Common endemic infections in the Middle East

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Endemic Area:

The constant presence of a disease or infectious agent in a population within a geographic area.

In Saudi Arabia:

Bacterial infections: Brucellosis & Enteric Fever (Typhoid fever).

Viral infections : MERS-COV & Dengue fever & COVID-19.

Parasitic infections: Visceral Leishmaniosi

Brucellosis: Mediterranean fever, Malta fever, and undulant fever.

Brucellosis is a zoonotic infection caused by the bacterial genus called Brucella that are transmitted from animals :

cattle, sheep, goats, camels, pigs, or other animal to humans through:

- A] Direct contact with an infected animal, or inhalation of aerosols: Slaughterhouse workers, farmers and shepherds.
- **B]** Consumption of unpasteurized dairy products (especially raw milk, soft cheese, butter, and ice cream) is the most common means of transmission).
- C] Laboratory workers with exposure to infected specimen during processing specimens (aerosols) without special precautions.

Brucella organisms: are small aerobic intracellular coccobacilli, localize in the reproductive organs of host animals, causing abortions.

They are shed in large numbers in the animal's milk, placental fluid, and other fluids.

To date, 4 species identified to have moderate-to-significant human pathogenicity:

Species Isolated from

- Brucella melitensis . (sheep and goats, as well as camels)
- Brucella suis . (swine)
- Brucella abortus . (cattle)
- Brucella canis . (dogs)

Pathophysiology

Brucella bacteria:

Possess a unique ability to invade both phagocytic and nonphagocytic cells and to survive in the **intracellular environment**.

Can involve almost every organ system.

Can gain entry into the human body through:

- A] Gastrointestinal (GI) tracts (Ingestion).
- B] Break in the skin.
- C] Conjunctival exposure through eye splash, and inhalation are the most common routes of entry.

Once within the bloodstream, the organisms quickly become intracellular pathogens contained within circulating polymorphonuclear cells (PMNs) and macrophages.

Pathophysiology

After ingestion by phagocytes:

Brucellae **that survive** are transported to and may replicate in any organ causing:

both localized and systemic infection the liver, spleen, central nervous system, heart, joints, and genitourinary system.

Development of **cell-mediated immunity** is the principal mechanism of recovery.

The host response to infection with B abortus is characterized by the development of tissue granuloma.

In contrast, infection with B melitensis and B suis (the more virulent species) more commonly results in visceral micro abscesses.

Epidemiology

The heaviest disease burden lies in countries of :

- The Mediterranean basin and Arabian Peninsula,
- Also common in India, Mexico, and South and Central America.
- ♦ 60% of cases of brucellosis occurred in individuals aged 13-40 years
- Brucellosis is generally uncommon in infants.

Clinical manifestation

A careful history is the most helpful tool in the diagnosis of brucellosis.

The incubation period : 2-4 weeks; occasionally, it may be take few months.

Brucellosis typically presents with insidious onset of:

Fever, malaise, night sweats (Drenching).

arthralgia, low back pain, headache, cough, and depression.

Physical findings (variable and nonspecific): hepatomegaly, splenomegaly, and/or lymphadenopathy.

Diagnosis:

Definitive diagnosis of brucellosis is based on **serologic techniques**, **culture** or **both**:

1] Standard Agglutination Test (SAT) sensitivity 95.6% & specificity 100.0%.

❖ Titers higher than 1:320 are considered to be diagnostic, especially in endemic areas

Blood culture:

. gram-negative coccobacilli

Sensitivity depends source of specimen:

Blood culture : 15 to 70 %

Bone marrow culture: 80 - 90%.

Complications:

Osteoarticular disease: is the most common form of focal brucellosis:

- **A] Sacroillitis:** occur later in the course of illness, usually 2-3 weeks after the onset of symptoms. Radiography reveals: blurring of articular margins and widening of the sacroiliac spaces.
- **B] Spondylitis:** The lumbar vertebrae (L4) are involved more frequently than the thoracic and cervical vertebrae.

Genitourinary involvement: In males, orchitis and/or epididymitis.

Neurologic involvement: meningitis (acute or chronic), encephalitis.

Cardiovascular involvement : Endocarditis :is the main cause of death attributable to brucellosis

Treatment:

General principles of brucellosis treatment include:

- A] Use of antibiotics with activity in acidic intracellular environments (such as doxycycline and rifampin),
- B] use of combination therapy (given high relapse rates with monotherapy),
- C] prolonged duration of treatment.

Doxycycline (oral) for 6 weeks PLUS streptomycin (parenteral) for the first 14 to 21 days

Prevention:

To avoid contact with possibly infected animals.

Avoid drinking raw milk (pasteurizing milk / boiling milk 60 degree for 10 min.

Eating processed meat,

Regular check-up of animals, and their vaccinations.

Taking care of health safety when dealing with infected animals,

Health safety during work in laboratories dealing with Brucella spp.

ENTERIC FEVER 'Typhoid fever'

Definition:

Enteric fever is characterized by severe systemic illness with fever and abdominal pain.

The organism classically responsible for the enteric fever syndrome is:

Salmonella Typhi.

Salmonella Paratyphi A, B, or C.

ENTERIC FEVER EPIDEMIOLOGY:

is more common in children and young adults

Worldwide, enteric fever is most prevalent in overcrowded areas with poor access to sanitation.

Incidence More than 100 cases per 100,000 person-years in :

South-central Asia, Southeast Asia, and southern Africa.

Humans are the only reservoir for S. Typhi and Infection therefore implies:

direct contact with an infected individual or **indirect contact** via contaminated food or water.

ENTERIC FEVER

Pathogenesis

S typhi ot Paratyphi are ingested and survive exposure to gastric acid before gaining access to the small bowel, where they penetrate the epithelium, enter the lymphoid tissue, and disseminate via the lymphatic or haematogenous route to the reticuloendothelial system: liver, spleen, and bone marrow.

These intracellular organisms are likely sources for relapsing infection.

Diarrhea and constipation appear to occur with approximately equal frequency.

ENTERIC FEVER

ROSE SPOTS





CLINICAL FEATURES:

Incubation period of 5 to 21 days.

Abdominal pain, rising fever ("stepwise") reaching >40°C and chills.

Headache is a frequent symptom.

Macular rash "rose spots" on the trunk and abdomen: may be seen.

Hepatosplenomegaly.

Relative bradycardia (pulse-temperature dissociation).

ENTERIC FEVER

Complications:

1] Intestinal perforation (necrosis of the Peyer's patches) usually occurs in the ileum during the third week.

2] Pneumonia, meningitis, osteomyelitis.

Diagnosis:

febrile patient living in, traveling from, or visiting from an endemic area.

Stool culture: Positive in 30 to 40 %

Blood culture. Positive in 50 to 70 %

Bone marrow culture: the most sensitive culture but is invasive procedure.

Serologic tests:

Widal test are of limited clinical utility in endemic

areas because positive results may represent previous infection. Not used.

In many cases the diagnosis of enteric fever is made presumptively in patients with protracted fever without alternative explanation.

Treatment:

A] Fluoroquinolones (e.g. ciprofloxacin) are the drugs of choice for empiric therapy.

B] Ceftriaxone 2gm Twice daily. (2nd choice)

Relapse — Relapse typically occurs two to three weeks after resolution of fever.

Chronic Salmonella carriage: Excretion of the organism in stool or urine >12 months after acute infection.

Rates of chronic carriage after S. Typhi infection range from **1 to 6 percent**Chronic carriers represent an infectious risk to others, particularly in the setting of food preparation.

Fluoroquinolone therapy (eg, ciprofloxacin 500 to 750 mg orally twice daily for 14 - 28 days eliminated carriage in 90 to 93 percent of cases.

Prevention:

Food and water safety: (avoid ingestion of contaminated food or water)

Access to fresh water, prioritization of sanitation and hygiene

Vaccination:

Several typhoid vaccines have been licensed.

None are completely effective against *S.* Typhi and none have been demonstrated to provide protection against paratyphoid fever caused by *S.* Paratyphi A.

Rift Valley fever



RVF is an acute zoonotic viral disease that affects ruminant animals[(cattle, buffalo, sheep, goats, and camels) and humans and caused by the Rift Valley fever virus.

The disease is named after the Rift Valley of East Africa, where the etiologic virus was first isolated in1930 among infected sheep on a farm in the Rift Valley in Kenya.

Several Outbreaks and epidemics of RVF were limited to the African continent until

Sept 2000 when it was reported in Jazan , then Tehama, and Al-Qunfuda. (Saudi Arabia). Then Yamen.

•Now Rift valley fever is considered to be at a low level of endemicity in Saudi Arabia.

Rift Valley fever

Transmission: to humans occurs via:

- A] Bites from infected mosquitoes or, through,
- B] Close contact with infected mammals (more frequently).

Clinical features:

Fever, headache, bleeding, malaise, muscle pain, back pain, and joint pain. abdominal pain, vomiting, diarrhoea, elevated liver enzyme levels progressing to liver failure, encephalopathy or encephalitis, disseminated intravascular coagulation (DIC), renal failure.

Rift Valley fever

Diagnosis:

Polymerase chain reaction (PCR) for detection of viral RNA

Enzyme-linked immunosorbent assay (Elisa) for detection of IgM antibodies against RVF virus.

Treatment:

Symptomatic treatment.

Vaccination for veterinary use are available.

Middle East respiratory syndrome coronavirus

History:

September 2012, a case of novel coronavirus infection was reported in Saudi Arabia involving a man who was admitted to a hospital with:

pneumonia and acute kidney injury in June 2012.

Subsequent cases and clusters of infections have been reported

		March and April 2014	May 2015	Feb -Aug 2015	Early 2019
,	Countries	Saudi Arabia United Arab of emirate	South Korea.	Saudi Arabia	Oman
	No of cases	More than 500 cases	Large outbreak	Outbreak: 153 cases	13 cases

MERS-COV is a **betacoronavirus** found in humans and camels that is different from the other human beta coronaviruses (severe acute respiratory syndrome coronavirus).

Possible sources and transmission:

A] Camels appear to be the primary animal host for MERS-CoV (Virus has been detected in dromedary camels in: Qatar, Saudi Arabia and Egypt).

Study has shown that 55% of infected patients had direct contact with camels in the 14 days preceding their illness.

B] Human-to-human transmission : Evidence:

- 1] Case clusters in the United Kingdom, Tunisia, and Italy and in healthcare facilities in Saudi Arabia.
- 2] In South Korea, a total of 186 cases were reported as a result of a single imported case.

Clinical feature: the median incubation period was 5 days.

Fever (>38°C) - 98%

Cough - 83 %

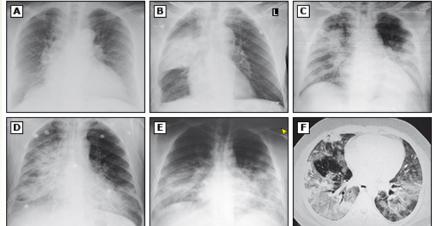
Shortness of breath

Sore throat –Myalgia.

Vomiting & Diarrhea

Abdominal pain

Several individuals had asymptomatic infection



Laboratory findings and diagnosis:

CBC: leukopenia, lymphopenia, lymphocytosis, thrombocytopenia.

LFT: elevated enzymes and LDH.

Renal function: rising blood urea nitrogen and creatinine (some patients).

Imaging findings:

Ground-glass opacity in a peripheral location (most common).

Airspace opacities, patchy infiltrates or consolidation.

Diagnosis:

Preferred tests and specimen types:

Real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) testing:

Nasopharyngeal swab specimen but Lower respiratory tract specimens:

Sputum, endotracheal aspirate, or Broncho alveolar lavage) are more sensitive.

Treatment:

Supportive only. No effective antiviral therapy is available

Prevention:

- 1] Use of standard, contact, and airborne precautions for the management of hospitalized patients with known or suspected MERS-CoV infection.
- 2] Avoiding camels.

كنضل اى مح ... Dengue fever

Dengue is a febrile illness caused by infection with one of four dengue viruses

(DENV-1, DENV-2, DENV-3, and DENV-4) transmitted by Aedes aegypti mosquitoes

- . Dengue viruses are members of the family Flaviviridae, genus Flavivirus .
- Infection may be:
- a] Asymptomatic or present with a broad range of clinical manifestations including:
- B) Mild febrile illness OR
- C] Life-threatening shock syndrome.

All dengue viruses are mosquito-borne human pathogens.

Dengue Clinical Syndromes:

- 1] Classic dengue fever
- 2] Dengue haemorrhagic fever
- 3] Dengue shock syndrome



Epidemiology:

Aedes aegypti mosquitoes: are widely distributed in tropical and subtropical areas from latitude 45°North to 35°South.(high humidity and a hot climate.)

Asia: (incidence of dengue infection is increasing).

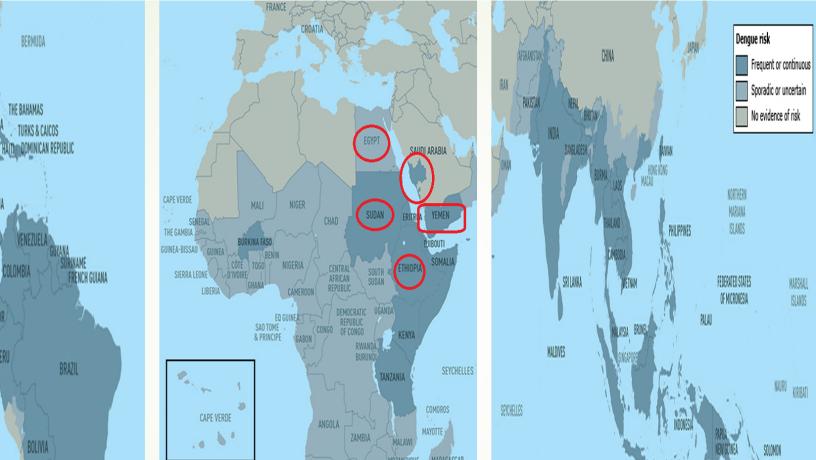
China, Thailand, Vietnam, Indonesia, India, Pakistan, and Sri Lanka.

Africa and Eastern Mediterranean: Ae. aegypti mosquitoes are present in most of sub-Saharan Africa and the Middle East.

North America: Ae. aegypti mosquitoes are present in most areas of Mexico and in the south-eastern United States

Others..

Dengue is common in more than 100 countries around the world with where 50 million DF occur annually, out of which 22,000 deaths affect mostly children.



Dengue fever (DF)

Dengue fever in Saudi Arabia:

Jeddah 1994:

The first experience of 289 confirmed cases of virus isolation during a DF outbreak.

Jeddah 1997:

Emergence of DF occurred and identified during the rainy season.

Jeddah 2004:

Mecca.2004: The DF Virus was isolated were isolated.

Jeddah 2005, 2006 cases were isolated

Al-Madinah 2008: Cases were isolated

MOH reported a total of <u>3350 cases</u> of DF in the Kingdom and estimated the case fatality rate to be 4.6/1000.

Classic dengue fever : The incubation period is 3 to 14 days symptoms typically develop between 4 and 7 days after the bite of an infected mosquito.

It is an acute febrile illness defined by the presence of fever and two of the followings:

Headache & Retro-orbital or ocular pain

Myalgia and/or bone pain & Arthralgia

Rash and blood test might shows Leukopenia.

Haemorrhagic manifestations: petechiae,

Positive tourniquet test, epistaxis, gum bleeding, blood in urine, or stool, or vaginal bleeding.



Microvascular fragility
may be demonstrated by
a positive "tourniquet test"

Dengue haemorrhagic fever (DHF): Characterized by:

Plasma leakage due to increased vascular permeability leading to ascites and pleural effusion in addition to features of Dengue fever.

Dengue shock syndrome:

DHF with marked plasma leakage that leads to circulatory collapse (shock) as evidenced by

- 1] Cold, clammy skin and restlessness.
- 2] Narrowing pulse pressure or hypotension
- 3] Rapid and weak pulse.

Diagnosis:

DX should be suspected in any febrile individuals with typical clinical manifestations and relevant epidemiologic exposure [residence in or travel within the past two weeks to an area with mosquito-borne transmission of DENV infection]

Provisional diagnosis of DENV infection is usually established clinically.

DÉFINITE TESTS:

Detection of viral nucleic acid BY reverse-transcriptase polymerase assay.:

high specificity but is more labor intensive and costly.

RT-PCR



Genome detection

Detection of viral antigen has high specificity.



Serology test: to detect presence of Immunoglobum. Igus or IgG.

(unreliable in vaccinated patient)





Serology IgM Serology IgG

Leishmaniasis is a diseases caused by a caused by the protozoan Leishmania parasites which are transmitted by the bite of infected female

phlebotomine sandflies (Phlebotomus Papatasi)

There are 3 main forms of the disease:

Cutaneous: The most common. [Cutaneous leishmaniosis]

Mucocutaneous [Mucocutaneous leishmaniosis

Visceral: The most serious form. [Visceral leishmaniosis]



Cutaneous leishmaniosis:

Cutaneous lesions tend to occur on exposed areas of the skin(face is the commonest site). begins as a pink-colored papule that enlarges and develops into a nodule (often with central softening), leading to a painless ulceration with an indurated border. Multiple lesions may be present,

The disease is endemic in many parts of KSA:

Qaseem, Riyadh, Al-Hassa, Asser, Hail, and Al-Madinah.

The main causative species are:

1]/Leishmania major (L. major) infection.

[2] Leishmania tropica (L. tropica) infection.



Psammomys obesus



Meriones libycus

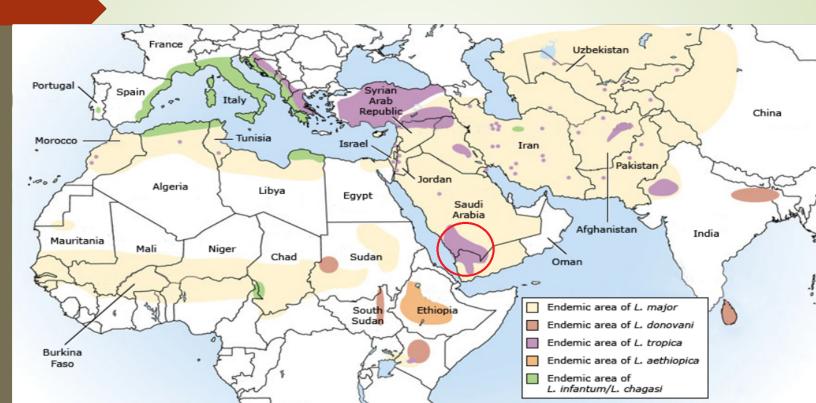




Have been defined as the principal reservoir hosts of zoonotic CL in Al-Hassa oasis, Al-Madinah, and Al-Qaseem provinces.

Face is the most commonly affected site, and ulcerative pattern accounts for 90% of lesions.

Leishmaniasis Distribution of cutaneous leishmaniasis







Diagnosis:

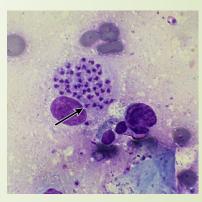
Definitive diagnosis requires demonstration of the parasite in a clinical specimen (usually skin) by:

1] <u>Histology</u>:

- The Leishmania amastigote is an oval to round organism
- The cytoplasm is blue, the nucleus violet-blue, and the kinetoplast red to violet (diagnostic characteristic)

2] Culture:

- Liquid media consists of Schneider's media.
 - 3] Molecular analysis via PCR:(Sensitive diagnostic tests).



Leishmania amastigote

Treatment:

Cutaneous leishmaniasis (CL) is **not life-threatening** but it can have disfiguring lesions and devastating effects on local communities

Many CL infections eventually resolve with spontaneous healing occurring over months to years.

local cryotherapy:

- A] Cryotherapy immediately followed by intralesional pentavalent antimony.
- B] Topical paromomycin may be used for treatment of ulcerative lesions due to L. major.
- C] Parenteral sodium stibogluconate (SSG).

Visceral leishmaniasis (VL), also known as kala-azar, is a disease caused by:

Leishmania donovani and L. infantum that is transmitted by phlebotomine sandflies.

The incubation period is usually **two to six months**.

Onset of symptoms is usually insidious,

Parasites replicate in the **reticuloendothelial system**, very high parasite loads accumulate in the spleen, liver, and bone marrow.

Clinical features:

Fever, weight loss.

Splenomegaly [The spleen is usually firm].

Marked cachexia (wt loss)

Kala-azar ("black fever") refers to darkening

of the skin, which is a common symptom in South Asia but not elsewhere.

Laboratory findings:

Severe anemia, Leukopenia, Thrombocytopenia

Hypergammaglobulinemia.

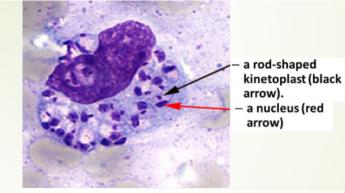
Hypoalbuminemia, and edema.

Immunosuppression increases risk for secondary bacterial infections.

Kala-azar is nearly always lethal without treatment.



Leishmaniosis.



Tissue Diagnosis –skin, spleen, bone marrow

Diagnosis:

Histopathology: bone marrow or spleen aspirations.

Bone marrow aspirates are generally safer than splenic aspirates.

Diagnosis requires visualization of **amastigotes** [**spherical or ovoid bodies** that measure 1- 5 microns long by 1 - 2 microns wide within macrophage] under microscope.

Treatment:

Liposomal amphotericin

Miltefosine

pentavalent antimonial (sodium stibogluconate (Pentostam)

Nutritional support.

Pregnancy: VL infection in the setting of pregnancy has been associated with congenital infection and fetal death

<u>Liposomal amphotericin B</u> is the drug of choice for treatment of VL in pregnancy

Response to treatment is generally assessed clinically, based on resolution of fever, decrease in spleen size, and weight gain.



Coronaviruses are important human and animal pathogens.

At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in China.

It rapidly spread, resulting in an epidemic throughout China, followed by a global pandemic.

In February 2020, the World Health Organization designated the disease COVID-19.

The virus that causes COVID-19 is designated (SARS-CoV-2).

Coronavirus virology:

Coronaviruses are enveloped positive-stranded RNA viruses.

Full-genome sequencing and analysis indicated that SARS-CoV-2 is a **betacoronavirus** in the same subgenus as:

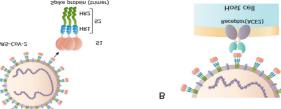
- 1] Severe acute respiratory syndrome (SARS) virus as well as
- **2**] Several bat coronaviruses.

The closest RNA sequence similarity is to two bat coronaviruses, and it appears likely that bats are the primary source. But intermediate host is unknown.

The host receptor for SARS-CoV-2 cell entry is the

angiotensin-converting enzyme 2 (ACE2).

SARS-CoV-2 binds to ACE2 through the receptor-binding gene region of its spike protein.



EPIDEMIOLOGY:

Globally, over 100 million confirmed cases of COVID-19 have been reported.

Transmission:

A] Person-to-person: respiratory transmission occur mainly through close-range contact (within approximately six feet or two meters) via respiratory particles;

When infected patient **coughs**, **sneezes**, or **talks**, **the virus is released** in the respiratory secretions which might infect another person if it **is inhaled** or makes **direct contact** with the mucous membranes.

- **B]** A person's hands are contaminated by secretions from contaminated surfaces.
- **C] Airborne transmission:** inhalation of particles that remain in the air over time and distance).

Manifestation:

The incubation period is within 14 days following exposure (most cases 4 -5 days)

The spectrum of illness associated with COVID-19 is wide, ranging from

1] asymptomatic infection.... To 2] life-threatening respiratory failure

1] ASYMPTOMATIC INFECTIONS:

2] Symptomatic:

A] maild cases: 80% Of Patients:

Fever, fatigue, and dry cough.

Headache, rhinorrhea, and sore throat are less common.

Smell and taste disorders have also been reported.

Gastrointestinal symptoms are not frequently reported but may be the presenting feature. (abdominal pain, vomiting, diarrhoea)

- **B] Severe cases**: 20 to 30% of patients (five to eight days after symptom).
- Respiratory failure: Dyspnoea which might Progress to acute respiratory distress syndrome (ARDS) rapidly requiring mechanical ventilation (10 20%).

Thus, the onset of dyspnoea is generally an indication for hospital evaluation and management.

- Cardiac complications: arrhythmias, acute cardiac injury.
- Neurologic complications Encephalopathy is a common particularly among critically ill patients.
- Thromboembolic complications: pulmonary embolism and acute stroke

LABORATORY EVALUATION

Lymphopenia (up to 90%)

Elevated aminotransaminase levels [AST, ALT]

Elevated lactate dehydrogenase levels [LDH]

Elevated inflammatory markers (eg, ferritin, C-reactive protein, and erythrocyte sedimentation rate).

Chest Imaging:

Chest x-ray: Consolidation and ground-glass opacities, with bilateral, peripheral, and lower lung zone distributions.

CT- SCAN: (more sensitive than chest radiograph):

DIAGNOSTIC TESTING:

RT-PCR for SARS-CoV-2 is the primary test used to diagnose active COVID-19.

The test is performed primarily on upper respiratory specimens:

Nasopharyngeal swabs, nasal swabs, and saliva.

The optimal time to test for COVID-19 following exposure is uncertain; five to seven

days following exposure

Serology: Measure antibodies to SARS-CoV-2 (indicate past infection).

Treatment

Suupportive.

No specific and effective medication.

Prognosis:

The overall case **fatality rate** is estimated to be between **2 and 3**%.

Risk factors for poor outcome:

- 1] Increased age.
- 2] Presence of chronic illnesses : CVS, Pulmonary, diabetes mellitus, kidney disease, and cancer.

Recovery and long-term sequelae — The time to recovery from COVID-19 is highly variable:

- A] Mild infection: recover relatively quickly (within 2 weeks).
- B] Severe disease: have a longer time to recovery (2 3 months).

The most common persistent symptoms include fatigue, dyspnea, chest pain, cough, and cognitive deficits..

Thank you! Questions or comments?