An Experience from a Tertiary Care Center in North India. Indian J Pediatr. 2010;77(9):981-985.

5) Vijaydeep Siddharth, Vineet Goyal, Vipin Kumar Koushal Clinical - Epidemiological Profile of Influenza A H1N1 Cases at a Tertiary Care Institute of India. Indian J Community Med. 2012 Oct-Dec; 37(4): 232–235.

6) Vincent Racaniello, Dickson Despommier, Alan Dove, Rich Condit, and Kathy Spindler, College of Physicians and Surgeons of Columbia University, USA. This week in Virology blog, May 5th, 2009

7) CDC.gov. Influenza Antiviral Medications: Summary for Clinicians | Health Professionals | Seasonal Influenza (Flu) (Available from: http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm) accessed July 22, 2015.

8) Monthly Newsletter of National Centre for Disease Control, Directorate General of Health Services, Government of India, Aug - Sept 2009, Vol. 13: No.2

9) Dept of Public Health and Preventive Medicine, Govt. of Tamil Nadu. Available from : (www.tnhealthorg/ aphpm.php) accessed 23rd Jan, 2015

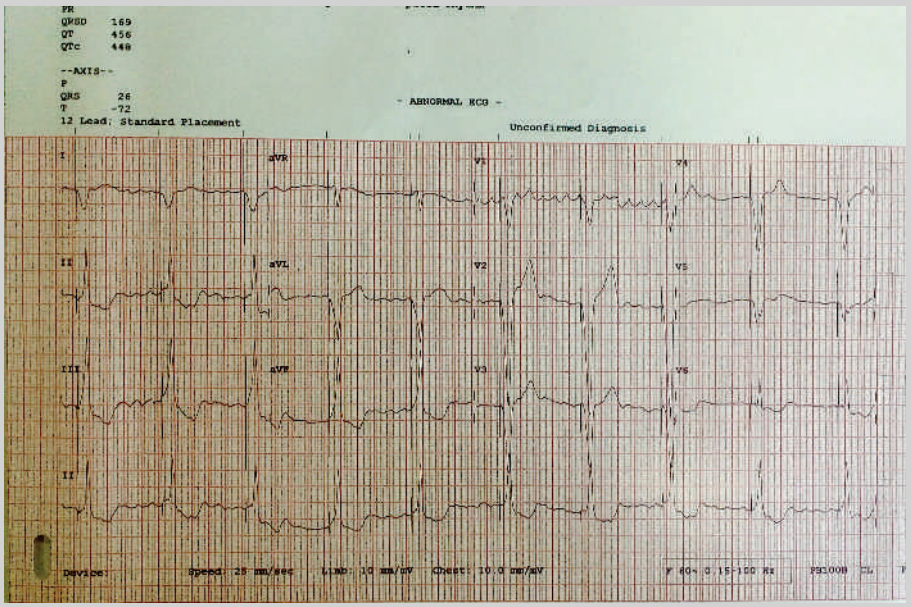
10) Girish L. Dandagi and Sujata M. Byahatti, An insight into the swine-influenza A (H1N1) virus infection in humans, Lung India. 2011 Jan-Mar; 28(1): 34–38.

11) Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2011. American Journal of Transplantation. 2011; 11(10):2250-2255.

12) Recommended composition of Influenza Virus Vaccines for use in the 2015. Southern hemisphere influenza season. World Health Organisation. Available from (http://www.who.int/influenza/vaccines/virus/recommendations/ 2015-south/en)

Diagnose the condition

65 year old male came for routine checkup.
He had undergone a procedure one year back for syncope.



Dr. M.Chokkalingam, Consultant Cardiology, CSSH.

Answer in page : 104