An Overview on the First Wave of COVID-19 from February to October 2020 in Arab World

Welcome letter from Editor-in-Chief

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It is with great pleasure that I write this editorial to welcome you to the IJCBR. This journal provides a platform for publication of original and reviews research articles, short communications, letter to editor, thesis abstract, conference report, and case studies. These types of publication are directed at the interface of the fields of cancer and biomedical research.

The IJCBR relies on a distinguished expert of the Advisory and Editorial Board Members from the top international league covering in depth the related topics. They timely review all manuscripts and maintain highest standards of quality and scientific methodology and ethical concepts. Meanwhile, we take all possible means to keep the time of the publication process as short as possible.

I take this chance to welcome your contributions to the IJCBR and have every expectation that it will soon become one of the most respected journals in both the fields of cancer and biomedical research.

Mohamed L. Salem,
Editor in Chief
An Overview on the First Wave of COVID-19 from February to October 2020 in Arab World

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ABSTRACT

The world faces a severe challenge to fight COVID-19 pandemic caused by SARS-CoV-2. Millions of calls for medical help were reported due to SARS-CoV-2 infection. Till now, no fixed protocols are known to cure this virus, therefore novel procedures and technologies have been made to avoid infection and death. SARS-CoV-2 belongs to the coronaviruses, which caused several epidemics in the past. Coronavirus started to invade the world from Wuhan until the present time causing fatal human and economic damages. Given that coronavirus spread in the world in a short time with high severity, the World Health Organization announced that coronavirus is a world pandemic on March 11, 2020. This review article highlights the prevalence and mortality of COVID-19 in the Arab countries during the first wave from February to October 2020. We analyzed the data that were registered monthly in all Arab countries and calculated the indices using correlation analysis. In addition, we discussed the possible routes of infection, clinical symptoms, and biochemical alternation post-SARS-CoV-2 infection, the susceptibility of diabetic patients, immunity against SARS-CoV-2, and new approaches for the treatment of COVID-19. The presented information about COVID-19 in Arab countries can be of help to policymakers, epidemiologists, and medical specialists.

Keywords: Diabetes; insect; outbreak; SARS-CoV-2; treatment.

INTRODUCTION

Coronaviruses are re-emerging viruses that infected millions of people around the world (Shi et al, 2020). On 31st December 2019, the first infected case with SARS-CoV-2 was reported in Wuhan city, Hubei Province, China (Adhikari et al, 2020). SARS-CoV-2 is the causative of COVID-19 (Guo et al, 2020; Qu et al, 2020). It has been reported that it is likely to be a zoonotic disease (Rothan & Byrareddy, 2020). The virus spread in different cities in China and within a short period, it began to spread to other countries such as Italy, the United States of America, and Germany. Lately, COVID-19 has spread in the entire world (WHO, 2020a). The World Health Organization (WHO) announced that COVID-19 is a world pandemic disease (Peng et al, 2020; Sarzii-Puttini et al, 2020). By 29th January 2020, it permeated the Arab world. The United Arab Emirates was the first Arab country that recorded the transmission of SARS-CoV-2. Later, SARS-CoV-2 overspread to other countries such as Lebanon, Iraq, Tunisia, Saudi Arabia, and Egypt, respectively (WHO, 2020a). In April 2020, COVID-19 spread to all Arab world. As the rate of spread and death due to COVID-19 pandemic in Arab countries is of top priority to the policymakers, epidemiologists and medical specialists, this review aims to describe the prevalence and distribution of COVID-19 during the first wave of SARS-CoV-2 infection from February -October 2020. So that the numbers of infected cases and death
reported in the Arab world from February to October 2020 were extracted from WHO websites. This information was registered monthly in all Arab countries and the calculated indices were analyzed using correlation analysis. The review also covers other related topics such as symptoms, the possible role of insects in transmission, the entry mechanism of SARS-CoV-2, the relation between COVID-19 infection and diabetes, the beneficial role of natural products for protection, and different approaches of COVID-19 treatment.

**Structure of coronavirus**

Coronavirus (SARS-CoV-2) has a poly or spherical shape with a diameter that varies from 150 to 160 nm. Due to its small size, the virus becomes ultra-filterable. Structurally, SARS-CoV-2 virus is coated with proteins and a lipid membrane-embedded a single positive-strand RNA. This RNA is about 30,000 nucleotides encodes structural proteins (SP) and nonstructural proteins (NSP). The SPs are four types, including nucleocapsid protein (N), an envelope protein (E), membrane protein (M), and spike protein (S). Coronavirus enveloped a single positive RNA strand randomly (Chen et al, 2007). Nucleocapsid protein interacts with several host-cells and has an antigenic effect. Spike glycoprotein binds to the host receptor that lets the SARS-CoV-2 enter the body cell. This process converts human cells into viral factories to let the virus invade other tissues (Boopathi et al, 2020). SARS-CoV-2 differentiates from other coronaviruses by coding supplemental glycoproteins with acetyl esterase and hemagglutination properties (Kannan et al, 2020).

**Entrance mechanism of SARS-CoV-2 into cell**

SARS-CoV-2 has two spike proteins known as S1 and S2 subunits. The virus enters inside the host cells through the attachment of S1 protein subunit with the cellular angiotensin-converting enzyme 2 (ACE2) receptors that are widely expressed in the respiratory tract, heart (pericytes), kidney, intestine (enterocytes), brain neurons, vascular endothelium, immune cells, renal tubules and pancreatic cells (Wang et al, 2020b). The S2 subunit, containing the fusion peptide and transmembrane domain, led to viral and host cell membrane attachments (Bergmann & Silverman, 2020). The S protein subunit promotes viral envelope fusion with the cell membrane of the host cells through the endocytosis pathway. Inside the cell, the virus releases its genomic RNA. This viral RNA is translated into viral replicas polyprotein (pp1a and 1 ab) then cleaved into small products by viral proteases. The viral protein compartments (S, M, and E) and viral genomes were subsequently assembled into viral particles in the endoplasmic reticulum and Golgi apparatus and then transported through vesicles and released out of the cells (Figure 1).

**Routes of COVID-19 infection**

Recently, SARS-CoV-2 rabidly spread everywhere due to several factors (Yuen et al, 2020). Transportation ways such as airplanes, ships, and trains between countries and cities led to the fast spread of COVID-19 (Wang et al, 2020a). Infection occurs on direct contact with an infected person through respiratory droplets and saliva that are emitted by breathing, sneezing, and coughing causes infection. Indirect contact with the infected objects, droplets, fomites, focal-oral, blood transfusion. Vertical transmission, an animal to the child, and inhalation droplets of airborne could also cause infection (Asadi et al, 2020; Moghadas et al, 2020; Yu & Yang, 2020). However, recent studies showed that the increase in temperature and humidity has accompanied by decreasing infection rate and daily death (Tosepu et al, 2020; Xie et al, 2020).

**COVID-19 and insects: perspectives**

Person-to-person transmission is thought to occur mainly via respiratory droplets when an infected person coughs or sneezes (Kramer et al, 2006). However, other transmission routes of infection such as stool contamination or by different vectors are possible, but no empirical data are available till now. Previous studies pointed out that SARS-CoV-2 is attacking lymphocytes and shed its particles into the patient’s plasma (Grant et al, 2003; Ng et al, 2003). As SARS-CoV-2 appeared in the peripheral circulation of some viraeic patients, they will be available to blood-sucking insects during feeding. Therefore, there is still a theoretical risk of transmission of SARS-CoV-2 through blood transfusion or via blood-sucking
insects such as mosquitoes and bed-bugs (WHO, 2020b). The transmission of SARS-CoV-2 by insects has been unexpected by some researchers (Dicke et al, 2020), although some insects such as *Aedes* sp. as well as ticks are very specific vectors of Arboviruses (Dehghani & Kassiri, 2020). For the researchers who support the idea that insects cannot transmit SARS-CoV-2 infection, several justifications are suggested. Even though, there are few viruses able to infect both humans and insects, however, in general, viruses that infect humans rarely infect insects. The ability of non-blood-feeding insects to humans is restricted and will be only through passive action. Therefore, non-blood-feeding insects contribute no significance to human health (Dicke et al, 2020). However, a scenario that is considered more logical highlighted the probability of transmission of SARS-CoV-2 by insects. Several arguments may support this hypothesis. SARS-CoV-2 is much related to SARS-CoV and Middle East respiratory syndrome (MERS-CoV). These are bat coronaviruses (Kramer et al, 2006). It is very recommended that these viruses are zoonotic, switch into intermediate hosts like civet, pangolin, or camels before they can infect humans (Leitner & Kumar, 2020). Most bats and pangolin feed on insects (Corman et al, 2014). Moreover, several blood-sucking insects may harbor nidovirales (Nga et al, 2011). Mosquitoes especially *Aedes* transmit several viruses such as Dengue, Zika, West Nile, Chikungunya, St. Louis encephalitis, Eastern equine encephalitis, and yellow fever viruses (Rosenberg et al, 2018). Recently, Zika and hepatitis C viruses were reported to be transmitted by *Culex pipiens* (El-Kholy et al, 2018; Guo et al, 2016). Given that some blood-sucking insects can take blood contaminated with SARS-CoV-2 from patients, these particles may have one of two ends. If the virus can get into the gut-lining cells, it may be able to replicate or at least drops down from the mouthparts (Calibéo-Hayes et al, 2003). Good support may come from the fact that insects such as *Drosophila melanogaster* and *Anopheles gambiae* have ACE analog receptors in gut epithelium, heart cells and the reproductive system (Harrison & Acharya, 2014; Holt et al, 2002). This receptor is the main point of entry for the virus. It has been demonstrated that the S2 subunit of the spike glycoprotein of Bovine Coronavirus can mediate membrane fusion in *Spodopera frugperda* (Sf9) cells. So that the possibility that insects especially the blood-sucking ones still open (Yoo et al, 1991). There is no confirmed data that insects cannot transmit the virus. Hence, it is much recommended to further examine the ability of blood-sucking insects to keep or transmit SARS-CoV-2 to exclude this route.

**Clinical symptoms and biochemical alterations of COVID-19**

The influence of COVID-19 revealed a variety of symptoms, ranged from asymptomatic, mild symptoms to severe respiratory failure, and maybe lethal (Esakandari et al, 2020). There is clear evidence that a lot of asymptomatic COVID-19 individuals may spread the virus to other people (Gao et al, 2020). The path of infection gets mild or asymptomatic in about 80 to 90% of cases. It becomes extreme in about 10% of cases (Pascarella et al, 2020). The minor symptoms include headache, dizziness, diarrhea, anorexia, nausea and vomiting, and conjunctivitis. Additionally, there are common clinical symptoms of COVID-19 patients that were viral pneumonia, including respiratory distress (dyspnea), high body temperature (fever), severe cough, sore throat, nasal congestion, and myalgia (muscle pain). It is, therefore, hard to distinguish COVID-19 from other respiratory diseases (Li et al, 2020a; Li et al, 2020b). Growing data indicates that coronavirus is not only limited to the respiratory system but also may enter the central nervous system that triggers neurodegenerative disorders (Li et al, 2020a). Besides causing pneumonia, COVID-19 can also damage multiple organs, such as the heart, liver, kidney, as well as multiple systems, such as the blood, immune system, eventually leading to death (Huang et al, 2020; Wang et al, 2020b). After infection with SARS-CoV-2, the patients begin to develop clinical symptoms and signs, for instance, a significant increase in serum proinflammatory cytokine levels, including cytokine storms characterized by IL-6, IL-1β, IL2, IL-8, IL-7, CSF, GMCSF, IP10, MCP1, and TNF (Qin et al, 2020; Xu et al, 2020). Due to severe infection with SARS-CoV-2, high levels of proinflammatory cytokines may lead to shock and tissue damage in the heart, liver,
kidney, as well as respiratory failure or multiple organ failure (Shi et al, 2020). Infected patients also developed abnormal myocardial enzyme profiles, such as an increase of creatine kinase (CK) and lactate dehydrogenase (LDH). Additionally, infected patients showed an increase in liver enzymes, alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Also, kidney function has been influenced by infection with SARS-CoV-2 showing increased blood urea nitrogen and serum creatinine (Cr) (Wang et al, 2020b). Also, age is considered as one of the susceptibility-determining factors in SARS-CoV-2 infection. Recent studies showed that the elderly are more susceptible to infection than young people (Garcia et al, 2020; Santesmasses et al, 2020).

**Diabetes and COVID-19**

Diabetes is considered one of the most common diseases in the entire world. It consists of 2 types: type 1 diabetes is a metabolic disease that lacks insulin secretion, unlike type 2 diabetes, is the insufficient use of the insulin it produces, and both of them reduce the body's immune response (Angelidi et al, 2020; Yin et al, 2010). Blood glucose regulation has influenced many characteristics of the innate and adaptive immune response. These immunity defects, including insufficient T-cell action, defective natural killer cell activity, complement defects, irregular secretion of adipokines and cytokines such as tumor necrosis factor-alpha (TNF-α) and interferon due to diabetes, lead to immune defects which in turn facilitate COVID-19 infection (Cai et al, 2020; Gupta et al, 2020). A previous study revealed that there is a positive relationship between type 2 diabetes, obesity, and COVID-19 infection (Johnsson et al, 2015). Also, some studies found that level of D-Dimer and fibrinogen was higher in diabetic patients which may increase the hypercoagulable state caused by COVID-19 inflammations than non-diabetic (Gao et al, 2020).

**Immunity to COVID-19**

Immune response to SARS-CoV-2 involves cytokines storm development, toll-like receptors (TLRs), complement activation, augment interferons secretion, increasing monocytes, macrophages, and neutrophils (Shah et al, 2020; Totura et al, 2015). Activation of ACE2 negatively impacts the physiological process of the body by downregulation of the renin-angiotensin system (RAS) (Corrêa Giron et al, 2020). Association of spike proteins with ACE2 upon the invasion of SARS-CoV-2 virus seems to release a considerable amount of cytokine in the body, mainly interleukin-6 (IL-6) that activates the immune response (Conti et al, 2020). Several studies showed that elevation of systemic IL-6 exacerbates SARS-CoV-2 infection side by side to fibrinogen, D-dimer, and inflammation (Gubernatorova et al, 2020; Hayiroğlu et al, 2020). SARS-CoV-2 infection causes an increase in neutrophil count and decreases lymphocyte. Moreover, it able to induce neutrophil extracellular traps in plasma, tracheal aspirate, and lung tissue that may induce the apoptotic pathways in the lung epithelial cells (Veras et al, 2020). Upon infection with the COVID-19, various proinflammatory cytokines are released from the epithelial cells and fibroblasts that chemoattract massive monocytes to the sites of infection. Then, the activated monocytes-macrophages induced exaggerated cytokine release and, consequently, cytokine release syndrome (CRS) responsible for the acute respiratory distress syndrome (ARDS) typical of severe patients (Gómez-Rial et al, 2020). T-lymphocytes recognize S protein, which correlates with both IgG and IgA antibody titers (Braun et al, 2020; Grifoni et al, 2020a). It has been reported that T-cells from patients infected with the SARS-CoV-2 virus recognize only 3 epitopes among 29 shared epitopes of six HLA types. This may suggest that vaccines may confer a short-term immunity against SARS-CoV-2 infection, and novel targets needed to be epitomized for natural CD8+ T cells (Ferretti et al, 2020).

The development of vaccines against SARS-CoV-2 should induce a natural CD8+ T-cell response, not just confers a short-term immune activation against that virus. Also, considering the variable neutralization activity of patients’ serum antibodies (French & Moodley, 2020; Grifoni et al, 2020b). The appearance of different genetic mutations in the SARS-CoV-2 genome suggests that SARS-CoV-2 virus is unremittingly developing across the whole world (Shah et al,
2020). Moreover, in most severe cases of SARS-CoV-2, significantly decreased count of T cells, helper T-cells, and suppressor T-cells showing lower levels associated with remarkably increased serum levels of pro-inflammatory cytokines such as IL-6 and TNF-α. This indicating loss of effector T-cells and exhaustion of the immune system leading to a poorer immune response and evasion (Chiappelli et al, 2020; Qin et al, 2020). Using TLRs antagonists may become potential therapeutics for SARS-CoV-2 infection. TLR7 is specifically bound to single-stranded RNA viruses such as SARS-CoV-2 and hepatitis C virus, activating the downstream protein MyD88 and subsequently activate NF-kB nuclear translocation and mitogen-activated protein kinase (MAPK) pathway (de Marcken et al, 2019; Onofrio et al, 2020). Another potential immunotherapeutic approach is using the cleavage inhibitor to complement system components named Eculizumab (human mAb) that is involved in the assembly of the membrane attack complex (Birra et al, 2020; Cugno et al, 2020).

**Confirmed infection and mortality of COVID-19 in the Arab world**

WHO (2020a) reported the confirmed cases and mortalities in different Arab countries starting from February 2020. We generated a regression line for each Arab country from February till October 2020. The highest confirmed cases of coronavirus-infected patients in the Arab world during this period were represented as 127113, 103052, 94111, 59257, and 43305 in Iraq (September), Saudi Arabia (June), Morocco (October), Jordan (October), and Egypt (June), respectively. In contrast, low numbers of confirmed cases were represented 2 and 3 cases in Mauritania (April) and Somalia (March), respectively (Figure 2A). The high number of mortalities were reported as 2832, 1959, 1473, 1270, and 1007 in Iraq (July), Egypt (June), Morocco (October), Saudi Arabia (July), and Tunisia (October), respectively. Low numbers of mortality were represented in Comoros, Djibouti, Somalia, Mauritania (Figure 2B).

**Total cumulative confirmed cases of COVID-19 in the Arab world**

The total cumulative COVID-19 infected cases in all Arab world till 31, October 2020 showed that Iraq, Saudi Arabia, and Morocco reported the highest number of coronavirus-infected cases with 470633, 34688, and 21529, respectively. Qatar, Kuwait, Oman, and Egypt showed moderate confirmed cases with 132343, 125337, 114434, and 107385, respectively. While Syria, Somalia, Yemen, and Comoros represent the lowest infected cases with 5683, 3941, 2066, and 53, respectively. The highest percentage of confirmed cases was found in Iraq that represented 21.85%. While the lowest percentage of confirmed cases was represented 0.02% in Comoros (WHO, 2020a) (Figure 3).

**Total cumulative mortalities of COVID-19 in the Arab world**

The total cumulative mortalities due to coronavirus infection in the Arab world from February to October 2020 reported that Iraq, Egypt, Saudi Arabia, and Morocco showed the highest number of mortalities with 10862, 6258, 5383, and 3625, respectively. Lebanon, Yemen, Palestine, and the United Arab Emirates showed moderate mortalities with 625, 600, 553, and 490, respectively. Mauritania, Somalia, Djibouti, and Comoros represented the lowest mortalities with 163, 104, 61, and 7, respectively (WHO, 2020a) (Figure 4).

**Correlation between confirmed cases and mortality**

In the present review, a correlation between the confirmed and mortalities of coronavirus patients in all Arab world till October 2020 was reported (Table 1). Iraq, Saudi Arabia, and Morocco represented the highest countries in confirmed and mortalities. While Comoros, Djibouti, and Somalia showed the lowest countries are confirmed and deaths cases among all Arab world (WHO, 2020a) (Figure 5).

**Approaches to COVID-19 treatment**

The antiviral chemical drugs such as Remdesivir, Chloroquine, Tocilizumab, Hydroxychloroquine, Umifenovir, Lopinavir, Oseltamivir, Favipiravir, and many adjunctive curative drugs such as zinc, vitamin D, azithromycin, ascorbic acid, nitric oxide, corticosteroids, and IL-6 antagonists are considered against COVID-19 (Esakandari et al, 2020).
Figure 1. The entrance mechanism of SARS-CoV-2 into the cell.

Figure 2. The confirmed cases (A) and death (B) due to COVID-19 in the Arab world from February to October 2020. The numbers of cases and death presented in this figure were obtained from WHO (2020a).
Figure 3. The total cumulative confirmed cases > 65,000 (A) and < 65,000 (B) of COVID-19 patients in the Arab countries till 31st October 2020. The numbers of the cumulative cases used in this figure were obtained from WHO (2020a).
Figure 4. The total cumulative death > 750 (A) and < 750 (B) due to COVID-19 in the Arab countries till 31, October 2020. The numbers of the cumulative death used in this figure were obtained from WHO (2020a).
COVID-19 infection in Arab countries...

Figure 5. Correlation between the confirmed cases and death in COVID-19 patients in the Arab world till October 2020. The numbers of the cumulative cases and death used in this figure were obtained from WHO (2020a).

Table 1. Pairwise Pearson correlation between total cases, total deaths, total cases per million, total deaths per million, population, population density, median age, aged 65 older, aged 70 older, GDP per capita, cardiovascular death rate, Diabetes prevalence, life expectancy, human development index.

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<th>Total deaths</th>
<th>Total cases per million</th>
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<th>Population</th>
<th>Population density</th>
<th>Median age</th>
<th>Aged 65 older</th>
<th>Aged 70 older</th>
<th>GDP per capita</th>
<th>Cardiovascular death rate</th>
<th>Diabetes prevalence</th>
<th>Life expectancy</th>
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The correlation between variables was calculated based on data registered by Roser et al. (2020). Values in bold red are statistically significant (P < 0.05).
In Egypt, Azithromycin, Ceftriaxone, Ribavirine, Lopinavir/Ritonavir, and Hydroxychloroquine were used to treat COVID-19 (Mostafa et al., 2020).

Natural herbal medicines as curcumin, cinnamon, basil, chili, ginger, turmeric, lemon, fenugreek, neem garlic, onion, black pepper, green tea, and black tea polyphenols have a lot of benefits against symptoms associated with COVID-19 (Mhatre et al., 2020; Thota et al., 2020). Several reports found that red algae (lectin griffithsin and phycocollod carrageenan), brown algae (fucoidans), green algae (ulvans), and marine algae may have possible antiviral agents against COVID-19 (Pereira & Critchley, 2020). Convalescent plasma transfusion has been used as an immune therapeutic approach for COVID-19 treatment. These approaches of treatment were applied in some countries around the world such as Egypt, USA, China, Guinea, and Italy (Rajendran et al., 2020). Recently, it was found that the main protease (Mpro) and spike (S) receptor antagonists for SARS-CoV-2 have a significant role during the virus entry into the host cell, which is considered as the primary target for the production of anti-COVID-19 drugs (Sen et al., 2020).

**CONCLUSION**

COVID-19 pandemic is a major global health disaster in recent times and considered an unresolved dilemma to the universe. COVID-19 cumulative prevalence differs depending on the country and incidences have been confirmed in almost all continents. The outbreak of the SARS-CoV-2 has not only showed the incapability of the worldwide medical system or the public health infrastructure but also caused an economic crisis and social problems that need decades for recovery. Elderly and immunocompromised patients also are susceptible to the virus's mortal impacts. Currently, there is no report for a successful remedy. However, we hope the suggested vaccines could make a difference in the recent future and afford long-time immunity for a human being. Therefore, the virus can be controlled with appropriate prevention strategies. Also, attempts must be made to formulate systematic strategies to prevent such future zoonotic outbreaks. At present, it is imperative to control the wellspring of contamination, reduce the transmission ways, and utilize the current medications and intends to control the advancement of the malady proactively.

**CONFLICT OF INTEREST**

All authors have approved this article and declare no conflicts of interest.

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**References**


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Egyptian Association for Cancer Research (EACR)
http://eacr.tanta.edu.eg/

EACR is an NGO society that was declared by the Ministry of Social Solidarity (Egypt) No. 1938 in 19/11/2014 based on the initiative of Prof. Mohamed Labib Salem, the current Chairman of EACR. EACR aims primarily to assist researchers, in particular young researchers in the field of cancer research through workshops, seminars and conferences. Its first international annual conference entitled "Anti-Cancer Drug Discovery" was successfully organized in April 2019 (http://acdd.tanta.edu.eg). Additionally, EACR aims to raise the awareness of the society about the importance of scientific research in the field of cancer research in prediction, early diagnosis and treatment of cancer. EACR is also keen to outreach the scientific community with periodicals and news on cancer research including peer-reviewed scientific journals for the publication of cutting-edge research. The official scientific journal of EACR is "International Journal of Cancer and biomedical Research (IJCBR: https://jcb.journals.ekb.eg) was successfully issued in 2017 and has been sponsored by the Egyptian Knowledge Bank (EKB: www.ekb.eg).

EACR Chairman,
Prof. Mohamed Labib Salem, PhD
Professor of Immunology
Faculty of Science, Tanta University, Egypt
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International Journal of Cancer and Biomedical Research (IJCBR), a publication of the Egyptian Association for Cancer Research (EACR), is a peer-reviewed online journal published quarterly. The journal allows free access (Open Access) to its contents and permits authors to self-archive a final accepted version of the articles on any OAI-compliant institutional / subject-based repository.

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INSTRUCTION TO AUTHORS

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